

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Centers for Medicare & Medicaid Services****42 CFR Parts 433, 438, 447, and 456**

[CMS–2482–F]

RIN 0938–AT82

Medicaid Program; Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value-Based Purchasing (VBP) for Drugs Covered in Medicaid, Revising Medicaid Drug Rebate and Third Party Liability (TPL) Requirements

AGENCY: Centers for Medicare & Medicaid Services (CMS), Department of Health and Human Services (HHS).

ACTION: Final rule.

SUMMARY: This final rule will advance CMS' efforts to support state flexibility to enter into innovative value-based purchasing arrangements (VBPs) with manufacturers, and to provide manufacturers with regulatory support to enter into VBPs with payers, including Medicaid. To ensure that the regulatory framework is sufficient to support such arrangements and to promote transparency, flexibility, and innovation in drug pricing without undue administrative burden, we are finalizing new regulatory policies and clarifying certain already established policies to assist manufacturers and states in participating in VBPs in a manner that is consistent with the law and maintains the integrity of the Medicaid Drug Rebate Program (MDRP). This final rule also revises regulations regarding: Authorized generic sales when manufacturers calculate average manufacturer price (AMP) for the brand name drug; pharmacy benefit managers (PBM) accumulator programs and their impact on AMP and best price when manufacturer-sponsored assistance is not passed through to the patient; state and manufacturer reporting requirements to the MDRP; new Medicaid Drug Utilization Review (DUR) provisions designed to reduce opioid related fraud, misuse and abuse; the definitions of CMS-authorized supplemental rebate agreement, line extension, new formulation, oral solid dosage form, single source drug, multiple source drug, innovator multiple source drug for purposes of the MDRP; payments for prescription drugs under the Medicaid program; and coordination of benefits (COB) and third party liability (TPL) rules related to the

special treatment of certain types of care and payment in Medicaid and Children's Health Insurance Program (CHIP).

DATES: These regulations are effective on March 1, 2021, except for amendatory instructions 7, 10.a., 14, 16, and 17, which are effective on January 1, 2022, and amendatory instructions 9 and 11, which are effective on January 1, 2023.

FOR FURTHER INFORMATION CONTACT:

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Christine Hinds, (410) 786–4578, for issues related to value-based purchasing.

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SUPPLEMENTARY INFORMATION:**I. Background**

Under the Medicaid program, states may provide coverage of prescribed drugs as an optional benefit under section 1905(a)(12) of the Social Security Act (the Act). Section 1903(a) of the Act provides for federal financial participation (FFP) in state expenditures for these drugs. In the case of a state that provides for medical assistance for covered outpatient drugs (CODs), as provided under section 1902(a)(54) of the Act, the state must comply with the requirements of section 1927 of the Act. Section 1927 of the Act governs the MDRP and payment for CODs, which are defined in section 1927(k)(2) of the Act. In general, for payment to be made available for CODs under section 1903(a) of the Act, manufacturers must enter into a National Drug Rebate Agreement (NDRA) as set forth in section 1927(a) of the Act. See also section 1903(i)(10) of the Act. The MDRP is authorized under section 1927 of the Act, and is a program that includes CMS, state Medicaid agencies, and participating drug manufacturers that helps to partially offset the federal and state costs of most outpatient prescription drugs dispensed to

Medicaid beneficiaries. The MDRP provides specific requirements for rebate agreements, drug pricing submission and confidentiality requirements, the formulas for calculating rebate payments, drug utilization reviews (DUR), and requirements for states for CODs.

The Covered Outpatient Drugs final rule with comment period (COD final rule) was published in the February 1, 2016 **Federal Register** (81 FR 5170) and became effective on April 1, 2016. The COD final rule implemented provisions of section 1927 of the Act that were added by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively referred to as the Affordable Care Act) pertaining to Medicaid reimbursement for CODs. It also revised other requirements related to CODs, including key aspects of Medicaid coverage and payment and the MDRP under section 1927 of the Act. The regulations implemented through the COD final rule, and those proposed in the "Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value-Based Purchasing (VBP) for Drugs Covered in Medicaid, Revising Medicaid Drug Rebate and Third Party Liability (TPL) Requirements" proposed rule that appeared in the June 19, 2020 **Federal Register** (85 FR 37256) (hereinafter referred to as the June 2020 proposed rule) are consistent with the Secretary's authority set forth in section 1102 of the Act to publish regulations that are necessary to the efficient administration of the Medicaid program.

A. Changes to Coordination of Benefits/Third Party Liability Regulation Due to Bipartisan Budget Act (BBA) 2018

Medicaid is the payer of last resort, which means that other available resources—known as third party liability, or TPL—must be used before Medicaid pays for services received by a Medicaid-eligible individual. Title XIX of the Act requires state Medicaid programs to identify and seek payment from liable third parties, before billing Medicaid. Section 53102 of the Bipartisan Budget Act of 2018 (BBA 2018) (Pub. L. 115–123, enacted February 9, 2018) amended the TPL provision at section 1902(a)(25) of the Act. Specifically, section 1902(a)(25)(A) of the Act requires that states take all reasonable measures to ascertain legal liability of third parties to pay for care and services available under the plan. That provision further specifies that a third party is any individual, entity, or

program that is or may be liable to pay all or part of the expenditures for medical assistance furnished under a state plan. Section 1902(a)(25)(A)(i) of the Act specifies that the state plan must provide for the collection of sufficient information to enable the state to pursue claims against third parties. Examples of liable third parties include: Private insurance companies through employment-related or privately purchased health insurance; casualty coverage resulting from an accidental injury; payment received directly from an individual who has voluntarily accepted or been assigned legal responsibility for the health care of one or more Medicaid recipients; fraternal groups, unions, or state workers' compensation commissions; and medical support provided by a parent under a court or administrative order.

Effective February 9, 2018, section 53102(a)(1) of the BBA 2018 amended section 1902(a)(25)(E) of the Act to require a state to use standard COBs cost avoidance when processing claims for prenatal services which now included labor and delivery and postpartum care claims. Additionally, effective October 1, 2019, section 53102(a)(1) of the BBA 2018 amended section 1902(a)(25)(E) of the Act, to require a state to make payments without regard to third party liability (TPL) for pediatric preventive services unless the state has made a determination related to cost-effectiveness and access to care that warrants cost avoidance for 90 days.

Section 53102(b)(2) of the BBA 2018 delays the implementation date from October 1, 2017 to October 1, 2019 of the provision from the Bipartisan Budget Act of 2013 (Pub. L. 113–67, enacted December 26, 2013) (BBA 2013), which allowed for payment up to 90 days after a claim is submitted that is associated with medical support enforcement instead of 30 days under previous law. Medical support is a form of child support that is often provided through an absent parent's employers health insurance plan.

Effective April 18, 2019, section 7 of the Medicaid Services Investment and Accountability Act of 2019 (Pub. L. 116–16, enacted April 18, 2019) (MSIAA) amended section 202(a)(2) of the BBA 2013 to allow 100 days instead of 90 days to pay claims related to medical support enforcement under section 1902(a)(25)(F)(i) of the Act.

B. Changes to the Calculation of Average Manufacturer Price (AMP) Regarding Authorized Generic Drugs Due to the Continuing Appropriations Act, 2020, and Health Extenders Act of 2019

On September 27, 2019, the President signed into law the Continuing Appropriations Act, 2020, and Health Extenders Act of 2019 (Health Extenders Act) (Pub. L. 116–59), which made changes to sections 1927(k)(1) and 1927(k)(11) of the Act, revising how manufacturers calculate the AMP for a COD, for which the manufacturer permits an authorized generic to be sold and redefines the definition of wholesaler. Manufacturers that approve, allow, or otherwise permit any drug to be sold under the manufacturer's own new drug application (NDA) approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (Pub. L. 75–717, enacted June 25, 1938) (FFDCA), shall no longer include sales of these authorized generics in the calculation of AMP of the brand name drug, regardless of the relationship between the brand name manufacturer and the manufacturer of the authorized generic. That is, a separate AMP would be calculated for the sales of the brand name drug and the authorized generic.

Specifically, section 1603 of the Health Extenders Act of 2019 (Pub. L. 116–59, enacted September 27, 2019), which is titled “Excluding Authorized Generic Drugs from Calculation of Average Manufacturer Price for Purposes of the Medicaid Drug Rebate Program; Excluding Manufacturers from Definition Of Wholesaler,” amended the statute as follows:

- Section 1927(k)(1)(C) of the Act to replace the term “Inclusion” with “Exclusion” in the title and further amended paragraph (C) to state that, in the case of a manufacturer that approves, allows, or otherwise permits any drug of the manufacturer to be sold under the manufacturer's NDA approved under section 505(c) of the FFDCA, such term shall be exclusive of the average price paid for such drug by wholesalers for drugs distributed to retail community pharmacies.

- The definition of wholesaler at section 1927(k)(11) of the Act to remove references to manufacturers from the definition of wholesaler.

Typically, an authorized generic is a product that a manufacturer (primary manufacturer) allows another manufacturer (secondary manufacturer) to sell under the primary manufacturer's Food and Drug Administration (FDA) approved NDA but under a different National Drug Code (NDC) number. The

authorized generic is typically the primary manufacturer's brand product offered at a lower price point. Primary manufacturers may sell the authorized generic product to the secondary manufacturer they are allowing to sell an authorized generic of their brand product, and such sales are commonly referred to as transfer sales, or they may allow a subsidiary manufacturer to sell the authorized generic.

Under the amendments made to section 1927 of the Act, a primary manufacturer that sells the authorized generic version of the brand drug to the secondary manufacturer can no longer include the price of the transfer sale of the authorized generic to the secondary manufacturer in its calculation of AMP for the brand product. The exclusion of these transfer sales from the primary manufacturer's brand drug AMP will likely result in higher AMPs for the brand drugs and a potential increase to a manufacturer's Medicaid drug rebates to states.

The amendments to section 1927 of the Act authorized under section 1603 of the Health Extenders Act are effective October 1, 2019. Therefore, manufacturers must reflect the changes to the calculation of their AMPs for rebate periods beginning October 1, 2019 (reported to CMS no later than 30 days after the end of the rebate period). To assist manufacturers, CMS provided guidance in Manufacturer Release #111¹ and Manufacturer Release #112.² Furthermore, in accordance with 42 CFR 447.510(b), manufacturers have 12 quarters from the quarter in which the data were due to revise AMP, if necessary. The amendments to section 1927 of the Act have not changed the inclusion of authorized generic drugs in best price; therefore, we did not propose any amendments to the regulatory requirements at § 447.506(c) and (d).

C. Changes as Result of the Bipartisan Budget Act of 2015

Under the Medicaid program, states may provide coverage of prescribed drugs as an optional service under section 1905(a)(12) of the Act. Section 1903(a) of the Act provides for FFP in state expenditures for these drugs. Section 1927 of the Act governs the MDRP and payment for CODs, which are defined in section 1927(k)(2) of the Act. In general, for payment to be made available under section 1903(a) of the Act for CODs, manufacturers must enter into an NDRA as set forth in section

¹ <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/mfr-releases/mfr-rel-111.pdf>

² <https://www.medicaid.gov/prescription-drugs/downloads/mfr-rel-112.pdf>

1927(a) and (b) of the Act. Section 1927 of the Act provides specific requirements for rebate agreements, drug pricing submission and confidentiality requirements, the formulas for calculating rebate payments, and requirements for states for CODs. Section 602 of the Bipartisan Budget Act of 2015 (Pub. L. 114–74, enacted November 2, 2015) (BBA 2015) amended section 1927(c)(3) of the Act to require that manufacturers pay additional rebates on their non-innovator multiple source (N) drugs if the AMPs of an N drug increase at a rate that exceeds the rate of inflation. This provision of BBA 2015 was effective beginning with the January 1, 2017 quarter, or in other words, beginning with the unit rebate amounts (URAs) that are calculated for the January 1, 2017 quarter. This additional inflation adjusted rebate requirement for N drugs was discussed in Manufacturer Release Nos. 97 (Manufacturer Release 97) and 101 (Manufacturer Release 101).

D. Current MDRP and Value-Based Purchasing (VBP) Arrangements

In the preamble of the COD final rule, in response to a comment (81 FR 5253), we recognized the importance of VBPs, especially when such arrangements benefit patient health care outcomes. We acknowledged that, given the uniqueness of each VBP arrangement, we had to consider how to provide more specific guidance on the matter, including how such arrangements affect a manufacturer's calculation of a drug's best price and Medicaid drug rebate obligations. Thereafter, we released a state and manufacturer notice on July 14, 2016 (available at State Release 176³ and Manufacturer Release 99⁴) to inform states and manufacturers on how to seek guidance from us on their specific VBP, as well as to encourage states to consider entering into VBP as a means to address high cost drug treatments.

Since the release, manufacturers and states have shown an increased interest in VBP as a possible option for better managing and predicting drug spending, which helps to assure that manufacturers have some vested interest in assuring positive patient outcomes from the use of their drugs. To this end, we have approved nine state plan amendments (SPAs) submitted by states that allow states to negotiate

supplemental rebates under CMS-authorized rebate agreements with drug manufacturers based on evidence-based measures or outcomes-based measures for a patient or beneficiary based on use of the drug.

In addition, manufacturers have approached us with their issues and questions regarding the impact of various types of VBP proposals on their MDRP price reporting obligations (that is, AMP and best price), as well as the regulatory challenges they encounter when structuring and implementing VBP. Finally, manufacturers have noted MDRP reporting challenges with VBP programs, whose evidence or outcomes-based measures extend beyond 3 years, particularly given that manufacturers have limited ability to make changes to reporting metrics outside the 12-quarter MDRP reporting period. In the June 2020 proposed rule, we addressed some of the manufacturer concerns with regards to these MDRP requirements.

E. Definition of Line Extension, New Formulation, and Oral Solid Dosage Form for Alternative URA

Section 2501(d) of the Patient Protection and Affordable Care Act (Pub. L. 111–148, enacted March 23, 2010), as amended by section 1206 of the Health Care and Education Reconciliation Act of 2010 (Pub. L. 111–152, enacted March 30, 2010) (collectively referred to as the Affordable Care Act) added section 1927(c)(2)(C) of the Act effective for drugs paid for by a state on or after January 1, 2010. This provision establishes an alternative formula for calculating the URA for a line extension of a single source drug or innovator multiple source drug that is an oral solid dosage form. We refer to the URA calculated under the alternative formula as the “alternative URA.” Additionally, the Affordable Care Act defined “line extension” to mean, for a drug, a new formulation of the drug, such as an extended release formulation. Section 1927(c)(2)(C) of the Act was further amended by section 705 of the Comprehensive Addiction and Recovery Act of 2016 (Pub. L. 114–198, enacted July 22, 2016) (CARA) to exclude from that definition an abuse-deterrent formulation of the drug (as determined by the Secretary), regardless of whether such abuse-deterrent formulation is an extended release formulation. The determination of whether a drug is excluded because it is an abuse deterrent formulation is explained in at

Manufacturer Release 102.⁵ The CARA amendment applies to drugs paid for by a state in calendar quarters beginning on or after the July 22, 2016 date of enactment of CARA (that is, beginning with 4Q 2016). Finally, section 1927(c)(2)(C) of the Act was further amended by section 53104 of the BBA of 2018, which provided a technical correction such that the rebate for a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form shall be the greater of either (1) the standard rebate (calculated as a base rebate amount plus an additional inflation-based rebate) or (2) the base rebate amount increased by the alternative formula described in section 1927(c)(2)(C)(iii)(I) through (III) of the Act. We refer to the additional inflation-based rebate as the “additional rebate.” Additionally, as we have used the term “initial brand name listed drug” in the “Medicaid Program; Covered Outpatient Drugs” proposed rule published in the February 2, 2012 **Federal Register** (77 FR 5318, 5323 through 5324) (hereinafter referred to as the February 2, 2012 proposed rule), the Covered Outpatient Drugs final rule with comment published on February 1, 2016 (81 FR 5197), and § 447.509(a)(4)(iii) to refer to the initial single source drug or innovator multiple source drug, we continued to do so in the June 2020 proposed rule. The BBA of 2018 amendment applies to rebate periods beginning on or after October 1, 2018.

We proposed a definition of “line extension” in the February 2, 2012 proposed rule (77 FR 5323 through 5324) and received numerous comments. In the COD final rule, we did not finalize the proposed definition and requested additional comments with a 60-day comment period that closed on April 1, 2016. The additional comments received, although instructive of the public's thoughts at the time, were not informed by the then-current statutory framework. Therefore, we did not finalize a definition of “line extension” in the April 1, 2019 final rule (84 FR 12132). We reiterated in the April 1, 2019 final rule that manufacturers are to rely on the statutory definition of “line extension” at section 1927(c)(2)(C) of the Act, and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension. We also stated that if we later decide to develop a regulatory definition of “line extension,” we

³ <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/state-releases/state-rel-176.pdf>.

⁴ <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/mfr-releases/mfr-rel-099.pdf>.

⁵ <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/mfr-releases/mfr-rel-102.pdf>.

would do so through our established Administrative Procedures Act (APA) compliant rulemaking process and issue a proposed rule. In the June 2020 proposed rule (85 FR 37294 through 37296), we proposed definitions of “line extension”, “new formulation”, and “oral solid dosage form”.

The line extension provision has been in effect since January 1, 2010, and the Drug Data Reporting (DDR) for Medicaid system was modified in 2016 to implement the data reporting requirements for line extensions.

However, we have found that some manufacturers are unclear about their line extension reporting obligations, for example, whether a particular drug satisfies the statutory definition of line extension and the identification of the initial brand name listed drug. Therefore, in addition to proposing definitions of “line extension”, “new formulation”, and “oral solid dosage form”, we provided the clarification below regarding manufacturers’ reporting obligations in the June 2020 proposed rule (85 FR 37289).

Details regarding how to calculate the additional rebate (calculated as a percentage of AMP) and the alternative URA can be found in the “Medicaid Program; Covered Outpatient Drug; Line Extension Definition; and Change to the Rebate Calculation for Line Extension Drugs” final rule and interim final rule with comment period that was published in the April 1, 2019 **Federal Register** (84 FR 12133) (hereinafter referred to as the April 1, 2019 final rule). We note that under § 447.509(a)(4)(iii), manufacturers are required to calculate the alternative URA if the manufacturer of the line extension also manufactures the initial brand name listed drug or has a corporate relationship with the manufacturer of the initial brand name listed drug. As noted in the June 2020 proposed rule (85 FR 37295), although a drug that meets the definition of a line extension should be identified as such in DDR, a manufacturer is not required to calculate the alternative URA unless the manufacturer of the line extension also manufactures, or has a corporate relationship with the manufacturer of, the initial brand name listed drug.

To apply the alternative formula described in section 1927(c)(2)(C)(iii)(I) through (III) of the Act for each line extension and rebate period, the manufacturer must determine which NDC represents the initial brand name listed drug that will be used to calculate the alternative URA. First, the manufacturer must identify all potential initial brand name listed drugs by their respective NDCs by considering all

strengths and dosage forms of the initial brand name listed drug in accordance with section 1927(c)(2)(C)(iii)(II) of the Act. Additionally, only those potential initial brand name listed drugs that are manufactured by the manufacturer of the line extension or by a manufacturer with which the line extension manufacturer has a corporate relationship should be considered. Then, the manufacturer must evaluate the additional rebate (calculated as a percentage of AMP) for each potential initial brand name listed drug. The potential initial brand name listed drug that has the highest additional rebate (calculated as a percentage of AMP) is the initial brand name listed drug that must be identified in DDR and used to calculate the alternative URA for the rebate period.

Section 1927(c)(2)(C)(i) of the Act requires the manufacturer to calculate the alternative formula for each quarter to determine the initial drug for each quarter that has the highest additional rebate (calculated as a percentage of AMP). Therefore, the manufacturer must re-evaluate the additional rebate (calculated as a percentage of AMP) for each potential initial brand name listed drug each quarter. Because the additional rebate (calculated as a percentage of AMP) for any potential initial brand name listed drug may change from one quarter to the next, the initial brand name listed drug used for the alternative URA calculation may also change from one quarter to the next. Additionally, the NDC for the initial brand name listed drug must be active in MDRP for the quarter, that is, an NDC that is produced or distributed by a manufacturer with an active NDRA and the NDC does not have a termination date that occurred in a rebate period earlier than the rebate period for which the calculation is being performed. Because drugs may come on and off the market, an initial brand name listed drug that was used to calculate the alternative URA for one quarter may not be active in MDRP for the next quarter. However, a different initial brand name listed drug may be active in MDRP and available to use to calculate the alternative URA for the next quarter.

F. Impact of Certain Manufacturer Sponsored Patient Assistance Programs (“PBM Accumulator Programs”) on Best Price and AMP

Manufacturer-sponsored patient assistance programs can be helpful to patients in obtaining necessary medications. However, PBMs contend that manufacturer-sponsored assistance programs steer consumers towards more

expensive medications when there may be more cost saving options available to health plans. Therefore, as a cost saving measure, PBMs have encouraged health plans in some cases to not allow the manufacturer-sponsored assistance provided under such programs to be applied towards a patient’s health plan deductible for a brand name drug not on a plan’s formulary. In the June 2020 proposed rule, we provided proposed instruction to manufacturers on how to consider the implementation of such programs when determining best price and AMP for purposes of the MDRP.

G. State Drug Utilization Data (SDUD) Reported to MDRP

Section 1927(b)(2)(A) of the Act requires each state agency to report to each manufacturer not later than 60 days after the end of each rebate period and in a form consistent with a standard reporting format established by the Secretary, information on the total number of units of each dosage form and strength and package size of each COD dispensed after December 31, 1990, for which payment was made under the plan during the period, including such information reported by each Medicaid managed care organization (MCO), and shall promptly transmit a copy of such report to the Secretary. In accordance with this requirement, states are required to send state drug utilization data (SDUD) using OMB-approved Rebate Invoice Form, the CMS–R–144 (the data fields and descriptions are included as Exhibit X in the June 2020 proposed rule) to manufacturers and transmit a copy of this report to CMS.

While many states subject their SDUD on the CMS–R–144 to edits to uncover outliers/inaccuracies in the invoices to manufacturers before sending copies to CMS, some states send unedited copies of the SDUD to CMS, resulting in discrepancies that do not conform with the statutory requirement at section 1927(b)(2)(A) of the Act. The statute requires such reporting to be in a form consistent with a standard reporting format established by the Secretary, and we believe that such a copy means that the data submitted on the invoice (CMS–R–144) to the manufacturer must be accurate and identical to the report (copy) states send to CMS. Further, we expect that when states send SDUD updates or changes to manufacturers, they transmit those changes to us concurrently in a copy to CMS. However, in some cases, states fail to submit these updates causing the data to be mismatched. This results in states not complying with section 1927(b)(2)(A) of the Act and CMS not

having an accurate account of rebates billed in the MDRP.

H. Changes Related to the Substance Use-Disorder Prevention That Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act

The epidemic of opioid overdose, misuse, and opioid use disorders is a critical public health issue that affects the lives of millions of Americans. Research shows the opioid overdose epidemic has a disproportionate impact on Medicaid beneficiaries and the consequences have been tragic. In 2017, 47,600 people in America died of an opioid overdose per the Centers for Disease Control and Prevention (CDC).⁶ Inappropriate opioid prescribing can result in costly medical complications such as abuse, misuse, overdoses, falls and fractures, drug to drug interactions and neonatal conditions. The use of multiple opioids is associated with a higher risk of mortality, with mortality risk increasing in direct relation to the number of opioids prescribed concurrently.^{7 8} Beneficiaries who receive multiple opioids may lack coordinated care and are at higher risk for opioid overdose.⁹ These complications are costly, preventable, and result in avoidable healthcare expenditures.¹⁰ Moreover, according to the National Institute on Drug Abuse (NIDA), research suggests that misuse of prescription pain relievers may actually open the door to heroin use, as four in five new heroin users started out misusing prescription pain reliever.¹¹ More than half of the individuals misusing prescription opioids obtained the medication they used from a friend or relative;¹² this emphasizes the need

for safe disposal¹³ of unused medications, including opioids.

Since 1993, section 1927(g) of the Act has required each state to develop a DUR program targeted, in part, at reducing abuse and misuse of outpatient prescription drugs covered under the state's Medicaid Program. The DUR program operates to help ensure that prescriptions are appropriate, medically necessary, and are not likely to result in adverse medical events. Each state DUR program consists of prospective drug use review, retrospective drug use review, data assessment of drug use against predetermined standards, and ongoing educational outreach activities.

Consistent with section 1927(g)(3)(D) of the Act, we require each state Medicaid program to submit to us an annual report on the operation of its Medicaid DUR program for the fee-for-service (FFS) delivery system, including information on prescribing patterns, cost savings generated by the state's DUR program, and the state's DUR program's overall operations, including any new or innovative practices. Additionally, § 438.3(s)(4) and (5) require state contracts with any MCO, prepaid inpatient health plan (PIHP) or prepaid ambulatory health plan (PAHP) that covers CODs to require the MCO, PIHP, or PAHP to operate a DUR program that complies with section 1927(g) of the Act and 42 CFR part 456, subpart K, and to submit detailed information about its DUR program activities annually. For the purposes of this final rule, managed care program (MCP) references MCOs, managed care entities (MCEs), PAHPs and PIHPs.

The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (Pub. L. 115–271, enacted October 24, 2018) (the SUPPORT Act) includes measures to combat the opioid crisis in part by reducing opioid related abuse and misuse by advancing treatment and recovery initiatives, improving prevention, protecting communities, and bolstering efforts to fight deadly illicit synthetic drugs. There are several Medicaid-related DUR provisions for FFS and MCP pharmacy programs contained within section 1004 of the SUPPORT Act. These provisions establish drug review and utilization standards in section 1902(a)(85) and (oo) of the Act to supplement existing requirements under section 1927(g) of the Act, in an effort to reduce opioid-related fraud, misuse and abuse. State

implementation of these strategies was required by October 1, 2019, and states must include information about their implementation in their annual reports under section 1927(g)(3)(D) of the Act. In turn, the Secretary is required to report to Congress on the information submitted by the states, starting with information from states' FY 2020 reports.

Consistent with section 1927(g) of the Act, the SUPPORT Act has the goal of improving the quality of care received by Medicaid recipients by reducing their exposure to hazards resulting from the inappropriate prescribing, gross overuse, or inappropriate or medically unnecessary care. In this context, strategies to assure the appropriate use of opioids are now being implemented in clinical settings, health care systems and public health agencies. Efforts to prevent harms associated with overuse and misuse of opioids must be integrated to ensure patients are receiving appropriate pain care. Pain is a common condition; estimates of chronic pain and high impact chronic pain in adults 65–84 years of age were 28 percent and 11 percent respectively, based on 2016 National Health Interview Survey Data.¹⁴ Estimates of acute pain in people under 65 years range from 7 to 52 percent, with headache, joint, and neuropathic pain commonly cited.¹⁵ We recognize efforts involving multiple stakeholders including the pain management community are needed to address the opioid crisis, to assure the health and well-being of Medicaid beneficiaries, and decrease any related health care expenditures. We are committed to ensuring there are basic minimum standards implemented through Medicaid DUR programs nationwide to help ensure that prescriptions are appropriate, medically necessary and align with current standards of care, under our authority to implement section 1927(g) of the Act and section 1004 of the SUPPORT Act.

I. Single Source Drug, Multiple Source Drug, Innovator Multiple Source Drug

Section 6(c) of the MSIAA modified the definitions in section 1927(k) of the Act for single source drug, multiple source drug, and innovator multiple source drug. In the June 2020 proposed rule, we proposed to revise the definitions of these terms at § 447.502 to reflect these statutory changes.

⁶ <https://www.cdc.gov/drugoverdose/data/statedeaths.html>.

⁷ Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Prescription of Long-Acting Opioids and Mortality in Patients with Chronic Noncancer Pain. *JAMA*. 2016 Jun 14; 315(22):2415–23.

⁸ Baumblatt JA, Wiedeman C, Dunn JR, Schaffner W, et al. High-risk use by patients prescribed opioids for pain and its role in overdose deaths. *JAMA Intern Med*. 2014 May; 174(5):796–801.

⁹ Bonnie, Richard J., et al. Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. The National Academies Press, 2017.

¹⁰ Davis, Cory. "Naloxone for Community Opioid Overdose Reversal." Naloxone for Community Opioid Overdose Reversal | Public Health Law Research, Public Health Law Research (PHLR), 22 June 2015. <http://phlr.org/product/naloxone-community-opioid-overdose-reversal>.

¹¹ "Opioid Addiction 2016 Facts & Figures—ASAM Home Page." American Society of Addiction Medicine, www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf.

¹² <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>.

¹³ <https://www.fda.gov/consumers/consumer-updates/where-and-how-dispose-unused-medicines>.

¹⁴ https://www.cdc.gov/nchs/nhis/nhis_nhsr.htm.

¹⁵ *Ibid*.

II. Summary of the Provisions of the Proposed Regulations, Analysis of and Response to Public Comments, and Provisions of the Final Rule

The following summarizes comments received in response to the June 2020 proposed rule (<https://www.regulations.gov/docket?D=CMS-2020-0072>) in general, or about issues not addressed in the proposed regulations.

Comment: A few commenters expressed concern that the proposed rule will jeopardize future drug development or enable drug manufacturers to rush drugs to market.

Response: We understand the concern about the possible impact of a new regulation on drug development; however, we do not believe the rule will jeopardize future drug development or enable drug manufacturers to rush drugs to the market. The rule, as it relates to VBP, is meant to help improve patient access to new medications, particularly new high cost therapies such as gene or cell therapies, by facilitating the use of VBP arrangements when purchasing such medications. We believe this rule helps create incentives for manufacturers to bring new drugs to market, and depending on the nature of the VBP arrangements could also create incentives for manufacturers to complete their clinical trials post marketing.

We note that this rule has no impact on the processes manufacturers must follow to bring new drugs to the market. Processes for review, approval, and marketing of drug products are the responsibility of FDA.

Comment: A few commenters expressed concern that the proposed changes to regulations will place additional burden on healthcare providers and the Medicaid program which are already overburdened by the novel coronavirus pandemic, both financially and administratively. A few commenters specifically expressed concern that the proposed changes will exacerbate access barriers and financial hardships for patients who are already experiencing increased barriers to care and financial hardship due to the coronavirus disease 2019 (COVID-19) pandemic and did not believe that the proposed changes were appropriate at the time of a public health emergency (PHE). The commenters suggested that the result of this rule on patients during this time will lead to increased healthcare costs that force patients to skip needed healthcare and lead to increased health issues and debilitating harms. One commenter also noted that the proposed rule was inconsistent with

the President's Executive Order 13924, "Regulatory Relief to Support Economic Recovery," that requires the heads of federal agencies to remove regulatory barriers to support the nation's economic recovery following the COVID-19 pandemic.

Response: We appreciate the concerns expressed by the commenters. As noted in the "EFFECTIVE DATE" section of this rule, these provisions will be effective March 1, 2021. However, we recognize that some final policies established in this final rule will require additional time to make necessary operational and administrative changes in order to ensure compliance, specifically those final policies related to the Definition of Line Extension, New Formulation, Oral Solid Dosage Form at § 447.502; Changes to Medicaid drug rebates (MDR) at § 447.509(a)(4); Changes to the Requirements for States at § 447.511 (SDUD and State Certification); Changes to State plan requirements, findings, and assurances at § 447.518(d) (CMS-Authorized Supplemental Rebate Reporting); and therefore these sections will not be effective until January 1, 2022. Similarly, changes to the Determination of AMP at § 447.504(c) and (e) and determination of Best price at § 447.505 (c) will not be effective until January 1, 2023. These final policies are discussed further in the applicable sections of this final rule.

Comment: Several commenters believed that the 30-day comment was not sufficient for the public and industry to analyze the impact of the policies being proposed. One commenter in particular did not agree that it was a not an economically significant rule, and that industry have only 30 days to comment.

Response: CMS provided a 30-day comment period, which is consistent with the Administrative Procedure Act. CMS believes that interested stakeholders had adequate opportunity to provide comment on the policies established in this final rule.

Comment: A few commenters suggested that proceeding to a final rule at this stage will raise APA issues because any final rule must be a "logical outgrowth" of its proposal.

Response: We disagree with the commenter that this rule raises logical outgrowth concerns. In the proposed rule, we described the substance and alternatives to the proposed rule and described the subjects and issues covered by the rule. Where this final rule is different from that discussed in the proposed rule, it does not deviate sharply from the proposed rule. We provided adequate notice in the

proposed rule that those changes were possible. Accordingly, we provided interested parties sufficient notice that they should have anticipated that those changes were possible.

After consideration of public comments, we are issuing this final rule, as discussed in greater detail in the sections that follow.

Comment: A few commenters suggested that CMS specify a later effective date for the final rule, such as at least 4 quarters from final rule publication to allow CMS to issue additional guidance, manufacturers to evaluate each drug in their portfolio, and manufacturers and state Medicaid agencies to make necessary system changes to price and data reporting systems.

Response: We are issuing this rule with an effective date of March 1, 2021. However, certain sections of this final rule as noted above, will not be effective until January 1, 2022 or January 1, 2023.

Comment: Several commenters expressed concern that the proposed rule will increase outpatient prescription drug prices and out-of-pocket costs for patients, and therefore, decrease patient access to needed care and medications. Furthermore, commenters noted that the regulation may intrude into the provider and patient relationship. One commenter urged CMS to withdraw the proposed rule and reconsider the proposed changes or include express protections to ensure that Medicaid beneficiaries continue to have access to medically necessary outpatient prescription drugs.

Response: We appreciate the commenters concerns regarding patient protections, but we disagree that this rule negatively impacts access to needed care and medications. In particular, and as discussed in the preamble to the June 2020 proposed rule (85 FR 37288), CMS supports manufacturer and state's use of VBP arrangements because we believe it will assist states with providing Medicaid patients access to needed therapies while providing a payment arrangement that allows the state flexibility, including an option to only pay for a drug when an evidence-based or outcomes-measures are achieved. For such arrangements to work for Medicaid, we need to balance changes to MDRP regulations to address manufacturers' concerns with offering such innovative payment arrangements to Medicaid programs, while ensuring the required economies, efficiencies, and quality of care continue to be provided under the Medicaid program. If we do not address a number of potential regulatory hurdles, states may not be able to provide such methods and

procedures relating to the utilization of, and payment for care and services as may be necessary to safeguard against unnecessary utilization of such care and services and assure that consistent with section 1902(a)(30)(A) of the Act, Medicaid payments are consistent with efficiency, economy, and quality of care (85 FR 37291).

A. Third Party Liability: Payment of Claims (42 CFR 433.139)

In 1980, under the authority in section 1902(a)(25)(A) of the Act, we issued regulations at part 433, subpart D establishing requirements for state Medicaid agencies to support the coordination of benefits (COB) effort by identifying TPL. Effective February 9, 2018, section 53102(a)(1) of BBA 2018 amended section 1902(a)(25)(E) of the Act to require states to cost avoid claims (for example, when the state Medicaid agency has determined there is a legally liable third party responsible for paying the claim, it will reject (“cost avoid”) the claim) for prenatal care for pregnant women including labor and delivery and postpartum care, and to allow the state Medicaid agency 90 days instead of 30 days to pay claims related to medical support enforcement services, as well as requiring states to collect information on TPL before making payments. Effective April 18, 2019, section 7 of the MSIAA amended section 1902(a)(25)(E) of the Act to allow 100 days instead of 90 days to pay claims related to medical support enforcement services, as well as requiring states to collect information on TPL before making payments.

Section 433.139(b)(2), (b)(3)(i), and (b)(3)(ii)(B) detail the exception to standard COB cost avoidance by allowing pay and chase for certain types of care, as well as the timeframe allowed prior to Medicaid paying claims for certain types of care. Specifically, we proposed to delete § 433.139(b)(2). We also proposed to revise § 433.139(b)(3)(i) by removing “prenatal care for pregnant women, or” from pay and chase services, and § 433.139(b)(3)(ii)(B) by removing “30 days” and adding “100 days.”

The following is a summary of the public comments we received on our proposal to revise § 433.139.

Comment: One commenter requested that CMS provide guidance to Medicaid MCOs on how they can more reliably and efficiently identify other payers through the state Medicaid agency. The commenter stated this will facilitate implementation of CMS’ proposals to require states to reject claims for pregnancy-related services in cases where a third party is legally

responsible for payment and to allow states a period of 100 days to pay claims related to medical support enforcement services.

Response: COB/TPL requirements apply in Medicaid MCOs, as well as Medicaid FFS programs. MCOs are required to pay certain types of claims and then seek recovery—“pay and chase”—in the same circumstances as the SMA Medicaid FFS program is required to do so. SMAs have options for ensuring that they meet the COB/TPL requirements in Medicaid MCOs. Regardless of how SMAs choose to allocate responsibility for COB/TPL activities, the contract between the SMA and the MCO must list any COB/TPL responsibilities of the SMA and the MCO must list any COB/TPL responsibilities of the plan see for example, 42 CFR 438.3(t). For more information on general COBs/TPL requirements under managed care, please see our guidance published on [Medicaid.gov](https://www.medicaid.gov/https://www.medicaid.gov/medicaid/eligibility/downloads/cob-tpl-handbook.pdf) at <https://www.medicaid.gov/https://www.medicaid.gov/medicaid/eligibility/downloads/cob-tpl-handbook.pdf>.

Comment: One commenter recommended that CMS should ensure that providers bear the responsibility of ensuring all third parties are notified and payments are retrieved citing their belief that the burden should be removed from the state and federal government.

Response: If there is no established liable third party, the state Medicaid agency (SMA) may pay claims to the maximum Medicaid payment amount establish for the service in the state plan. If the SMA later establishes that a third party was liable for the claims, it must seek to recover the payment. The SMA should first seek recovery from the liable third party. If that is not feasible (for example, Medicare will not accept a claim directly from an SMA), it may be necessary to recoup the payment from the provider and ask the provider to rebill correctly. Section 433.139(d)(2) states that SMAs must seek reimbursement within sixty days from the end of the month in which it learns of the existence of the liable third party.

Comment: One commenter expressed concern that the proposed revisions to § 433.139 will not permit states to elect to cost avoid claims for pediatric services as allowed under the BBA 2018. The commenter stated the BBA allows states to pursue cost avoidance for pediatric services upon determination that cost-effectiveness and access to care “warrants cost avoidance for 90 days.” The commenter recommended that CMS revise the proposed provision to allow states to pursue cost avoidance for pediatric care.

Response: The BBA 2018 did not eliminate pay and chase for pediatric preventive services; The BBA 2018 amended the statute to eliminate pay and chase for prenatal services. Therefore, this request is outside of the scope of our regulation change authority under § 433.139(b)(3)(i) and the BBA of 2018 as identified within. For additional guidance on this change in law, please see our guidance published on www.Medicaid.gov at <https://www.medicaid.gov/federal-policy-guidance/downloads/cib111419.pdf> and <https://www.medicaid.gov/medicaid/eligibility/downloads/cob-tpl-handbook.pdf>.

Comment: One commenter recommended that CMS provide states with an alternative option to the required cost avoidance determinations of cost-effectiveness and access to care. The commenter stated that current cost avoidance determination process is burdensome for states to perform and recommended that CMS allow an alternative option where state Medicaid agencies may attest that their program is compliant, has an “exception, grievance, fairing hearing” process, and does not have known access issues for beneficiaries seeking pediatric preventive services.

Response: This request is outside of the scope of our regulation change authority under § 433.139(b)(3)(i) and the BBA 2018 as identified within.

Comment: One commenter requested clarification from CMS on the application of the 100-day waiting period application to preventive pediatric services. The commenter indicated that the provision’s reference to § 433.139(b)(3)(ii)(B) appears to apply to child support enforcement services. The commenter requested CMS clarify whether the 100-day waiting period applies to both preventive pediatric services and child support enforcement services as it may impact implementation and cost-effectiveness.

Response: The 100-day waiting period only applies to medical support enforcement and not preventative pediatric services. Preventive pediatric service claims must be “paid and chased” without regard to a liable third party unless the state has made a determination related to cost-effectiveness and access to care that warrants cost avoidance for 90 days.

Section 53102(b)(2) of the Bipartisan Act of 2018 delayed the implementation date from October 1, 2017 to October 1, 2109 of the BBA 2013 provision, which allowed for payment up to 90 days after a claim is submitted that is associated with medical support enforcement instead of 30 days under previous law.

Medical support is a form of child support that is often provided through an absent parents employers health insurance plan. Effective April 18, 2019, section 7 of the MSIAA amended section 202(a)(2) of the BBA 2013 to allow 100 days instead of 90 days to pay claims related to medical support enforcement under section 1902(a)(25)(F)(i) of the Act.

Additionally, effective October 1, 2019, section 53102(a)(1) of the BBA 2018 amended section 1902 (a)(25)(E) of the Act, to require a state to make payments without regard to TPL for pediatric preventive services unless the state has made a determination related to cost-effectiveness and access to care that warrants cost avoidance for 90 days.

Comment: One commenter noted that the provisions as written will not allow a state Medicaid agency to implement a cost avoidance period of less than 90 days. The commenter noted that their state requires a 60-day timeframe after finding that a 90-day period was not cost-effective and that access to care issues may result from provider abrasion. The commenter requested clarification from CMS that state Medicaid agencies may continue to keep a shorter cost avoidance period based on cost-effectiveness and access to care evaluations.

Response: Our November 14, 2019¹⁶ guidance clarified that a state can allow up to 100 days to pay claims related to medical support enforcement. States are permitted the flexibility to pay and chase medical support enforcement claims within that 100-day time period if they have made a determination that the full waiting period creates a cost-effectiveness or access to care issue.

As background, section 53102(b)(2) of the BBA 2018 delays the implementation date from October 1, 2017 to October 1, 2019 of the BBA 2013 provision, which allowed for payment up to 90 days after a claim is submitted that is associated to medical support enforcement instead of 30 days under the previous law. Medical support is a form of child support that is often provided through an absent parents employers health insurance plan.

Effective April 18, 2019, section 7 of the MSIAA amended section 202(a)(2) of the BBA 2013 to allow 100 days instead of 90 days to pay claims related to medical support enforcement pursuant to section 1902(a)(25)(F)(i) of the Act. We are finalizing as proposed.

B. Changes To Address Medicaid Access to Drugs Using Value-Based Purchasing Arrangements (VBP)

In the preamble of the COD final rule, in response to a comment (81 FR 5253), we recognized the importance of VBP especially when such arrangements benefit Medicaid patients' access to drug treatments. We acknowledged that given the uniqueness of each VBP arrangement, we had to consider how to provide more specific guidance on the matter, including how such arrangements affect a manufacturer's best price and Medicaid drug rebate obligations. Thereafter, we released a state and manufacturer notice on July 14, 2016 (State Release 176 and Manufacturer Release 99) to inform states and manufacturers on how to seek guidance from us on their specific VBPs, as well as encourage states to consider entering into VBPs with manufacturers as a means to address high cost drug treatments.

Since those releases, manufacturers and states have shown an increased interest in VBP as a potential option for better managing and predicting drug spending, which helps to assure that manufacturers have some vested interest in assuring positive patient outcomes from the use of their drugs. However, some manufacturers hesitate to offer VBP arrangements to payers, including Medicaid, because of concerns that the existing Medicaid COD statute and applicable regulations do not specifically address, for price reporting, the rebating or discounting of drugs based on evidence or outcomes-based measures. Specifically, CMS had not addressed the possible impact of offering VBP arrangements on manufacturer compliance with applicable MDRP price reporting obligations, including best price and AMP reporting.

We support VBP because we believe it will assist states with providing Medicaid patients access to needed therapies while providing a payment arrangement that allows the state flexibility, including an option to only pay when a therapy actually works. For such arrangements to work for Medicaid, we need to consider changes to MDRP regulations to address manufacturers' concerns with offering Medicaid such innovative payment arrangements, while also ensuring the required economies, efficiencies, and quality of care provided under the Medicaid program. As discussed in the June 2020 proposed rule, if we do not consider addressing a number of potential regulatory hurdles in this regulation to increase patient access to

new medications, manufacturers may not be willing to offer VBP arrangements in the marketplace to commercial payers or to states. As a result, states may not be able to take advantage of these arrangements to afford new high priced medications such as gene and cell therapies, among others, limiting their availability to Medicaid patients. Subsequently, states may not be able to provide such methods and procedures relating to the utilization of, and payment for care and services as may be necessary to safeguard against unnecessary utilization of such care and services, and assure that, consistent with section 1902(a)(30)(A) of the Act, Medicaid payments are consistent with efficiency, economy, and quality of care.

One potential regulatory hurdle manufacturers have raised with us is a manufacturer's quarterly best price reporting. Section 1927(c)(1)(C) of the Act defines best price in relevant part to mean for a single source drug or innovator multiple source drug of a manufacturer *the lowest price available* from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization (HMO), non-profit entity, or governmental entity within the United States, with certain exclusions enumerated at sections 1927(c)(1)(C)(i)(I) through (VI) of the Act. One of the issues manufacturers face in determining best price with the advent of VBP arrangements is that a manufacturer's best price can be reset based upon the outcome of a drug treatment for one patient or one unit of the drug because of the VBP. When this occurs, the price for that single use of the drug during a quarter that resulted in a negative outcome will reset the best price to a significantly lower amount, sometimes zero, prompting a significantly higher rebate (sometimes 100 percent of the drug's AMP) for all uses of the drug during that quarter.

This being the case, manufacturers have questioned how they should calculate best price and account for these units when an outcome of a VBP arrangement results in "a lowest price available" of zero or at a significant discount. Manufacturers have expressed concern to CMS that without further guidance from CMS in regulation regarding the determination of best price in this scenario, the manufacturer could be at risk of understating rebates and may potentially be subject to False Claims Act liability, a risk which further diminishes manufacturer interest in offering VBP payment arrangements in either the commercial or Medicaid market. In turn, this may hinder Medicaid access to the care and services

¹⁶ <https://www.medicaid.gov/sites/default/files/Federal-Policy-Guidance/Downloads/cib111419.pdf>.

provided as part of these VBP arrangements (for example, to gene therapies and potentially curative orphan drug treatments) that are available in the general population.

In the June 2020 proposed rule, we proposed changes to the MDRP price reporting (in particular best price) to address the changing market atmosphere and regulatory challenges manufacturers encounter when structuring and implementing VBP, and therefore, to give manufacturers a greater ability to offer these programs to commercial payers or Medicaid without the negative impact on best price or the potential for manufacturers' non-compliance when calculating best price.

1. Overall VBP Comments

Comment: Several commenters supported CMS' efforts to increase adoption of, and foster more meaningful value-based payment arrangements for, prescription drugs as a step to ensuring affordable, high value healthcare and lowering drug prices. Commenters expressed appreciation for efforts to relieve the regulatory requirements that have prevented manufacturers and states from developing VBP arrangements. A few commenters noted that manufacturers, commercial payers, state Medicaid agencies and health plans, and other commenters are well-suited to negotiate VBP arrangements and associated measures.

Commenters also noted that VBP arrangements:

- Increase patient access to drug therapies, especially for breakthrough, gene, and other novel therapies including therapies for treatment of rare diseases.
- Accelerate research and new treatment development while also fostering greater patient safety.
- Support manufacturer accountability as a result of a shared-risk model.
- Promote transparency in manufacturers' production processes, costs, and the distribution of drug therapies.
- Improve healthcare system sustainability by decreasing overall treatment costs and incentivizing improved treatment modalities.
- Hold drug manufacturers liable for drug effectiveness.

Response: We appreciate these comments of support for value based purchasing (VBP) arrangements.

Comment: Several commenters did not support the proposed rule to accommodate VBP arrangements due to concerns of unintended consequences on patient access to prescription drugs and on drug prices. Commenters

expressed concerns that evidence and outcomes-based contracts do not address the underlying price of a therapy and noted the proposal does little to ensure that the VBP arrangements incentivized by the proposed changes to best price actually meet the objectives to increase therapeutic value while reducing cost for consumers and insurers. A few commenters noted that the proposed changes may allow manufacturers to manipulate program rules to increase drug prices, and therefore, increase their profits. Other commenters noted that they did not see VBP arrangements as a comprehensive solution to high drug prices and suggested that CMS reconsider the provisions in the proposed rule and take additional actions to control drug prices. One commenter expressed concern that the proposed rule introduced major policy changes without articulating substantial policy justifications in the proposed preamble text.

A few commenters also expressed concern that the VBP arrangement proposals and the definition of such arrangements lack the requisite clarity for manufacturers to undertake the operational overhauls necessitated by these proposals. Commenters requested that CMS work with commenters to develop a more specific regulatory proposal and reissue a new proposed rule before moving forward with any changes. The commenter requested that CMS provide additional detailed guidance before implementing provisions of the rule.

Response: We believe that access to pharmaceutical manufacturer VBP arrangements by both state Medicaid programs and commercial payers is one of many negotiating tools that payers may take advantage of in today's pharmaceutical market. We are not requiring states or payers enter into VBP arrangements as part of this final rule. Instead, we are clarifying and amending the regulatory framework so it is sufficient to support such arrangements and to promote transparency, flexibility, and innovation in drug pricing without undue administrative burden. These rules clarify certain already established policies to assist manufacturers and states in participating in VBP arrangements in a manner that is consistent with the law and maintains the integrity of the MDRP.

Comment: Many commenters expressed concerns that CMS' proposals related to VBP arrangements may negatively impact state Medicaid programs in several ways including compromising the integrity of the MDRP and noting that states would likely

experience smaller Medicaid drug rebates and increased Medicaid spending as a result of the rule if finalized. A few commenters recommended that CMS establish specific guardrails to ensure that state Medicaid programs benefit from the value of VBP arrangements. The commenters noted that manufacturers could reduce their Medicaid rebate obligations by shifting their commercial rebating strategy to VBP arrangements (sheltered from being included in best price) by refusing to negotiate VBP arrangements with state Medicaid programs at all.

Commenters also noted that they believe the cost savings generated under the VBP arrangement must exceed those currently available under the MDRP framework and be inclusive of administrative costs to implement the VBP arrangement. Another commenter requested that CMS provide additional guidance on how VBP arrangements might address barriers to treatment that are unique to the Medicaid population.

One commenter expressed concern that the proposed regulations will have serious consequences to state Medicaid programs and their ability to provide access to vital healthcare services to the state's Medicaid beneficiaries.

Response: The new VBP approach would build upon the approach that exists in current law regarding how manufacturers pay rebates to states for a dosage form and strength of a drug. Manufacturers are required to report a best price each quarter to CMS which is used by CMS to calculate the state's unit rebate amount (URA) for the drug, and that reporting will continue. Under this new approach, manufacturers that offer a value based purchasing arrangement (as defined at § 447.502) to all states, may report a best price that includes varying best price points for a single dosage form and strength as a result of that VBP arrangement.

Otherwise, manufacturers that do not offer VBP arrangements to states will be required to report a single best price (which would include all prices, including applicable discounts, rebates, or other transactions that adjust prices to the best price eligible entities, including such transactions from VBP arrangements not offered to states). This would address the commenters' concerns that this approach would compromise the integrity of the rebate program, shift manufacturer rebates to VBP programs, or allow manufacturers to not offer these VBP programs to states. States would not be required to participate in these arrangements, but can do so if they so choose. Manufacturers that choose to offer their

VBP arrangement to the states and report multiple best prices would continue to report a non-VBP best price for this dosage form and strength of this drug for the quarter. States that opt not to participate in a multiple best price arrangement that is being offered by manufacturers would receive rebates based on the manufacturer's non-VBP best price for this dosage form and strength of the drug.

Therefore, each state should consider the value of entering into VBP arrangements and potential consequences, be it impact on access to health care in their state or the administrative costs associated with operationalizing a VBP arrangement, and make the appropriate decision for their state.

Comment: One commenter requested that CMS maintain incentives for providers to choose the lower-cost therapeutic option that is clinically appropriate and for ongoing development of lower-cost therapies, including biosimilars in addition to permitting flexibilities around VBP arrangements.

Response: This rule does not require providers to participate in VBP arrangements or to discontinue offering lower-cost therapeutic options when clinically appropriate. Like states and commercial payers, providers have the option to participate in VBP arrangements and may choose to forgo these arrangements and avail their patients of lower cost therapies that the provider believes may be just as effective.

Comment: A few commenters requested CMS address the potential incentive for manufacturers to expedite market entry (VBP for accelerated approval pathway drugs) for drug therapies that may be the subject of a potential VBP arrangements.

Response: We believe that the commenter may be concerned that the use of VBP may create incentives for manufacturers to attempt to use FDA's accelerated approval pathway to bring a drug to market, and then use a VBP approach to market the drug as payers, including state Medicaid agencies, might not believe that the drug has a fully-determined clinical benefit. This rule does not address drug development and how drugs are approved for marketing in the United States by FDA. We do not believe that manufacturers make decisions about developing or marketing a drug based on the existence of VBP approaches. However, we do think that accelerated approval drugs might be good candidates for VBP, as these drugs can meet the definition of covered outpatient drug under the

Medicaid Drug Rebate Program, and payers may want some additional evidence that they will be paying for a drug that will provide a clinical benefit to the patient, and thus seek a VBP arrangement from the manufacturer.

Comment: A few commenters commented on the timing of the final rule and encouraged CMS to finalize the proposed rule this calendar year and develop further subregulatory guidance based on their belief it will improve access to cell and gene therapies coming to market. Another commenter recommended that CMS work through CMS' Center for Medicare and Medicaid Innovation (CMMI) to test broader VBP arrangements and other payment innovations for drug therapies. A few commenters requested that CMS clarify that existing VBP arrangements established prior to the final rule will be grandfathered in if they are not found to be compliant with definitions articulated in the final rule.

Response: While this rule will be effective 60 days after its publication, we are delaying the effective date of certain amendments in this final rule until January 1, 2022, including the policy permitting manufacturers to report multiple best prices under a VBP arrangement. This will allow manufacturers, states and CMS to make the necessary system changes, and CMS to issue operational guidance regarding the final policy permitting multiple best price reporting, as necessary. The definition of VBP arrangement will be effective 60 days after the rule publication in order to apply the changes made to the bundled sales definition as discussed later in this rule.

While we appreciate the request to test these innovative payment arrangements, we do not believe VBP arrangements need to be tested under the CMMI authority in order to issue this final rule. Many state Medicaid programs (nine states via CMS-authorized supplemental rebates) and commercial payers already have VBP arrangements in place that have provided some initial evidence about the pros and cons of these programs. This final rule addresses potential regulatory hurdles manufacturers and states face when choosing to offer and participate in VBP arrangements.

Comment: A commenter was concerned that the proposals with regard to VBP arrangements and the definition of such arrangements lack the requisite clarity for manufacturers to undertake the operational overhauls necessitated by these proposals. For example, the commenter questioned whether outcomes-based measurement metrics create bundled sales under

arrangements that do not meet the proposed definition of a VBP arrangement (including the as yet undefined requirement that the outcomes-based measure "substantially" link the cost of the drug to that of the drug's actual performance). The commenter indicated that without further detail regarding the operation of CMS' VBP arrangement proposals, manufacturers will lack the certainty needed to invest in operationally-complex innovative payment arrangements.

Some commenters raised concerns about how states will become aware that a manufacturer is in fact offering a multiple best price VBP arrangement to states for a drug, how such information will be reported to CMS and accessed by states, whether states and manufacturers would have to enter into side agreements regarding the VBP arrangement, and how such future price adjustments under the VBP program would be reported to and made by states and manufacturers, among others.

Response: We understand that there may be unresolved issues regarding some aspects of the VBP policies that are being implemented in this regulation, and if necessary and appropriate, expect to address any such issues that may arise in the future through operational guidance.

We note that some manufacturers have been using the bundled sales approach for VBP arrangements, under the reasonable assumption that a VBP arrangement represents a type of performance requirement. Regulations found at § 447.502 allow manufacturers to allocate discounts in a bundle across the entire bundle if tied to a performance requirement. After the regulation is finalized, any VBP arrangement would have to meet the new definition of VBP arrangement in order to avail itself of potential regulatory flexibilities, whether the manufacturer reports pricing using a bundled sale or multiple best prices approach (effective January 1, 2022). To be clear, with respect to the bundled sales approach, a manufacturer could only use the bundled sales approach, and thus allocate any VBP discounts across the products in the bundle, if the manufacturer's value-based payment arrangement met the new definition of VBP arrangement, as adopted in this final rule as discussed below.

We also believe that the commenter's reference to operational complexity is referencing the technology and systems that may have to be developed or modified to accommodate the necessary tracking of patients that are enrolled in VBP arrangements. We appreciate the

comment, and recognize that VBP arrangements can be complex to design and implement. However, this rule does not require manufacturers, states or payers to enter into VBP arrangements but rather makes changes to price reporting requirements to allow manufacturers to report multiple best prices associated with such arrangements. We know that some Medicaid programs are already implementing these VBP arrangements, as are some commercial payers, so there is some experience in the marketplace with implementation of these programs. We also understand that state Medicaid programs, commercial payers and manufacturers, as well as CMS, will have to make some operational changes to accommodate the reporting of multiple best prices associated with VBP arrangements being offered to the states.

We are also developing a new Medicaid Drug Program (MDP) system that will replace both the current Drug Data Reporting (DDR) and Medicaid Drug Reporting (MDR) systems, and this new system is expected to be fully functional in July 2021. We expect that this new system will help support the reporting by manufacturers of multiple best prices, as well as the reporting by CMS of VBP-related unit rebate amounts to the states, that would obviate the need for manual reporting of these prices by manufacturers to CMS and to the states. We will need to provide operational guidance on these and other related issues over the next year.

For these and other reasons, the final policy permitting multiple best prices reporting will not be effective until January 1, 2022 so that all affected stakeholders have sufficient time to address these operational technology and system challenges. We believe that delaying the effective date until January 1, 2022 after the new MDP system is expected to come on line will provide sufficient time to test the system and assure that it can support the new multiple best price reporting options.

2. Subpart I—Payment for Drugs (Definitions (§ 447.502))

a. Value-Based Purchasing (VBP) Arrangement

A VBP arrangement is not expressly defined or addressed in section 1927 of the Act or the MDRP implementing regulations. To address the issues, we proposed a definition of VBP to apply, as appropriate, in implementation of the MDRP. More specifically, we proposed to define VBP at § 447.502 to further clarify for manufacturers how discounts, rebates, pricing etc. as a result of VBP

arrangements should be accounted for in a manufacturer's determination of AMP and best price for an applicable COD.

At this time, manufacturers are permitted to make reasonable assumptions in the absence of applicable statute, regulation or guidance regarding how to treat pricing as a result of VBP. However, because of the uncertainty or lack of assurances as to the propriety of those reasonable assurances, we understand manufacturers may be discouraged from offering VBP to payers including Medicaid. Therefore, we proposed to define VBP as an arrangement or agreement intended to align pricing or payments to an observed or expected therapeutic or clinical value in a population (that is, outcomes relative to costs) and includes (but is not limited to):

- Evidence-based measures, which substantially link the cost of a drug product to existing evidence of effectiveness and potential value for specific uses of that product;
- Outcomes-based measures, which substantially link payment for the drug to that of the drug's actual performance in a patient or a population, or a reduction in other medical expenses.

We have observed that some examples of evidence or outcomes-based measures used by manufacturers in their VBP proposals may be derived by observing and recording the absence of disease over a period of time, reducing a patient's medical spending, or improving a patient's activities of daily living thus resulting in reduced non-medical spending. In response to the proposed definition of VBP, we solicited suggestions for other measures and a rationale for the suggested measures that could be used to reflect value from a drug therapy and considered as we develop a final definition. We also solicited suggestions as to how to interpret "substantially" as used in the definition. That is, how much of the drug product's final cost should be associated with the evidence or outcomes based measure in order for the arrangement to be considered a VBP (for example, a drug product cost with less than 90 percent of the discounts/rebates tied to the drug's performance not be considered a VBP arrangement).

a. Definition of VBP Arrangement

Comment: Many commenters encouraged CMS to maintain a broad definition of VBP arrangements and expand the definition to ensure that all contracting parties have the flexibility needed to develop arrangements that best meet their priorities for a wide

range of drug therapies, including cell and gene therapies, as well as oral small-molecule drugs dispensed in retail settings based on their belief that evidence and/or outcomes-based approaches can be used independent of whether a drug is or is not classified as specialty. A few commenters requested that CMS clarify that VBP arrangements are not limited to one-time, high-priced therapies to enable use of these arrangements for therapeutic areas that require recurring treatment, have a substantial prevalence and overall disease burden to patients, and/or drive substantial cost to Medicaid and payers (for example, chronic condition).

However, several commenters expressed concern with CMS' proposed definition of VBP arrangements because they noted it was not detailed enough to operationalize and had potential for fraud, waste, and abuse. One commenter further noted that the proposed definition does not include any guardrails or features to ensure that VBP arrangements meet reasonable thresholds for providing value for a drug.

A few commenters requested CMS to revise the definition to reflect the following: "An arrangement or agreement intended to align pricing and/or payments to observed or expected therapeutic or clinical values in select populations (that is, outcomes relative to costs) and including (but not limited to): Evidence-based measures, which link the cost of drug products to existing evidence of effectiveness and potential value for specific uses of products included under the arrangement; Outcomes-based measures, which link drug costs to the actual performance (actual endpoints and direct or indirect surrogate markers, including duration of therapy or discontinuation) in a patient or a population, or a reduction in other medical expenses." One commenter recommended that CMS review current state VBP arrangements to refine the proposed definitions.

Several commenters emphasized the need to maintain the option for VBP arrangements to include evidence- or outcomes-based measures to provide maximum flexibility for payers and manufacturers when negotiating contracts. The commenters requested that CMS include an "or" between the two examples of measures to make clear that both are not required for VBP arrangements. A few commenters recommended that CMS only consider outcomes-based measures for VBP arrangements eligible for alternative best price calculations. One commenter noted that the parenthetical phrase,

“that is, outcomes relative to costs” is confusing and should be removed from the definition.

One commenter recommended that CMS only allow outcomes-based VBP arrangements to be allowed to perform alternative best price calculations based on their belief that they are likely to have significant best price implications from a single sale. The commenter distinguished outcomes-based VBP arrangements from evidence-based ones further, expressing their opinion that evidence-based contracts are more likely to have a value-based price across multiple sales. One commenter suggested CMS should require manufacturers to demonstrate a drug’s outcome effectiveness prior to market entry. The commenter noted that this change will enable payers to negotiate payments based on proven outcomes.

Response: We believe the definition of VBP arrangement is sufficiently broad to include most VBP structures currently on the market and would not exclude specific drugs on the market—be it highly utilized drugs that treat large populations for chronic conditions or one-time gene therapies that are used in small populations. Therefore, we are maintaining a broad definition to ensure such arrangements are recognized for purposes of determining and reporting best price and AMP; however, we agree with commenters that the evidence or outcomes-based measures used in a VBP arrangement should be evaluated in a select population and are therefore adding the term “select” before populations to clarify that VBP arrangements are arrangements that are specific to select population groups using the drug therapy (for example, gene therapy specific to a specific cancer type). We are also adding “and/or” between the two measures in the definition to further clarify that either evidence-based and/or outcomes-based measures could be used in a VBP arrangement. Furthermore, we agree that the parenthetical “that is, outcomes relative to costs” is confusing given outcomes measures is already part of the definition of VBP arrangement. Therefore, we are removing it to reduce redundancy. Also, in response to commenters concerns that the drug covered by the VBP arrangement has demonstrated effectiveness, we are clarifying that VBP arrangements apply to CODs as defined at section 1927(k)(2) of the Act.

Comment: One commenter requested CMS to clarify the definition of the terms “effectiveness” and “performance” within the definition of VBP arrangement.

Response: We do not agree that the definition of VBP arrangement should be revised to further define “effectiveness” or “performance.” Each VBP arrangement will be fact-specific to the drug, the diagnosis it is treating, and patient population being treated, and we expect such terms will be defined as part of the VBP agreement itself.

Comment: A few commenters recommended that CMS use an alternative term to “value-based purchasing arrangements.” Commenters recommended that CMS use “value-based pricing” arrangements to reflect that VBP arrangements can be entered into between manufacturers and customers that do not “purchase” a product (for example, payers). A few commenters recommended that CMS use “value-based arrangements,” or VBAs, to reflect common industry terminology. One commenter requested that CMS use “value-based contracts,” or VBCs, instead.

Response: For the purpose of this rule, we will continue to use the term value-based purchasing (VBP) arrangement as proposed. However, we recognize there may be arrangements already available on the market that manufacturers may label differently, yet still align with the definition of VBP arrangement as finalized in this rule.

Comment: One commenter recommended that CMS require VBP arrangements to include minimum, maximum, and expected percentage rebates that will be offered and limit permissible VBP arrangements to drugs meeting certain characteristics, such as a floor for average annual cost, course of treatment cost, and/or genetic therapies and other similarly specialized drugs.

Response: CMS will not be requiring manufacturers offer specific percentage rebates or limit VBP arrangements to only certain drugs as part of the definition of VBP arrangement. Instead we will be maintaining a broad definition of VBP arrangement so that manufacturers and payers (including states) have the flexibility to design the VBP arrangement, taking into consideration the specifics of the drug treatment and patient population served. The final definition will include the language that there be a substantial link between an outcomes-based measure and the payment for the drug; or, evidence-based measure and the cost of the drug as discussed later in this preamble.

b. Evidence-Based Measures

Comment: Several commenters either supported or did not support the inclusion of evidence-based measures in the definition of VBP.

Commenters that supported the inclusion of evidence-based measures noted it was sufficiently flexible to account for the breadth of potential measures that may be considered in VBP arrangements. A few commenters urged CMS to preserve a broad definition of evidence-based measures to allow manufacturers and payers to identify appropriate measures for each VBP arrangement, tailored to a particular drug therapy and patient population. Another commenter suggested that CMS ensure that the definition of evidence-based measures be sufficiently broad to allow clinical endpoints and direct or indirect surrogate endpoints to be used in VBP arrangements. Commenters also noted that use of evidence-based measures is already allowed under current best price reporting requirements and CMS-authorized supplemental rebate agreements (SRAs).

Some commenters did not support CMS’ inclusion of “evidence-based measures” in the definition of VBP arrangements, claiming the inclusion of such measures leaves the VBP arrangement definition excessively broad. The commenters stated that the inclusion of evidence-based measures is unnecessary because these measures are currently used to negotiate regular discounts for formulary or preferred drug list (PDL) placement between manufacturers and commercial payers or states. Several commenters noted that including evidence-based measures in the definition of VBP arrangements will likely undermine best price reporting requirements and allow manufacturers to reduce their Medicaid rebate obligations.

A few commenters opposed inclusion of evidence-based measures in the definition of VBP arrangements because they noted that CMS did not provide sufficient details in the proposed rule. A few commenters expressed concern with the proposed inclusion of evidence-based measures in the definition of VBP arrangements citing their belief that the administrative burden associated with reporting will be significant. One commenter noted that the inclusion of evidence-based measures in the definition of VBP is redundant based on their belief that external entities like the Institute for Clinical and Economic Review (ICER) already account for evidence-based measures.

Some commenters requested that CMS clarify that evidence-based measures may be based on a limited clinical data set, health economics, outcomes research or other documented evidence. A few commenters also

encouraged CMS to clarify that clinical effectiveness is defined more broadly than required under FDA regulatory requirements and requested that CMS provide clarity on how clinical effectiveness will be determined, especially for new drugs.

Other commenters requested CMS to require evidence-based measures be developed through a patient-centered approach that requires patient input on measure selection and desired outcomes. Several commenters emphasized the importance of CMS' consideration of a patient-centered approach to measuring value because they noted that they believe in the need for patients to be involved throughout the design of VBP arrangements, including the selection of measures that are important and relevant to patients. A few commenters recommended that CMS include patient-reported measures that signal improvement in patient health or quality of life as an indicator of a drug's value. One commenter suggested that long-term benefits for patient health, or durability, also be considered to measure value.

One commenter encouraged CMS to provide guidance refining the definition of evidence-based measures in the context of therapies treating rare diseases with limited availability of data and small target populations that require highly personalized treatment. A few commenters noted that they believe there are often limited evidence-based measures for rare disease groups given limited natural history data, small patient populations and other challenges.

Response: We appreciate the comments regarding the use of evidence-based measures as part of the definition of a VBP arrangement, but we will not be revising the definition to provide additional refinement to what is meant by evidence-based measures. We believe further clarification to the term evidence-based measures will unnecessarily limit the potential for VBP arrangements using such measures. While we support VBP arrangements that establish evidence-based measures using patient-centered approaches such as quality of life indicators and believe that evidence-based measures must be based on clinical data sets and documented evidence, we believe determining the appropriate features of a VBP arrangement are more appropriately left to the manufacturer and further negotiated with the payer (be it a health plan, provider, or patient).

Comment: A few commenters noted that the proposed definition of evidence-based measures could result in

inconsistent interpretations of requirements for best price calculations between manufacturers, which may result in a smaller rebate obligations under VBP arrangements as compared to current Medicaid supplemental rebate agreements (SRAs).

Response: There may be differences between rebates offered under a CMS-authorized SRA and the VBP arrangements under the multiple best price approach. States will be in the best position to determine which arrangement meets the financial and patient care needs of their state's Medicaid program. A state is not required to participate in a manufacturer's VBP arrangement as offered on the commercial market. They may negotiate their own arrangement under a CMS-authorized SRA, and those arrangements do not have to meet the definition of VBP arrangement. States may choose to negotiate participation in both types of arrangements as well. However, a manufacturer who wishes to utilize the multiple best price approach or the bundled sales approach must ensure that their VBP arrangements satisfies the definition of a VBP arrangement in this final rule, and with respect to using the best price reporting flexibilities, offer such VBP arrangements to all states, in order to avail themselves of such regulatory flexibilities.

Comment: One commenter requested CMS to clarify that VBP arrangements that rely solely on evidence-based measures are sufficient to meet the proposed definition of VBP arrangements. The commenter further noted that there may be circumstances in which the combination of evidence and outcome-based measures may not be feasible.

Response: VBP arrangements may be based on either evidence-based or outcomes-based measures or both, as provided in the final definition of a VBP arrangement.

Comment: One commenter recommended CMS clarify in the final rule that the list of evidence-based measures in the preamble to the proposed rule is not an exhaustive list of acceptable measures to meet the definition of VBP arrangements.

Response: The commenter is correct that the list of examples provided in the preamble to the proposed rule (85 FR 37292) is not an exhaustive list of evidence-based measures and CMS does not intend to further define or limit evidence-based measures based upon these examples as part of this final rule. Therefore, manufacturers may make reasonable assumptions, in the absence of any further guidance on such

measures; as part of their determinations as to whether an arrangement satisfies the definition of a VBP arrangement and retain such documents in accordance with recordkeeping requirements at § 447.510(f).

Comment: One commenter suggested that CMS require VBP arrangements to be either cost-based or outcomes-based unless the state Medicaid agency finds an evidence-based VBP arrangement to be appropriate. It is the opinion of the commenter that evidence-based measures alone are not sufficient to ensure value.

Response: We will not be requiring the VBP arrangements be cost-based or outcomes-based as part of this final rule. Furthermore, states will not be required to enter into a VBP arrangement in instances when the state does not agree with entering into an evidence-based VBP arrangement.

c. Outcomes-Based Measures

Comment: Several commenters requested CMS provide additional clarification regarding what is meant by outcomes-based measures in VBP arrangements. Commenters indicated that outcomes measures should be easily measurable, clinically relevant, and associated with clinical and/or financial improvements and must rely on documented evidence. One commenter expressed concern that the proposed rule did not provide information around the process for developing performance (outcomes) measures and how those measures will be established for new treatments.

Other commenters supported maximum flexibility in CMS' proposed definition of outcomes-based measures to account for the breadth of potential measures, diseases, and populations that may be considered in VBP arrangements.

Response: We are not defining what is meant by outcomes-based measures as part of the definition of VBP arrangement, or a process to develop such measures. With this final rule, we intend to provide the greatest flexibility to manufacturers and states (and other payers) to develop and design VBP arrangements, as appropriate. We believe that a broad definition of VBP arrangement allows manufacturers and payers to develop, structure and implement VBP arrangements in the ever-evolving health care environment, as well as allow manufacturers and payers to consider future changes in the scope and nature of such arrangements. Providing overly prescriptive performance or outcomes-based measures to be used by manufacturers

and payers in these arrangements may impede this flexibility.

Comment: A few commenters recommended that CMS clarify the difference between evidence-based and outcomes-based measures included in the proposed definition of VBP arrangements. One commenter suggested that the proposed definition of both measures included confounding language based on their belief that performance measures in outcomes-based arrangements are based on effectiveness derived from evidence.

Response: We do not believe additional clarification is necessary to distinguish between evidence-based and outcomes-based measures within the definition, as doing so may impede manufacturer and payers ability to negotiate VBP arrangements. We believe that the final definition of VBP arrangement provides manufacturers and payers substantial flexibility to develop, structure and implement VBP arrangements in the evolving health care environment, and the capacity to adapt future changes in the scope and nature of these programs. An example of an evidence-based measure is a situation where a manufacturer may use documented evidence that its cancer drug results in complete remission for 80 percent in a population. The manufacturer may then negotiate with the payer that if 80 percent of the payer's patients do not enter complete remission as based on this evidence-based measure, the payers cost of the drug will be rebated for a portion of their patient's population. On the other hand, an example of an outcomes-based measure is that the manufacturer and payer agree to a payment based upon whether or not a patient reaches an agreed upon clinical outcome. The outcome may include a reliance upon documented evidence or not.

Comment: One commenter recommended that CMS remove from the outcomes-based part of the definition of VBP arrangement "reduction in other medical expenses" and replace it with "an impact to other medical expenditures" based on their belief that it will provide more flexibility to payers and manufacturers.

Response: We decline to make this change as the phrase "an impact to other medical expenditures" is overly broad and could be interpreted to mean something other than decreases to medical expenditures. For example, "impact" to other medical expenditures could mean that medical expenditures could increase under a VBP arrangement. This would seem to be counter intuitive to the use of VBP arrangements. For example, a

manufacturer may offer a VBP arrangement for a drug that will keep the patient out of the hospital, or require fewer emergency room visits. If the use of the drug did not reduce these other health care expenditures, then payers may not be willing to enter into these arrangements or discontinue participation. We believe that the reduction in other medical expenses should be a primary outcome of the use of VBP arrangements.

Comment: Several commenters suggested various types and considerations for selecting outcomes-based measures, including disease-specific measures, patient or population total cost of care, healthcare utilization rate, clinical and direct or indirect surrogate endpoints, biomarkers, survival and recovery, cure rate, adverse event rates, laboratory values, quality of life, medication adherence, drug persistence, or tied to additional doses of therapy. A few commenters encouraged CMS to require alternative treatments to be considered when developing VBP arrangements, in particular comparing cost and outcomes of new treatments to existing therapies. One commenter recommended that outcomes-based measures adhere to the HHS OIG's October 2019 proposed rule (84 FR 55694; RIN: 0936-AA10)¹⁷ requiring outcome measures grounded in legitimate, verifiable data or other information from a credible external source (such as a medical journal, social sciences journal, or scientific study), an established industry quality standards organization, or results of a payor or a CMS-sponsored model or quality program.

Response: We appreciate these recommendations but do not believe we need to revise the definition of a VBP arrangement to account for these considerations. The manufacturers will enter into these agreements with commercial payers and state Medicaid programs, and we encourage the manufacturers to work very closely with payers and patient groups when developing their VBP arrangements in a process that is transparent and free of financial conflict such that there is confidence in the outcomes-measures chosen.

Comment: A few commenters requested that CMS allow VBP arrangements to be evaluated with outcomes-based measures that were not included in clinical trials and provide guidance on how manufacturers should

report initial prices under a VBP arrangement if those prices vary based on patient outcomes that were not documented during clinical trials. The commenter noted that narrowing VBP arrangements to evidence generated in a limited number of single trials will limit VBP arrangements and fail to meet desired patient outcomes.

Response: We appreciate the commenter's suggestions. We hope that manufacturers and payers will take note of them. However, we do not believe we need to revise the definition of a VBP arrangement to account for these considerations. Manufacturers and payers will determine the development and evaluation of these VBP arrangements, and determine whether such VBP arrangements satisfy the regulatory definition and avail themselves of the regulatory flexibilities being finalized in this final rule, as appropriate.

Comment: A few commenters expressed concern that the proposed outcomes-based measures included in the proposed definition of VBP arrangements may not align well with rare diseases, especially if the outcomes-based measure(s) is further restrictive. The commenter also claimed that rare disease products are developed through the Accelerated Approval Pathway, and thus limited clinical data is available at the time when an application is reviewed and approved. One commenter suggested that reliance solely on clinical outcome assessments for small patient populations may obscure a therapy's true value and patient feedback when evaluating VBP arrangements.

Response: We believe that drugs for rare diseases approved under FDA's accelerated approval authority could make good candidates for VBP arrangements for the very reason that the commenter mentions. FDA approval in these instances may be dependent upon further studies to confirm the clinical benefit of the drug. The VBP program could, for example, have some connection to the manufacturer completing these additional studies, or be based on the evidence from the additional trials that the manufacturer is conducting during the period of the VBP arrangement.

Comment: A few commenters recommended that CMS clarify in the final rule that outcomes-based measures based upon quality of life or age are discriminatory and devalue the lives of persons with disabilities and older adults. Another commenter encouraged CMS to require that VBP arrangements account for complex conditions experienced by Medicaid beneficiaries,

¹⁷ <https://www.federalregister.gov/documents/2019/10/17/2019-22027/medicare-and-state-healthcare-programs-fraud-and-abuse-revisions-to-safe-harbors-under-the>.

including mental illness, and account for how those medical comorbidities may affect outcomes.

Response: We appreciate these comments regarding outcomes-based measures and how they should not discriminate against certain populations. In accordance with legal obligations under section 504 of the Rehabilitation Act, the Americans with Disabilities Act, the Age Discrimination Act, and section 1557 of the Affordable Care Act, manufacturers and payers, including state Medicaid agencies, may not make use of measures that would unlawfully discriminate on the basis of disability or age when designing or participating in VBP arrangements.

d. Defining Substantially Under VBP Arrangement Definition

Comment: A few commenters encouraged CMS to include input from patient groups and the National Health Council (NHC) when defining the term substantially. The commenters recommended CMS consider the NHC's patient-centered approach to establishing criteria for "substantially", including the six domains of patient partnership, transparency, representativeness, diversity, outcomes that patients care about, and patient-centered data sources and methods.

Response: While we appreciate the recommendation, we will not further define the term "substantially" as used in the definition of VBP arrangement in this final regulation. Instead, we expect information regarding the link between the evidence or outcomes-based measures will be included in the VBP arrangement itself and that manufacturers will retain records of how the measures link to the payment/cost of the drug consistent with the recordkeeping requirements at § 447.510(f). For example, a drug sale may be subject to two types of sales arrangements: A 5 percent discount based upon formulary placement and 50 percent rebate linked to an outcomes-based measure. The second arrangement would be a VBP arrangement because there is a substantial link between the cost of the drug and the outcome. CMS may consider providing additional examples in subregulatory guidance as more arrangements become available and we gain more experience on the various arrangements available or offered in the marketplace.

Comment: Several commenters recommended potential prescriptive or percentage thresholds to define substantially or that CMS further define the term substantially in regulation while some commenters noted they

believe a prescribed percentage would be arbitrary.

Specifically, a few commenters recommended that CMS establish a minimum threshold at the current mandatory rebate percentages of AMP (that is, 23.1 percent of AMP for single source or innovator multiple source drugs or 17.1 percent of AMP for drugs for pediatric indications or eligible clotting factors) to define substantially. The commenters claimed this will ensure the Medicaid program is eligible to receive larger rebates and will ensure the amount of risk and discounts during VBP arrangement negotiations will be acceptable to payers and manufacturers.

A few commenters recommended that CMS define "substantially" as a maximum possible discount that is greater than the current minimum mandatory rebate percentages, where the maximum possible discount accounts for all VBP arrangement and all non-VBP arrangement best price-eligible discounts. They noted that under the scenario where the maximum possible discount is less than the applicable mandatory rebate percentage of AMP, Medicaid URA calculations will align with current statutory requirements, eliminating the need for regulatory relief to promote VBP arrangements under the proposed rule.

A few commenters requested that CMS define "substantially" by requiring a threshold average of at least 50 percent of AMP over the life of a VBP arrangement. The commenters noted this threshold will allow manufacturers and payers the flexibility to adjust the rebate percentage throughout the agreement. A few commenters recommended that CMS ensure a robust definition of substantially and apply a "significantly high threshold." The commenters stated that a high threshold will disincentivize gaming on the part of manufacturers seeking to reduce rebate obligations.

One commenter suggested that CMS set the threshold for "substantially" at greater than 33–50 percent of the ingredient cost of a drug rather than the current minimum mandatory rebate percentages. The commenter noted this threshold will allow payers to hold manufacturers accountable for the value of drugs. One commenter noted that if CMS includes the term "substantially" in the final rule, CMS should set the threshold at a minimum of 25–30 percent of AMP based on their belief that it will incentivize broader uptake of VBP arrangements. One commenter suggested that CMS define substantially with a threshold of at least 80 percent. Another commenter requested that CMS consider the dictionary definition of the

term "substantially" to leverage an ordinary meaning of the term for the final rule.

However, many commenters expressed concern with CMS' application of a prescriptive or percentage threshold to define the term "substantially". Several commenters suggested that a percentage threshold will be arbitrary and could stifle innovative contracting arrangements and if CMS were to define examples of a VBP arrangement narrowly, by reference to a specific or high percentage threshold, manufacturers could be led to believe they can no longer subject VBP arrangements that do not meet that threshold to bundled sale treatment.

A few commenters recommended that CMS delay defining "substantially" until after the final rule when commercial and Medicaid payers gain additional experience with VBP arrangements.

Response: We appreciate the recommendations from commenters on how CMS should define substantially when it comes to the manufacturer determining if it is offering a VBP arrangement.

First, we appreciate the commenters' concern that the manufacturer's VBP arrangement provide at least the minimum Federal Medicaid rebate as determined in accordance with § 447.509, and that any additional VBP rebates paid to the state by a manufacturer over time as a result of the VBP arrangement be additive to that rebate. We want to assure states that the minimum rebate that the states would receive in the quarter in which the drug is administered, whether under a VBP arrangement or non-VBP program, would be the minimum Medicaid rebate—that is, a rebate for single source/innovator multiple source drugs, equal to the greater of the minimum 23.1 percent of AMP or the difference between the AMP and "best price" in a quarter for a dosage form and strength of a drug.

Should the state participate in a VBP arrangement for which the manufacturer reports multiple best prices, the state will at least receive the Federal Medicaid rebate based upon the non-VBP best price in the quarter in which the drug is administered, and additional rebates based upon the multiple best prices reported as a result of the manufacturer VBP arrangement, if the state has opted to participate in the VBP arrangement and therefore, eligible to receive such additional rebates under the VBP arrangement.

If the state is participating in a VBP arrangement under a CMS authorized

supplemental rebate program, that state-negotiated supplemental rebate as a result of the VBP arrangement is supplemental to the Federal Medicaid rebate, as well as exempt from AMP and best price. A VBP arrangement offered pursuant to a CMS-authorized supplemental rebate agreement should not be confused with a VBP arrangement that satisfies the regulatory definition of such that is being finalized in this rule.

With respect to designating an actual rebate percentage that would represent a “substantial” link to satisfy the new VBP definition, this will likely be a function of several factors, including the number of patients that might be enrolled in the health plan as well as the evidence of the drug’s effectiveness, among others. For a plan with a few number of patients, for a drug with limited clinical evidence, the threshold of a “substantial” link would likely be different than a plan with a significant number of patients, for a drug with significant clinical evidence. The amount could even be different for the same drug. Therefore, it would be difficult to designate an amount or range of rebates that might represent a substantial link.

After further consideration of the commenters’ recommendations, we will not be defining substantially or requiring a specific percentage threshold to determine whether or not there is a substantial link between the cost/payment for the drug and either of the measures in the definition of VBP arrangement. We do not want the manufacturer and the payer (state or otherwise) to be held to a specific threshold when making the determination as to the link between the cost/payment for the covered outpatient drug and outcome within the agreement and believe the parties involved should have the flexibility to determine the link. As stated earlier, VBP arrangements are voluntary and payers, including states, will not be required to participate in them if they believe the arrangement does not result in a price they are willing to pay. Also, we provided an example in the proposed regulation that used a 90 percentage threshold as an example of a possible “substantial” financial link between the expected outcome of a therapy in a patient and the compensation that a manufacturer might be expected to provide to a payer if the drug didn’t meet the expected outcomes. That is, the manufacturer would refund 90 percent of the initial purchase price to the payer if the therapy failed. The 90 percent example that was provided was an illustration of a substantial financial

link for a VBP arrangement and was not meant to be a firm regulatory threshold for the establishment of a VBP arrangement. The example demonstrates further that the intent of a VBP arrangement is that the cost/payment for the covered outpatient drug is driven by the outcome in the arrangement and that the cost/payment for a drug that is driven by other factors beyond the outcomes or evidence-based measures would not qualify the VBP arrangement under our definition. Therefore, manufacturers should ensure that in order to satisfy the definition of a VBP arrangement under our rules, any arrangement they have as a VBP arrangement with payers, provides that the cost/payment is substantially linked to outcomes.

Since we are not further defining “substantially” as part of this final rule, manufacturers may make reasonable assumptions and should document how its arrangement substantially links the payment/cost of the drug to the outcome in the arrangement and therefore qualifies as a VBP arrangement under this final rule. Manufacturers should continue to maintain records of reasonable assumptions consistent with Federal recordkeeping requirements at § 447.510(f). We may also consider issuing further subregulatory guidance on policy and operational issues relating to the definition of VBP arrangement given the nature and scope of the various arrangements coming to the market. We note that VBP arrangements offered on the commercial market before this regulation that do not meet the new regulatory definition of VBP arrangement (which goes into effect within 60 days of the publication of this final rule) will have to be restructured to meet the new definition and requirements of this final regulation if a manufacturer wants to take advantage of the regulatory flexibilities included in this final rule. Since the revised definition of VBP arrangement does not apply to arrangements negotiated under a CMS-authorized supplemental rebate agreement, those arrangements will not need to be restructured.

e. Other Measures of Value

Comment: A few commenters recommended CMS consider certain measures of value such as work productivity, patient satisfaction with treatment, and medical spending to assess a drug’s value. A few commenters suggested that CMS consider healthcare utilization like reduction in hospitalization rates and emergency department visits as a measure of a drug’s value. One commenter noted further that a reduction of utilization of

services should be controlled for maintenance of healthcare quality standards. A few commenters identified measures like laboratory tests or screenings or use of electronic health records (EHRs) as measures of a drug’s value based on their belief that such measures incentivize providers to give high quality care. A few commenters recommended that CMS consider disease-specific measures to measure value for patients with rare disorders, including rare cancers, because they believe they are inherently disease-specific and highly variable across patients.

Some commenters recommend revising the VBP arrangement definition to include individual patient cost-limiting arrangements that reduce pricing for an individual patient for greater-than-expected usage based on available evidence, discounts based on the achievement of patient-testing benchmarks, patient-reported measures that signal improvement in patient health or quality of life as an indicator of a drug’s value and expected therapeutic, clinical, or patient-centric value in a population.

Other commenters recommended that CMS measure the value of a particular drug by comparing its performance to a competing therapy or treatment option. One commenter noted that such a comparison will facilitate the cultivation of comparative effectiveness research available for drug therapies. One commenter recommended comparative effectiveness of target immunomodulatory treatments in particular for the psoriatic disease community.

Response: We appreciate the suggestions raised by the commenters and believe that all of these measures could be used by a manufacturer and payer as part of a VBP arrangement; however, we will not be amending the regulatory text to further define value. While we will not be specifically directing manufacturers to use specific measures as part of an arrangement in order to meet the definition of VBP arrangement, we believe these recommendations may be considered in the structuring of VBP arrangements as manufacturers and payers negotiate arrangements specific to a particular drug treatment. After reading all the comments, and reflecting on the best approach to help make these VBP arrangements succeed, we believe that the key is giving the most flexibility to payers and manufacturers in structuring these arrangements. Each VBP arrangement is fact-specific; therefore, the recommended measures to assess a drug’s value will be driven by a number

of factors including, but not limited to, the drug's indication, patient population treated, the availability of clinical evidence for the drug, and treatment setting. Therefore, we are not revising our proposed definition of a VBP arrangement to require specific measures beyond outcomes-based or evidence based measures.

Comment: Many commenters provided suggestions for other measures that could be used to reflect the value of a drug therapy. A few commenters recommended that CMS consider total cost of care as an additional measure of value tied to cost savings resulting from VBP arrangements and should involve a comparison of the total cost of care (inclusive of medical and pharmacy costs) to a payer for a patient (or cohort of patients) who is prescribed the contracted drug to another patient (or cohort) with equivalent disease type and severity that is not prescribed the drug. Another commenter further recommended that CMS require manufacturers to report cost savings for VBP arrangements prior to and after a VBP arrangement was implemented to promote transparency. One commenter also noted that a reduction in total cost of care should be controlled for maintenance of healthcare quality standards.

Several commenters encouraged CMS to provide flexibility and finalize broad categories of measures, especially when determining the value of drug therapies. Commenters noted that finalizing a broad definition with broad categories of measures will provide maximum flexibility between payers and manufacturers to specify more detailed medical and non-medical metrics, incentivize uptake of VBP arrangements, and avoid stifling innovation.

Response: We appreciate the commenters' suggestions for additional measures of drug value; however, we will not be amending the regulatory text to further define value, and we will not be requiring these measures as part of the final definition of VBP arrangement in order to ensure that the definition is sufficiently broad to permit flexibility by manufacturers and payers to negotiate the specific terms of each VBP arrangement. We encourage manufacturers and payers to consider these measures of value as recommended by the commenters, such as a comparison between the cost of the drug under the VBP versus other therapies, the impact of the VBP on total cost of care, such as a reduction in hospitalizations or other medical interventions, when evaluating a drug's value and designing and negotiating the specific terms of a VBP arrangement.

Comment: One commenter noted it is important that VBP arrangements facilitate access to high-value products by appropriately accounting for the actual clinical outcomes a specific product achieves. Appropriate measures include primary and secondary clinical trial endpoints, serious adverse effects avoided, total cost of care savings, episode-based reductions in spending below established benchmarks, and other clinically relevant measures that are substantially related to the underlying performance of the product and the overall improvement of the patient's health. Requiring that VBP arrangements be linked to actual clinical outcomes will help facilitate the types of arrangements CMS hopes to promote and limit the opportunities for gaming the flexibilities introduced by this rule.

Response: We appreciate the suggestion that actual clinically-relevant measures be used when measuring the performance of a drug product in a patient. We are not providing a specific definition of performance measure or giving specific examples of acceptable performance measures as part of the VBP definition and instead believe such measures may be addressed as part of the VBP agreement between the manufacturer and the payer.

Comment: A few commenters encouraged CMS to require that measures of value or effectiveness must be person-centered and based on individual assessments of patient needs, excluding measures that are discriminatory against individuals with disabilities or older adults based upon quality of life or age. A few commenters requested that CMS specify that VBP arrangements may not lock-in patients or prevent them from determining the best treatment(s) in consultation with their providers. One commenter recommended that CMS require patient management and support services be included in VBP arrangements to promote medication compliance and adherence. Several commenters suggested that the proposed rule does not ensure coverage or access to prescription drugs is preserved, especially for Medicaid enrollees, individuals with disabilities, and patients with rare or complex genetic disease. A few commenters suggested that CMS require VBP arrangements to have substantive input from patients on their needs, priorities, and desired outcomes. A few commenters requested that CMS require a simple, transparent appeals process and patient safety monitoring protocols that they believe could serve to inform patients and providers of the effectiveness of a particular drug therapy.

Response: With the exception of non-discrimination obligations required under federal civil rights law, patient protections provided under manufacturer and payer arrangements are not a subject of this final rule. Therefore, while we agree with the commenters that measures adopted under VBP arrangements should not endanger certain patients, providers, or impede access to other available medications and treatments, or interfere with the practice of medicine generally, we are not imposing patient protection requirements on manufacturers or payers embarking on VBP arrangements as part of this final rule beyond previously articulated non-discrimination obligations.

f. Transparency and CMS Oversight

Comment: Many commenters requested that CMS require certain transparency elements in the definition of VBP arrangements. Specifically, commenters recommend that CMS require manufacturers share details of VBP arrangements with states and payers, including cost-related and comparative effectiveness data and information available prior to FDA approval. In addition, they suggest that we report on measures included in VBP arrangements, including a description of the measure, justification for the measure selection, and the amount of the product's cost that is tied to the measure; and publicly release outcomes-based data associated with VBP arrangements.

Commenters also requested CMS issue guidance on the timing of negotiations for VBP arrangements with states, describe the process for maintaining confidentiality, identify information manufacturers are required to share with states and payers, establish a robust legal framework to allow all commenters to participate in VBP arrangements. They also requested that manufacturers be required to provide legal details in a timely manner to minimize gaps between VBP arrangements being implemented and a state beginning to participate in the arrangement.

Commenters also suggested that CMS mandate that states be allowed to participate in the VBP arrangement, that specific details of contract structures of VBP arrangements remain confidential and disallow direct marketing or outreach by manufacturers to patients using manufacturer gathered data from VBP arrangements.

Response: We believe the list of suggestions for CMS requirements on manufacturers, payers and states as they relate to transparency in VBP

arrangements are good suggestions and may be considered as part of the negotiation of a VBP arrangement between the manufacturer and payer. However, we are not establishing them as requirements on manufacturers and payers, including states, when participating in VBP arrangements in this final rule and we will not revise the definition of a VBP arrangement to specify such terms.

As further arrangements may emerge as a result of this final rule, CMS may consider engaging states and other industry experts regarding best practices when negotiating VBP agreements.

In order to clarify manufacturer obligations when reporting multiple best prices, we are revising the proposed regulation text at § 447.505(a) in this final rule to state that if a manufacturer offers a value based purchasing arrangement (as defined at § 447.502) to all states, the lowest price available from a manufacturer may include varying best price points for a single dosage form and strength as a result of that value based purchasing arrangement. However, states will not be required to participate in these VBP arrangements. In addition, if a state does not participate in the VBP arrangement, the best price that sets the rebate for that state will be the non-VBP arrangement best price point that must also be offered by the manufacturer and reported to CMS along with the multiple best price points reported by the manufacturer.

Comment: Several commenters encouraged CMS to consider establishing oversight processes for VBP arrangements. Specifically, a few commenters suggested the Secretary of the Department of Health and Human Services (the Secretary) should establish a pre-certification process where outcomes-based VBP arrangements must be reviewed and approved before implementation and a process to validate performance measures used in VBP arrangements to ensure that measures are meaningful and rigorous. Another commenter requested that CMS establish a pre-certification process to ensure that manufacturers do not owe lesser Medicaid rebates under VBP arrangements.

Response: We did not propose that we would provide specific oversight of the nature of VBP arrangements as part of this final rule. The federal oversight of VBP arrangements in the context of this rule would be related to the accuracy of manufacturer government price reporting and certification (for example, calculation and reporting of AMP and best price as described in § 447.510) and the manufacturer payment of required

Medicaid drug rebates. Therefore, manufacturers should maintain records of their VBP arrangements as part of their recordkeeping requirements at § 447.510(f). However, while we will not review or certify VBP arrangements offered under the multiple best price approach, we will continue to review and approve SPAs associated with CMS-authorized supplemental rebate agreement templates for state arrangements with manufacturers if a state chooses to use a VBP approach.

We also note that as discussed later in this regulation, we will require state Medicaid programs under § 447.518 that have VBP arrangements under CMS-approved SRAs to report on a quarterly basis certain information regarding the program, such as the drugs covered, costs to administer the program, and savings generated. This will help provide feedback to states and CMS on the value of these programs to Medicaid, and the operational and policy issues that states may face with implementation. This requirement will go into effect on January 1, 2022.

Otherwise, we will not be providing ongoing oversight or an approval process for VBP arrangements or the agreements between a manufacturer and payer.

g. Patient and Provider Engagement

Comment: Several commenters recommended that CMS require payers, including states, and manufacturers to engage patients and providers when determining outcomes-based measures and metrics for VBP arrangements. Several commenters emphasized the importance of including patient-reported outcomes in VBP arrangements and that there was concern that a therapy successful in achieving outlined outcomes may still leave a patient with significant medical needs and medical costs. A few commenters recommended that CMS consider the National Health Council's (NHC's) patient-centered approach when establishing criteria for outcomes-based measures, including the six domains of patient partnership, transparency, representativeness, diversity, outcomes that patients care about, and patient-centered data sources and methods. A few commenters encouraged CMS to mandate substantive input from patients on factors like disease mitigation and management, impact on patient out-of-pocket (OOP) costs, ease of adherence, and improved aspects of quality of life. Another commenter noted patients, patient advocates and physicians without financial interest in a drug therapy must be included in the process of reviewing VBP arrangements.

Response: We appreciate the comments summarized above and agree that patient and provider input in VBP arrangements are important, but we are not mandating patient or provider input with respect to VBP arrangement design or development in this final rule. We believe commercial payers and state Medicaid programs are in the best position to evaluate the benefits of a particular manufacturer's value-based arrangement for their particular enrolled patient population and may ask manufacturers to engage with patient and provider groups as part of the VBP arrangement. We note that commercial payers generally have a mechanism to evaluate the costs and benefits of such programs through pharmacy and therapeutics committees, which often include health professional participation. Furthermore, state Medicaid DUR Boards that make coverage and criteria decisions for states may also assist states with the evaluation of evidence-based or outcomes-based measures associated with particular drug therapies available under VBP arrangements, and these Boards often include providers and patients or consumers.

h. Burden of VBP Operations and Data Collection

Comment: Many commenters expressed concern that there are administrative burdens, operational requirements and significant costs borne by providers, payers, and/or manufacturers to monitor patients and collect data to evaluate VBP arrangements. A few commenters identified patient portability, especially as a result of patients that may move in and out of the Medicaid program, as a significant challenge to operationalizing VBP arrangements as it may disrupt the ability to monitor and evaluate patient outcomes over longer periods of time.

One commenter noted that manufacturers may further complicate data collection by requiring measures that labs might be incapable of testing and require involvement of third-party vendors and additional costs. Another commenter noted that manufacturers may increase data collection and monitoring burdens on providers and payers to gather data valuable for marketing, applications for FDA approval of supplemental indications, or post-marketing studies.

Several commenters recommended that CMS provide additional guidance to address these operational barriers and the additional costs associated with the adoption of VBP arrangements, including developing internal state capacity and cross-sector, multi-payer

databases, and best practices for data collection and sharing. One commenter recommended that CMS partner with FDA and the Office of the National Coordinator for Health Information Technology (ONC) to provide guidance addressing these challenges.

Response: We do not plan to issue guidance or best practices at this time as to how to operationalize, evaluate, or monitor VBP arrangements because each arrangement will have its own set of specific facts and circumstances associated with the VBP, such as the drug, the anticipated outcomes, and population included in the arrangement. In other words, a one-size fits all approach to operationalizing a VBP arrangement is not possible because of the many different arrangements on the marketplace.

We also note that we are not requiring any entity to enter into VBP arrangements. Therefore, any entity that wants to voluntarily participate in a VBP arrangement (be it a provider, payer, or state) should evaluate the complexity of entering into a specific arrangement by noting the obligations required, such as increased data collection responsibilities, monitoring burden, patient-specific portability challenges, and patient monitoring associated with the outcomes or evidence-based evaluation under the VBP arrangement. Payers, including states, should take into consideration whether participating in these VBP arrangements are of value to their beneficiaries and consider the additional costs that they will likely incur for provider or other third party services as they evaluate the final price that they may pay for the drug being purchased under the VBP arrangement.

Comment: A few commenters questioned whether VBP discounts (inclusive of administrative fees paid by manufacturers) are large enough to cover the additional operational costs (that is, staff, expertise, technical resources) to states to perform multiple and complex outcomes analyses.

Response: Participants in VBP arrangements will need to determine if the price for the drug, as discounted by the manufacturer, through the VBP arrangement, will be significant enough to cover administrative and operational costs. Both state Medicaid programs and commercial payers should be mindful of these costs before entering into VBP arrangements with manufacturers.

Comment: A few commenters recommended that CMS consider what state-level coordination is needed to track health outcomes for Medicaid beneficiaries involved in VBP arrangements. A few commenters noted

that state Medicaid agencies may not have the capacity to perform data collection to validate performance of drug therapies under VBP arrangements and that Medicaid agencies will need to coordinate monitoring and data collection efforts across Medicaid managed care plans (MCPs), as well as states. Another commenter noted that states engaging in VBP arrangements should not impose additional data collection and reporting requirements on hospitals and providers as a condition of participation.

Response: As noted earlier, we are not requiring state Medicaid agencies or their providers to enter into VBP arrangements as part of this final rule. Therefore, states will need to determine, when entering into VBP arrangements, if they have the capacity to operationalize and administer the various data collection efforts that may be required of a VBP arrangement.

States should also consider the impact of a VBP arrangement's data collection and reporting on Medicaid MCOs and Medicaid providers participating in these arrangements and whether or not these parties are interested in participating. Since the provider costs associated with a manufacturer's VBP arrangement are not reimbursable under Medicaid (unless it is a Medicaid covered service paid for under the state plan), providers, manufacturers and states (including Medicaid MCOs) should evaluate the compensation offered (if available) for the provider tasks under the arrangement and whether or not such compensation is sufficient for the tasks to be performed.

Comment: A few commenters requested that CMS offer reimbursement to providers when data collection is required. One commenter suggested that CMS should not allow VBP arrangements to place burden on providers to track and report on outcomes. One commenter noted that providers administering drug therapies will be better suited to evaluate patient outcomes and encouraged CMS to reimburse for monitoring and reporting costs. One commenter expressed concern that any savings associated with successful VBP arrangements are not shared with hospitals and providers.

A few commenters recommended that CMS acknowledge the role of providers in patient monitoring and performance measure reporting in the final rule and noted that providers administering drug therapies will be better suited to evaluate patient outcomes and encouraged CMS to reimburse for monitoring and reporting costs. One commenter requested CMS to clarify if savings associated with VBP

arrangements will be shared with providers through higher reimbursement rates furnished to Medicaid beneficiaries.

Response: We understand that depending upon the VBP arrangement, providers may have a significant role in providing or administering the drug, evaluating of patient outcomes, and monitoring patient and other clinical details associated with the VBP arrangement. Each VBP arrangement will have its own set of criteria that are needed to evaluate outcomes; therefore, it should be up to the parties participating in the VBP arrangement to negotiate terms regarding the source of payment or reimbursement relating to the performance of these activities. We did not propose and is not finalizing a new payment authority as part of this rule for Medicaid providers to perform these activities.

i. Patient Considerations

Comment: A few commenters expressed concern that VBP arrangements may compromise patient safety based on their belief that manufacturers might be encouraged to bring a drug to market with potential outcomes, not proven ones. The commenters also noted that if a drug proves to be more effective than initially demonstrated, the manufacturer should have the opportunity to demonstrate the increased benefit and re-apply for payment that reflects the new outcome effectiveness.

Response: We disagree with the commenter that this rule, which gives manufacturers and payers flexibility to enter into VBP arrangements will allow manufacturers to market suboptimal drugs or compromise patient safety. The safety and effectiveness of a drug is not the subject of this final rule. And we further add that the final definition of VBP arrangement at § 447.502 is limited to covered outpatient drugs as defined at section 1927(k)(2) of the Act which with very limited exceptions have already been approved by FDA.

Comment: A few commenters requested that CMS prohibit manufacturers from using data for direct marketing to patients or clinicians, applications for FDA approval of supplemental indications, or post-marketing studies.

Response: The proposed rule did not address the use of data by manufacturers as part of their VBP arrangement, therefore it is not a topic of this final rule. We believe any data use as a result of a VBP arrangement should be negotiated between the parties of the VBP agreement.

We also remind states that the use of a VBP arrangement in the Medicaid program does not modify the Section 1927 requirements regarding state coverage of the covered outpatient drugs of those manufacturers that have a rebate agreement in place with the Secretary of HHS. Moreover, we reiterate that CMS will not be overseeing the specific VBP arrangements or the specific pricing agreements entered into between states and manufacturers with respect to multiple best prices. Our role will be limited to receiving best price and other price information that manufacturers are required to send us under law and regulation, as well as making states aware that such multiple best prices have been reported to us for a specific drug.

Comment: A few commenters requested that CMS reject VBP arrangements and other alternative payment arrangements that unduly limit Medicaid enrollee access to medically necessary outpatient prescription drugs.

Response: This rule, and the development of a various VBP approaches under this regulation, including the multiple best price approach, does not change state Medicaid program drug coverage requirements under section 1927 of the Act, and therefore, we do not believe there will be an access issue to medically-necessary covered outpatient drugs as a result of this final rule or VBP arrangements offered by manufacturers.

States are still required to cover drugs that satisfy the definition of a covered outpatient drug subject to a manufacturer rebate agreement, whether that drug is subject to a VBP arrangement or not. If the drug is subject to a VBP arrangement and the state decides to participate in the manufacturer's VBP arrangement, the state would have to cover the drug under the VBP arrangement similar to how it would cover it if it chose not to participate in the VBP. The difference is the state would be able to collect additional rebates based upon the VBP arrangement design and presumably, the multiple best prices reported by the manufacturer under the VBP arrangement. Moreover, this rule does not establish any CMS review and approval process for VBP arrangements.

j. AMP/Best Price Reporting and MDRP

Comment: A few commenters expressed concern that manufacturers may be able to set artificially low initial prices to delay when they have to pay the full rebates they owe, and requested CMS clarify how manufacturers will report their initial prices.

Response: Manufacturers that offer VBP arrangements (as defined at § 447.502) would report AMP and best price to CMS as they currently do each quarter. They would report a best price that was not tied to a VBP arrangement, and then report the multiple best prices for any VBP arrangements that they are willing to offer to the states. We will provide additional guidance to manufacturers on how such reporting would be made, as well how we would report these non-VBP and VBP prices to states so they can evaluate their participation.

The establishment of drug launch prices is outside the scope of this rule. However, to the extent that manufacturers increase prices on their products faster than the CPI-U, manufacturers would pay additional rebates (that is, inflation penalties) as required under section 1927(c) of the Act.

Comment: Several commenters recommended that manufacturers be permitted to report AMP as the full price of the drug at the time the drug is administered, even if installment payments would extend to subsequent quarters. A few commenters recommended CMS clarify that any installment that is forgiven under a VBP arrangement will be treated as a lagged price concession for purposes of the AMP smoothing methodology.

Response: Manufacturers must include the full price of the drug in the quarter in which the drug is sold in the determination of AMP in accordance with the definition of AMP at section 1927(k)(1) of the Act regardless of the payment arrangements negotiated with payers. Both the statutory and regulatory definition of AMP at § 447.504(a) require that AMP reflect "the average price paid" to the manufacturer for the drug in the United States by wholesalers for drugs distributed to retail community pharmacies and retail community pharmacies that purchase drugs directly from the manufacturer. Installment payments do not represent the price of the drug, but rather a partial payment of the drug's price.

We also believe it is appropriate that an installment payment not made because of a VBP arrangement outcome which would result in a significant discount, be treated as a lagged price concession (as defined at § 447.502) for purposes of the determination of AMP in accordance with § 447.504(f)(3) and best price in accordance with § 447.505(d)(3).

Comment: One commenter recommended that until a manufacturer has VBP arrangements in place that

cover 50 percent of the treated disease-state population, Medicaid should continue to exclude VBP arrangements from the manufacturer's calculation of best price. Another commenter recommended CMS implement standardized process for manufacturers to correct best price data generated under a VBP arrangement.

Response: The proposed regulation did not propose that VBP arrangements be excluded from the determination of best price. Moreover, best price, as defined at section 1927(c)(1)(C) of the Act, does not permit the exclusion of prices available under VBP arrangements. Instead, we expanded § 447.505(a) to revise best price to state that a lowest price available from a manufacturer may include varying price points for a single dosage form and strength as a result of a VBP arrangement defined at § 447.502. We further discuss this policy in the multiple best prices section in the preamble below.

Comment: A few commenters recommended that CMS require manufacturers to provide separate payments for data collection and monitoring services in VBP arrangements and to expressly characterize them in the contract as either discounts or bona fide service fees paid separately from the VBP contract. This separation will provide clarity for all parties for legal and regulatory price reporting obligations (for example, AMP and best price).

Other commenters noted that manufacturer payment to third parties to track patient outcomes and fees associated with the administrative services should be excluded from best price and AMP calculations and reporting and requested CMS to provide guidance on the appropriate fair market value reimbursement for pharmacy services provided under VBP arrangements.

Response: We made no proposals about how manufacturers or other parties pay for data collection and monitoring associated with VBP arrangements in this rule. We believe payments for data collection and monitoring services as part of a VBP arrangement should be addressed during negotiations with the parties involved in the VBP arrangement. Furthermore, if a manufacturer pays a fee to any entity for data collection, administration or evaluation of a patient in a VBP arrangement, the manufacturer should evaluate whether or not that fee represents a fair market value for the service in accordance with the definition of bona fide service fee at § 447.502, as such fees shall be excluded

from the determination of AMP and best price (see §§ 447.504(c)(14) and (e)(5) and 447.505(c)(16)). Further discussion regarding the definition of bona fide service fees and fair market value is provided in the preamble (81 FR 5176 through 5181) to the COD final rule.

Comment: One commenter requested that CMS clarify how a manufacturer should structure rebates under VBP arrangements to account for a delay in data for outcome measures.

Response: We understand that there may be a delay in the reporting to a manufacturer of patient outcomes data under a VBP arrangement. We expect that manufacturers, under a VBP arrangement that will result in multiple best prices, will report to us a set of best prices that are associated with outcomes or evidence based measures which will be used for the Federal Medicaid drug rebate calculation. Based on the agreement the state (or other payer) has with the manufacturer relative to the VBP arrangement, states will report outcomes data to the manufacturers when they are available, and states will receive Federal Medicaid rebates based on the outcome measure observed in the quarter it was measured. This means a state may experience revisions to the initial Medicaid drug rebate paid to the state because of a failed outcome for a patient that occurs after the drug has been administered, and the initial rebate would need to be supplemented to account for one of the multiple best prices as a result of the outcome of the VBP arrangement. In other words, a prior period adjustment to a Medicaid Federal rebate that has already been paid to the state may be necessary.

k. Other Payment Models (Warranty, Pay-Over-Time, Subscription, Indication-Based Pricing)

Comment: Several commenters encouraged CMS to provide that additional innovative arrangements that could qualify under the definition of VBP arrangements such as payment-over-time, license or subscription arrangements, indication-based pricing, combination pricing, warranty type models, subscription models and financial risk-based models. One commenter suggested that CMS refine the definition of VBP arrangements to allow payment-over-time arrangements that do not rely on evidence- or outcomes-based measures and recommended that the definition be revised to read: “(1) an arrangement containing measures (which can be outcome-based, evidence-based, or use other standards) that link the cost of a drug product to a specific outcome in patient or population, whether measures

in health outcome, cost savings, or any metric agreed to by the parties, or (2) payment over time arrangements not contingent on specific health outcomes.”

Commenters also requested that “warranty-type” insurance models (this model obligates a premium payment by the manufacturer to a health plan to pay for a patient’s future healthcare costs if the therapy fails) be outside of the proposed definition of VBP and that the revisions adding VBP arrangements to the proposed bundled sale definition and multiple best price calculations would not apply to such warranty models.

Some commenters suggested that some subscription models may not meet the definition of VBP arrangements; however, those (subscription) models that link to evidence-based or patient outcomes should be included in the definition proposed by CMS.

Response: We recognize that there may be a variety of payment models that industry may adopt that may, or may not satisfy the definition of a VBP arrangement. We do not want to inadvertently narrow the definition of VBP arrangements by identifying specific models or structures and believe the definition of VBP arrangement in this final rule is sufficiently broad to potentially capture the various arrangements noted by the commenters when it would be appropriate.

We note that not all pay-over-time arrangements will meet the definition of a VBP arrangement at § 447.502. For example, while there may be some pay-over-time arrangements that allow payers to pay in increments based upon evidence-based or outcomes-based measures, we do not agree that every pay-over-time or subscription model should be considered in the definition of VBP arrangement. Some pay-over-time measures are simply payment schedules negotiated between the manufacturer and payer and do not have any linkage to the value of the drug to the patient or selected population.

One of our main objectives is to ensure that any VBP arrangement must include evidence-based measures that substantially link the cost of a covered outpatient drug to existing evidence of effectiveness and potential value for specific uses of that product; or, outcomes-based measures that substantially link payment for the covered outpatient drug to that of the drug’s actual performance in a patient or a population, or a reduction in other medical expenses. If one of these models noted above satisfies the definition of a VBP arrangement, then it

may appropriately avail itself of applicable regulatory flexibilities.

However, there are questions regarding whether the premiums paid by the manufacturer to a third party can be excluded from, or included in, best price when a manufacturer adopts a warranty-type models. Section 1927(c)(1)(C) of the Act defines best price, in part, to mean with respect to a single source drug or innovator multiple source drug of a manufacturer, the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity or governmental entity within the United States, with certain exclusion applying. The statutory definition of best price is implemented in regulation at § 447.505 and provides that a drug’s best price be net of certain transactions including incentives (see § 447.505(d)(1)).

The premium paid by the manufacturer to a third party to warrant a drug and provide benefits to payers and patients when certain clinical or performance measures are not achieved serves as an incentive to payers, providers, and patients to purchase the drug. Therefore, the premium paid by a manufacturer reduces the drug’s price, and must be included in “best price.” However, the benefits paid by the third party in the event the drug did not meet certain clinical or performance measures are exempt from “best price” because payments made from the third party to the payer do not represent a price available from the manufacturer to any best price eligible entity as provided in § 447.505(a) and does not represent a manufacturer sale to an AMP eligible entity consistent with § 447.504(b) or (d).

Therefore, under this warranty model, a manufacturer would pay both Section 1927 rebates for the drug, as well as pay for a premium for a warranty policy, the value of which they would have to be included in the calculation of their best price, regardless of whether the manufacturer uses a VBP arrangement that results in multiple best prices.

Comment: One commenter encouraged CMS to explore carving VBP arrangements out of government price reporting metrics, while creating a mechanism for direct payment of discounts to states could encourage broader adoption of VBP arrangements.

Response: This comment is outside the scope of the rule.

Comment: A commenter requested clarification from CMS regarding two-sided risk VBP arrangements and how they would operate within the context

of the proposed Medicaid best price accommodations.

Response: It is not clear from the comment what is meant by two-sided risk VBP arrangements. However, we believe that any adjustments to the prices available from the manufacturer, including adjustments made by the payer or manufacturer under a VBP arrangement, that adjust the prices available from the manufacturer must be included in the determination of best price as provided at section 1927(c)(1)(C)(ii)(I) of the Act and § 447.505(d)(3).

1. Other Concerns With VBP Arrangements

Comment: Many commenters recommended that CMS work with HHS OIG and Office of Civil Rights (OCR) to provide guidance to address other regulatory obstacles to uptake and operationalization of VBP arrangements, including the Anti-kickback Statute, the Physician Self-Referral Law (Stark Law), privacy laws (such as HIPAA), and civil monetary penalty (CMP) rules relating to beneficiary inducements. A few commenters suggested that CMS collaborate with HHS OIG to issue guidance on relevant safe harbors to accommodate the collection and sharing of patient outcomes data to evaluate VBP arrangements. A few commenters requested that CMS clarify how safe harbors can accommodate for, among other issues, the collection and sharing of data to adjudicate a contract and VBP arrangements that tie payment to outcome measures that are meaningful to manufacturers, payers, and patients but that are not included in a drug's FDA-approved label.

Response: We appreciate the suggestions and will consider whether additional guidance may be needed at a later date. Furthermore, commenters concerns regarding safe harbors under HHS OIG should be addressed directly with the OIG.

Comment: A few commenters requested CMS to clarify whether the new flexibility for state Medicaid programs to enter into VBP arrangements would include claims paid under, or could be applied to, Medicaid MCOs. One commenter encouraged CMS to require Medicaid MCOs to have a VBP agreement signed in the quarter preceding implementation based on their belief that the requirement would address post facto adverse selection.

Response: Medicaid MCOs may enter into their own VBP arrangements with manufacturers including the VBP arrangement offered by the manufacturer on the commercial

market. However, the prices negotiated under those VBP arrangements would not be exempt from best price given that the prices are not negotiated pursuant to a CMS-authorized supplemental rebate agreement under the exclusion at § 447.505(c)(7).

Comment: A commenter suggested that CMS should engage in a Request for Information (RFI) process to gather more stakeholder feedback to develop more detailed proposals before finalizing the proposed rule definition of a VBP arrangement. One commenter noted that CMS' request for public comment on additional measures to reflect value from a drug therapy is indicative of a need for a RFI process prior to the release of formal notice and comment rulemaking.

Response: We do not believe feedback via a RFI is necessary before finalizing this rule as there are numerous manufacturers and payers already involved in VBP arrangements and the goal of this rule was to enhance flexibility around Medicaid drug rebate pricing rules for manufacturers and payers as they enter into these arrangements. We appreciated the suggestions that commenters gave regarding the measures to determine a drug's value, which we hope will generate ideas and considerations as manufacturers and payers continue participating in VBP arrangements. CMS may consider issuing best practices in Medicaid regarding VBP arrangements in the future based upon the experiences realized by states, payers, and manufacturers.

Comment: A commenter recommends that CMS work with its fellow agencies to develop and implement strategies and programs to improve the availability, quality, and access to real-world data (RWD) for research and other population health purposes and CMS should establish privacy-related policy principles and recommendations to support the use of RWD and real-world evidence to include patient-generated data for clinical research, regulatory evaluation, and VBP decision-making. The commenter further noted that CMS should collaborate with FDA on ways to generate shared evidence in support of their (CMS) decisions.

Response: While the availability of data to measure and evaluate drug therapies is an essential part of VBP arrangements, improving upon the availability, quality and access of real world data for research and other purposes, is outside the scope of this final rule.

Comment: One commenter recommended CMS consider creating a new type of Healthcare Common

Procedure Coding System (HCPCS) code, potentially a modifier, associated with a gene therapy's HCPCS Level II code, preferably issued at the time of FDA approval, which could be used to report whether or not a health outcome was achieved to facilitate payment and financial reconciliation of a value-based contract.

Response: The creation of new types of HCPCS codes associated with this regulation is outside the scope of this final rule.

Comment: One commenter recommended that CMS require state Medicaid agencies that enter into VBP arrangements to provide the manufacturers with audit rights to any data collected for purposes of tracking performance. The commenter noted that access to the data is important to adjudicate the rebates associated with VBP arrangements and to facilitate lessons learned for both parties.

Response: This final rule does not require state Medicaid agencies provide manufacturers with the data collected for purposes of tracking a drug's performance. This final rule focuses on providing manufacturers and payers additional regulatory flexibility to enter into VBP arrangements. We believe if manufacturers desire to seek audit rights as part of the VBP arrangement, manufacturers may consider negotiating these terms as part of the arrangement with the state.

Comment: One commenter noted the proposed rule facilitates uptake of individual-level VBP arrangements for one-time or curative treatments, rather than arrangements requiring population-based approaches. The commenter also noted that without further clarification, uptake of population-based VBP arrangements for chronic conditions would be limited as a result of the administrative burden born by payers and manufacturers to calculate the value of a drug at the individual-level.

Response: We do not agree that the proposed rule facilitates only individual level VBP arrangements for one-time or curative treatments instead of population based approaches because the definition of VBP arrangement does not make such limitations. We also believe that by adopting a broad definition of VBP arrangement, manufacturers will have the flexibility to develop VBP arrangements specific to either individual or population-based approaches.

Comment: A few commenters expressed concern that payers may deny coverage of FDA-approved therapies as a result of not meeting expected outcomes for VBP arrangements, especially for gene therapies and

contraception. Another commenter requested CMS clarify that the lack of a VBP arrangement does not release the state from the drug coverage obligations of section 1927 of the Act.

Response: This final rule does not affect Medicaid coverage of covered outpatient drugs as defined at section 1927(k)(2) of the Act. States are required to cover all covered outpatient drugs of manufacturers that participate in the MDRP, whether the state enters into a VBP arrangement or not.

Comment: A few commenters recommended that CMS consider waiving cost-sharing requirements for beneficiaries participating in VBP arrangements or develop other approaches for sharing savings with beneficiaries.

Response: This comment is outside the scope of this final rule.

After considering the comments received, we believe the definition of VBP arrangement should be broad enough so that manufacturers and payers, including states, have the flexibility to structure a VBP arrangement specific to the drug therapy being offered. Therefore, we are maintaining a broad definition to ensure such arrangements are recognized for purposes of determining and reporting best price and AMP; however, we agree with commenters that the evidence or outcomes-based measures used in a VBP arrangement should be evaluated in a select population and are therefore adding the term “select” before populations in the definition to clarify that VBP arrangements are specific to select population groups using the drug therapy, such as a gene therapy specific to a patient with a particular type of cancer. We are also adding the terms “and/or” between the two measures in the definition to further clarify that either evidence-based or outcomes-based measures could be used in a VBP arrangement. Furthermore, we agreed with commenters concern that the parenthetical “that is, outcomes relative to costs” is confusing given outcomes-based measures are already part of the definition of VBP arrangement. Therefore, we are removing it to reduce redundancy. Also, in response to commenters concerns that the drug covered by the VBP arrangement has demonstrated effectiveness, we are clarifying that VBP arrangements apply to covered outpatient drugs; that is, products that satisfy the definition of a covered outpatient drug, as defined at section 1927(k)(2) of the Act. We are finalizing the definition of a VBP arrangement to mean an arrangement or agreement intended to align pricing and/or payments to an observed or

expected therapeutic or clinical value in a select population and includes, but is not limited to:

- Evidence-based measures, which substantially link the cost of a COD to existing evidence of effectiveness and potential value for specific uses of that product; and/or,
- Outcomes-based measures, which substantially link payment for the COD to that of the drug’s actual performance in patient or a population, or a reduction in other medical expenses.

3. Inclusion of VBP as a Performance Requirement Under a “Bundled Sale”

As stated in the June 2020 proposed rule, one of the issues manufacturers contend with in determining best price with the advent of VBP arrangements is that a manufacturer’s best price can be reset based upon the outcome of a drug treatment for one patient or one unit of the drug because of the VBP arrangement. When this occurs, the rebate due for that single use of the drug during a quarter that results in a negative outcome will reset the best price to a significantly lower amount, sometimes zero, prompting a significantly higher rebate (sometimes 100 percent of the drug’s AMP). We have received stakeholder comments and inquiries regarding how rebates or discounts as part of a VBP arrangement could be considered in a bundled sale when determining best price. Some manufacturers have made reasonable assumptions that such discounts, as a result of a VBP, should be considered part of a bundled sale as defined at § 447.502.

In the COD final rule, we defined bundled sale at § 447.502 as any arrangement regardless of physical packaging under which the rebate, discount, or other price concession is conditioned upon the purchase of the same drug, drugs of different types (that is, at the nine-digit NDC level) or another product or some other performance requirement (for example, the achievement of market share, inclusion or tier placement on a formulary), or where the resulting discounts or other price concessions are greater than those which would have been available had the bundled drugs been purchased separately or outside the bundled arrangement. Specifically, the discounts in a bundled sale, including those discounts resulting from a contingent arrangement, are allocated proportionally to the total dollar value of the units of all drugs or products sold under the bundled arrangement. Also, for bundled sales where multiple drugs are discounted, the current definition indicates that the aggregate value of all

the discounts in the bundled arrangement must be proportionally allocated across all the drugs or products in the bundle. (See § 447.502; 81 FR at 5182.) We noted that we understand that based on the bundled sale definition, which provides that the rebate, discount or other price concession is conditioned upon the purchase of the same drug, drugs of different types, or another product or some other performance requirement, some manufacturers have made reasonable assumptions to take into account the discounts from a VBP arrangement that has a performance requirement when a measure (such as a performance-based measure) is not met. When manufacturers recognize the VBP arrangement as a bundled sale, the manufacturer, for example, may assume that the discount that resulted from a performance requirement of a single unit is distributed proportionally to the total dollar value of the units of all the drugs sold in the bundled arrangement. This smooths out the discount over all the units sold under the arrangement in the rebate period and does not reset the manufacturer’s best price based upon the ultimate price of one unit of a drug.

For example, a manufacturer could structure a VBP arrangement such that to qualify for a patient outcome rebate, the bundled sale VBP arrangement requires the sale of 1000 units of the same drug at \$200 per unit, and if one patient fails to achieve an outcomes-based performance measure the manufacturer agrees to a \$100 price concession on that one unit. In this example, because all of the drugs in the bundle were subject to the performance requirement, the manufacturer’s scheme qualified as a bundled sale VBP arrangement, and thus, the manufacturer’s rebate of \$100 on that one unit would be allocated across all units in that bundled sale as follows:

$$1000 \text{ units} \times \$200 = \$200,000 - \$100 \text{ price concession} = (\$199,900/1000 \text{ units}) = \$199.90.$$

Best price could be set at \$199.90 if that \$100 rebate available in a qualifying bundled sale resulted in the lowest price available from the manufacturer, and not at \$100 (\$200/unit – \$100).

We agree with the applicability of the bundled sale definition in this context because it will permit manufacturers to have a best price that is not based upon the failure of one patient taking the drug. Therefore, to facilitate the appropriate application of a bundled sale offered in the context of a VBP arrangement to the best price determination, we proposed to revise the definition of bundled sale at § 447.502 to add paragraph (3) that

states VBP arrangements may qualify as a bundled sale, if the arrangement contains a performance requirement such as an outcome(s) measurement metric. We noted that we expect manufacturers, consistent with the manufacturer recording keeping requirements at § 447.510(f), to maintain documentation of the VBP arrangement, including documentation of how the programs meets the new definition of VBP arrangement, to support their calculation of AMP and best price.

We received the following comments on the definition of bundled sale in § 447.502.

Comment: Many commenters expressed support for CMS' proposed changes to the bundled sale definition which would permit manufacturers to allocate discounts or price concessions as a result of a VBP arrangement across a bundled sale. Several commenters expressed support for the proposed revision to the definition of bundled sale to include the "performance requirement" and that the bundled sale authority requires a VBP with a performance requirement, like an outcomes metric, but noted that the performance requirement does not need to be an outcomes metric as set forth in the VBP arrangement definition. Another commenter disagreed with the inclusion of the performance requirement and requested that CMS consider changing the language "if the arrangement contains a performance requirement such as an outcome(s) measurement metric" to explicitly state "a value-based purchasing (VBP) arrangement may be treated as a bundled sale."

Response: We appreciate the support and suggestions related to the proposed revisions to the bundled sale definition at § 447.502. We agree with the commenters, and are revising the proposed definition to remove "if the arrangement contains a performance requirement such as an outcomes measures metric" because this phrase is redundant to the definition of VBP arrangement defined at § 447.502 which already requires VBP arrangements include outcomes based measures. We also note that the measures listed in the preamble to the proposed rule (85 FR 37292) are examples for manufacturers to consider and we do not intend to limit VBP arrangements to only those examples.

Comment: A few commenters requested CMS to clarify in the regulations that the "VBP arrangement" referenced in the bundled sale proposed regulatory text is or is not associated with the proposed definition of VBP arrangement to be codified at § 447.502.

Response: The definition of VBP arrangement, as finalized at § 447.502 by this final rule, will apply to the bundled sale definition.

Comment: Several commenters did not support the proposed changes to the definition of bundled sale. One commenter noted this change would make the best price requirement "highly vulnerable to manufacturer gaming and inaccurate reporting that could substantially reduce or delay drug rebate payments." Another commenter opined that the proposed changes would "water down existing discounts, raise best price and lower rebate amounts." One commenter expressed the belief that the proposed changes would permit manufacturers to offer a low price to commercial purchasers and payers that would not be available to Medicaid.

Response: It is not completely clear what the commenter means by "gaming"; however, we do not agree that this clarification to the bundled sale definition makes it highly vulnerable to manufacturer gaming in the context of best price or AMP that would reduce Medicaid drug rebates. Some manufacturers have already been allocating discounts in a bundled arrangement as a result of a performance requirement under a VBP arrangement using reasonable assumptions and have shared those approaches with CMS. While we have not opined on those manufacturer-specific approaches, we have not detected any significant impact on these manufacturers' best price or AMP, or decreases in Medicaid drug rebates. Manufacturers continue to be potentially subject to penalties, including CMPs, for failure to follow pricing and product reporting requirements.

The clarification made to the definition of bundled sale was necessary to specifically address situations when best price is reset based upon the outcome of a drug treatment for one patient or one unit of the drug because of the VBP arrangement. As stated in the preamble to the proposed rule, a single use of the drug in a patient can result in a negative outcome which will reset the best price to a significantly lower amount, sometimes zero, prompting a significantly higher Medicaid drug rebate for the manufacturer (sometimes 100 percent of AMP) (85 FR 37292). We believe the impact of these significantly-higher Medicaid drug rebate deters manufacturers from offering VBP arrangements on the commercial market, as well as Medicaid.

Comment: A few commenters stated that manufacturers should not be permitted to mix prices under a VBP

arrangement with those under a non-VBP arrangement. Another commenter recommended the bundled calculation occur at the individual purchaser and individual VBP contract level and that best price for an individual purchaser should equal the average price paid per unit after including (or stacking) all discounts that a purchaser received, whether the discounts were within or outside of a VBP arrangement. One commenter requested from CMS a clearer definition of "proportional allocation" of discounts within a bundled sale arrangement with regards to VBP arrangements. Another commenter expressed concern that the proposed rule does not adequately address how stacked discounts would be handled in a bundled arrangement, allowing manufacturers to use evidence-based VBP to spread stacked discounts across all purchases, ultimately, in the commenter's opinion, reducing Medicaid rebates.

Response: The definition of bundled sale at § 447.502(1) indicates that discounts in the bundled sale, including those discounts resulting from a contingent arrangement, are allocated proportionally to the total dollar value of the units of all drugs or products sold under the bundled arrangement. The policy that is being finalized in this rule is that VBP arrangements may qualify as a bundled sale. Therefore, if the manufacturer determines that its VBP arrangement qualifies as a bundled sale, the manufacturer allocates the VBP discounts in the VBP arrangement so that it is proportional to the total dollar value units of all drugs or products sold under the bundled arrangement to the best price (or AMP) eligible entity. Any discounts provided for those units sold to the best price (or AMP) eligible entity outside of the VBP arrangement would not be part of the allocation. Moreover any non-VBP discounts provided to the best price (or AMP) eligible entities should be considered when determining the actual price realized by the entity and would not be part of the bundled sale allocation. That is, the single actual price realized by the entity for the quarter when using a bundled sales approach for a drug would have to be considered by the manufacturer along with any non VBP prices for the same drug.

Comment: A commenter suggested that aggregation of sales and discounts across purchasers under a VBP arrangement to arrive at a bundled sales best price should only be allowed for very small purchasers (such as when that the number of patients expected to take the drug is extremely low). Another commenter requested that CMS change

the rule to require manufacturers to include all VBP rebates in the calculation of a single best price using the bundled sale methodology.

Response: We appreciate the comments; however, we do not agree that the bundled sales approach only applies in certain situations (for example, drug usage in a small number of individuals) or that all discounts of a VBP arrangement could be used in the calculation of a single best price using the bundled sale methodology. Manufacturers may determine that they want to work with one or more different best price eligible entities on a VBP program using a bundled sales approach, whether a small number or large number of patients are involved for each best price eligible entity. Manufacturers would have a distinct price for each entity, taking into account price concessions or discounts inside and outside of the bundled sale arrangement available to the entity, and compare the prices amongst all eligible entities in a quarter to determine the product's lowest price available. That lowest price available amongst the best price eligible entities would presumably be the best price.

We do not believe that the statute supports the inclusion of all VBP prices offered by a manufacturer into the calculation of a single best price under a bundled sales methodology, as the determination of a best price is based on a lowest price available to a specific best price eligible entity, not a price that is an aggregation of sales/discounts/rebates across multiple entities as suggested by the commenter.

Comment: A few commenters expressed concern that the bundled sales approach may not be a workable approach to determining best price because VBP arrangements involving very small patient populations, such as gene therapy or drug therapies that treat rare and orphan diseases, and may not be able to take advantage of the smoothing effect of the bundled sale methodology. Commenters requested whether manufacturers may choose either a bundled or multiple best price approach or whether the manufacturer may determine both depending on the preferences of their negotiating partners and the product characteristics.

Response: We agree that the manufacturer may not want to use the bundled sale approach based upon the characteristics of the drug, such as drugs that treat small populations, rare and orphan disease drugs, and certain gene therapies covered under its VBP arrangement. As discussed in this section, the definition of bundled sale at § 447.502 is being finalized to state that

VBP arrangements may qualify as a bundled sale. We believe manufacturers may choose between the bundled sale arrangement approach to calculating best price, or use the multiple best price reporting approach, understanding that it is dependent upon the design of a manufacturer's VBP arrangement such as the product and population characteristics of the drug therapy offered under the VBP arrangement, and whether that arrangement meets the regulatory definition of a VBP arrangement.

We believe that the concern regarding treating small populations will be addressed by the reporting of multiple best prices approach. For example, in the event a state enters a VBP agreement with a manufacturer and a single Medicaid beneficiary has an outcome that results in a very high rebate under the VBP arrangement, the best price used by the manufacturer to set the rebate for that single unit dispensed will be based upon the VBP arrangement best price for that specific outcome. All other Medicaid units dispensed during a quarter that are eligible for rebates but not dispensed to Medicaid beneficiaries enrolled in the VBP arrangement will reflect the best price outside of the VBP arrangement.

Comment: One commenter requested CMS consider replacing the phrase "may qualify as a bundled sale" with "may constitute a bundled sale" as it is the commenter's opinion that the term "qualify" appears to invite a degree of judgment on a matter where there is no clear arbiter.

Response: Bundled sale is already specifically defined in regulation at § 447.502. We believe manufacturers will need to determine whether or not their VBP arrangement qualifies as a bundled sale, and do not believe the suggested regulatory text change is necessary, as we do agree a degree of judgement is required to determine whether a VBP arrangement should be viewed and treated as a bundled sale.

Comment: One commenter noted VBP bundling regulations do not address pro-rating, which may prove burdensome for manufacturers and may increase the possibility of gaming.

Response: This comment is outside the scope of this rule.

Comment: A commenter requested CMS to clarify whether outcomes-based measures created under bundled sales arrangements meet the proposed definition of a VBP arrangement.

Response: A manufacturer may use a bundled sales approach if the payer's or purchaser's rebate or discount is, among other situations, contingent on the existence of a performance requirement.

We are finalizing in this regulation that a VBP arrangement could qualify as a bundled sale. Going forward after the effective date of this regulation, a VBP arrangement that does not meet the definition of VBP arrangement in this regulation (which would include evidence and/or outcomes-based measures) will not be recognized as part of the bundled sale definition.

After consideration of the comments received, we are finalizing subparagraph (3) of the definition of bundled sale to remove the phrase "if the arrangement contains a performance requirement such as an outcome(s) measurement metric" and read, "Value-based purchasing (VBP) arrangements may qualify as a bundled sale."

4. Definitions—Best Price (§ 447.505(a)) and Reporting of Multiple Best Prices, Adjustments to Best Price (§ 447.505(d)(3))

In the preamble to the COD final rule (81 FR 5253), we indicated that we recognized the value of pharmaceutical VBP arrangements in the marketplace, and that we were considering how to give specific guidance on this matter, including how such arrangements affect a manufacturer's "best price." In addition to CMS, States, manufacturers, and commercial payers all have an interest in making new innovative therapies available to patients, and we have heard that there are challenges with the current interpretation of statutes and regulations for how "best price" can affect the availability of VBP arrangements. Because the statute was drafted more than 30 years ago, when such arrangements were not prevalent in the market, it is understandable that such interpretations by CMS to date regarding "best price" have been limited to one "best price" per drug.

The Medicaid statute defines best price in relevant part to mean, for a single source drug or innovator multiple source drug of a manufacturer, the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, HMO non-profit entity, or governmental entity within the United States, with certain exclusions enumerated at sections 1927(c)(1)(C)(i)(I) through (VI) of the Act. Historically, we have interpreted this language to result in only one best price per drug. The current Medicaid "best price" regulation at § 447.505 generally tracks the statutory language, but reads in relevant part that "best price" means, for a single source drug or innovator multiple source drug, the lowest price available from the manufacturer during the rebate period *in any pricing*

structure (including capitated payments), in the same quarter for which the AMP is computed (emphasis added).

The current regulation is interpreted further in the preamble language to the COD final rule and MDRP releases where we have indicated that the lowest price available means the lowest price “actually realized” by the manufacturer or the lowest price at which a manufacturer sells a covered outpatient drug—that is, one lowest price available per dosage form and strength of a drug. Applied to the VBP arrangement context, this interpretation could result in setting a best price that is either at a greatly reduced price or possibly zero, if a single dosage form or strength dispensed to one patient is subject to a full or very large rebate under a VBP arrangement.

Thus, we need to reconcile the interpretation of the statute in regulation, which currently contemplates that for any quarter, the “best price” is a single price for each dosage form and strength of a drug that represents the actual revenue realized by the manufacturer for that drug—in any pricing structure offered by the manufacturer (such as capitated payments)—with the realities of the current evolving marketplace which contemplate that multiple prices could be made available by the manufacturer for a particular drug based on the drug’s performance (such as the case with VBP arrangements that use evidence or outcomes-based measures) in a quarter.

In that regard, because VBP and other innovative payment arrangements sometimes result in various price points for a dosage form and strength of a single drug or therapy being available in a quarter, we proposed to reflect this possibility in the June 2020 proposed rule. Specifically, we proposed that a single drug may be available at multiple price points, each of which may establish a “best price”, based on the relevant or applicable VBP arrangement and patient evidence-based or outcome-based measures.

We explained in the June 2020 proposed rule that we believed we have this authority because we previously interpreted the statutory definition of best price at § 447.505(a) to reference the best price “in any pricing structure,” contemplating the possibility of various pricing structures, such as capitated payments. With the new VBP pricing structures that are available in the marketplace, we believe it is appropriate and reasonable to further interpret what pricing structures are available, and account for new VBP pricing structures, which may include introducing the

offering of a drug at multiple price points. That is, we proposed to expand our interpretation of “in any pricing structure” and also the term “lowest price available” by proposing that the price realized in a VBP arrangement by the manufacturer when a measure is not met for a single patient would not reset the best price for the drug in the quarter. That is, a single patient failure on the drug, or lack of attainment of an expected clinical outcome, would not result in the manufacturer having to give that same rebate as a result of the VBP arrangement to Medicaid for that drug as they would have to give to the commercial plan in which that patient was enrolled. However, if a state chooses to participate in the VBP arrangement offered by the manufacturer, the state could receive a URA for each patient’s particular outcome that is reflective of the VBP arrangement best price.

Rather, we proposed that, given our interpretations of the statutory phrase “lowest price available”, and the phrase “in any pricing structure” at 42 CFR 447.505, that multiple prices could be realized by the manufacturer for the same drug in a quarter when the prices are tied to a particular VBP outcomes structure. Therefore, multiple price points (price points are offered and available as a result of a VBP program, and price points absent a VBP program) may be reported for one dosage form and strength in a rebate period.

Manufacturers could offer the same or a different set of best price points each quarter for a drug, and those best price points would be applicable to the patient to whom the drug was administered in that particular quarter. Any future best price adjustments for that patient would be reflected in the outcomes that the patient achieves over the period of time of the VBP arrangement, and any price adjustments due to the state (if they participate in the VBP arrangement) would be based on the additional best price rebates reported in that quarter by the manufacturer in which the drug was first administered. Manufacturers would have to make any adjustments to both sets of best prices (VBP and non-VBP best prices) reported if any adjustments are made by the manufacturer subsequent to the quarter in which they are reported.

As an example, when a manufacturer offers a VBP arrangement, and the state chooses to participate, the manufacturer would report a single best price for the drug for the quarter for sales of the drug in that quarter (a non-VBP arrangement best price), and in addition, the manufacturer would also report a

distinct set of “best prices” that would be available based on the range of evidence-based or outcomes measures for that drug that are possible under the VBP arrangement.

The manufacturer would provide a best price rebate to the state in the quarter in which the drug is administered, and then could offer varying additional rebates based on a patient’s response after the drug is administered. The calculated additional MDRP rebate due to the state using the VBP best price would be a function of whether or not the Medicaid rebate is being paid on a unit of a drug dispensed to a Medicaid patient that participated in a VBP, and the level of rebate associated with that patient’s outcome. The additional rebate paid for that patient would only represent the amount of rebate due to the state from the manufacturer for that patient, not all patients. That is, the rebate would be specific to that patient’s outcome and that price actually realized by the manufacturer, as that price is the lowest price available from the manufacturer based on that patient’s outcomes. Otherwise, the best price used in the Medicaid rebate formula would mirror the lowest price available absent a VBP arrangement.

Therefore, we proposed to further interpret the regulatory language “in any pricing structure” to include VBP arrangements. Then, we proposed to interpret the statutory and regulatory phrase “lowest price available” as used in the definition of best price, to permit, in the context of a VBP arrangement, to include a set of prices at which a manufacturer makes a product available based on that pricing structure. This being the case, we proposed that the definition of best price be expanded at § 447.505(a) to provide that a lowest price available from a manufacturer may include varying best price points for a single dosage form and strength as a result of a VBP (as defined at § 447.502). We noted that we understand the operational challenges this may bring to MDRP systems and that it will take us time to make such system changes. We solicited comments on the proposal, its impact on the MDRP, the commercial market, and its operational implications. Specifically, we requested comments regarding the potential impact of these changes on supporting payment innovation and health care quality. We also sought comment on steps which would be needed by manufacturers and states to implement these Best Price changes, including how states would track health outcomes for Medicaid beneficiaries to align with the outcomes developed in a private market VBP.

Also, to provide consistency between AMP and best price, as we did in the COD final rule (81 FR 5170), we proposed to revise § 447.505(d)(3) to make it consistent with § 447.504(f)(3). Section 447.504(f)(3) provides that the manufacturer must adjust the AMP for a rebate period if cumulative discounts, rebates, or other arrangements subsequently adjust the prices actually realized to the extent that such cumulative discounts, rebates, or other arrangements are not excluded from the determination of AMP by statute or regulation. We proposed to add a similar qualifying phrase at the end of § 447.505(d)(3) to state that the manufacturer must adjust the best price for a rebate period if cumulative discounts, rebates or other arrangements subsequently adjust the prices available, to the extent that such cumulative discounts, rebates, or other arrangements are not excluded from the determination of best price by statute or regulation. We believe this is consistent with the requirement at section 1927(c)(1)(C)(ii)(I) of the Act, which provides that best price shall be inclusive of cash discounts, free goods that are contingent on any purchase requirement, volume discounts and rebates, and therefore, best price must account for these to the extent they are not excluded by statute or regulation.

We received the following comments on the definitions—Best Price (§ 447.505(a)) and Reporting of Multiple Best Prices, Adjustments to Best price (§ 447.505(d)(3)).

Comment: A few commenters expressed support for CMS' proposed changes regarding the reporting of multiple best prices, specifically regarding adjustments for cumulative discounts, rebates or other arrangements. Several commenters also suggested alternative approaches to CMS' proposals for best price and reporting of multiple best prices such as:

- Include all payments related to VBP arrangements, including administrative fees, in the best price calculation.
- Allow the discounts across various VBP agreements to be pooled together to create an Average Best Price from the VBP agreements or pool outcomes (both successes and failures) across all VBP agreements and apply them to the most favorable VBP agreement to determine a VBP Best Price.
- Require manufacturers to report only one VBP best price in any given quarter in addition to the current best price calculations.
- Use CMS authority under the MDRP to provide technical clarifications about how best price could be reasonably

reported under contracts in which discounts vary based on patients' clinical outcomes, without eliminating or dramatically weakening the best price requirement.

- Provide incentives to manufacturers to have VBPs for all new curative therapy drugs for a defined period (for example, 5 years) following a drug's approval, applicable to all Medicaid recipients.

- Administer value-based payments and best price as a true-up model that would allow state Medicaid programs to continue to obtain whatever best price was agreed to at the time a VBP was created and that, by updating the definition of VBP and extending the Best Price adjustment period for VBP only, they would allow for a true-up/rebate adjustment for the MDRP.

Response: We appreciate the support for the proposed changes to best price and the alternatives proposed by commenters, and may consider them in future rulemaking. We are finalizing our proposal that manufacturers be permitted to report multiple best prices based upon commercially-available VBP arrangements made available to states that satisfy the regulatory definition of a VBP arrangement. We believe that we have attempted to address via this regulation technical clarifications about how best price could be reasonably reported without eliminating or dramatically weakening the best price requirement. That is, by permitting manufacturers to report multiple best prices in accordance with § 447.505(a) for VBP arrangements offered to states that satisfy the regulatory definition of a VBP arrangement we are finalizing in this rule, it guarantees those states that agree to participate receive the best price under the VBP arrangement. Furthermore, as explained in section II. G. of this final rule, we are finalizing a policy to permit manufacturers to request a change as a result of a VBP arrangement, as defined in § 447.502, outside of the normally applicable requirement to report within 12-quarters from the quarter in which the data were due, when the outcome must be evaluated outside of the 12-quarter period. Otherwise, states that do not participate will continue to receive a Medicaid rebate based upon the non-VBP best price as reported by the manufacturer.

Comment: Several commenters did not support the proposed changes to best price reporting and stated that these changes violate the Medicaid rebate statute, exceed CMS's authority, and disregard Congressional intent. A few commenters noted that the proposed MDRP best price requirements

undermine competition and recommended CMS consider additional reforms to the MDRP to correct the impact it has had on drug market dynamics. One commenter noted that the current Medicaid rebate program is an effective tool for states to control drug prices, combat inflation and egregious price increases and to allow multiple best prices would put states at risk for incorrect price reporting. Several commenters expressed opposition to CMS' proposed changes regarding the language "in any pricing structure", and noted that CMS' proposal is inconsistent with the Medicaid Drug Rebate statute's definition of best price and contrary to CMS's treatment of other similar transactions in AMP and best price. Another commenter noted that the proposal contradicts the best price statute citing their belief that "lowest price" is understood to be a single lowest price. A few commenters noted that the proposal does not limit the number of unique VBP arrangements a manufacturer may create, nor does it limit the number of pricing tiers within each VBP arrangement and believes that the segmentation this creates significantly weakens best price protection, while one commenter stated that the proposed changes would create higher rebates across all Medicaid units.

Response: We do not believe the policy permitting manufacturers to report multiple best prices in accordance with § 447.505(a) for VBP arrangements offered to states that satisfy the regulatory definition of a VBP arrangement we are finalizing in this rule weakens the best price requirement or exceeds our authority. As discussed above, manufacturers will be required to continue to report, and states not participating in the VBP arrangement would be able to access, a separate best price based upon prices available outside of the VBP arrangement to best price eligible entities for the dosage form and strength of the drug. If a manufacturer chooses not to offer a VBP arrangement to states, or simply chooses not to report multiple best price points resulting from a VBP arrangement, then manufacturer reporting would follow all existing laws and regulations regarding the best price determination.

We reiterate that states will not be required to participate in these VBP arrangements and in cases when a manufacturer is reporting multiple best prices pursuant to a VBP arrangement will receive a Medicaid drug rebate based upon the non-VBP best price for the drug for the quarter in which the drug is administered. The final policy simply permits manufacturers to report

a distinct set of multiple best prices for a VBP arrangement (or multiple sets if there is more than one in the marketplace), in addition to reporting a single best price for the drug not affiliated with a VBP arrangement. This ensures that when a state agrees to participate in one of the manufacturer's VBP arrangements, the additional rebates that could be paid to a state reflects the best prices associated with the VBP arrangement. We reiterate that the initial rebate to all states in the quarter in which the drug is administered, under either the non VBP or VBP arrangement, will be at least equal to the greater of 23.1 percent of the AMP or AMP minus best price (be it a multiple best price or the non-VBP best price).

In order to report multiple best prices, the manufacturer must make available to the states the VBP arrangement (or multiple VBP arrangements) being offered on the commercial market. States may have the option to participate in that VBP arrangement. Manufacturers may also choose not to report multiple best prices approach for their VBP program, and follow existing rules, or, as appropriate, choose another approach to determining best price (and AMP) such as the bundled sales approach. For example, when a manufacturer follows the bundled sales approach, the manufacturer will not report multiple best prices associated with the arrangement and will report one best price using the bundled sales approach. Please see the discussion in section II.G.3. of this final rule, for a more detailed explanation of the bundled sales approach to VBP arrangements.

The rationale for the proposed changes is to give manufacturers the ability to offer VBP arrangements to commercial payers and Medicaid without having the current interpretation of best price result in disincentives for manufacturers to offer these innovative pricing strategies because doing so could dramatically increase their Medicaid drug rebates based on a single sale.

The expanded interpretation of best price, such that a manufacturer could offer multiple best prices for a single dosage form and strength of a drug, in addition to a non-VBP best price, is consistent with the statute, as the MDRP was structured to reduce the cost of drug therapies to all states by allowing Medicaid to take advantage of the negotiating abilities of the private sector. Given the evolution in the marketplace since the original law was drafted in 1990, and the availability of new expensive gene therapies that could

have different clinical outcomes in different patients, we believe that it is reasonable for the agency to make an interpretation of the statute and regulations that the "lowest price available" "in any pricing structure" could be interpreted as a VBP arrangement under which different prices are available based on different outcomes.

Comment: A few commenters noted the proposed changes to multiple best price reporting structure will increase burden on manufacturers. One commenter noted that reporting individual patient prices would not add value to the healthcare system and would create an unnecessary administrative burden upon both CMS and manufacturers.

Response: We do not agree that there is unnecessary burden on manufacturers as we are not requiring manufacturers engage in VBP arrangements or report individual patient prices under this final rule. Instead, this rule gives manufacturers the ability to report more than a single best price (multiple best prices), at their option, when offering a VBP arrangement on the commercial market that they also offer to states. State Medicaid programs will have the option to either participate or not in the commercially available VBP arrangement. Therefore, the change does not place any additional burden on manufacturers or the states, but rather establishes a tool (the ability to report more than one best price) to reduce the disincentives for manufacturers to offer these innovative pricing strategies because doing so could dramatically increase their Medicaid drug rebates based on a single sale.

Comment: Some commenters noted that CMS should determine if the proposed new options in best price reporting will complement, or perhaps inspire, private sector innovations in reinsurance, stop-loss protection and other business insurance products that will make VBP arrangements feasible for payers.

Response: These comments are outside the scope of this rule.

Comment: One commenter recommended CMS remove the option to report multiple best prices in VBP arrangements, and instead use the bundled sale methodology to incorporate all VBP best prices into one URA, such that commercial VBP payments are not treated differently from any other rebate and limit the number of VBP arrangements a manufacturer may offer.

Response: We do not believe using the bundled sale approach will be workable for all manufacturers in all situations,

which is why we proposed the change to the determination of best price to permit multiple best prices. Specifically, certain manufacturers of drugs indicated for use in limited populations will not have a large number of sales in a quarter to spread out discounts as a result of a bundled sale. This being the case, a VBP arrangement that results in a significant discount (for example, 75 percent discount) will impact best price significantly if only 1–3 units are dispensed per quarter.

Comment: Several commenters requested clarifying guidance regarding the best price and inclusion of prices from VBP arrangements, as well as the reporting requirements, operational timelines, and the treatment of non-VBP arrangement rebates. A few commenters recommended that CMS update the DDR system to accommodate non-manual reporting of multiple best prices to align with the effective date of the final policy and ensure such system updates accommodate products with both VBP and non-VBP arrangements. A few commenters requested more guidance on CMS' URA reporting mechanism and methodology.

Some commenters recommended CMS not finalize the proposed change to the definition of best price that includes a reference to "varying price points" until guidance has been developed and all of the implications on program integrity and other prices have been thoroughly considered. Several commenters urged CMS to establish clear and specific regulatory provisions for codification in the CFR for manufacturers to follow in applying the multiple best prices authority set forth in the proposed rule.

A few commenters also expressed concern regarding the operational implications for manufacturers with CMS' proposals related to best price reporting, as well as the possible resource constraints that, in their opinion, may be too great to overcome. One commenter noted that the multiple best price approach imposes an unreasonable administrative burden on VBP arrangement participants because a drug manufacturer would require data from PBMs and health plans with sufficient detail to support a per product, per customer, per quarter, per unit price to report and certify an accurate best price. Many commenters noted additional resources, including staffing and information technology may need to be invested by CMS, payers, and manufacturers to support the proposed price reporting methodology, with a few commenters further suggesting CMS utilize a single federal contractor to

monitor VBP arrangements available in the market and support data collection and analysis; and allowing multi-state VBP contracts to support pooling of state administrative resources and a larger pool of covered lives for VBP negotiations. One commenter cautioned that the proposal would introduce complexities that would outweigh the benefits for states that the proposal envisions and instead proposed that CMS adopt the weighted average multiple best price calculation as facilitated by the revised bundled sales provision.

Response: We agree with the commenters regarding the operational and administrative challenges for CMS, manufacturers, states and payers and we intend to provide additional necessary technical and operational guidance regarding various aspects of the program, such as the reporting of multiple best prices in MDRP systems. In addition, we have decided to delay the effective date of the revised definition of best price at § 447.505(a) until January 1, 2022, which will permit manufacturer reporting of varying best price points for a single dosage form and strength as a result of a value based purchasing arrangement that meets the definition at § 447.502.

The delayed effective date of this new policy is the direct result of many commenters who described some of the implementation complexities with this new approach. Over the next year, states, CMS, manufacturers and payers will need to make the necessary policy, clinical, contractual, system, and administrative modifications that will be necessary to give the program the best chance for success. We expect manufacturers may want to initially focus the development of these VBP programs on those drugs and therapies that are the most expensive to the Medicaid program, such as gene and cell therapies, and accelerated approval drugs, so that the VBP arrangement can have the most potential impact on making these drugs more available to Medicaid patients.

Comment: A few commenters requested clarification as to whether the manufacturer reporting multiple best prices is voluntary and requested clarification that if a state does not want to track outcomes or participate in a VBP arrangement, their best price will automatically revert to the traditional method as calculated based on the price of the therapy when it is sold outside of a VBP arrangement.

Response: Manufacturers that want to report multiple best prices associated with its VBP arrangement must offer those VBP arrangements to the states.

Otherwise manufacturers will not be permitted to report multiple best prices for their VBP arrangements. If a manufacturer does not want to offer the VBP arrangement to the states, it will only be permitted to report one best price for that drug or biological, and that best price must be inclusive of any and all prices as a result of a VBP arrangement offered on the commercial market. When manufacturers offer the VBP arrangement to the states, states will have the option to enter into these VBP arrangements and be guaranteed a Medicaid rebate based upon the multiple best prices. Or, the state may opt not to participate and continue to receive Medicaid drug rebates calculated based on the best price of the drug outside of a VBP arrangement and that rebate would not be impacted by the multiple best prices reported by the manufacturer for its VBP arrangement.

States that choose not to participate in the VBP arrangement that the manufacturer has made available under the multiple best price approach may want to consider entering into their own CMS-authorized VBP supplemental rebates agreement with the manufacturer. States will need to ensure that a supplemental rebate agreement with the manufacturer is approved by CMS via the existing SPA template process. Rebates received as a result of the CMS-authorized supplemental rebate agreement will be exempt from best price.

Comment: A few commenters urged CMS to clarify that states do not need to seek SPAs to enter into VBP arrangements, whether based upon manufacturer arrangements with commercial payers or on their own.

Response: States are not required to submit a SPA if they seek to enter into VBP arrangements offered by manufacturers as part of the multiple best price approach as these arrangements are not CMS-authorized SRAs. States that wish to enter into their own VBP arrangements with manufacturers, where such prices would be exempt from best price, will continue to be required to submit a template that CMS can approve as part of a SPA process.

Comment: Several commenters wanted states to be protected under the expansion of the definition of best price. Several commenters asserted the proposed changes could bar states from benefiting from the best price under VBP arrangements if a manufacturer chooses to report a range of best prices rather than through a bundled sale and if the state's Medicaid program does not have a VBP arrangement with that manufacturer. One commenter

expressed concern that manufacturers could potentially exclude states from a VBP arrangement by extending VBP opportunities exclusively to private payers, leaving states subject to only mandatory rebates on high list price products.

Response: There is no risk to states under the multiple best prices reporting. Manufacturers that want to report multiple best prices associated with their VBP arrangements available on the commercial market must make these arrangements available to the states. In order to participate in the VBP arrangement, states must meet the requirements of the VBP arrangement as offered by the manufacturer. While states will be given the opportunity to participate in these VBP arrangements, they will not be required to enter into these arrangements. States will need to assess whether or not they want to participate in these VBP arrangements and if they do not want to participate in the VBP arrangements using the multiple best prices approach, they may continue to receive Medicaid drug rebates based solely upon the best price available outside of the VBP arrangement (even if the manufacturer offers a VBP arrangement and reports multiple best prices to CMS) and may continue to negotiate supplemental rebates with manufacturers under a CMS-authorized SRA, which could include their own VBP arrangements.

Comment: Commenters expressed concern that the proposed rule will facilitate manufacturers entering into VBP arrangements with commercial payers and will provide little benefit to state Medicaid programs, and stated that the proposal would increase Medicaid drug costs citing their belief that the proposed changes would reduce the total rebates drug manufacturers pay to Medicaid. A few commenters opined that the proposed changes would exacerbate existing best price reporting challenges and make it more difficult for states to ensure drug manufacturer compliance with best price requirements. One commenter noted the proposed changes to best price to facilitate adoption of VBP arrangements would undermine the MDRP and enable manufacturers to significantly reduce or delay the rebates they would otherwise have to pay under current law, thereby increasing Medicaid drug costs.

Response: States will benefit from these multiple best price VBP programs as this approach will allow all states to take advantage of and participate in the VBP arrangements which manufacturers may have been heretofore reluctant to offer because of various reasons, including the requirement that

manufacturers only report one best price per quarter. For example, a significant rebate to a commercial payer for a drug that did not achieve its clinical objectives under a VBP arrangement could reset the best price in Medicaid, and require the manufacturer to give that significant rebate to all Medicaid patients, even if the Medicaid patient taking the drug met the clinical objective.

This multiple best price approach will also protect states that do not want to participate in VBP by requiring that, for a dosage form and strength for a drug for each quarter, that a manufacturer report a best price unrelated to a VBP arrangement, and such best price will reflect the lowest price available to a best price eligible entity that is not participating in the VBP arrangement.

This approach may also reduce the need for additional states, beyond the nine that have approved CMS-authorized SRA VBP SPAs, to submit a SPA to CMS to obtain approval for a template to enter into their own CMS-authorized SRAs with a VBP arrangement. This multiple best price approach will allow any state that wants to participate in a manufacturer VBP arrangement to have the option to do so. As always, states may continue to negotiate additional rebates using CMS-authorized SRAs if they so choose.

Thus, we do not believe states will realize a reduction in the federal Medicaid rebate with the implementation of this policy, and/or if they decide not to participate in the VBP arrangement being offered because in all cases the manufacturer will be required to report a separate best price available outside of the VBP arrangement. The separate best price will be the basis for the Medicaid drug rebates for states that choose not to participate.

Comment: A few commenters expressed concern that the rule as written, does not include a mechanism for states to be aware of commercial VBP arrangements or to ensure outcomes measures in VBP arrangements will exactly match those of any commercial payer in any given quarter during the VBP negotiation process. One commenter noted that states would need to know the terms of the commercial patient outcome-based price concession arrangement to ensure Medicaid rebate amounts are properly determined under the multiple best price approach. Another commenter recommended requiring manufacturers to share specific details of their VBP arrangements with CMS and to allow CMS to develop a mechanism to share

certain details with states, so the states may consider a similar arrangement.

Response: Manufacturers that want to report multiple best prices associated with their VBP arrangements in the commercial market will be required to offer these arrangements to the states. We will share these multiple best prices with states as we do other manufacturer pricing benchmarks, such as AMP and unit rebate amounts. The mechanism of how these arrangements will be communicated to the states will be set forth in CMS operational guidance. We will not be a party to any of these VBP arrangements, and therefore, will not be privy to the specifics of the VBP arrangements (for example, the terms of the patient outcomes price concession or responsibility of fees associated with data collection and evaluation) negotiated between the payers, including states, and the manufacturer.

Comment: A few commenters expressed concern that commercial VBPs available on the market may be difficult to apply to the Medicaid market. The commenters noted that this would result in states not being eligible for a best price URA based on payments made under a commercial VBPs. One commenter questioned the validity of applying VBP arrangements from the commercial markets to a Medicaid population as the commenter noted the measures are tied to certain evidence- or outcomes-based measures that were carefully selected and tailored to a specific, commercially-insured population. A few commenters requested CMS clarify that a state Medicaid agency should have in place data collection and adjudication processes, inclusive of dispute resolution, that are sufficiently robust to administer the VBP arrangement to the same degree of reliability as it is administered between a drug manufacturer and a commercial payer.

Response: We appreciate the commenters' concerns about the applicability of some commercial VBP arrangements to the Medicaid population. It is our general impression that in some cases, both Medicaid and commercial payers may have similar patient population characteristics that would allow for the applicability of a commercial payer VBP to Medicaid, and in other cases it may not. In those latter cases, the state will have to determine whether it wants to participate in the VBP arrangement that is being offered on the commercial market, and that the manufacturer is reporting to us and offering to all states. While we are not requiring that manufacturers design their VBP arrangements with Medicaid in mind, we would expect that they will

consider this to avail themselves of the regulatory flexibilities being finalized in this rule. We believe this policy will help achieve the goal of increasing Medicaid patient access to new innovative drug therapies.

We also believe that there may be multiple manufacturer VBP arrangements in the market, and our policy requires that manufacturers that want to report multiple best prices associated with their VBP arrangements must offer them to states in order to avail themselves of this regulatory flexibility being finalized in this rule. A state will determine which VBP arrangements might work best with its patient population.

Finally, states can use a CMS-approved supplemental rebate agreement to enter into their own VBP agreements with manufacturers for a drug if none of the multiple best price VBP arrangements reported by manufacturers to CMS for that drug would be useful in that state's Medicaid populations.

With respect to dispute resolution, we would expect that states and manufacturers would continue to work cooperatively to resolve any rebate disputes whether they are related to rebates paid under non VBP or VBP arrangements. We have issued several guidances on dispute resolution (see *Manufacturer and State Releases*¹⁸).

Comment: Several commenters requested CMS provide funding for VBP arrangements to provide state Medicaid agencies with funding for IT infrastructure needed for performance tracking and interstate or cross-payer interoperability. Commenters believe that the breadth of possible VBP arrangements could pose a serious financial burden for state Medicaid agencies to monitor and would require significant modification of state and vendor rebate systems to incorporate multiple URAs based on each outcome. Another commenter questioned if states are permitted to contract with vendors to perform patient monitoring of outcomes for VBP arrangements. A few commenters requested CMS offer forms of federal support to help commenters build appropriate infrastructure for these proposed arrangements.

Response: We have no plans to provide federal funding to facilitate states' participation in VBP

¹⁸ https://www.medicaid.gov/medicaid/prescription-drugs/program-releases/index.html?search_api_fulltext=dispute+resolution&field_date%5Bmin%5D=03%2F21%2F1991&field_date%5Bmax%5D=11%2F16%2F2020&sort_by=field_date&sort_order=DESC&items_per_page=10%23content#content.

arrangements. States are not required to participate in VBP arrangements and will have to make those decisions based on their own administrative and operational considerations. As stated in response to prior comments, states will have a choice as to whether or not they want to enter into VBP arrangements.

Comment: A few commenters suggested that CMS require manufacturers to submit their commercial VBPs to CMS so that it can inform states of the drugs and outcome measures in those commercial VBPs. Another commenter suggested CMS require manufacturers to “lock in” an estimated Best Price for the duration of the contract and apply a CMS-overseen reconciliation process to protect states from the uncertainty the proposed change may create, and that CMS could use the commercial VBPs submitted by manufacturers to develop a VBP contract template that states could use to ensure that they were in alignment.

Response: CMS will be looking at ways to make information regarding manufacturer VBP arrangements that are offered on the commercial market available to states. We will not, however, be involved in the approval or review of the specifics of any VBP arrangements offered by manufacturers to commercial payers; nor will we be engaged in the negotiation of terms between manufacturers and payers or states. Furthermore, we will not be imposing additional requirements or requesting manufacturers change their VBP arrangements when they make their arrangements available to the states. At a minimum, as discussed earlier in this section, states will continue to receive the Medicaid drug rebate for a covered outpatient drug consistent with the separate best price reported by the manufacturer outside of the VBP.

Comment: One commenter requested clarification that the duration of a VBP arrangement contract is a term that a state Medicaid agency would need to adhere to in order to take advantage of the proposed multiple best price approach, as it is central to a VBP arrangement (in the commercial sector or otherwise).

Response: This rule does not speak to the specific terms that should or should not be included in VBP arrangement contracts.

Comment: A commenter recommended that the VBP exemption from best price apply only when a pharmaceutical manufacturer pays for the entire cost of a drug during the entire length of the prescription.

Response: We assume the commenter is under the impression that the

multiple best prices as they pertain to VBP arrangement offered on the commercial market allows the manufacturer to exempt those prices from “best price.” We are not exempting VBP prices from a manufacturer’s best price. Rather, we are allowing manufacturers to report both a non-VBP best price for a drug and multiple best prices for a drug based on a VBP arrangement when the manufacturer offers the VBP arrangement to all states.

Comment: One commenter requested CMS clarify if manufacturers would initially calculate the best price they report to the federal government by looking at the expected net price under the VBP arrangement, based on the expectations of the manufacturer and the private purchaser using available clinical data.

Response: Manufacturers permitted to report multiple best prices pursuant to a VBP arrangement would make two best price reports each quarter to CMS, one that includes the best price of the drug net of any discounts or offsets that are unrelated to the VBP arrangement, and the other that includes the set of multiple best prices offered under the VBP arrangement (offset by applicable discounts) based upon the outcomes of the VBP arrangement.

Comment: One commenter urged CMS to ensure that methods other than the bundled sale concept and the multiple best prices are available to accommodate the unique factors associated with extremely rare disorders.

Response: We believe that the final policies in this rule with respect to reporting best price under a VBP arrangement will accommodate manufacturers of covered outpatient drugs for rare diseases because manufacturers will not face the same rebate consequences if one patient fails on the therapy. Furthermore, the publication of this final regulation does not mean CMS may not consider other approaches addressing unique circumstances as part of a future rulemaking.

Comment: One commenter requested CMS mandate that a manufacturer base its best price reporting on the lowest price available in the marketplace, including one that arises from a VBP arrangement offered in the commercial marketplace (either by using the bundled sale calculation rules or reporting multiple best prices), as well as what the manufacturer offers to any state Medicaid program or Medicaid MCO that wishes to engage in the VBP arrangement.

Response: Manufacturers are already required to report the lowest price

available to most entities on the commercial market, as included in the definition of best price at § 447.505(a). This rule does not change that, but rather allows manufacturers to report varying best price points for a single dosage form and strength when it offers a VBP arrangement to all states. If the VBP arrangement is not offered to states, the manufacturer will report one best price for the dosage form and strength of the drug which would include any and all prices and rebates, and subsequent adjustments, associated with the manufacturer VBP arrangements in accordance with the best price requirements at § 447.505.

Comment: Some commenters noted that CMS should clarify that “any pricing structure” in the definition of best price is inclusive of any and all pricing structures.

Response: We do not believe it is necessary to further clarify the regulatory language “any pricing structure” as used in 42 CFR 447.505(a). We are expanding the definition of best price to allow manufacturers to include the lowest price available from a manufacturer to include varying best price points for a single dosage form and strength as a result of a VBP arrangement. The reference to any pricing structure in this case is made to indicate that we consider a VBP arrangement to be a form of a pricing structure.

Comment: A commenter suggested that for a patient to be deemed to have participated in a VBP, the patient must be a patient covered by a state that has an executed, signed agreement with the manufacturer setting forth the same terms and conditions set forth in the corresponding commercial VBP on which the multiple best prices are based.

Response: Manufacturers will be required to offer the same terms and conditions to states as set forth in its corresponding commercial VBP that is used to set its multiple best prices.

Comment: A few commenters noted that expanding the definition of best price to provide that a lowest price available from a manufacturer may include varying best price points for a single dosage form and strength as a result of a VBP could allow pharmaceutical companies to raise the prices of life indispensable medications. One commenter requested CMS clarify the proposal citing their concern that a single best price for a less effective dosage form and strength could limit the ability of coming to VBPs for other dosages.

Response: We do not believe that this regulation encourages pharmaceutical

companies to raise prices for a single dosage form and strength of a drug. The current Medicaid drug rebate regulation continues to include an inflation penalty in the form of an additional rebate if AMP for the dosage form and strength of a drug increases at a rate greater than inflation (as measured by the consumer price index for all urban consumers—United States average) (see sections 1927(c)(2) and (c)(3)(C) of the Act and § 447.509(a)(2) and (7)). These would apply to drugs that are included under a VBP arrangement. Therefore, the Medicaid drug rebate calculation continues to include a disincentive to manufacturers increasing drug prices.

Comment: One commenter recommended excluding any price concessions received under a VBP arrangement from the best price calculation citing their belief that this would increase the adoption of VBP arrangements.

Response: Section 1927(c)(1)(C)(ii) of the Act provides that the term best price shall be inclusive of cash discounts, free goods that are contingent on any purchase requirement, volume discounts, and rebates (other than rebates under section 1927 of the Act). Therefore, manufacturers must include all discounts available, including discounts as a result of a VBP arrangement in best price. This rule did not propose to add an exclusion of all prices as a result of a VBP arrangement when determining best price. Instead, it allows manufacturers to report multiple best prices associated with a VBP arrangement to reflect the discounts/prices available under these arrangements. Manufacturers must make adjustments to best price for a drug (either for a single reported best price or multiple best price arrangement) as a result of any subsequent discounts or price concessions that may occur.

Comment: One commenter requested guidance on how multiple best prices will be audited, especially if predicated on the attainment of patient-specific outcomes that rely on personal health information that may need to be protected under the Health Insurance Portability and Accountability Act of 1996 (Pub. L. 104–191, enacted August 21, 1996) (HIPAA) and/or other law or regulation.

Response: We will not audit how multiple best prices will be determined or how the parties participating in the VBP arrangements will measure patient-specific outcomes using potentially protected health information under HIPAA. However, parties participating in these VBP arrangements should be aware of potential HIPAA requirements when patient-specific data is used to

measure outcomes. Manufacturer information reported under section 1927 of the Act for purposes of the Medicaid rebate (for example, AMP and best price) is subject to audit by the Inspector General of the Department of Health and Human Services in accordance with section 1927(b)(3) of the Act.

Comment: A few commenters urged CMS to safeguard proprietary pricing information, such as the multiple best prices under a VBP arrangement, the terms of which are confidential between the state or payer and manufacturer.

Response: Information disclosed by manufacturers to CMS in accordance with manufacturer reporting requirements set forth at section 1927(b)(3) of the Act, including pricing information related to the reporting of multiple best prices, will be subject to the confidentiality of information requirements at section 1927(b)(3)(C) of the Act.

Comment: One commenter noted the proposed rule does not explain how manufacturers will report initial prices under a VBP arrangement if those prices vary based on anticipated patient outcomes.

Response: Manufacturers will submit a non-VBP best price following the methodology for determining best prices in accordance with § 447.505. We intend to have the manufacturer report the multiple best prices as a separate file in MDRP systems which we will grant access to states that choose to participate in the manufacturer's VBP arrangement. More information regarding the reporting of multiple best prices in our system will be provided in operational guidance.

Comment: One commenter recommended the Medicaid rebate amount true-up process could utilize one of two existing Reconciliation of State Invoice (ROSI) functionalities: A ROSI functionality applicable to SRA or a ROSI functionality applicable to "extra rebates."

Response: We will take this recommendation and welcome additional recommendations regarding the intersection between multiple best prices and the functionality of the ROSI.

Comment: A commenter recommended that CMS require manufacturers to pay interest fees based on the statutory late payment penalty rate in the event that evaluation of outcomes-based measures causes rebates to be delayed.

Response: In accordance with the NDRA, manufacturers will continue to be responsible for timely payment of applicable rebates within 30 days so long as the state invoice contains, at a

minimum, the number of units paid by NDC under the state plan in accordance with section 1927(b)(1)(A) of the Act. Manufacturers that do not pay rebates in time, regardless of the reason, must follow existing operational guidance relating to interest application found in various Program Releases, including State Releases #29, and #166, as well as Manufacturer Release #7. Program Releases are here—Medicaid Program Releases.

Comment: One commenter recommended CMS consider coupling this final rule with an OIG proposed rule to create a safe harbor for VBP arrangements for medical products or pursuing future rule-making to produce a new safe harbor from the Anti-Kickback Statute, which might consider manufacturers' data monitoring and outcome tracking activities as unlawful inducement.

Response: This regulation is specific to the impact of VBP arrangements on price reporting associated with the MDRP. We will not be providing guidance to manufacturers regarding how their particular VBP arrangements, including data monitoring and tracking activities, may violate the Anti-kickback statute.

Comment: Many commenters requested clarification of the impact of the proposed multiple best price approaches to AMP, average sales price (ASP), and 340B ceiling price. Several commenters urged CMS to issue additional rulemaking before allowing 340B covered entities to leverage VBP-associated prices and clarify the best price to be used when calculating 340B ceiling price as well as ASP. A few commenters requested that HRSA and Medicare Part B be involved so that CMS can carefully examine the impact of VBP agreements on state budgets, safety net provider participation in the 340B program and other government pricing programs such as Part B (including calculation of ASP). Several commenters recommended that CMS consider revising its proposed approach to VBP arrangements to exclude the arrangements from required government price reporting metrics. The commenter noted this is necessary to incentivize broader adoption of VBP arrangements.

Another commenter expressed their belief that that it is essential to exclude drugs purchased through VBPs from ASP determinations. Commenters expressed concern that outcomes-based price discounts made for VBP arrangements could lower the Medicare Part B Drug ASP, reducing ASP-based reimbursements to providers or pharmacies that purchase the drug therapy. The commenters noted that

discounts under VBP arrangements are granted to payers while providers and pharmacies would experience reduced revenue.

Another commenter requested CMS address the uncertainty VBP arrangements may have on 340B ceiling prices, as well as AMP. Another commenter requested that CMS consider the scope of the discounts that could be included in a bundled sale under the proposed change and what the impact would be on Medicaid rebates and, by extension, the 340B program.

Response: While this regulation allows manufacturers to report multiple best prices associated with their VBP arrangements, manufacturers will continue to be required to report a best price for each dosage form and strength of a drug paid for outside of the VBP arrangement (non-VBP best price). Therefore, the 340B ceiling price will continue to reflect a Medicaid drug rebate based upon the non-VBP best price.

Also, while we do not anticipate that this rule will reduce a drug's AMP, manufacturers should also consider the effects of their VBP arrangements on payment amounts that are determined for use in other parts of Medicare, for example the effects of VBP arrangements on AMP if AMP is used to determine payment allowance for a drug in Part B as authorized in section 1847A(d) of the Act.

In consideration of comments received, specifically those comments that requested clarification regarding the manufacturer's allowance to report multiple best prices, we are revising the definition of best price at § 447.505(a) to state that if a manufacturer offers a value based purchasing arrangement (as defined at § 447.502) to all states, the lowest price available from a manufacturer may include varying best price points for a single dosage form and strength as a result of that value based purchasing arrangement. However, in order to address the operational and administrative challenges facing CMS, states, and manufacturers, as noted in the comments, we are delaying the effective date of this final policy at § 447.505(a) such that the revised definition of best price to permit multiple best price reporting will not be effective until January 1, 2022.

C. Changes to Update Definitions in § 447.502 To Reflect Recent Statutory Changes Made by the MSIAA, BBA 2018 and the Affordable Care Act

1. Innovator Multiple Source Drug

The MSIAA clarified the definition of innovator multiple source drug at

section 1927(k) of the Act by removing the phrase "an original new drug application" and inserting "a new drug application," removing "was originally marketed" and inserting "is marketed," and inserting ", unless the Secretary determines that a narrow exception applies (as described in § 447.502, Code of Federal Regulations (or any successor regulation))" before the period. Section 1927(k)(7)(A)(ii) of the Act now defines innovator multiple source drug to mean a multiple source drug that is marketed under a NDA approved by the FDA, unless the Secretary determines that a narrow exception applies (as described in § 447.502 (or any successor regulation)). To align the regulatory definition with the definition in the statute, as clarified by the MSIAA, we proposed to define innovator multiple source drug in § 447.502 as a multiple source drug, including an authorized generic drug, that is marketed under a NDA approved by FDA, unless the Secretary determines that a narrow exception applies (as described in the section). We noted that the proposal also included a drug product marketed by any cross-licensed producers, labelers, or distributors operating under the NDA and a COD approved under a biologics license application (BLA), product license application (PLA), establishment license application (ELA) or antibiotic drug application (ADA).

We have received the following comments regarding the proposed definition of innovator multiple source drug:

a. Prospective Application

Comment: One commenter requested that CMS revise their proposed definition of innovator multiple source drug to only apply prospectively from October 2019 forward, citing their belief that since this is the date the Congress amended the MDRP statute, it would be in accordance with the recent ruling in the United States District Court for the District of Columbia case of *STI Pharma, LLC v. Azar*.

Response: The revision to the definition of innovator multiple source drug is to conform the rule with the amended statute. Our longstanding interpretation of the statute (both before and after the 2019 amendments) is that an innovator multiple source drug is a drug approved under an NDA, and noninnovator drugs are those approved under an ANDA. We believe *STI Pharma, LLC v. Azar* was wrongly decided. Prior to the 2016 COD final rule, there was no narrow exception to that general rule. Therefore, any drug approved under an NDA that is reported as a noninnovator multiple source drug

for quarters prior to 2Q2016 is improperly categorized and the drug manufacturer should request a drug-category change or risk enforcement action.

b. Narrow Exception

Comment: One commenter recommended that CMS maintain and codify the current factors used to determine if a product meets the narrow exception citing their belief that this would provide clarity to both current and future manufacturers, helping to ensure these products are available and do not go into shortage, and therefore, are available to the patients who need them.

Response: We do not agree that we should codify the factors used to determine if a drug qualifies for a narrow exception to the rule that drugs marketed under an NDA should be reported to us as a single source drug or an innovator multiple source drug. Each request for a narrow exception is evaluated individually and we consider many factors in determining whether to use our discretion to grant such an exception. When reviewing a request for a narrow exception, we may reach out to the manufacturer to request additional information to aid in the review of the request, thereby ensuring that we are making decisions based on all of the information pertinent to the request. We are finalizing the definition of innovator multiple source drug as proposed.

2. Line Extension, New Formulation, and Application of Oral Solid Dosage Form Requirement

Section 1927(c)(2)(C) of the Act defines line extension to mean, for a drug, a new formulation of the drug, such as an extended release formulation, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary), regardless of whether such abuse deterrent formulation is an extended release formulation. As discussed in the June 2020 proposed rule (85 FR 37288 through 37289), we proposed to define line extension in the February 2, 2012 proposed rule, but did not finalize a definition in the COD final rule or the April 1, 2019 final rule. We reiterated in the April 1, 2019 final rule that manufacturers are to rely on the statutory definition of line extension at section 1927(c)(2)(C) of the Act, and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension (81 FR 5265).

As discussed in the June 2020 proposed rule (85 FR 37294), after several years of experience with manufacturers self-reporting their line extensions, and numerous inquiries from manufacturers regarding the identification of drugs as line extensions, we have noted inconsistency among manufacturers in their identification of drugs as line extensions. In addition, we expressed concern that manufacturers may have a financial incentive to be underinclusive in their identification of drugs as line extensions because a drug identified as a line extension may be subject to a higher rebate. We noted that if manufacturers underreport their line extensions, rebates may be calculated incorrectly and underpaid.

To ensure that section 1927(c)(2)(C) of the Act is fully implemented and the universe of line extensions is comprehensively identified, we proposed to provide further interpretation of the statute in the June 2020 proposed rule.

Based on the definition of line extension that was included in the Affordable Care Act, we believed that the statute gives us discretion and authority to interpret the term “line extension” broadly. We expressly solicited comments on our proposed definitions of “line extension” and “new formulation,” specifically on whether these terms should be interpreted more narrowly. Moreover, if commenters believed that a narrower interpretation is appropriate, we solicited comments on how to identify those drugs that constitute a line extension and a new formulation to apply the alternative URA calculation when required by statute. The comments we received in response to this solicitation are addressed in section II.C. of this final rule.

In the June 2020 proposed rule (85 FR 37294), we proposed that only the initial single source drug or innovator multiple source drug (the initial brand name listed drug) must be an oral solid dosage form. In the 2012 proposed rule (77 FR 5338, 5339), we proposed that both the initial brand name drug and the line extension drug had to be an oral solid dosage form. However, as noted in the June 2020 proposed rule, we did not finalize a regulatory definition of line extension, and instructed manufacturers to make “reasonable assumptions” regarding whether a drug is a line extension (81 FR 5265). The statute states that the alternative calculation must be performed in the case of a drug that is a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form.

Upon further evaluation of this statutory language, we believed that the statutory text can be reasonably construed to provide that only the initial single source drug or innovator multiple source drug must be an oral solid dosage form. We believed this interpretation is appropriate because the alternative construction (requiring both the line extension and the initial single source drug or innovator multiple source drug to be an oral solid dosage form) may inappropriately limit the universe of line extension drugs in a manner which would allow a manufacturer to circumvent rebate liability when creating a line extension and to potentially avoid inflation-based additional rebates, in cases where such rebates should apply. Therefore, we proposed that when determining whether a drug is a line extension, only the initial single source drug or innovator multiple source drug must be an oral solid dosage form. That is, we proposed that the line extension of the initial brand name listed drug does not need to be an oral solid dosage form. We believed this is consistent with the statutory language and will assist in appropriately identifying drugs that may be line extension drugs. Therefore, we proposed to amend § 447.509(a)(4)(i) and (ii) to refer to “a drug that is a line extension of a single source drug or an innovator multiple source drug provided that the initial single source drug or innovator multiple source drug is an oral solid dosage form,” and § 447.509(a)(4)(i)(A) and (a)(4)(ii)(A) to refer to “a single source drug or an innovator multiple source drug” in the regulatory text that describes the alternative rebate calculation.

We received the following comments regarding our proposal that when determining whether a drug is a line extension, only the initial single source drug or innovator multiple source drug must be an oral solid dosage form:

Comment: A few commenters disagreed with the proposal to require that only the initial single source drug or innovator multiple source drug be an oral solid dosage form when determining whether a drug is a line extension because they claim the proposal does not align with Congressional intent. They stated that the legislative history shows that Congress intended that the line extension provision applies only to drugs that were “slight alterations” of the previous drug, and that a change from an oral solid dosage form to a different dosage form is a significant alteration. A few commenters stated that if the change requires submission of clinical data to FDA, it would be a

significant alteration. Some commenters, in discussing fixed-dose combination tablets in treating diseases such as HIV, noted that innovations that improve patient compliance provide significant improvements that benefit patients.

Response: We believe that our proposal is consistent with section 1927(c)(2)(C) of the Act. Additionally, the statute does not require that in order for a drug to be a line extension, the change to a drug must be a slight alteration. Had Congress intended to limit the definition of line extension to only those drugs for which a slight alteration had been made, we believe they would have included that requirement in the statute. Notably, the example of a new formulation that Congress provided in the statute is “an extended release formulation.” The change from an immediate release formulation to an extended release formulation may be considered more than a slight alteration. We agree with commenters that innovations that improve patient compliance provide significant improvements that benefit patients and believe this may include extended release formulations. Had Congress intended to limit the line extension provisions to drugs that were only slight alterations, we believe they would have provided an example of a less significant change than “an extended release formulation.”

Comment: A few commenters stated that requiring that only the original single source drug or innovator multiple source drug be an oral solid dosage does not align with the statute. One commenter stated that in the statutory language, in the case of a drug that is a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form, Congress plainly intended for the phrase “that is an oral solid dosage form” to modify the term “line extension.” They stated that because Congress directly addressed this issue, the agency lacks discretion to define “line extensions” to include products that are not oral solid dosage forms.

Response: As stated in the June 2020 proposed rule, we believe that the statutory text can be reasonably construed to provide that only the initial single source drug or innovator multiple source drug must be an oral solid dosage. We disagree that the statutory language clearly indicated that the phrase “that is an oral solid dosage form” modifies the term “line extension.” Although the structure of the sentence does not make it clear which subject is modified by “that is an oral solid dosage form,” we believe that

the better reading is that the phrase modifies “a single source drug or an innovator multiple source drug” because it appears directly following that subject.

Comment: A few commenters stated that the proposal to require that only the original single source drug or innovator multiple source drug be an oral solid dosage form is contrary to prior guidance and that the existing interpretation is more reasonable and should be retained. Several commenters agreed with CMS’ proposal that the line extension of the initial brand name listed drug does not need to be an oral solid dosage form. A few commenters noted that these definition clarifications will expand the universe of drugs that can be line extensions. One commenter noted that requiring that only the initial drug must be an oral solid dosage form would prevent manufacturers from switching forms to avoid higher inflation-related rebates.

Response: We do not agree that our proposal is less reasonable than the interpretation we discussed in the COD final rule. We acknowledge that in the February 2, 2012 proposed rule, we proposed that both the initial brand name listed drug and the drug that is a line extension were required to be an oral solid dosage form in order for the alternative rebate calculation to be required. However, that proposal was not finalized in the COD final rule. Instead, we stated that we will continue to consider the issues and may consider addressing the issues in future rulemaking (81 FR 5265). We are doing so in this final rule.

After consideration of public comments, we are finalizing our proposal that only the initial single source drug or innovator multiple source drug be an oral solid dosage form when determining whether a drug is a line extension. While we initially proposed amending § 447.509(a)(4)(i) and (ii), we are making a technical change to that proposal to more accurately reflect the prospective applicability of the revised policy. In addition, as discussed in section II.C. of this final rule, we are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension. We are amending § 447.509(a)(4)(ii) to change “beginning on or after October 1,

2018” to “beginning on October 1, 2019 through December 31, 2021”, redesignating § 447.509(a)(4)(iii) as § 447.509(a)(4)(iv) and adding § 447.509(a)(4)(iii).

3. Definition of Line Extension

In response to requests to provide more specific guidance on how to identify a line extension drug, we proposed to define “line extension” and “new formulation” at § 447.502. Specifically, we proposed that as provided in section 1927(c)(2)(C) of the Act, the term “line extension” means, for a drug, a new formulation of the drug, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary).

Most of the comments we received regarding our proposed definition of “line extension” more accurately pertain to our proposed definition of “new formulation,” and therefore, we will discuss those comments in section II.C.4. of this final rule. We received the following comment regarding our proposed definition of “line extension”:

Comment: One commenter supported CMS’ proposal to exclude abuse-deterrent formulations from the proposed definition of line extension, citing their belief that this exclusion aligns with the Administration’s public health goals, as well as other efforts to reduce rates of opioid abuse in communities.

Response: We thank the commenter for the support and note that section 1927(c)(2)(C) of the Act requires that we exclude abuse deterrent formulations from the definition of “line extension”.

After consideration of public comments, we are finalizing the definition of “line extension” as proposed. In addition, as discussed in section II.C. of this final rule, we are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension.

4. Definition of New Formulation

Additionally, we proposed to define “new formulation” to mean, for a drug, any change to the drug, provided that the new formulation contains at least one active ingredient in common with the initial brand name listed drug. As discussed in the June 2020 proposed rule (85 FR 37295), new formulations

(for the purpose of determining if a drug is a line extension) would not include abuse deterrent formulations but would include, but would not be limited to: Extended release formulations; changes in dosage form, strength, route of administration, ingredients, pharmacodynamics, or pharmacokinetic properties; changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC); and combination drugs, such as a drug that is a combination of two or more drugs or a drug that is a combination of a drug and a device. We requested comments about whether a drug approved with a new indication that is not separately identifiable should be considered a new formulation and, if so, how such a drug could be identified in DDR for purposes of calculating the alternative URA.

We received the following comments regarding our proposed definition of “new formulation”.

Comment: We received many comments that provided general support for our proposed definition of new formulation. Commenters noted that the proposed definition will help ensure that manufacturers identify all their drugs that are line extensions and will prevent manufacturers from circumventing inflation-based rebates. One commenter stated that the current ambiguity has allowed manufacturers to use “product hopping” strategies for financial gain and blocking generic competition.

Response: We appreciate the support from the commenters.

Comment: We received several comments generally opposing the proposed definition. Some commenters generally disagreed with any expansion of the definition of line extension. One commenter opposed any measure that expands rebates because it distorts market dynamics and pushes costs onto every other payer. Another commenter stated that CMS was proposing an expansive change to line extension policies without providing context for the programmatic purpose and goals for a substantial change in disposition impacting many products. One commenter stated that the proposed language is filled with inconsistencies that make the proposals impossible to operationalize.

Response: As explained in the June 2020 proposed rule (85 FR 37294), we have noted inconsistency among manufacturers in their identification of drugs as line extensions. In addition, we expressed concern that manufacturers may have a financial incentive to be under-inclusive in their identification of drugs as line extensions because they

may be able to avoid some of the inflation-based rebates they had incurred because of the increases in the price of the original drug that exceeded the rate of inflation. By making certain changes to the original drug, they were often able to establish a new baseline AMP for the line extension drug and essentially start fresh, without the burden of the inflation-based rebates on the original drug. By proposing a definition which clarifies the attributes of a drug that make it qualify as a line extension drug, we believe manufacturers will have a clearer explanation about how to identify their drugs that are line extensions. We disagree that any measure that expands rebates distorts market dynamics and pushes costs onto other payers and the commenter did not substantiate that assertion. We do not believe that the definitions we are finalizing in this rule contain inconsistencies, and CMS staff is available to assist manufacturers with any operational questions.

a. Statutory Concerns

Comment: We received one comment stating that our proposed definition is grounded in statute.

We received many comments stating that our proposed definition of new formulation exceeds statutory authority because it is too broad or exceeds what Congress authorized (that is, slight alterations). A few commenters stated that CMS exceeds reasonable statutory interpretation by including several product categories clearly not within the common understanding of new formulation.

A few commenters stated that our use of the term “any change” is inconsistent with statute. They stated that because the statute provides an example of a change that is a new formulation (that is, an extended release formulation), that only a change in formulation that is similar to an extended release formulation can qualify as a line extension. A few commenters cited the principle of *ejusdem generis*, stating that per that principle, a general term that follows an enumerated list of more specific terms should be interpreted to cover only matters similar to those specified. One commenter stated that the subset of drugs that can be a new formulation must be directly tied to the physical formulation of the two products.

Response: We disagree that our proposed definition of new formulation exceeds statutory authority or that it is not reasonable. The statute does not define new formulation and it provides only one example of a new formulation, that is, an extended release formulation.

The example provided does not expressly limit the types of new formulations that are to be treated as line extensions; rather, using the term “such as,” Congress provided one example of a new formulation. Had Congress intended to limit the definition to certain types of changes to a drug, it could have done so in the statute.

Regarding our proposed use of the phrase “any change”, that phrase was followed by specific inclusions and exclusions so that the final definition did not state that any change to a drug qualified the drug as a new formulation. However, the definition we are finalizing in this rule does not contain that phrase.

We disagree that the principle of *ejusdem generis* applies because Congress did not provide a list of types of changes to a drug that should be considered a new formulation. Had they provided a list of changes to a drug that all had similar attributes, then it possibly could be interpreted that a new formulation must have a similar attribute to the types of changes in that list. Additionally, the general term (new formulation) precedes the more specific term (extended release formulation), further indicating that *ejusdem generis* is not applicable here. We do not believe that the language Congress selected limits the definition of new formulation to include only an extended release formulation of the original drug or a change that is closely related to an extended release formulation. Congress merely provided one example of a new formulation, that is, an extended release formulation.

b. Congressional Intent

Comment: A few commenters stated the proposed definition of new formulation is consistent with the intent of Congress. One commenter stated that the intent was to provide protection to taxpayers from drug company pricing practices which are the primary factors in spending increases and that the proposed definition furthered that intent. Another commenter stated that if Congress wanted a more limited definition, it would have included that in the statute; however, it left the interpretation to the Administration. The commenter noted that committee reports show that Congress knew there were multiple ways that a drug could be modified to avoid additional rebate obligations.

Response: We thank those commenters who agreed that our proposed definition is not contrary to Congressional intent. We believe that our proposal is consistent with section

1927(c)(2)(C) of the Act. We do not believe that the modification has to have been made for the purpose of avoiding inflation-based rebates. Rather, the alternative rebate calculation would result in a unit rebate amount that is higher than the standard unit rebate amount when price increases of the initial brand name listed drug exceed the rate of inflation regardless of the reason for the modification.

Comment: Many commenters stated that the proposed definition disregards the intent of Congress and the legislative history. Commenters stated that Congressional intent was to capture slight alterations of existing drugs and the legislative history mandates a narrow reading of the statute. One commenter stated that the legislative history makes it clear that a new formulation is only a slight alteration in an existing drug where no additional studies are required by FDA but the proposed definition captures more than slight alterations. Commenters stated that Congress did not intend to include innovative products and new formulations that provide significant benefits to patients in the definition of line extension. One commenter stated that even after CMS recognized that many combination drugs are not slight alterations, we nonetheless included them in the proposed definition.

Response: We disagree that our proposed definition exceeds what Congress intended in the line extension provisions. We are aware that there have been discussions about slight alterations made to a drug and those alterations permitted a manufacturer to mitigate the effect of inflation-base rebates on the original drug, however, Congress chose not to include that language, or any similar language, when constructing the statutory language. Additionally, Congress did choose to include an example of one change that is a new formulation. The example given is an extended release formulation, which in general is a change to a drug for which FDA requires additional studies and may be considered a significant change to an original drug. Had Congress intended that the change be slight in order to be considered a new formulation, it could have stated so. The change from an immediate release drug to an extended release drug is not a slight change; there may be significantly different technology involved. Therefore, as Congress had considered slight alterations to a drug in their discussions of line extensions, but chose not to include that limitation in statute, and, as Congress ultimately included a more complex change (that is, an extended release formulation) as an

example of a new formulation, we believe that section 1927(c)(2)(C) of the Act is not limited to only slight alterations.

Similarly, Congress could have included language that excluded new formulations that were innovative or provided significant benefits to patients. However, not only was such language not included in the statute, but the only example of a new formulation that was provided (that is, extended release formulation) can provide significant benefits to patients.

c. Prior Guidance

Comment: Several commenters pointed out that some parts of the proposed definition of new formulation conflicts with prior guidance. One commenter stated that prior guidance provided that both the original drug and the line extension drug must be an oral solid dosage form for the application of the alternative rebate formula to be required and that manufacturers have been relying on that guidance for a long time. The commenter stated that the prior guidance is reasonable and appropriate.

Several commenters noted that in the COD final rule, CMS stated that a new strength is not a line extension and provided rationale that the statute did not contemplate that it is. A few stated that our reversal of that position is being done without adequate justification and is arbitrary and capricious.

A few commenters stated that prior guidance instructed manufacturers to rely on the statutory definition to determine if a drug is a line extension and that they may use reasonable assumptions to make that determination.

Response: In the COD final rule, we advised that we were not finalizing a definition of line extension at that time and we reiterated that manufacturers are to rely on the statutory definition of line extension and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension drug. We also stated that if we later decide to develop a regulatory definition of line extension drug, we will do so through our established Administrative Procedures Act compliant process and issue a proposed rule. We have done so by issuing the June 2020 proposed rule and this final rule. We have 10 years' experience with various aspects of the line extension provisions that were enacted in the Affordable Care Act and are using our experience to develop a definition of new formulation that we believe is supported by the statute, and supports

the MDRP. We do not believe that any changes we have made to prior guidance conflict with the statute or are unreasonable or unjustified in light of the proposed changes.

d. Effect on Patients

Comment: We received many comments that the proposed definition of new formulation would negatively affect patients. Several commenters stated that patients might be denied access to drugs that are line extensions, as designating some of these new drugs as line extensions might create disincentives for manufacturers to develop such new formulations. Several commenters stated that the proposals will cause states to change their preferred drugs list which will cause changes in patients' drug regimen, resulting in increased medical and drug expenditures due to health consequences of medication changes. Some commenters stated that manufacturers would be less likely to make drugs that would be subject to the alternative rebate calculation, thereby decreasing patients' access to innovative drugs that may benefit them in terms of compliance or side effects. Some commenters stated that this would lead to poorer health outcomes. One commenter stated that the broad definition would impact its ability to provide discounts outside of the Medicaid program that aid patients in other safety-net programs.

Response: We do not agree with the commenters who stated that patients would be harmed because manufacturers will not have incentive to research and develop innovative alternatives that may be considered new formulations and therefore subject to the alternative rebate calculation. Based upon the comments received in response to the proposed definition of line extension and new formulation, the definition was further refined to limit the scope of drugs that are new formulations and thereby subject to the alternative rebate calculation. Because we are not finalizing that certain changes to a drug result in a new formulation, as described later, there is a significantly smaller universe of drugs that will be subject to the alternative rebate calculation. We believe that with the exclusion of these proposed changes from the final definition of line extension, that we have maintained incentives for manufacturers to bring such advances to the market.

Market forces and competition may help determine whether such new formulations are in fact significant clinical advances, given that payers are likely to impose utilization restrictions

around their use if they are not. Manufacturers' decisions regarding those drugs to research and market depend on multiple factors, including clinical significance of the drug, prescriber and patient demand, costs of research and development, and possible revenues generated. Whether the drug is a line extension, which could subject it to the alternative rebate calculation, is only one factor in these decisions. The financial effect of the alternative rebate calculation would only be applicable in the Medicaid program, and the new drug may have only limited use in Medicaid. For these and other reasons, we believe that it will continue to be in the interest of a manufacturer to broaden the use of its existing drugs in the form of line extensions, which will lead to increased revenue for the manufacturer.

For those drugs that have a broader use in Medicaid, such as HIV combination drugs, we note that we have decided at this time not to include new combinations in the final regulatory definition of new formulation. We also point out again, that the development of a new formulation does not automatically mean that a manufacturer will be penalized by the alternative rebate calculation for marketing that new formulation. There would only be an alternative inflation penalty on the new formulation to the extent that the increase in price on the initial drug was greater than inflation. Thus, manufacturers that have excessively inflated the price of their older existing drugs, and attempt to market a new formulation to avoid paying inflation penalties on those older existing drugs, may have to pay the alternative inflation penalty on the new formulation. The possibility of paying this penalty would be one consideration that manufacturers would have to take into account when developing a new formulation of an existing oral solid drug, but any increase that they would have to pay over the standard rebate amount would be a result of an increase in prices faster than inflation on these drugs.

We believe that the existence of the alternative inflation calculation requirement can also help serve the interests of the broader population with respect to drug pricing. A manufacturer that knows that an intended new formulation could be subject to an alternative inflation penalty if it excessively inflates the price of its initial oral solid drug, could limit price increases on the initial drug.

We understand that states may wish to reevaluate their preferred drug lists if manufacturers alter their existing state

supplemental rebate agreements. However, we understand that such reevaluation by states occurs on a regular basis, as it does with non-Medicaid insurers. We are confident that state Medicaid programs can continue to effectively manage shifting preferred drug lists and provide appropriate, cost-effective therapies to their beneficiaries as they have been doing. As a result of possible potential increases in the net cost of drugs that are line extensions to a state due to loss of rebates, the state may prefer a drug that is not a line extension. However, per section 1927(d)(4)(D) of the Act, the state plan is required to cover a non-preferred drug pursuant to a prior authorization program that is consistent with section 1927(d)(5) of the Act.

e. Effect on Innovation

Comment: We received many comments addressing the effect that the proposed definition of new formulation will have on innovation. A few commenters stated that they believed the broad definition would be unlikely to have a negative effect on innovation. A few commenters stated that the proposed definition would encourage “true innovation” and discourage manufacturer’s incentive to “product hop” or to seek approval for so-called “me too” or patent-extending formulations.

We received many comments discussing that the proposed definition will have a negative effect on innovation by discouraging, disincentivizing or penalizing innovation. In addition, one commenter stated that CMS should not disrupt the innovation cycle that allows manufacturers to take on the challenges of innovation. One commenter stated that the proposed definition could make innovation financially untenable for manufacturers. Several commenters discussed that reducing incentives for innovation, research and development, which are long-term, high-risk and expensive investments, will affect clinical outcomes. A few commenters expressed concern that the proposed definition will stifle the development of new and innovative therapies with particular concern for drugs that treat rare diseases. One commenter stated that the proposed definition distorts incentives to innovate because new active ingredients would be incented over other changes, even though new uses, dosage forms, and combination drugs require significant innovation and may lead to important advancements. Several commenters stated that the proposed definition undermines, or is inconsistent with FDA policies and incentives that encourage innovation.

One commenter stated that the proposed definition of new formulation will result in higher rebates for drugs that are line extensions and because of the higher rebates, 340B prices will be decreased. They stated that lower 340B prices will lead to less incentive for manufacturers to invest in research and development.

Response: We disagree that the definition of new formulation penalizes innovation. If the alternative calculation for a drug that is a line extension results in a higher URA than the standard rebate calculation, it is because the original drug was subject to inflation-based penalties. Therefore, the most important variable that determines if the applicable URA is based on the alternative rebate calculation, rather than the standard calculation, is whether the original drug increased faster than the rate of inflation. The perceived “penalty” for a drug that is a line extension is not a penalty on the new drug, rather it is a continuation of the “penalty” on the original drug. We agree that the treatment of a line extension drug may result in a URA that is greater than the standard rebate amount, however we do not believe that this treatment would prevent a manufacturer from pursuing innovation. The fact that the innovation may lead to a higher rebate obligation for a drug that is a line extension is not the result of the innovation. Manufacturers will continue to have incentives to innovate based on multiple factors, as noted in the previous response to a comment. In addition to previously described factors, we understand various FDA policies encourage innovation. We do not believe the proposed definition of new formulation changes those FDA policies and incentives.

Regarding the comments that Medicaid rebates will increase and 340B prices will decrease, it is important to note that the alternative calculation does not categorically result in a higher URA for a drug, as there are many factors that enter into the calculation. One of the most important factors in the calculation is the inflation-based rebate that is applied to the initial brand name listed drug for the rebate quarter being calculated. Regardless of the price of the new formulation, if the initial brand name listed drug did not increase in price in excess of the rate of inflation, then the alternative rebate calculation for the line extension should not result in a higher URA than the standard calculation for the drug that is a line extension. However, even in the event that the definition of new formulation results in a decrease to a 340B price, we believe our proposed definition is

consistent with section 1927(c)(2)(C) of the Act. We do not believe that decreases in 340B prices will lead to less research and development for same reason that we believe that URA increases will not lead to less innovation.

f. Effect on Manufacturers

Comment: A few commenters described the negative effects that the proposed definition of new formulation will have on manufacturers. A few commenters stated that the proposal would reduce revenue for manufacturers, including decrease revenue due to reduction in 340B prices. One commenter stated that the proposed definition is unnecessarily burdensome on manufacturers. One commenter stated that the proposed definition will cause manufacturers to use existing rebates from the original drug that could be years old.

Response: Applying the alternative rebate calculation should not categorically lead to decreased revenue for a manufacturer; rather, it continues to apply the inflation-based rebate that applies to the initial brand name listed drug. The alternative rebate calculation limits the ability of a manufacturer to negate those inflation-based rebates. We understand that if the alternative rebate calculation leads to a URA that is higher than the standard URA for a new formulation, a manufacturer may not ultimately attain the same revenue as if the alternative rebate calculation was not required. However, by interpreting the statutory definition, and providing this clarification to manufacturers, we are assisting manufacturers in ensuring their compliance with section 1927(c)(2)(C) of the Act.

g. Effect on States

Comment: A few commenters pointed out that any increase in rebates due to the alternative rebate calculation for drugs that are line extensions are offset to the federal government. The commenters stated that states would likely suffer a loss because of the offset and because manufacturers that were providing supplemental rebates to the states for these drugs would likely discontinue those supplemental rebates. Commenters stated that this change in supplemental rebates would lead to the states having to reevaluate their preferred drug lists to ensure that preferred drugs are most cost-effective.

One commenter noted that if the definition was enacted retroactively, it would create an administrative burden for the states and that states would owe money to CMS back to 2011.

Response: The statute provides that any increase in rebates resulting from the alternative calculation for drugs that are line extensions are to be treated as an offset to federal financial participation provided to a state as specified at section 1927(b)(1)(C) of the Act. We understand that states may wish to reevaluate their preferred drug lists if manufacturers alter their existing state supplemental rebate agreements. However, we understand that such reevaluation by states occurs on a regular basis, as it does with non-Medicaid insurers. We are confident that state Medicaid programs can continue to effectively manage shifting preferred drug lists and provide appropriate, cost-effective therapies to their beneficiaries as they have been doing.

The definitions of line extension, new formulation, and oral solid dosage form being finalized in this rule will be effective beginning on January 1, 2022 and will therefore not result in states owing money to CMS for retrospective application.

h. Recognizing Benefits of New Formulations

Comment: A few commenters stated that the proposed definition of new formulation fails to take into account the value of improvements and innovation. One commenter stated that the policy explicitly fails to differentiate between innovation and non-substantive formulation changes. A few commenters stated that CMS fails to recognize the effort and expense that go into developing new formulations and combinations drugs.

Response: We do not believe that the statute requires that the treatment of a drug that is a line extension is dependent on the extent of the improvements, the value of the innovation, or the expense that manufacturers incur when developing new formulations. If Congress had intended these factors to limit the scope of drugs that are line extensions, it would have provided as much in statute. While CMS recognizes the value of innovation and improvements, we also recognize the importance of giving full effect to the statute.

i. New Combination Drugs and Drug/Device Combinations

The statutory definition of line extension does not expressly exclude new combination drugs, such as a drug that is a combination of two or more drugs or a drug that is a combination of a drug and a device, and, as noted in the June 2020 proposed rule (85 FR 37295), our proposed definition of new

formulation includes new combination drugs provided that the new formulation contains at least one active ingredient in common with the initial brand name listed drug. It also provided that a drug/device combination is a new formulation.

As noted in the COD final rule (81 FR 5197, 5265 through 5267), we received numerous comments regarding our proposal in the February 2, 2012 proposed rule to include combination drugs in the definition of line extension. In particular, commenters were concerned that our proposal required sharing of proprietary pricing information with competitors. We believed that the commenters' concerns have been mitigated by § 447.509(a)(4)(iii), which requires the additional rebate to be calculated only if the manufacturer of the line extension also manufactures the initial brand name listed drug or has a corporate relationship with the manufacturer of the initial brand name listed drug. Therefore, in the June 2020 proposed rule, we clarified that while our proposed definition of new formulation includes combination drugs, the alternative URA calculation is only required under § 447.509(a)(4)(iii) for a rebate period if the manufacturer of the line extension also manufactures the initial brand name listed drug or has a corporate relationship with the manufacturer of the initial brand name listed drug.

Furthermore, we noted that in the event that the initial brand name listed drug is a combination drug, neither the statutory definition of line extension nor our proposed definitions of line extension or new formulation exclude new formulations of combination drugs. For example, if an initial brand name listed drug is a combination drug consisting of an approved drug plus a new molecular entity, and FDA subsequently approves a new drug consisting only of the new molecular entity, then we would consider the new drug to be a new formulation of the initial brand name listed drug because it would constitute a change to the initial brand name listed drug and contains at least one active ingredient in common with the initial brand name listed drug.

As previously stated, we believed we have the discretion and authority to include a broad range of drugs as a line extension, including combination drugs. However, we also noted that we are aware that some combination drugs appear to be slightly different from an existing drug while other combination drugs are very different drugs than the initial brand name listed drug. For

example, if a new combination drug contains a new molecular entity in combination with a previously approved drug, the resultant new combination may appear to be very different from the initial brand name listed drug, however, we believed that it is a new formulation of an initial brand name listed drug. Conversely, we believed that a new combination of two previously approved drugs, or a combination of a previously approved drug and a non-drug product (for example, a dietary supplement or a device), may not be a significant alteration even though it also is a new formulation of an initial brand name listed drug. Given that different commenters have differing thoughts on what constitutes a new formulation of an initial brand name listed drug, and our attempt to provide a reasonable interpretation of the statute to define or describe what constitutes a change that should be considered a new formulation, we solicited comments that may provide a way to define and identify those combination drugs that should be identified as line extensions while excluding those combination drugs that should not be so identified.

We did not receive any comments specific to our solicitation regarding a method to differentiate between combination drugs that should be identified as line extensions while excluding those that should not be so identified. However, we received the following comments regarding our proposal to include a drug that is a new combination in the definition of new formulation:

Comment: A few commenters supported CMS' proposal to include combination drugs in the proposed definition of line extension citing their belief that the proposal could incentivize investment in new drug development rather than less innovative changes and is not expressly excluded by statutory language. One commenter encouraged CMS to recognize as line extensions all combination drugs that include a previously approved drug citing their belief that this would ensure that the Medicaid program is not unduly harmed by manufacturers' choices in product life cycle management.

Many commenters disagreed with CMS' proposal to include combination drugs in the proposed definition of line extension citing their belief that it is contrary to Congressional intent, FDA policies, and statute, minimizes the significant advancements represented by combination drugs, undermines clinical breakthroughs/innovations, especially in the HIV treatment arena, and could be difficult to implement.

One commenter noted that CMS proposes to include certain combination drugs despite the fact that these products may offer a treatment for a novel patient population or even include a new molecular entity. Another commenter noted the proposal is unreasonable, stating that it is impossible to apply the alternative URA formula to combination products. One commenter stated that subjecting combination drugs to the alternative rebate calculation will have unintended pricing consequences. Several commenters disagreed with CMS' proposal to include combination drugs because they stated that the Congress intended the line extension rebate calculation to apply to a single drug as demonstrated by the Congress's deliberate and intentional use of the singular form to describe each drug subject to the line extension drug provision. One commenter disagreed with CMS' proposed definition of new formulation to include a drug that is a combination of a drug and a device citing their belief that combination products, which could include without limitation a drug/biologic active ingredient combined with a medical device, are not similar to extended release formulations, and therefore, cannot qualify as a line extension under the statutory definition. One commenter expressed concern that combination products currently account for substantial federal and supplemental rebates and the high federal rebates on the original products would severely weight the rebate distribution in favor of the federal government, causing an impact to states, who may in turn move line extension products to non-preferred status even if utilization is high, assuming comparable clinical options exist.

Response: We believe that we have statutory authority to include new combination drugs and drug device combinations in the definition of new formulation; however, based on the comments, we have decided not to include a new combination of drugs, and a drug/device combination as a new formulation.

It is important to note that combination drugs are not necessarily excluded from the definition of a new formulation. If an initial brand name listed drug is a combination of two or more drugs, and then a manufacturer begins selling a new formulation of that combination drug, then the new drug satisfies the definition of a new formulation and must be identified as a line extension. For example, consider two single-ingredient drugs, Alpha and Beta. A new combination of these two

drugs, AlphaBeta, is not considered a new formulation for the purposes of the line extension alternative rebate calculation. However, a later developed new formulation of AlphaBeta, for example, AlphaBeta XR, is a new formulation with AlphaBeta representing the initial brand name listed drug.

Based on the comments received, we will not be finalizing our proposal that a drug that is a new combination is included in the definition of new formulation.

j. Active Ingredient

Comment: A few commenters agreed with CMS' proposal that "the new formulation contains at least one active ingredient in common with the initial brand name listed drug" citing their belief that this would allow manufacturers and CMS to readily answer the threshold question as to whether a product is a line extension. One commenter specifically supported CMS's proposed use of active ingredient to identify a new formulation.

A few commenters disagreed with CMS' proposal that "the new formulation contains at least one active ingredient in common with the initial brand name listed drug" citing their belief that comparing active ingredients is technically complicated, the proposal is unworkable in practice and indicative of a policy that stretches beyond CMS' authority. One commenter expressed their belief that defining "new formulation" by reference to active moiety would require manufacturers to unnecessarily expend time and resources in identifying original drugs, when doing so could be unlikely to lead to the application of the alternative URA formula. One commenter recommended that CMS modify the proposed definition of new formulation to expressly exclude combination products and clarify that a new formulation must contain the same one active ingredient in common with the original drug, not "at least one." Another commenter requested that CMS clarify that each line extension should have only a single original drug, which is the drug first approved by FDA that contains the same active ingredient as the line extension.

Response: We included the proposal that a new formulation that contains at least one active ingredient in common with the initial brand name listed drug because we proposed that a drug that is a new combination should be identified as a line extension if the new combination contained one of the same active ingredients as the initial drug. We were using that common active ingredient to make the link between the

original drug and the drug that is a new combination. As stated, we are not finalizing that new combinations are new formulations and therefore we are not finalizing that the original drug and the drug that is a new combination have an active ingredient in common.

k. New Indication

In the February 2, 2012 proposed rule, we proposed that a drug approved with a new indication for an already approved drug would be a line extension (77 FR 5323). We received several comments stating that the proposal was not feasible because the approval of a new indication for an already approved drug may not result in a different drug product and it would not be logical that a drug is a line extension of itself. Additional commenters noted that it is not possible to apply the alternative line extension calculation to rebate invoices for an NDC only for those claims that were prescribed the newly approved indication. In the June 2020 proposed rule, we agreed that if following the approval of a new indication a manufacturer markets its drug in such a way that it is not a separately identifiable drug product the alternative URA calculation would not apply. However, if following the approval of a new indication the manufacturer markets the drug in such a way that it is a separately identifiable drug product, we proposed that the alternative URA calculation would apply. Thus, as discussed in the June 2020 proposed rule, we proposed a definition of new formulation that included changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC).¹⁹ We requested comments about whether a drug approved with a new indication that is not separately identifiable should be considered a new formulation and, if so, how such a drug could be identified in DDR for purposes of calculating the alternative URA.

We believed that the Congress included the alternative URA calculation for a line extension to address changes to a drug that allow a manufacturer to avoid inflation-based additional rebates by establishing a new

¹⁹ An NDC comprises three segments. The first segment is a labeler code, associated with the labeler, the second segment is a product code, which in association with a specific labeler code identifies the product, and the third segment is a package code, which, in association with the preceding segments, identifies the package size and type. For purposes of reporting to the MDRP, FDA's 10-digit NDC must be converted to an 11-digit NDC. The 9-digit NDC cited here is a combination of the labeler code plus the product code. FDA requirements for an NDC are at 21 CFR 207.33.

market date and base date AMP for the drug. We noted that we agreed with the comments suggesting that if there is a change to a drug but that drug is not separately identifiable, then it is not feasible for the manufacturer to identify the drug as a line extension and perform an alternative URA calculation.

In response to our request for comments about whether a drug approved with a new indication that is not separately identifiable should be considered a new formulation and, if so, how such a drug could be identified in DDR for purposes of calculating the alternative URA, we did not receive specific suggestions. However, we received one comment asking for clarification on what marketing measures, other than a different NDC, would qualify a drug with a new indication as a new formulation. We received the following comments regarding the inclusion of “new indication” in the definition of new formulation:

Comment: Many commenters disagreed with CMS’ proposal to include “changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC)” as part of the proposed definition for new formulation citing their belief that the proposal is overly broad, conflicts with Congressional intent, FDA policies, and CMS’ statutory authority, it would disincentivize manufacturers to provide treatment options for rare disease patients, the proposal does not reference the scope of the changes involved where FDA approves a new indication, could freeze or slow research and investment into orphan drug indications, and could adversely impact the COVID-19 pandemic by chilling innovation. One commenter requested that CMS not consider new or expanded indications to treat chronic conditions such as psoriatic disease as a new formulation under the proposed “line extension” definition. One commenter expressed their belief that in the case of a new indication—the parent and child drug are the very same drug—and applying the alternative rebate formula will pose problems as the line extension and the parent drug would have the same AMP, and thus, the same rebate. One commenter expressed concern that obtaining approval for new indications of existing therapies can require significant investments in research and development, including new clinical studies. One commenter noted that the introduction of a new indication can have significant benefits for patients. Another commenter was concerned that when a drug is approved with a new

indication that is not separately identifiable, considering it a new formulation would create a number of implications on stakeholders throughout the drug delivery system. One commenter stated that a new indication of a drug is not a new formulation because a change to the label of a drug to reflect a new indication does not change the chemical composition of a drug, even if the new indication is marketed as a “separately identifiable drug.” One commenter recommended that CMS limit the definition of “line extension” to those formulations that are not legitimately distinct products.

A few commenters agreed with CMS’ proposal to include “changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC)” as part of the proposed definition for new formulation. As stated previously, one commenter recommended that CMS clarify what marketing measures other than a separate NDC would qualify to minimize confusion between manufacturers and CMS.

Response: We believe that we have statutory authority to include a drug that has been approved for a new indication in the definition of new formulation, however, based on the comments, we have decided not to include a new indication accompanied by marketing as a separately identifiable drug (for example, a different NDC) in the definition.

It is important to note that drugs approved for a new indication accompanied by marketing as a separately identifiable drug are not necessarily excluded from the definition of a new formulation. If a drug is approved for a new indication and is marketed as a separately identifiable drug, and also includes one of the changes in formulation that qualifies a drug as a new formulation, then that drug is included in the definition of a new formulation. For example, if an initial brand name listed drug is approved for a new indication, assigned a different NDC, and marketed in a different dosage form than the initial drug, such drug is a new formulation subject to the alternative rebate calculation.

Based on the comments received, we will not be finalizing our proposal that a change in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC) is included in the definition of new formulation.

1. New Strengths

In the COD final rule (81 FR 5267), we indicated that we do not consider a new

strength of the same formulation of the initial brand name listed drug to be a line extension because section 1927(c)(2)(C) of the Act does not expressly contemplate that a new strength is a line extension. As noted in the June 2020 proposed rule though, we did not finalize a regulatory definition of line extension, and instructed manufacturers to make “reasonable assumptions” regarding whether a drug is a line extension. As noted in the June 2020 proposed rule (85 FR 37295), we proposed to interpret the definition of line extension more broadly, which included proposing a much broader definition of new formulation. The statutory definition of line extension does not expressly exclude a new strength of a drug, and we believed a change in strength is a relatively simple modification to a currently marketed product. Furthermore, changing the strength of an initial brand name listed drug allows a manufacturer to establish a new base date AMP, thereby avoiding inflation based rebate liability, which may incentivize a manufacturer to change the strength of a drug that is losing its exclusivity or patent protection to prolong the lifecycle of the drug, preventing money saving generic substitution. Therefore, we believed that a new strength of a drug, produced or distributed at a later time than the initial strength(s), should be identified as a line extension and made subject to the line extension alternative URA calculation. Therefore, as noted in the June 2020 proposed rule, we proposed a definition of new formulation that included changes in strength.

We received the following comments in response to including a new strength in the definition of new formulation:

Comment: A few commenters agreed with CMS’ proposal that “a new strength of a drug, produced or distributed at a later time than the initial strength(s), should be identified as a line extension and made subject to the line extension alternative URA calculation” citing their belief that this will expand the universe of drugs that can be line extensions and that CMS is correct in its characterization of manufacturer product life cycle gaming and the unintended consequences for both patients and the Medicaid program that results from this behavior.

Response: We appreciate the support.

Comment: Several commenters disagreed with the proposal that “a new strength of a drug, produced or distributed at a later time than the initial strength(s), should be identified as a line extension and made subject to the line extension alternative URA calculation” citing their belief that the

proposal conflicts with prior CMS guidance, statute and Congressional intent. A few commenters stated that since CMS previously stated that they did not believe the statute indicated that a new strength was a line extension, and that the statute did not change, that CMS is making a change in policy without appropriate explanation. They noted that CMS does not provide a policy rationale for why a new strength of an existing formulation would meet the statutory definition for a new formulation. A few commenters pointed out that CMS stated that the statute does not prohibit a new strength from being identified as a line extension but that the lack of prohibition does not mean that it is permissible or advisable.

Response: We believe that our proposed definition of new formulation is consistent with section 1927(c)(2)(C) of the Act, and that it give us discretion to include a new strength in the definition. Although in the 2016 COD final rule we did not include a new strength in the definition of line extension, our continued experience with the application of the statutory provisions for drugs that are line extensions resulted in a reevaluation of our prior position.

Comment: A few commenters stated that the proposed definition of new formulation conflicts with the FFDCA and FDA regulatory understanding of “formulation”.

Response: FDA and CMS each have different functions and responsibilities and we do not believe that the same terms need to be defined or interpreted in the same manner. We note that CMS and FDA may use the same terms differently for purposes within their own programs and consequently do not agree that the interpretation of terms must always be the same. Until the January 1, 2022 effective date of the definition of new formulation, manufacturers may continue to refer to the statutory definition of line extension and use reasonable assumptions, if necessary, to determine if their drug is a new formulation.

Comment: A few commenters expressed their belief that CMS does not understand the patient needs and/or reasons that different strengths serve, manufacturers may be discouraged from taking steps that would expand patients’ treatment options, and manufacturers may be penalized for investing in and pursuing additional improvements to a drug. One commenter stated that despite the proposed rule’s suggestion that a new strength is a “simple modification,” such a change must be supported by data—which may require conducting clinical trials—and receive

FDA approval. One commenter suggested that a new strength might be approved for a drug in connection with a new indication for a drug and that would be a significant change.

Response: We disagree that we do not understand the reasons that different strengths may be developed. We believe that the introduction of a new strength of a drug, regardless of the reason a manufacturer may begin marketing such new strength, is a new formulation that is subject to the alternative rebate calculation. Although we understand there may be a variety of reasons a manufacturer may pursue FDA approval of a new strength of a drug, we do not believe that the reason for creating a new strength affects whether the new strength is a new formulation and thereby required to calculate the alternative rebate for a drug that is a line extension.

We also do not believe that the requirement to perform the alternative rebate calculation penalizes a manufacturer for pursuing changes to a drug. If the initial strength(s) of the drug did not increase in price faster than the rate of inflation, then the alternative calculation for the new strength will generally not result in a higher rebate than the standard calculation. Although the alternative rebate calculation may result in a higher URA for a drug, as compared to the standard URA, the higher URA is not due to the innovations in the new formulation. Rather, if the alternative rebate calculation results in a URA that is higher than the standard calculation, it is because the *original* drug increased in price faster than the rate of inflation and therefore was subject to inflation-based additional rebates.

Thus, an alternative rebate calculation that results in a higher rebate than the standard calculation is not a result of the improvement to the drug, but rather the price increases on the original drug that exceeded the rate of inflation.

Comment: A few commenters stated that the statute was focused on a change in dosage form, and did not discuss a change in strength. A few commenters expressed their belief that the inclusion of a new strength in the definition of new formulation conflates the concepts of “strength” and “dosage form”—concepts that the statute treats as distinct—in a way that is contrary to Congressional intent. The commenters point out that either a change in strength or a change in dosage form may lead to the establishment of a new base date AMP. They noted that since the line extension provision provides a different dosage form as an example of a line extension (that is, an extended

release formulation), that only a change to the dosage form (that is, not a change in strength) qualifies a drug as a line extension.

Response: We do not agree that we are conflating “strength” with “dosage form.” We agree with the commenter that a change in strength or a change in dosage form may be reason to establish a new base date AMP. However, the line extension provision in the statute does not rely on whether the change to a new formulation is a reason to establish a new base date AMP, nor does it preclude considerations of changes in strength.

Comment: Several commenters expressed concern with operational challenges if a new strength could be a line extension. They stated that since one of the variables in the alternative rebate calculation was subject to *any* strength of the original drug, the calculation is difficult, illogical, or impossible.

Response: We understand that the statutory requirement to apply the alternative rebate calculation to a drug that is a line extension may be operationally confusing and difficult, but we do not believe that that it is illogical or impossible. As always, CMS staff is available to assist manufacturers with operational concerns.

Comment: A few commenters stated that CMS presupposes that a manufacturer creates a new strength for the purpose of avoiding inflation-based rebates, or to avoid generic competition. One commenter stated that concerns about generic competition is irrelevant to whether a drug is a line extension and CMS does not have authority to address patent or generic competition issues.

Response: We do not believe that a new strength is necessarily created for the purpose of avoiding inflation-based rebates or to address generic competition. We also do not believe that our language in the proposed rule concerning reasons why a manufacturer may seek approval for a new strength is inappropriately addressing patent or generic competition issues. Rather, we proposed a definition of new formulation in order to provide guidance to manufacturers on how to identify which of its drugs should be identified as a line extension, regardless of the reasons the new formulation was developed.

We are finalizing our proposal that a new strength of a drug is included in the definition of a new formulation.

m. Extended Release Formulation

Comment: One commenter stated that including an extended release

formulation in the definition would undermine the significant improvement Long Acting Injectable (LAI) Antipsychotics offer to people with mental illness.

A few commenters disagreed with CMS' inclusion of any new formulation other than an extended release formulation or similar to an extended release formulation in the proposed definition of new formulation, citing their belief that the proposal conflicts with statute and Congressional intent, and would undermine longstanding statutory incentives that encourage innovation.

Response: The statute defines a line extension, in part, as a new formulation of a drug and provides an extended release formulation as an example. As a result, we do not believe we have discretion to exclude an extended release formulation from the definition of new formulation. Nevertheless, we believe that our proposed definition is consistent with section 1927(c)(2)(C) of the Act and appropriate for the reasons discussed in the June 2020 proposed rule. We do not agree that the alternative rebate calculation required for a drug that is a line extension undermines drug improvements, whether the line extension is an extended release formulation, or any other new formulation. As stated, the alternative calculation does not categorically result in a higher URA for a drug as there are many factors that enter into the calculation. If the initial brand name listed drug did not increase in price in excess of the rate of inflation, then the alternative rebate calculation for the line extension should not result in a higher URA than the standard calculation for the drug that is a line extension.

The application of the alternative rebate calculation does not nullify statutory incentives that encourage innovation as those incentives continue to be a factor in the calculation of the URA for the drug that is a line extension. For example, if FDA has approved a drug exclusively for pediatric indications, or if a drug is identified as a clotting factor, section 1927(c)(1)(B)(iii) of the Act continues to allow for a lower percentage of AMP for the rebate calculation.

n. Change in Pharmacodynamics or Pharmacokinetic Properties

Comment: We received one comment regarding the proposal to include changes in pharmacodynamics or pharmacokinetics in the definition of new formulation. The commenter stated that these types of changes involve more than a slight alteration of an existing

product and may result in changes to an active moiety such that it would be considered a different active ingredient.

Response: After considering the comment, we concluded that using the terminology "pharmacodynamics or pharmacokinetics" incorporated a broader range of changes than we intended with this language. Therefore, we are simplifying the language to incorporate the more limited types of change in the drug that we intended to capture, using less complex language. Rather than including a change in pharmacodynamics or pharmacokinetic properties, we are modifying the language to include a change in release mechanism. Examples of a change in release mechanism include, but are not limited to, a change from an immediate release formulation to a delayed release formulation, a change from an extended release formulation to an immediate release formulation, and a change from a non-coated tablet to an enteric coated tablet.

After consideration of public comments, we are finalizing a modification of our proposal. Specifically, we are including in the definition of a new formulation a change in release mechanism, rather than changes in pharmacodynamics or pharmacokinetic properties as proposed.

o. Route of Administration

Comment: A few commenters disagreed with CMS' inclusion of changes to route of administration in the proposed definition of new formulation, citing their belief that the proposal fails to consider the benefits of new routes of administration and conveys a lack of recognition of the value of incremental improvements in new formulations. One commenter also stated their belief that there would be fewer financial incentives to develop new and improved drugs, including highly anticipated, long-acting HIV medications for both prevention and treatment.

Response: We believe that our proposal to include a drug with a new route of administration in the definition of new formulation is consistent with section 1927(c)(2)(C) of the Act. The statute does not limit a line extension to only those drugs that do not provide additional clinical benefits over the initial brand name listed drug. Additionally, the statute does not direct that the new formulation of the drug has to be administered by the same route of administration as the original drug. Moreover, we do not agree that when determining if the alternative rebate calculation is required for a drug that is

a line extension, it is required to consider the benefits of new routes of administration or the benefits of any other new formulation. As stated, the alternative calculation does not categorically result in a higher URA for a drug as there are many factors that enter into the calculation. If the initial brand name listed drug did not increase in price in excess of the rate of inflation, then the alternative rebate calculation for the line extension should not result in a higher URA than the standard calculation for the drug that is a line extension.

After consideration of public comments, we are including a change in route of administration in the definition of a new formulation as proposed.

p. Recommendations for Modifications to Proposals

We received a few comments that are out of the scope of the proposed rule and we are not addressing those comments in this final rule.

Comment: One commenter recommended that the definition of line extension should follow the statute exactly because it would be less confusing.

Response: We disagree that adopting the statutory language as the regulatory definition of line extension or new formulation would be less confusing. One important reason is that the statute only provides one example of a type of new formulation, that is, an extended release product. In addition, experience has shown us that since the publication of the 2016 final rule, there has been confusion and questions regarding the identification of drugs that are line extensions. In the interest of fairness to all affected parties, including states and manufacturers, therefore, we believe a more detailed regulatory definition, along with the information in the preamble of this rule, will provide more clarity for manufacturers on how to correctly identify their drugs that are line extensions.

Comment: A few commenters stated that although they support the proposed clarification related to line extensions, they believe the proposal could be further strengthened. One commenter recommended that we add non-oral drugs and biosimilars to the definition. Another commenter recommended that CMS explicitly add "authorized generics" to the definition of "line extension" for purposes of the inflation rebate.

Response: We do not agree with the suggestion that we add authorized generics to the definition of line extension. As discussed in the COD final rule (81 FR 5268), we do not read

section 1927(c)(2)(C) of the Act as treating authorized generic products differently.

Similarly, we do not believe it is necessary to provide separate language regarding biosimilars and non-oral drugs because we do not read section 1927(c)(2)(C) of the Act as treating biosimilars and non-oral drugs differently. Both of those categories of drugs will be treated according to the provisions set forth in this regulation.

Comment: We received a few comments that recommended that a drug should only be identified as a line extension or new formulation if FDA requires only bioequivalence or bioequivalence and bioavailability studies for a drug.

Response: We disagree that we should rely on these types of studies. We are not proposing that bioequivalence or bioavailability are among the criteria for determining if a product is a line extension. Therefore, these studies are not relevant to evaluating whether a drug is a line extension.

Comment: A few commenters stated that CMS should make it clear that the original drug must be the “truly original drug” and identify that as the “first drug approved.” They wanted it specified that drugs that were approved after the initial drug but before the line extension are not to be treated as an initial brand name listed drug. One commenter stated that the original drug should be based on the chronology of the approval of the original drug. One commenter recommended that it should be written into the regulatory text that a drug must be active in the applicable quarter in order to be considered as a potential initial brand name listed drug.

Response: We do not agree with the commenters who requested us to clarify that the initial brand name listed drug should be limited to the “truly original drug.” As stated in the preamble in the proposed rule (85 FR 37289), “[t]o apply the alternative formula described in section 1927(c)(2)(C)(iii)(I) through (III) of the Act for each line extension and rebate period, the manufacturer must determine which NDC represents the initial brand name listed drug that will be used to calculate the alternative URA. First, the manufacturer must identify *all* potential initial brand name listed drugs by their respective NDCs by considering *all* strengths of the initial brand name listed drug in accordance with section 1927(c)(2)(C)(iii)(II) of the Act.” (emphasis added). In order to perform the calculation as instructed, all strengths of potential initial drugs must be considered, regardless of the chronology of a drug’s approval, or date first marketed. Potential initial brand

name listed drugs may be excluded from consideration if they are not manufactured by the same manufacturer of the drug that is a line extension or by a manufacturer with which the line extension manufacturer has a corporate relationship. Also, if a potential initial brand name listed drug is not active in the MDRP during the quarter, it is excluded from consideration for that quarter and we do not believe it is necessary to include that language in the regulatory text.

Comment: A few commenters suggested that CMS revise the proposed definition of line extension to exclude those drugs that have not been assigned a different baseline AMP. The commenters noted that this would minimize administrative burden and would also be consistent with Congressional intent, which is focused on situations where a line extension is subject to a lower additional rebate than the original drug.

Response: We do not agree with revising the definition of line extension or new formulation to exclude those drugs that have not been assigned a new base AMP. The URA for a drug that is a line extension may derive from the standard rebate calculation or the alternative rebate calculation, and the applicable calculation may vary from quarter to quarter. One of the required fields in the product data is an indicator to identify whether a drug is a line extension. If a drug is a line extension, a determination must be made every quarter whether there is an initial brand name listed drug to report for the quarter. If there is more than one potential initial brand name listed drug for the quarter, an evaluation must be conducted to determine which of the potential initial brand name listed drugs has the highest additional rebate (calculated as a percentage of AMP) for that quarter. That NDC must be reported as the initial brand name listed drug for that quarter. Using that NDC for the initial brand name listed drug, if the alternative rebate calculation results in a higher URA than the standard URA, then the alternative URA is used for that quarter. As there are numerous variables considered and utilized in the calculation of the URA for a drug that is a line extension, and the base AMP value is only one of those variables, it is not appropriate to exclude a drug from the definition of line extension or new formulation based only on the base AMP value.

Comment: One commenter recommended that CMS work with FDA to create an exceptions process for manufacturers where they develop criteria for evaluating any petition from

companies that believe their products are not line extensions.

Response: We do not agree that we should create an exceptions process and work with FDA to evaluate manufacturer petitions for exceptions to the definition of line extension or new formulation. We believe that the regulatory definition is reasonable, is consistent with section 1927(c)(2)(C) of the Act, and will assist manufacturers in appropriately identifying their drugs that must be reported as a drug that is a line extension.

Comment: We received a comment suggesting that we sever the line extension section of this rule, along with other sections that may interfere with research and development, from the rest of the rule.

Response: We do not believe there is a reason to sever sections of this rule. There is no evidence that the implementation of the line extension alternative calculation, which has been in effect for 10 years now, has affected research and development. Manufacturers have had to make determinations of which drugs constitute a line extension based primarily on reasonable assumptions over this period. This regulation provides more specific direction on identifying those drugs that represent line extensions.

q. Prospective Implementation

Comment: Several commenters requested that CMS confirm that any new regulation defining the terms should be prospective from the date of implementation. One commenter also noted that they believe if these definitions are applied retrospectively, this will dramatically increase the fiscal impact to the states. One commenter requested that CMS clarify that nothing would stop a manufacturer from voluntarily conforming its past reporting to the new definitions. Another commenter requested that CMS clarify that any regulatory definition of “new formulation” and application of the oral solid dosage form requirement would only apply for new products as of the effective date of this future final rule and that manufacturers may rely on their reasonable assumptions for existing products.

Response: The definitions of line extension, new formulation, and oral solid dosage form finalized in this final rule will not be applied retrospectively. These definitions become effective for all drugs in the MDRP beginning on January 1, 2022. Prior to the effective date, manufacturers may continue to rely on reasonable assumptions to determine if their drug is a new

formulation in order to comply with the statutory requirements and to use for potential future review of compliance prior to the effective date. If a subsequent review by us, by the Office of the Inspector General (OIG), or another authorized government agency determines or reveals that additional adjustments or revisions are necessary, the manufacturer is responsible for complying with that determination.

r. Delay Effective Date

Comment: A few commenters recommended that CMS consider narrowing the redefinition of line extension in future rulemaking with adequate time for commenters to consider the impact and comment, with one commenter requesting that if that is not possible, that CMS implement the new line extension definition with at least 12 months' notice prior to the effective date to permit states time to make preferred drug list decisions, notify patients, and implement changes. One commenter also requested that CMS specify a compliance date/effective date that is at least 4 quarters following the publication of the final rule, and that the rule should be prospective only.

Response: Based on the comments received, we are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension.

Based on the comments, we are revising the proposed definition of new formulation to read: For a drug, a change to the drug, including, but not limited to: An extended release formulation or other change in release mechanism, a change in dosage form, strength, route of administration, or ingredients. In addition, as discussed in section II.C. of this final rule, we are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension.

s. Corporate Relationship

In the June 2020 proposed rule (85 FR 37295), we noted that under § 447.509(a)(4)(iii), manufacturers are required to calculate the alternative URA if the manufacturer of the line extension also manufactures the initial brand name listed drug or has a corporate relationship with the manufacturer of the initial brand name listed drug. Although a drug may satisfy the definition of line extension, and therefore, should be identified in DDR as a line extension, a manufacturer is not required to calculate the alternative URA unless the manufacturer of the line extension also manufactures, or has a corporate relationship with the manufacturer of the initial brand name listed drug.

Although we did not propose any changes to this policy, we received some comments that were out of the scope of the proposed rule and we are not addressing them in this final rule.

5. Oral Solid Dosage Form

Oral solid dosage form is defined at § 447.502 to mean capsules, tablets, or similar drugs products intended for oral use as defined in accordance with FDA regulation at 21 CFR 206.3 that defines solid oral dosage form. As we now have more experience reviewing and dealing with the line extension provisions from the Affordable Care Act, we believed that manufacturers may not be interpreting the term oral solid dosage form consistently. To mitigate any potential confusion, we believed that manufacturers and other commenters would benefit from a more detailed definition. In the June 2020 proposed rule, we proposed to modify the definition of oral solid dosage form.

In the COD final rule (81 FR 5198), CMS interpreted an oral route of administration as any drug that is intended to be taken by mouth. Because there is potential confusion about whether a dosage form must be swallowed, or otherwise enter the gastrointestinal tract to be considered an orally administered dosage form, we proposed to interpret that an oral form of a drug is one that enters the oral cavity. This includes, but is not limited to, a tablet or film administered sublingually and a drug that is orally inhaled. We believed that this interpretation provides greater clarity to commenters regarding what constitutes an oral form of a drug.

Additionally, we believed that manufacturers may not be interpreting the term solid dosage form consistently. To mitigate any potential confusion, we proposed to interpret that a solid dosage

form is a dosage form that is neither a gas nor a liquid.

FDA regulation at 21 CFR 206.3 defines the term "solid oral dosage form" for the purpose of identifying drugs for which a code imprint is required to permit identification of the product. The phrase "capsules, tablets or similar drugs products" may not encompass the range of dosage forms that we believed should be considered for the application of the line extension provision in the Affordable Care Act. For example, a sublingual film is an oral solid dosage form; however, because of the physical attributes of the dosage form, there may not be a requirement to imprint an identifying code on the dosage form. Another example of an oral solid dosage form is a powdered drug administered by oral inhalation. Therefore, we proposed to modify the definition of oral solid dosage form at § 447.502 to read that it is an orally administered dosage form that is not a liquid or gas at the time the drug enters the oral cavity. Additionally, we noted that an oral solid dosage form that incorporates a medical device would not be exempt from this definition solely due to the addition of a device to the oral solid dosage form. For example, if a manufacturer adds a device to a tablet, the new drug would not be exempt from being a line extension solely due to the addition of a device to the tablet.

We received the following comments regarding the definition of oral solid dosage form:

Comment: A few commenters disagreed with CMS' proposal to expand the definition of an oral solid dosage form citing their belief that the expanded definition would exceed CMS' statutory or delegated authority. A few commenters disagreed with the proposed change because it no longer relies on an FDA definition of oral solid dosage form. One commenter noted the current definition that properly relies on the FDA definition has caused no practical problems. Another commenter noted that not relying on the FDA definition would result in needless confusion, requiring manufacturers to evaluate dosage forms under two incongruous legal standards.

Several commenters disagreed with CMS' proposed definition of oral solid dosage form citing their belief that modifying the definition would result in a substantial chilling effect on drug innovation. One commenter stated that the proposed definition fails to take into account that oral drugs, including inhaled drugs, become the threshold for any subsequent dose form of a particular product brought to market.

Several commenters supported the proposal to expand the definition of oral solid dosage form. One commenter agreed with CMS' proposal to include powdered inhalations and sublingual films in the proposed definition for an oral solid dosage form and also encouraged CMS to clearly state that liquid filled capsules are considered oral solid dosage forms.

One commenter requested that CMS clarify that any regulatory definition of new formulation and application of the oral solid dosage form requirement would only apply for new products as of the effective date of the final rule and that manufacturers may rely on their reasonable assumptions for existing products.

Response: The commenter did not explain how our proposed definition of oral solid dosage form would exceed our statutory or delegated authority. Nevertheless, we believe that our proposed definition is consistent with section 1927(c)(2)(C) of the Act and appropriate for the reasons discussed in the June 2020 proposed rule.

We do not agree that we should retain FDA's regulatory definition at 21 CFR 206.3 for purposes of identifying an oral solid dosage form for the MDRP. As we stated in the proposed rule, the FDA definition at 21 CFR 206.3 is for the purposes of identifying drugs that require a code imprint on the dosage form. Due to physical characteristics of some oral solid dosage forms, it may be impossible to imprint a code on them. Since FDA's regulatory definition is used for the specific purpose of determining when a code must be imprinted on a dosage form, and that identification bears no relationship to identifying what drugs are subject to the alternative rebate calculation for line extension drugs, we believe that it is reasonable to adopt a different definition than FDA's definition for the purposes of identifying an oral solid dosage form for the line extension provisions.

We also do not agree that modifying the definition of oral solid dosage form will necessarily discourage innovation. As stated, the alternative calculation does not categorically result in a higher URA for a drug as there are many factors that enter into the calculation. If the initial brand name listed drug did not increase in price in excess of the rate of inflation, then the alternative rebate calculation for the line extension should not result in a higher URA than the standard calculation for the drug that is a line extension. We also disagree that we failed to take into account that oral drugs become the threshold for any subsequent dose form. The statute

requires that the initial drug is necessarily the threshold drug for any line extension of that drug.

We appreciate the support of the commenter who agreed with our inclusion of inhaled powders and sublingual films as an oral solid dosage form and we do understand that adopting this interpretation includes the possibility that an inhaled drug that is an oral solid could be an initial brand name listed drug. We agree that liquid filled capsules satisfy the proposed definition of oral solid dosage form because when the liquid filled capsule enters the oral cavity, it is a solid dosage form.

We do not agree that only products introduced on or after the effective date of the final rule should be subject to the requirement that only the initial brand name listed drug must be an oral solid dosage form and the regulatory definitions of oral solid dosage form, line extension, and new formulation. Although manufacturers will not be required to apply the regulatory definitions and oral solid dosage form requirement when calculating rebates for periods prior to the effective date of the final rule, the definitions become effective for all drugs that are on the market as of and following that effective date.

We are finalizing the definition of oral solid dosage form as proposed. In addition, as discussed in section II.C. of this final rule, we are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension.

6. Multiple Source Drug

The MSIAA clarified the definition of multiple source drug in section 1927(k) of the Act by removing "(not including any drug described in paragraph (5))" and inserting ", including a drug product approved for marketing as a non-prescription drug that is regarded as a covered outpatient drug under paragraph (4),". Section 1927(k)(7)(A)(i) of the Act now provides that the term multiple source drug means, for a rebate period, a COD, including a drug product approved for marketing as a non-prescription drug that is regarded as a COD under section 1927(k)(4) of the Act for which there is at least 1 other drug product which: Is rated as therapeutically equivalent (under FDA's

most recent publication of "Approved Drug Products with Therapeutic Equivalence Evaluations"), except as provided in section 1927(k)(7)(B) of the Act, is pharmaceutically equivalent and bioequivalent, as defined in section 1927(k)(7)(C) of the Act and as determined by FDA, and is sold or marketed in the United States during the period.

We proposed to revise the definition of multiple source drug at § 447.502 to align with the statutory definition. Specifically, we proposed to revise the definition of multiple source drug to mean, for a rebate period, a COD, including a drug product approved for marketing as a non-prescription drug that is regarded as a COD under section 1927(k)(4) of the Act, for which there is at least 1 other drug product which meets all the following criteria:

- Is rated as therapeutically equivalent (under the FDA's most recent publication of "Approved Drug Products with Therapeutic Equivalence Evaluations" which is available at <http://www.accessdata.fda.gov/scripts/cder/ob/>).

- Except as provided at section 1927(k)(7)(B) of the Act, is pharmaceutically equivalent and bioequivalent, as defined at section 1927(k)(7)(C) of the Act and as determined by the FDA.

- Is sold or marketed in the United States during the period.

We did not receive public comments on the definition of multiple source drug, and therefore, we are finalizing as proposed.

7. Single Source Drug

The MSIAA clarified the definition of single source drug in section 1927(k) of the Act by removing the phrase "an original new drug application" and inserting "a new drug application", inserting ", including a drug product approved for marketing as a non-prescription drug that is regarded as a covered outpatient drug under paragraph (4)," after "covered outpatient drug", inserting "unless the Secretary determines that a narrow exception applies (as described in § 447.502 of title 42, Code of Federal Regulations or any successor regulation)" after "under the new drug application" and adding language to specify that such term also includes a COD that is a biological product licensed, produced, or distributed under a biologics license application approved by the FDA. Section 1927(k)(7)(A)(iv) of the Act now defines a single source drug to mean a COD, including a drug product approved for marketing as a non-prescription drug that is regarded

as a COD under section 1927(k)(4) of the Act, which is produced or distributed under an NDA approved by the FDA, including a drug product marketed by any cross-licensed producers or distributors operating under the NDA unless the Secretary determines that a narrow exception applies (as described in § 447.502 or any successor regulation) and the term includes a COD that is a biological product licensed, produced, or distributed under a biologics license application approved by the FDA. To align the regulatory definition with the definition in the statute at section 1927(k)(7)(A)(iv) of the Act, as clarified by the MSIAA, we proposed to revise the regulatory definition of single source drug at § 447.502. We proposed to define single source drug in § 447.502 to mean a COD, including a drug product approved for marketing as a non-prescription drug that is regarded as a COD under section 1927(k)(4) of the Act, which is produced or distributed under an NDA approved by the FDA, including a drug product marketed by any cross-licensed producers or distributors operating under the NDA unless the Secretary determines that a narrow exception applies (as described in § 447.502) and includes a COD that is a biological product licensed, produced, or distributed under a biologics license application approved by the FDA.

We received the following comments regarding the definition of single source drug at § 447.502:

Comment: One commenter requested that CMS revise their proposed definition of single source drug to only apply prospectively from October 2019 forward, citing their belief that since this is the date the Congress amended the MDRP statute, it would be in accordance with the recent ruling in the United States District Court for the District of Columbia case of *STI Pharma, LLC v. Azar*.

Response: The revision to the definition of single source drug is to conform the rule with the amended statute. Our longstanding interpretation of the statute (both before and after the 2019 amendments) is that a single source drug is a drug approved under an NDA, and noninnovator drugs are those approved under an ANDA. We believe *STI Pharma, LLC v. Azar* was wrongly decided. Prior to the 2016 COD final rule, there was no narrow exception to that general rule. Therefore, any drug approved under an NDA that is reported as a noninnovator multiple source drug for quarters prior to 2Q2016 is improperly categorized and the drug manufacturer should request a drug-

category change or risk enforcement action.

We are finalizing the definition of single source drug as proposed.

8. CMS-Authorized Supplemental Rebate Agreements (SRAs)

States may enter into separate or supplemental drug rebate agreements as long as such agreements achieve drug rebates equal to or greater than the drug rebates set forth under the NDRA. (See section 1927(a)(1) of the Act.) CMS approval to enter directly into such agreements with manufacturers is required under section 1927(a)(1) of the Act, and thus, states are required to use the SPAs process as a means to seek CMS authorization. Supplemental rebates must be considered a reduction in the amount expended under the state plan in the quarter for medical assistance as provided at section 1927(b)(1)(B) of the Act. See program guidance at <https://www.medicaid.gov/federal-policy-guidance/downloads/smd091802.pdf>.

The Affordable Care Act revised section 1927(b)(1)(A) of the Act to require that manufacturers provide rebates for CODs dispensed to individuals enrolled with a Medicaid MCO when the organization is responsible for coverage of such drugs. At that time, states had to re-assess whether or not to directly collect supplemental rebates related to CODs dispensed to Medicaid managed care enrollees if the MCO was responsible for such drug coverage. Some states required their MCOs to collect and share supplemental rebates under the CMS-authorized SRA, while other states permitted their MCOs to negotiate their own rebates with manufacturers outside of the CMS-authorized supplemental rebate agreement, allowing the MCO to keep the savings generated by the supplemental rebates.

The Affordable Care Act amendment to section 1927(b)(1)(A) of the Act also prompted some manufacturers to make assumptions with regard to AMP and best price calculations. Specifically, manufacturers made assumptions that all supplemental rebates paid by manufacturers for prescriptions dispensed to Medicaid managed care enrollees should be excluded from the manufacturer's determination of AMP and best price. That included those rebates paid directly to Medicaid MCOs, even if those rebates were not a result of a CMS-authorized SRA, and therefore, not shared with the state or eventually used to offset state drug expenditures prior to claiming FFP from the federal government. Since CMS-authorized SRA is not defined as it is

used at §§ 447.504(c)(19) and (e)(9) and 447.505(c)(7), manufacturers assumed that any supplemental rebates paid based on dispensing to Medicaid managed care enrollees are always a part of a CMS-authorized SRA with the states. However, rebates paid to Medicaid MCOs may be paid by manufacturers that are not part of a CMS-authorized SRA and are not shared with the state to offset drug expenditures prior to claiming FFP. Therefore, to clarify that such rebates paid by manufacturers are not part of a state's CMS-authorized SRA, in the June 2020 proposed rule, we proposed to define CMS-authorized supplemental rebate agreement to mean an agreement that is approved through a SPA by CMS, which allows a state to enter into single and/or multi-state supplemental drug rebate arrangements that generate rebates that are at least as large as the rebates set forth in the Secretary's national drug rebate agreement with drug manufacturers.

Furthermore, and consistent with section 1927(b)(1)(B) of the Act which provides that the amounts received by a state under paragraph (a)(1) (federal rebates) or an agreement under paragraph (a)(4) (the existing state rebates) in any quarter shall be considered to be a reduction in the amount expended under the state plan in the quarter for medical assistance for purposes of section 1903(a)(1) of the Act. As proposed, the definition further stated that the revenue from these rebates must be paid directly to the state and be used by the state to offset a state's drug expenditures resulting in shared savings with the federal government.

We received the following comments on the proposed definition of CMS-authorized SRA:

Comment: A few commenters requested that CMS confirm that the proposed definition of CMS-authorized SRA permits states and manufacturers to negotiate VBP arrangements with the state Medicaid program's approval and in compliance with this definition, without requiring further levels of approval or submission of a SPA. Another commenter further requested that CMS reinforce the need for states to obtain CMS approval prior to implementing changes to supplemental rebate policies.

Response: The proposed definition of CMS-authorized SRA permits the states and manufacturers to negotiate VBP arrangements; however, state Medicaid programs must seek approval via the SPA process to enter into a CMS-authorized SRA, including SRAs that reference VBP arrangements. We have

also encouraged states and manufacturers to consider negotiating supplemental rebates as part of VBP arrangements by directing them to review the September 18, 2002 State Medicaid Director Letter regarding supplemental rebates and seek authorization under section 1927(a)(1) of the Act from CMS to ensure compliance with section 1927 of the Act when entering directly into SRAs with manufacturers.²⁰

Comment: One commenter requested that CMS revise the first sentence of the definition to state that CMS-authorized SRA means an agreement that is approved through a SPA by CMS, which allows a state to enter into single and/or multi-state supplemental drug rebate arrangements that may generate rebates in addition to the rebates set forth in the Secretary's national rebate agreement with drug manufacturers. Another commenter requested CMS to revise the definition to clarify that rebates may fall within the definition of CMS-authorized SRA regardless of their amount and that a SRA may be approved by CMS as long as the combined rebate payment under the supplemental and national rebate agreements is greater than or equal to the rebate under the national rebate agreement alone.

Response: In the September 18, 2002 State Medicaid Director letter regarding supplemental rebate agreements, CMS directed that states seek CMS approval under section 1927(a)(1) of the Act to enter directly into agreements with manufacturers and in doing so, must ensure that any such agreement will achieve drug rebates that are at least equal to the rebates set forth in the Secretary's rebate agreements with manufacturers.²¹ We continue to believe this is an appropriate interpretation of the statute, and thus, we are not revising the definition of CMS-authorized supplemental rebate agreement as suggested by the commenters.

Comment: A few commenters recommended CMS clarify that any VBP arrangements that states already entered into with manufacturers will continue to be treated as "CMS-authorized supplemental rebate agreements", and therefore, exempt from Best Price and AMP calculations. Another commenter also requested that CMS provide confirmation that states will be permitted to use SRAs but would not be required to use the pre-approved

template. One commenter recommended that CMS provide additional guidance to enhance SRAs to align with flexibilities granted under the rule.

Response: States that have entered into CMS-authorized VBP SRAs have submitted a different template through the SPA approval process than that used under traditional non-VBP supplemental rebate agreements. Thus, states may have both a SRA approved for a non-VBP based template as well as a VBP-based template. Once CMS approves either template, rebates provided for under agreements entered into between states and manufacturers are exempt from best price. States do not need to submit a SPA to take advantage of the multiple best price VBP approach as described in this final regulation. However, a state could negotiate its own VBP arrangement outcomes based rebate approach under a CMS-authorized SRA, and those rebates would be exempt from Medicaid best price.

Comment: A few commenters supported CMS' proposed definition of CMS-authorized SRA with one commenter specifically recommending that CMS require any Medicaid MCO to utilize only CMS-authorized SRAs.

Response: Medicaid MCOs may enter into their own SRAs with manufacturers, but as noted in this rule, only prices pursuant to CMS-authorized SRAs would be exempt from best price. If a Medicaid MCO enters into their own SRAs with manufacturers, such prices are not exempt from best price. This rule does not address the types of SRAs a Medicaid MCO may enter into, and thus, a MCO is not required to only utilize CMS-authorized SRAs.

Comment: One commenter stated that although they generally support the proposed definition of CMS-authorized SRA, they also requested that CMS edit the definition as follows: "Revenue from these rebates must be paid directly to the state under section 1927 of the Act and be used by the state to offset a state's drug expenditures resulting in shared savings with the Federal government." The commenter noted this will ensure consistency with the existing regulations (see §§ 447.504(c)(19) and (e)(9) and 447.505(c)(7)).

Response: We appreciate the comment but believe the phrase "under section 1927 of the Act" is not necessary since it is already included in the exclusions listed in the determination of AMP and best price regulations at §§ 447.504(c)(19) and (e)(9) and 447.505(c)(7).

Comment: One commenter urged CMS to expressly confirm that a manufacturer may exclude rebates paid under a CMS-authorized SRA from AMP and best price, without having to verify that the rebate payments are in fact "used by the state to offset a state's drug expenditures" citing their belief that it would not be reasonable to hold manufacturers accountable for how a state uses a rebate payment.

Response: We agree that it is the responsibility of the state, not the manufacturer, to ensure that rebates paid by manufacturers under the CMS-authorized SRA are used by the state to offset a state's drug expenditures resulting in shared savings with the federal government. Manufacturer rebates paid under a CMS-authorized SRA must be excluded from AMP and best price in accordance with §§ 447.504(c)(19) and (e)(9) and 447.505(c)(7).

Comment: Several commenters disagreed with the language in the proposed definition of CMS-authorized SRA that states "Revenue from these rebates must be paid directly to the state". A few commenters recommended that CMS exclude rebates that are reported by MCOs from best price/AMP because the commenter noted rebates reported by MCOs are factored into a state's rate setting process, and therefore, are treated as if they had been received directly by the state.

Response: The issue is whether the rebates that are paid for these covered outpatient drugs are paid in accordance with a CMS-authorized supplemental rebate agreement, and thus exempt from inclusion in the calculation of the manufacturer's AMP and best price, or paid directly to the MCO, and are not exempt from the inclusion in the calculation of the manufacturer's AMP and best price.

As stated in the preamble to this final rule, the definition of CMS-authorized SRA is consistent with section 1927(b)(1)(B) of the Act which provides that the amounts received by a state under paragraph (a)(1) (federal rebates) or an agreement under paragraph (a)(4) (the existing state rebates) in any quarter shall be considered to be a reduction in the amount expended under the state plan in the quarter for medical assistance for purposes of section 1903(a)(1) of the Act. The proposed definition provides that these rebates must be paid directly to the state which the states then use to offset its drug expenditures, resulting in shared savings with the federal government. Therefore, any manufacturer rebate revenue collected by the MCOs on behalf of the state that are part of any

²⁰ <https://www.medicare.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/state-releases/state-rel-176.pdf>.

²¹ <https://www.medicare.gov/sites/default/files/Federal-Policy-Guidance/downloads/smd091802.pdf>.

CMS-authorized SRAs must be shared with the state directly in accordance with section 1927(b)(1)(B) of the Act. We also do not agree that manufacturers should exclude rebates that are directly paid to MCOs outside a CMS authorized supplemental rebate reported by MCOs from AMP or best price. That is because they are not provided directly to the state by the manufacturer under a CMS-authorized supplemental rebate agreement.

Comment: One commenter noted that Medicaid MCOs are critical in maintaining the cost-effectiveness and quality of care for the Medicaid program through medication adherence, care coordination, and timely provider interventions, and stated that it is critical that MCOs are retained as important partners during negotiations between states and manufacturers.

Response: This comment is outside the scope of this regulation.

In consideration of the comments received, we are finalizing the definition of CMS-authorized SRA at § 447.502 as proposed, to mean an agreement that is approved through a SPA by CMS, which allows a state to enter into single and/or multi-state supplemental drug rebate arrangements that generate rebates that are at least as large as the rebates set forth in the Secretary’s national rebate agreement with drug manufacturers. Revenue from these rebates must be paid directly to the state and be used by the state to offset a state’s drug expenditures resulting in shared savings with the federal government.

D. Exclusion of Certain Manufacturer Sponsored Patient Assistance Programs (“PBM Accumulator Programs”) From Determination of Best Price (§ 447.505) and AMP (§ 447.504)

Manufacturers participating in the MDRP are required to report certain pricing information to the Secretary, including a COD’s best price and AMP. Best price is defined at section 1927(c)(1)(C) of the Act to mean, for a single source or innovator multiple

source drug of a manufacturer (including the lowest price available to any entity for any such drug of a manufacturer that is sold under a NDA approved under section 505(c) of the FFDCFA), the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, HMO, nonprofit entity, or government entity within the United States, subject to certain exclusions. Section 1927(c)(1)(C)(ii) of the Act further defines the term best price to be inclusive of cash discounts, free goods that are contingent on any purchase requirement, volume discounts, and rebates (other than rebates under this section). The definition of best price is further defined at § 447.505(a) and includes the lowest price available from the manufacturer during the rebate period to any provider, which is defined to mean a hospital, HMO, MCO, or entity that provides coverage or services to individuals for illnesses or injuries or providers services or items in the provision of healthcare. Paragraph (b) further indicates that best price includes all prices, including applicable discounts, rebates, or other transactions that adjust prices either directly or indirectly to the best price eligible entities in paragraph (a).

We have learned that some health plans (which meet the definition of provider when determining best price) are being instructed or encouraged by their PBMs to apply manufacturer sponsored patient assistance programs, such as patient copay assistance programs, to the benefit of the plan, instead of entirely to the patient. (Note that Medicaid patients are not eligible for these manufacturer sponsored programs, but the administration of these programs by commercial health plans and PBMs can affect the rebates that the Medicaid program receives from the manufacturer-sponsor of these programs.)

For example, certain PBMs have instructed health plans to not allow the manufacturer-sponsored patient

assistance to be applied towards a patient’s plan deductible for a brand name drug not on a plan’s formulary. PBMs contend that such programs steer consumers towards more expensive medications when there may be more cost saving options, such as generic substitution. Therefore, PBMs offer health plans that are commonly referred to as PBM accumulator programs and tout them as cost saving measures. For instance, using a copayment assistance card program as an example, instead of applying the manufacturer sponsored patient assistance program in a manner that bestows the entire benefit of the program to the patient or consumer, and ensures no contingency on a purchase requirement, as applicable, the PBM (on behalf of the plan) identifies when a copayment card is used by a patient and adjusts the beneficiary’s deductible only in instances when the out-of-pocket contribution is made by the beneficiary. As a result, the manufacturer-sponsored assistance does not accrue towards a patient’s deductible and the patient sometimes does not realize this until the manufacturer copayment assistance runs out and the patient receives a significantly larger bill for the drug. This results in the health plan delaying the application of its plan benefit to the patient to the detriment of the patient or consumer, thus generating savings for the plan. We provide the following example in this rule:

Example:

Assume: \$2,500 Drug cost
 \$2,500 Patient Deductible
 \$10,000 Copayment Assistance Program Maximum

In the no PBM accumulator scenario below, the manufacturer’s copayment assistance accrues to the benefit of the patient because the patient has a high deductible, which is what we believed the manufacturer intended. In such cases, it is clear that the manufacturer’s program is directly assisting the patient’s copayment/deductible costs.

TABLE 1—COPAY ASSISTANCE PROGRAM WITH NO PBM ACCUMULATOR PROGRAM

	Jan	Feb	Mar	Apr	May	June
Plan Pays	\$0	\$2,000	\$2,000	\$2,000	\$2,000	\$2,000
Patient Pays	25	\$25	25	25	25	25
Manufacturer Pays	2,475	\$475 deductible reached. Manufacturer only pays \$475.	475	475	475	475

In the PBM accumulator scenario in Table 2, the PBM does not apply the manufacturer’s copayment assistance to the deductible of the patient thus delaying the patient satisfying his or her

deductible, which benefits the health plan. The patient usually is not aware of the change until he is subject to a larger cost share of the drug when the manufacturer’s support copay benefit

maximum is reached (see May column). At that time, the patient receives a significantly larger bill.

TABLE 2—COPAY ASSISTANCE PROGRAM WITH PBM ACCUMULATOR PROGRAM

	Jan	Feb	Mar	Apr	May	June
Plan Pays	\$0	\$0	\$0	\$0	\$0	\$2,000
Patient Pays	25	25	25	25	\$2,400	500
Manufacturer Pays	2,475	2,475	2,475	2,475	100 manufacturer copay benefit max. reached	0

As demonstrated in Table 2, the health plan is benefiting from the manufacturer sponsored copay assistance program instead of the patient (consumer). However, manufacturers, in these instances, claim they are not aware of when these practices by the health plans take place, and therefore, make reasonable assumptions that their discount programs meet the criteria at § 447.505(c) that exclude such programs from best price.

Specifically, manufacturers make reasonable assumptions that their programs meet the best price exclusions listed in § 447.505(c)(8) through (12) which provide:

- Manufacturer-sponsored drug discount card programs, but only to the extent that the full value of the discount is passed on to the consumer and the pharmacy, agent, or other entity does not receive any price concession (§ 447.505(c)(8)).

- Manufacturer coupons to a customer redeemed by a consumer, agent, pharmacy, or another entity acting on behalf of the manufacturer; but only to the extent that the full value of the coupon is passed on to the consumer, and the pharmacy, agent, or other entity does not receive any price concession (§ 447.505(c)(9)).

- Manufacturer copayment assistance programs, to the extent that the program benefits are provided entirely to the patient and the pharmacy, agent, or other entity does not receive any price concession (§ 447.505(c)(10)).

- Manufacturer-sponsored patient refund or rebate programs, to the extent that the manufacturer provides a full or partial refund or rebate to the patient for out-of-pocket costs and the pharmacy, agent or other entity does not receive any price concession (§ 447.505(c)(11)).

- Manufacturer-sponsored programs that provide free goods, including but not limited to vouchers and patient assistance programs, but only to the extent that the voucher or benefit of such program is not contingent on any other purchase requirement; the full value of the voucher or benefit of such program is passed on to the consumer; and the pharmacy, agent or other entity does not receive any price concession (§ 447.505(c)(12)).

As discussed in the June 2020 proposed rule, we understand from some manufacturers that they do not monitor or place parameters around how the benefits of their manufacturer-sponsored assistance programs are applied when an individual has health plan coverage. Therefore, we proposed to revise these paragraphs to provide expressly that the exclusions discussed in this rule apply only to the extent the manufacturer ensures the full value of the assistance or benefit is passed on to the consumer or patient. We believe manufacturers have the ability to establish coverage criteria around their manufacturer-sponsored assistance programs to ensure the benefit goes exclusively to the consumer or patient. We noted that nothing in the proposed change should be construed to contradict any OIG guidance. We welcomed comments on the proposal.

The current list of prices excluded from best price as noted in this rule also apply to AMP as specified in § 447.504(c) and (e). As stated in the COD final rule, to provide consistency between the AMP and best price sections, where applicable, and to help with streamlining and clarifying a manufacturer's price reporting responsibilities, the same methodology is applied to AMP (81 FR 5253), and for the same reasons already discussed in this rule, we proposed making corresponding changes for these exclusions in the context of AMP.

Accordingly, we proposed to revise the determination of best price § 447.505 to add a requirement that manufacturers ensure that the benefits of their assistance programs as provided at § 447.505(c)(8) through (12) are provided entirely to the consumer and proposed corresponding changes to the AMP regulations at § 447.504(c)(25) through (29) and (e)(13) through (17).

We received several types of comments on the issue of whether the manufacturer should ensure that the benefits of their assistance programs be provided entirely to the consumer, or are actually passed through to the patient. These comments could, in general, be grouped into the following categories: (1) Impact on Patients; (2) Legal Authority; (3) Existence of Mechanisms to Assist Manufacturers with Compliance; (4) Viability of

Manufacturer Assistance Programs; and (5) Impact on other Federal Programs and Policies.

We provide responses to the following comments on the exclusion of certain manufacturer sponsored patient assistance programs (“PBM Accumulator Programs”) from determination of best price (§ 447.505) and AMP (§ 447.504).

(1) Impact on Patients

Comment: Several commenters supported the proposals for manufacturers to account for patient assistance in Medicaid best price reporting when it is not passed through to the patient, and shared CMS' concerns about the role that health carriers and PBMs play in manipulating manufacturer-sponsored assistance programs, and wanted to ensure financial assistance benefits flowed to the patient and not the health plan.

Response: It is our understanding that PBM Accumulator Programs shift costs back to the patient prematurely by not applying the full value of the manufacturer-sponsored assistance to a patient's health plan deductible. Upon exhaustion of the value of the manufacturer's assistance (manufacturer sponsored drug discounts, coupons, copayment assistance or refund/rebate programs) the beneficiary of the manufacturer-sponsored assistance must pay the remaining amount of their deductible for the drug before the plan's benefit begins. We believe the final rule will encourage manufacturers to ensure the full value of manufacturer-sponsored assistance is extended to the patient, as described in greater detail below.

Comment: A few commenters expressed concern that CMS equates the “full” value and “exclusive” benefit of a manufacturer assistance program with reducing the patient's deductible and maximum out-of-pocket obligation and stated that there is no factual or statutory basis for this proposition. A few commenters stated that regardless of whether a patient is subject to a PBM accumulator program that appropriates part of their assistance, the patient has received the full benefit of manufacturer assistance as long as the manufacturer has helped the patient meet their point-of-sale cost and that manufacturers have

no control over what happens to the benefit after the point-of-sale. One commenter stated that CMS is not entitled to make the conclusion without any supporting evidence that manufacturers allow or acquiesce to a diversion of the manufacturer-sponsored assistance away from the patient to the plans when PBM accumulator adjustment programs are used.

Response: We do not agree with the commenter that, as long as the manufacturer has helped the patient receive manufacturer assistance at the point-of-sale, the patient has received the full benefit of manufacturer-sponsored assistance. By not applying the manufacturer assistance to a patient's deductible or other cost sharing obligations to obtain the drug, the assistance becomes a price concession to the health plan by delaying the point at which the health plan's contribution toward the patient's cost sharing begins, or reducing the value of the assistance to the patient, and thus should be counted in best price and, in certain cases, the calculation of the AMP. When the patient does not receive the full value of the manufacturer's assistance, the end result is that:

- The patient may be subject to a significant out-of-pocket drug bill in the event the manufacturer-sponsored assistance ends in the middle of the plan year, and the patient finds out that he or she is still in the deductible phase of a benefit. If this happens, the patient may need to switch to the less expensive alternative offered by the plan or pay the full bill for the non-formulary or non-preferred drug, neither of which are patient friendly scenarios.

- The patient is unaware of the other more cost effective drugs that his/her health plan offers on its drug formulary at the time that the original prescription is filled. Since the patient likely presents at the pharmacy with the manufacturer-sponsored assistance card, the manufacturer-sponsored assistance is automatically applied by the pharmacy (electronically) and the beneficiary is not made aware of other less expensive drug treatments offered by the health plan. In other words, it is not transparent to the patient at the pharmacy (point-of-sale) which drug may be more affordable to the patient in the long run.

Comment: Several commenters expressed concern about the impact of the proposal on patients with rare, life-threatening illnesses or complex chronic conditions who rely on discounts and copay assistance to access specialty medications, and disagreed that patient

assistance steers consumers towards more expensive medications because there is often no generic alternative or clinically appropriate substitute. Many commenters raised concerns about the potential impact of the proposals in this section on medication adherence, medical complications, outcomes, and hospitalizations and requested CMS to take patient's special needs into consideration.

Response: We do not believe that the final policies we are adopting in this final rule will negatively impact patients with rare, life-threatening illnesses who rely on manufacturer assistance programs. Rather, we do believe that there is a corollary benefit to this proposed policy, as it might lead to reforms in manufacturer assistance programs. We understand from many manufacturers and patient groups that PBM accumulator programs are increasing in number, and that the value of these programs to the patient is diminishing. It is not clear how these programs can continue to benefit patients without some modifications and reforms.

We believe manufacturers can implement a system to ensure the full benefit of its manufacturer-sponsored assistance passes on to the patient. By doing so, patients will continue to have access to much needed medication which will in turn increase positive outcomes and also improve adherence.

We are aware of situations when a patient has been subject to significant out-of-pocket costs because the patient has not progressed through the deductible phase of the health plan. That is because the value of the manufacturer-sponsored assistance was not applied to the patient's deductible. When this happens, the patient may be forced to stop taking the drug, switch to an alternative offered by the plan, or pay the full bill for the non-formulary drug, none of which are patient-friendly, especially for those patients with rare and life threatening conditions. The policies we are adopting in this final rule could help avoid these concerns because it will improve transparency in drug pricing and will ensure that the full value of the manufacturers-sponsored assistance programs is passed on to the patient. We believe this will also help assure patient compliance and adherence with medications.

Comment: Several commenters expressed concern that the proposed rule would encourage expansion of PBM accumulator programs and stated that if the federal government continues to permit PBMs to profit from the use of PBM accumulator programs, then manufacturers will either have to set

higher prices for new drugs to offset these incremental profits, or withdraw manufacturer-sponsored assistance altogether, resulting in harm to patients.

Response: We understand the concerns about PBM accumulator programs and the impact on manufacturer prices. As noted above, the current regulations at 42 CFR 447.504 and 447.505 already require that best price and AMP exclude manufacturer-sponsored assistance programs (copayment, patient refund/rebate, coupons, discount card programs) when the full value of the assistance is passed on to the consumer, and the pharmacy, agent or other entity does not receive any price concession.

The goal of this final policy is to not affect drug manufacturers' prices, but to make sure that Medicaid programs receive the rebates that they are owed from manufacturers if any value of the manufacturer assistance is accruing to a "best price" eligible entity rather than the patient. It is possible that manufacturers, knowing that any assistance not being passed through would have to factor in their Medicaid rebates, will improve their oversight of these manufacturer assistance programs such that they will not have to pay higher rebates to Medicaid. This could actually lead to lower drug prices, and increase the amount of manufacturer assistance that will actually go to patients. This will help reduce the potential for patient harm resulting from a lack of compliance with medications if the patient cannot afford them because they are not receiving the full value of their cost sharing assistance.

Thus, we believe the proposed rule and the policies we are adopting in this final rule will encourage manufacturers to monitor and track their manufacturer-sponsored assistance programs to ensure the full value of the manufacturer-sponsored assistance goes to the consumer and not to health plans.

Comment: Several commenters noted that another justification for prohibiting or increasing oversight of PBM Accumulator Programs is the surprise impact of receiving a significantly larger bill for the drug than expected due to lack of patient awareness of PBM policies that do not count manufacturer-sponsored assistance towards patient cost-sharing obligations.

A few commenters recommended requiring plans to give notice to a patient of its intent to withhold third party funds, and explain in plain language what benefits accrue to the patient, how manufacturer assistance will be affected and applied, and account for third-party assistance, as a potential alternative to the proposals in

this section. One commenter supported a policy alternative requiring health plans and PBMs to apply price reduction instruments for out-of-pocket expenses when calculating an insured individual's cost-sharing requirement.

Response: We appreciate the comments regarding the identification of certain mechanisms to increase patient awareness that the health plan that they are enrolled in may use a PBM accumulator program. We agree with the many comments that we received expressing concern about the impact of these programs on patients, including the sudden impact that such programs can have on patient out-of-pocket spending for their drugs, and lack of patients' awareness of the existence of such programs.

We are only able to regulate this issue within the scope of the Medicaid drug rebate program rules. That is, under the MDRP, the manufacturer can only exclude manufacturer assistance that is fully passed through to a patient/consumer from the calculation of best price, and when applicable, AMP for 5i drugs. We believe the final policies adopted in this rule will help ensure the full benefits of the manufacturer-sponsored assistance program are passed on to the patient, which hopefully, will have the added benefit of reducing some of the negative consequences that patients have faced as a result of manufacturers not making such assurances related to PBM accumulator programs.

Comment: Several commenters supported CMS' proposals on the basis that they may reduce spending on prescription drugs and noted that the use of manufacturer sponsored coupons and similar arrangements are designed to increase drug spending, needlessly drive consumers to high cost treatments and circumvent utilization management tools adopted by health plans. Several commenters stated that manufacturer copay coupons create anti-competitive effects, market disruptions, unreliable access for patients, and undermine more affordable generic or biosimilar drugs, and viewed CMS proposals as an effort to prevent manufacturers from increasing drug prices without market constraints.

Response: We appreciate the comments and agree that manufacturer-sponsored assistance may increase drug spending by circumventing health plan utilization management tools and steering patients towards more expensive treatments not necessarily covered by a patient's plan. We are also concerned that patient out-of-pocket spending will increase significantly when the manufacturer-sponsored

assistance runs out, and patients are required to pay for the drug in full much earlier than anticipated. We believe that this rule will encourage manufacturers to examine the structures of their manufacturer-sponsored assistance program(s) so that patients are not surprised by high drug costs when all or part of the cost sharing assistance is passed through to the plan rather than the patient.

Comment: A few commenters defended the existence of PBM accumulator programs as necessary to ensure that benefits will be administered as they are designed, rather than artificially reducing deductibles for patients on specific high cost drugs.

Response: We are aware that PBM accumulator programs are used by health plans to ensure their benefits are administered as they are designed. However, these PBM accumulator programs often do not allow for the full benefit of the manufacturer-sponsored assistance to accrue to the patient. This regulation requires that the manufacturer be aware of this action taken by the PBM so that the manufacturer complies with the regulations that set forth the determination of AMP and best price for the purposes of the MDRP.

Comment: One commenter cited several studies, one of which showed that for 23 branded drugs studied, coupons were associated with a 3.4 percent decrease in the rate of generic utilization and an estimated excess spending of 1.2 percent to 4.6 percent higher total drug spending over 5 years and requested that this be considered a well-documented problem rather than attributing concerned statements only to health plans and PBMs.

Response: We appreciate the information regarding the impact of manufacturer-sponsored assistance programs have on drug benefits and spending. However, as noted above, we believe the final policies adopted in this rule will ensure that the full benefits of the manufacturer-sponsored assistance program pass on to the patient, and that the exclusions to best price and AMP are applied appropriately.

Comment: A few commenters stated that PBM accumulator programs do not only apply to brand name drugs not on a plan's formulary, but to all drugs.

Response: We agree that PBM accumulator programs do not apply only to single source brand name drugs. The use of brand name drugs in the rule was an example of a particular situation where the PBM does not apply the benefit of the manufacturer sponsored assistance to the patient's health plan

deductible in circumstances when a health plan's formulary covers a lower cost generic (or brand) alternative. We believe this is one scenario, and not an exclusive example.

(2) Legal Authority

Comment: Several commenters stated that health plan enrollment in a PBM accumulator program, or the existence of the program, has no bearing on manufacturer exclusion of a manufacturer assistance program from AMP and best price. Several commenters stated that requiring manufacturers to include the value of manufacturer assistance that was subsequently taken away from patients by plans in the calculation of best price is contrary to the statutory definition of best price because patient assistance is not a price, or a price concession that is available from a manufacturer to plans. A few commenters suggested that to be consistent with CMS' prior interpretations of the statute, patient assistance can only be viewed as a price concession when the manufacturer develops that program specifically for patients of a particular payer or PBM, but absent such negotiation or coordination, and the assistance is not "designed to" adjust prices to the payer or PBM, then the assistance should be excluded from AMP and best price.

Several commenters noted that CMS lacks statutory authority for the proposals in this section, that they are based on erroneous interpretation of the Medicaid drug rebate statute, or that they are based on unexplained or unsupported assumptions, and thus requested that CMS rescind the proposals related to including patient assistance programs in best price and AMP unless manufacturers "ensure" that their assistance solely benefits patients and does not benefit third parties. These commenters noted that CMS has not articulated an overall context or reasoning behind their proposed change in treatment of manufacturer sponsored patient assistance programs, specifically the intended outcome for these changes and how this approach would achieve those goals. One commenter stated that implementation of such a dramatic change in the assistance available to patients across the country should not occur without additional explanation accompanied by concrete data and evidence to support it. A few commenters stated that basing the proposals in this section on what one group of commenters "contend" constitutes an "unsupported and conclusory statement" that renders

CMS' proposals arbitrary and capricious within the meaning of the APA.

Some commenters stated that it is unfair, infeasible, and contrary to statutory intent to hold manufacturers responsible for ensuring that the discount goes exclusively to the consumer or patient when manufacturers are not involved in the application of tools that change how assistance is applied to the patient's insurance benefit, and therefore, cannot monitor or place parameters around them. For these reasons, several commenters stated that these proposals cannot be operationalized if made final and that the agency's proposals are arbitrary and capricious.

Response: We do not agree with the commenters that manufacturer-sponsored assistance is not a price, or a price concession that is available from the manufacturer to the plans, in situations when health plans participate in PBM accumulator programs, and then the value of the assistance does not accrue in full to the patient. Nor do we agree that this proposal is arbitrary and capricious, as current regulations already provide that manufacturers can only exclude manufacturer-sponsored assistance if it is being passed through to the patient. See §§ 447.504(c) and (e) and 447.505(c).

Manufacturers are fully aware of the existence of PBM accumulator programs, and may not have taken action to date to address the potential that they may already be reporting in violation of the regulations at § 447.504(c) and (e) for AMP and § 447.505(c) for the calculation of best price. These sections of the regulation have always stated that the manufacturer-sponsored assistance (coupons, free goods, discounts, refund/rebate programs and copay assistance) exclusions apply only if such assistance is passed on to the consumer and the pharmacy, agent, or other AMP/best price eligible entity does not receive any price concession. In cases where the PBM accumulator programs do not allow any manufacturer-sponsored assistance to apply to the beneficiary' deductible, the health plan is receiving a price concession in the form of delaying the health plan's obligation to provide coverage of the drug under the patient's health plan benefit. This postponement in providing benefits to the patient, or the accrual of the benefit to the plan in whole or part, is a price concession to the health plan.

Since these programs are increasing in scope and number, such that it is no longer the case that such assistance is always passed through to the patient which is an existing requirement, we

believe a change in the regulatory text underpinning this exemption is needed. Under this final rule, manufacturers must ensure that the full value of the manufacturer-sponsored assistance is passed on to the consumer or patient regardless of the specific transactions that occur between payers, pharmacies and PBMs.

We believe that we have the statutory authority for this rule and have explained the overall context or rationale to support our proposed policies and now our final policies. Manufacturers participating in the MDRP are required to report certain pricing information to the Secretary, including a COD's best price and AMP. In the proposed rule, we noted that some health plans (which meet the definition of provider when determining best price) are being instructed or encouraged by their PBMs to apply manufacturer-sponsored assistance programs, such as patient copay assistance programs, to the benefit of the plan, instead of entirely to the patient.

Best price is defined at section 1927(c)(1)(C) of the Act to mean, for a single source or innovator multiple source drug of a manufacturer (including the lowest price available to any entity for any such drug of a manufacturer that is sold under a NDA approved under section 505(c) of the FDCA), the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, HMO, nonprofit entity, or government entity within the United States, subject to certain exclusions. Section 1927(c)(1)(C)(ii) of the Act further defines the term best price to be inclusive of cash discounts, free goods that are contingent on any purchase requirement, volume discounts, and rebates (other than rebates under this section). The definition of best price is further defined at § 447.505(a) and includes the lowest price available from the manufacturer during the rebate period to any provider, which is defined to mean a hospital, HMO, MCO, or entity that provides coverage or services to individuals for illnesses or injuries or providers services or items in the provision of healthcare. Paragraph (b) further indicates that best price includes all prices, including applicable discounts, rebates, or other transactions that adjust prices either directly or indirectly to the best price eligible entities in paragraph (a). We believe the reference to "other transactions that adjust prices either directly or indirectly" to the best price eligible entities in paragraph (a) includes the transactions made by the manufacturer indirectly to health plans via

manufacturer-sponsored assistance programs should be included.

Comment: Several commenters stated that treating patients as best-price eligible entities exceeds the scope of CMS' statutory authority. Several commenters stated the plain language of the statute requires that to be considered for best price calculations as a "price available from the manufacturer," the manufacturer had to intend to offer the price to a best-price eligible entity. However, several commenters stated that the Congress' only intended best price-eligible entities under the statute are purchasers, wholesalers, retailers, providers, HMOs, non-profit entities, and governmental entities. Several commenters further stated that manufacturer-sponsored assistance designed solely to benefit patients and reduce their out-of-pocket costs cannot constitute a "price available from the manufacturer" because the manufacturer did not intend to offer the price to an eligible third party such as the health plan, and therefore should not be required to include the value of assistance in its best price calculations when the health plan denies the manufacturer assistance apply to patients. Other commenters stated that a manufacturer can only have intended to make the price available to eligible entities if the manufacturer negotiated with the PBM to offer manufacturer assistance or designed the manufacturer assistance to benefit the PBM, and further stated that when such coordination, negotiation, or consideration is not present, the assistance cannot be a price "available from" the manufacturer and included in best price. One commenter stated that CMS confirmed that patients are not eligible purchasers in the COD final rule in 2016.

Response: This regulation does not treat patients as best price eligible entities. In accordance with current regulations at § 447.505(c)(8) through (12), prices excluded from best price include manufacturer-sponsored assistance programs, but only to the extent that the full value of the assistance is passed on to the consumer, and the pharmacy, agent or other entity does not receive any price concession (see further discussion on these existing policies in preamble to COD final rule at 81 FR 5254). As proposed and finalized in this rule, these regulations have been revised to require that a manufacturer ensure that the value of the manufacturer's assistance accrues to the benefit of the patient and not the plan (a best price eligible entity) before excluding the value of these assistance programs from the determination of best

price and AMP. As stated in current regulation, the manufacturer's assistance can be excluded from best price only if the full value of the assistance is passed through to the patient/consumer. However, if any of the manufacturer-sponsored assistance is diverted to the plan, those amounts should be included when a manufacturer calculates its best price and AMP in certain cases. This final policy requires manufacturers to ensure the full value is passed on to the consumer, consistent with the regulation.

Comment: A few commenters expressed concern about the impact of the proposals in this section on the ability of manufacturers to continue offering manufacturer assistance programs to individuals in the larger commercial market during the COVID-19 pandemic. These commenters stated that during the PHE and economic crisis, patients and families across the country would experience significant harm if the proposal is finalized and they lose access to medications.

A few commenters stated the proposals are contrary to an Executive Order urging federal agencies to rescind, modify, waive, or provide exemptions from regulations and other requirements that may inhibit economic recovery, consistent with applicable law and with protection of the public health and safety. A few commenters stated that to be consistent with that Executive Order, CMS should reconsider and modify its current policies for PBM accumulator programs and to withdraw the current proposal that would impose new standards for exclusions of manufacturer-sponsored assistance amounts to patients in connection with Best Price and AMP determinations.

Response: Since there is concern with the impact of this policy on manufacturer's ability to provide assistance during the COVID-19 crisis, and manufacturers are also concerned that they may not be able to ensure their manufacturer assistance is going to the patient and not being passed through to the health plan via an electronic means right away, we are finalizing this rule, as proposed, but are delaying the effective date until January 1, 2023. This will give manufacturers time to implement a system that will ensure the full value of assistance under their manufacturer-sponsored assistance program is passed on to the patient, such as contracting with a third party vendor to track their assistance when provided at the point of sale, or changing the structure of their manufacturer-sponsored assistance programs to require patients pay for the

drug first and then have the patient collect the rebate directly from the manufacturer (outside of the electronic claims process). Manufacturers may also choose to revise the manufacturer-sponsored assistance structure by requiring the patient to submit its claim for the manufacturer-sponsored assistance outside of the electronic claims process (this will allow a patient's cost sharing at the point of sale to apply to the patient's deductible because the pharmacy and PBM will be unable to identify that the patient used manufacturer-sponsored assistance.

(3) Existence of Mechanisms To Assist Manufacturers With Compliance

Comment: Several commenters stated that manufacturers do not have knowledge, visibility, or control over programs deployed by PBMs and health plans regarding the pass through of patient assistance, and suggested that CMS focus on imposing program efficiencies on plan managers and PBMs instead. Other commenters similarly stated that manufacturers are not party to arrangements between, nor do they receive consideration from, health plans and PBMs that withhold discounts from patients.

Several commenters stated that the use of PBM Accumulator Programs is a post-transaction or downstream cost adjustment mechanism into which manufacturers have no insight, and pointed to CMS' acknowledgement that even patients are often not aware when they are enrolled in such programs. Several commenters further stated that despite good faith efforts, they do not have access to data, plan policies, or an information exchange with enough specificity on PBM Accumulator Programs on a per-product, per-customer, per-quarter, or per-unit basis, and therefore, have no awareness of which patients are subject to PBM Accumulator Programs and which ones are not. Several commenters further stated that obtaining such data would create new administrative burdens, citing that documents are private, proprietary, or lengthy and complex.

One commenter challenged manufacturer arguments that there would be too many barriers to knowing when their coupons are absorbed by PBM Accumulator Programs and excluded from deductibles, stating that manufacturers can contract with third parties to obtain such data. Several commenters stated that PBM Accumulator Programs only exist to interfere with or prevent manufacturer-sponsored assistance from being applied to the patient's deductibles and maximum out-of-pocket costs from the

consumer, and that instead of ensuring patient accessibility, accumulators penalize patients for using coupons to lower their costs.

Response: We understand the concerns from the commenters that manufacturers may not currently have the ability to track their manufacturer assistance to ensure it is provided in full to the patient. However, we believe that the electronic prescription claims processing infrastructure that is currently in place can serve as a possible foundation for manufacturers to have the ability to ensure their manufacturer-sponsored assistance is going to the patient.

Almost all prescriptions are electronically processed at the pharmacy, and when transmitted from the pharmacy, are routed through a switch to the corresponding PBM based on the information on the patient's prescription card, such as BIN/PCN number. As noted, manufacturers do currently contract with switches and brokers that are electronically connected to this prescription claims processing "highway", and which apply manufacturer-sponsored assistance on the manufacturers' behalf at the point-of-service to reduce the amount that a patient might have to pay for a prescription.

Manufacturers also have relationships with PBMs, given that they pay rebates and other price concessions for formulary placement on the PBMs' formularies. Thus, the electronic and contractual infrastructure is in place for manufacturers to better understand how the PBMs are using the manufacturer assistance. We believe and have the expectation that PBMs will work with manufacturers to provide this information to the manufacturers to help them ensure that their assistance is passed through.

Alternatively, manufacturers may consider redesigning assistance programs to require patients pay for the drug first and then have the patient collect the rebate directly from the manufacturer (outside of the electronic claims process). Revising the manufacturer-sponsored assistance structure by allowing the patient to pay first and bill the manufacturer for the assistance after the claim has been processed will guarantee patient's cost sharing applies to the patient's deductible and that the payer does not receive any price concession from the manufacturer-sponsored assistance. This manual approach also allows the patient at the point-of-sale to consider alternatives offered by their own health plan to the drug offered under the manufacturer-sponsored assistance

program, and therefore, supports the Administration's quest for drug pricing transparency.

Comment: Many commenters stated the proposals in this section are unworkable for manufacturers due to the lack of transparency in PBM accumulator programs and rather than finalizing these proposals, requested that CMS ban the use of PBM accumulator programs entirely, or at least prohibit their use when generic alternatives are not available. These commenters noted that this would directly accomplish CMS' stated goals of ensuring that the full value of assistance be passed along to the patient.

Several commenters also requested CMS to regulate cost sharing, transparency, standards for access to plan information, marketing, and benefit design as a means of protecting patients from the potential negative clinical and financial consequences of PBM accumulator programs. A few commenters stated that PBM accumulator programs should not be necessary since health plans have many guardrails in place to ensure that patients are incentivized to use lower cost medications such as prior authorization and step therapy.

Response: While we appreciate the comments, this final rule only addresses situations when the value of manufacturer-sponsored assistance is not passed through to the patient and how that should be reflected by the manufacturer in the determination of best price and calculation of AMP in certain cases. The proposed rule requires manufacturers ensure that the full value of the manufacturer-sponsored assistance is passed on to the consumer and that the entity, in this case the health plan, does not receive any part of the value of the manufacturer assistance in order for that value to be excluded from best price and AMP. Banning PBM accumulator programs is outside the scope of this rule.

Comment: One commenter expressed concern that the proposed changes to the best price determination might require health plans and PBMs to provide additional information to manufacturers beyond what they already provide and stated that this risks giving manufacturers greater market insight that could be leveraged to circumvent plan designs that encourage use of cost effective drugs in new ways, thereby increasing prices for patients and plans alike. One commenter recommended that CMS clarify that drug manufacturers, not PBMs and health plans, are solely responsible for correctly characterizing

and accounting for amounts attributable to their manufacturer-sponsored assistance programs for the purposes of best price.

Response: This rule does not require PBMs and health plans disclose or disseminate information they believe to be proprietary to manufacturers. Manufacturers that offer assistance only need to know if the patient is receiving the full value of the assistance for their drug (that is, the assistance is being fully counted towards the patient's deductible and cost sharing). The mechanism by which the manufacturer determines whether or not the full value of its assistance is provided to the patient will be determined by the manufacturer, working with its brokers, the PBMs, and plans.

(4) Viability of Manufacturer Assistance Programs With This Policy

Comments: Several commenters expressed concern that the operational challenges to manufacturers would deter them from offering a broad range of manufacturer assistance currently exempt from best price reporting including coupons, drug discount card programs, patient rebate programs and copay assistance.

Several commenters challenged CMS' assertion that manufacturers can establish "parameters" or "coverage criteria" for ensuring the full value of assistance to patients' subject to PBM accumulators, stating that it has no factual support. Several commenters requested further explanation or guardrails on such parameters or coverage criteria from CMS to ensure the provision has its intended effect while protecting people who rely on assistance. A few commenters expressed concern that the proposals in this section would also affect the frequency of government price reporting if manufacturers are expected to investigate on a plan by plan basis every suspicion that manufacturer assistance funds were being appropriated by a health plan. One commenter stated that even diligent checks and oversight cannot reveal every instance of plan or PBM capture or misappropriation of patient assistance funds due to the plan's overall lack of transparency.

Response: We do not agree that this regulation creates an insurmountable burden for manufacturers to comply with this new regulatory requirement. This rule does not place a federal mandate on health plans, insurers, and pharmacies to provide specific data or verify data to manufacturers relating to the operation of their manufacturer-sponsored assistance programs. However, our expectation is that

manufacturers will work with their contracted patient assistance brokers, prescription claims processing switches, health plans and their contracted PBMs to ensure that they have the information necessary to comply with this regulatory requirement.

The mechanism by which manufacturers will ensure that the full value of the manufacturer-sponsored assistance will be going to the patient will be determined by the manufacturer. However, we believe that one of the approaches that manufacturers may be able to use to capture information regarding how their manufacturer-sponsored assistance is used is through an electronic feedback mechanism at the point-of-sale, which appears to be in place at the present time. We believe that the PBMs will have to work with the manufacturers and their switches and brokers to assure that the manufacturers have the information necessary to comply with this regulatory requirement.

Comment: A few commenters expressed concern that there is no way a manufacturer can certify to the accuracy of data obtained by health plans regarding PBM accumulator programs, subjecting manufacturers to penalties for false reporting or non-compliance with the MDRP requirements. One commenter stated that absent a federal mandate for health plans, insurers, and pharmacies to provide certified reports of the PBM accumulator transactions to manufacturers, manufacturers will not be able to provide accurate price reports.

Response: We understand manufacturers concerns regarding certification of the data that they are required to report to comply with MDRP reporting requirements. Manufacturers currently certify data that are required to be reported to us regarding the calculation of AMP and best price. These calculations currently require that manufacturer sponsored assistance programs be passed through to the patient in full in order to be excluded from the calculation of best price and AMP in certain cases. Manufacturers should only be exempting manufacturer-sponsored assistance from their AMP and best price now if the value of its assistance passed onto the patient in full. If manufacturers are certifying their AMP and best price data at this time, which they are required to do each quarter, they should be doing so only with the knowledge that such their manufacturer-sponsored assistance is being passed through to the patient in compliance with applicable statutes and regulations. This final regulation

emphasizes the need for manufacturers to ensure this is happening. As we have stated, it is our expectation that manufacturers will work with the various components of the electronic prescription processing system, such as PBMs, switches, and brokers, among others, to obtain the information they need to accurately determine the pricing benchmarks they need to report each quarter.

Comment: Several commenters requested that CMS not finalize its proposals in this section unless it establishes safe harbors that clearly identify actions that manufacturers can reasonably take to ensure they have met CMS standards. One commenter expressed concern that although manufacturers typically have terms and conditions governing their patient assistance programs, neither PBMs nor plans are a party to those terms and conditions. The commenter suggested that the only way for manufacturers to ensure that the full value of manufacturer copay assistance programs go exclusively to the patient is to create terms and conditions that prohibit a patient's acceptance of manufacturer support when a PBM accumulator program applies. The commenter recommended that if CMS finalizes its proposal, it should expressly state that such a prohibition would be sufficient to meet the regulatory standard if manufacturers are held responsible for ensuring the full benefit of patient assistance passes to the patient.

Response: We appreciate the commenter's suggestion, but do not agree that shifting the burden to patients is necessary for a manufacturer to be able to determine that the full value of manufacturer assistance has been passed through to the patient. Prohibiting patients from accepting assistance unless they know that an accumulator program does not apply in their plan places undue burdens on patients. We do not agree that such a regulatory standard would satisfy the requirement that a manufacturer ensures that manufacturer sponsored patient assistance is passed through to the patient in full before it may be excluded from the calculation of best price or AMP in certain cases. Satisfying this regulatory requirement is the responsibility of the manufacturer, which is the entity that is regulated by CMS. The patient may not understand what an accumulator is, how it works, or whether their health plan's PBM uses an accumulator.

As noted in prior responses, we believe that there may be multiple ways that manufacturers will be able to meet these new regulatory requirements to

ensure that manufacturer patient assistance is passed through fully to the patient or consumer, such as being able to electronically capture information regarding the value of manufacturer-sponsored assistance that is being passed through in PBM accumulator programs through some type of feedback mechanism at the point-of-sale, or by creating coverage criteria for the use of their patient assistance programs.

Comment: One commenter stated that any regulatory language that discourages the use of PBM accumulator programs would have a significant impact on a payer's ability to appropriately manage their prescription drug benefit and leads to increased costs when coupon and copay card amounts must apply to their members' deductibles and out of pocket maximums for certain drugs.

Response: The current regulation already requires that best price and AMP exclude manufacturer-sponsored assistance programs (copayment, patient refund/rebate, coupons, discount card programs) when the full value of the assistance is passed on to the consumer, and the pharmacy, agent or other entity does not receive any price concession. In the interest of program integrity, and to assure that the states receive the rebates that they are due, this final regulation is specifically requiring manufacturers to ensure compliance with that requirement that the manufacturer ensures the full value of the assistance is going to the patient.

We understand that PBMs may be using this accumulator approach to steer patients away from drugs for which lower-cost generics are available, thus potentially impacting the payer's ability to manage their prescription drug benefit if this proposed policy was adopted as final. In that regard, however, we understand that these programs are being used for both single source brands, as well as innovator off patent brands for which there are multiple lower cost generics on the market. However, there is no distinction made in the statute between single source and innovator multiple source drugs for which manufacturers would have to make a best price determination. That is, if a manufacturer's price concession is being realized by a best price eligible entity, whether it is for a single source or innovator multiple source drug, then that price should be considered in the determination of best price.

(5) Impact on Other Federal Programs and Policies

Comment: One commenter expressed concern that the proposals in this section would increase the risk of

manufacturers cutting off vital patient assistance. The commenter requested that we work with the HHS' OIG to revisit rebate pass-through policies to ensure patients benefit directly from manufacturer discounts and rebates provided to PBMs.

Response: We appreciate the comment, but do not agree that the final policy will have the effect of cutting off vital manufacturer assistance because manufacturers should only be exempting manufacturer-sponsored assistance from their AMP and best price now if the value of its assistance passed onto the patient in full. If manufacturers are certifying their AMP and best price data at this time, which they are required to do each quarter, they should be doing so only with the knowledge that such their manufacturer-sponsored assistance is being passed through to the patient in compliance with applicable statutes and regulations. This final regulation emphasizes the need for manufacturers to ensure this is happening.

The request to work with HHS' OIG to revisit other policies is outside the scope of this rule.

Comment: Several commenters suggested in response to CMS' concerns about the impacts of the growing use of PBM accumulator programs that CMS revert to the Notice of Benefit and Payment Parameters 2020 (NBPP 2020) proposals (85 FR 78572). Several commenters stated that CMS initially proposed to prohibit the use of PBM accumulator programs when the patient was prescribed a brand name medication for which a generic alternative was not available, and made clear that cost-sharing support for a brand drug on the formulary would always count toward the annual limitation on cost sharing. Several commenters noted that they preferred this earlier proposal, stating it would be simpler and more effective for creating guardrails to ensure provisions on cost-sharing assistance have their intended effect and to mitigate the harmful effects of such programs on patients.

Several commenters also noted that the proposals conflict with the recent Notice of Benefit and Payment Parameters Rule for 2021 final rule (85 FR 29164), that permitted, but did not require, issuers to count toward the annual limitation on cost sharing amounts paid toward reducing out of-pocket costs using any form of direct support offered by drug manufacturers to enrollees for specific prescription drugs. Several commenters stated that CMS did not provide that same degree of flexibility to plans in the proposed rule, and instead, preferred that

assistance programs are counted towards the patient's deductible. One commenter stated that the differing approaches in the two regulations create operational complications for plans participating in both the Marketplace and Medicaid programs, as they have different requirements under each program as it relates to the treatment of patient assistance programs, and expressed concern this would lead to competitive disadvantages for plans that operate in both spaces. A few commenters stated that it is important for plans to have the flexibility to manage pharmaceutical copay assistance programs, as such programs often incentivize enrollees to utilize more expensive medications and stated that the proposals in this section undermine formulary and benefit design and results in higher health care costs.

Response: The CMS Medicaid drug rebate program requires that manufacturers only exclude the value of manufacturer sponsored assistance to patients from the best price when the value of the assistance is passed through to the patient in full. This requirement is the focus of this rulemaking. In the Notice of Benefit and Payment Parameters Rule for 2021 final rule (hereinafter referred to as "2021 NBPP"), we permitted, to the extent consistent with state law, but did not require, issuers to count toward the annual limitation on cost sharing amounts paid toward reducing out-of-pocket costs using any form of direct support offered by drug manufacturers to enrollees for specific prescription drugs.

The policies we are adopting in this rule require manufacturers ensure that the full value of their assistance programs is passed on to the consumer, and the entity, in this case the payer, does not receive any price concession. In cases when some of the value goes to the payer, manufacturers must include the value of the assistance in their determination of best price and AMP.

In the 2021 NBPP, we stated that issuers and group health plans are allowed to continue longstanding policies with regard to how direct drug manufacturers' support accrues towards an enrollee's annual limitation on cost sharing. When the issuer does not permit the patient to realize the full benefit of the manufacturer's assistance, manufacturers must not exclude such amounts from best price calculations. We suggest ways that manufacturers can become aware of such circumstance and thus include the assistance as a price concession in the manufacturer's determination of best price and AMP. However, we are not prescribing a way

that this should be done. The policies we are adopting in this final rule will require manufacturers to ensure that the full benefit of the assistance program goes exclusively to the patient in order for the manufacturer to exclude the manufacturer's assistance from the calculation of best price and AMP. To allow manufacturers to develop mechanisms to obtain the information necessary to know whether the assistance has been in fact passed through to the patient, we are delaying the effective date for this requirement until January 1, 2023.

Comment: A commenter noted that there is no inherent False Claims Act risk in price reporting by properly treating coupon amounts as price concessions.

Response: The determination of whether a manufacturer is at risk of violating the False Claims Act is outside of the scope of this final rule.

Comment: A few commenters noted the proposal to include manufacturer-sponsored assistance in reporting for AMP, unless the manufacturer ensures the full value is passed on to the patient, would result in lowering the AMP, which in turn would lower manufacturers' rebate liability under the MDRP. These commenters stated that CMS' proposal may encourage manufacturers to set higher list prices and offer coupons, rather than simply starting with a lower list price, while not having any greater rebate liability under the MDRP. One commenter provided an example of a drug priced at \$10,000 with the offer of a \$5,000 coupon from the manufacturer, and stated that in order for that \$5,000 to be deducted from AMP, the full value must be passed directly to the patient under the proposal. The commenter expressed concern that this could mean the \$5,000 manufacturer copay assistance must count toward the patient's annual deductible and/or maximum out-of-pocket (MOOP) spending and that such a policy may incentivize utilization of higher-priced pharmaceutical products and increase overall health care spending. The commenter also noted that if the discount does have to apply towards the patient's deductible or MOOP, then the drug manufacturer would have subverted the patient's formulary and benefit design by skewing product choice and insulating the patient from financial liability intended to encourage responsible health care decision-making. The commenter suggested in contrast, if the manufacturer set the list price at \$5,000, the net price would be the same as the higher priced drug as reduced by the

coupon, and the AMP would be the same.

A few commenters expressed concern that CMS' proposal to ensure that the full value of manufacturer-sponsored assistance is passed through to the patient in order for it to be excluded from calculations of best price and AMP would have negative downstream effects on ASP and the 340B ceiling price. These commenters noted that CMS' proposals in this section could result in the inclusion of patient assistance in ASP leading to a reduction in ASP and payer reimbursement in this rule acquisition costs. These commenters stated that in order for drug reimbursement rates not to fall below their costs, manufacturers would discontinue assistance programs and harm patients in need.

One commenter stated that the ASP statute and regulations require that 103 percent of AMP be substituted for the ordinary Part B payment rate (106 percent of ASP) if the ASP for a drug exceeds AMP by 5 percent or more for 2 consecutive quarters, meaning that a decline in AMP could cause such a substitution and thus reduce the Part B drug payment rate. The commenter stated that reducing a drug's Part B payment rate (either through a decline in ASP or through a substitution of 103 percent of AMP) could have detrimental effects on Medicare Part B providers and could hinder patient access to critical drugs.

Response: We do not believe this final rule will have a significant impact on Part B drug payments. First, under section 1927(k)(1) of the Act, AMP is defined as the average price paid to manufacturers for a covered outpatient drug by wholesalers for drugs distributed to retail community pharmacies, as well as for drugs that retail pharmacies purchase directly from manufacturers. The calculation for AMP excludes payments to insurers as found at section 1927(k)(1)(B)(IV) of the Act, meaning these sales (with applicable exclusions) are not reflected in AMP.

However, many Part B drugs can also be classified as "5i" drugs under the MDRP, that is, instilled, infused, injected, intraocular, and implanted drugs. The manufacturer's calculation of the AMP for 5i drugs includes a broader set of manufacturer's transactions, including sales, nominal price sales and associated discounts, rebates, payments or other financial transactions to insurers. Thus, the 5i AMP for a drug, may be impacted if the manufacturer fails to ensure that the full value of its manufacturer-sponsored assistance accrues to the patient and the insurer realizes a price concession. In

circumstances when the manufacturer does not assure that the manufacturer assistance is passed through to the patient in full, and thus has to be included in the calculation of 5i AMP for the drug, such a situation could possibly reduce 5i AMP and impact Part B reimbursement.

However, since not all sales of a manufacturer's 5i drug utilizes a manufacturer-sponsored assistance program, we do not believe the amount associated with the manufacturer-sponsored assistance (value of discounts, coupons, rebates) will impact 5i AMP significantly to result in the substitution of AMP to the detriment of Medicare Part B providers and access to critical drugs. Thus, while it is possible that the inclusion of manufacturer assistance in the calculation of the 5i AMP for the drug could affect whether the Secretary makes such a substitution for the Part B drug, we do not believe it is likely. To the extent that manufacturer-sponsored assistance is passed fully through to the patient, there should be no reduction in the value of the 5i AMP. As a result, there should be no increased incidence of substituting 103 percent of AMP for ASP under section 1847A(d) of the Act, which creates an additional incentive for manufacturers to ensure that their assistance is being passed through fully to the patient.

For 340B ceiling prices, such prices are calculated by subtracting the URA (URA = AMP – best price when greater than the statutory rebate percentage based on drug classification) for a drug from the drug's AMP, as described in section 340B(a)(1) of the Public Health Service Act. The URA is the Medicaid rebate amount for a quarter for a dosage form and strength of a drug. To the extent that manufacturer-sponsored assistance is passed through to the payer, rather than the patient, it could be counted in best price, which could affect the calculation of the ceiling price, as it is one component of the URA. The impact on 340B ceiling prices would depend on the inclusion of the manufacturer-sponsored assistance in the best price, and in some cases the AMP, for the drug for that quarter.

Comment: One commenter supported the proposals and recommended that CMS conduct a regulatory impact analysis of the potential impacts on manufacturer pricing behavior before finalizing its proposal to adjust Best Price calculations to include manufacturer coupon payments to patients in copay PBM accumulator programs due to concerns about the unintended effect of manufacturers increasing their overall drug prices to

compensate for the additional price concessions.

Response: We do not believe this rule will have a major regulatory impact. More discussion can be found in section IV. of this final rule, the Regulatory Impact Analysis section.

Comment: One commenter recommended as an alternative to the proposed changes to best price and AMP regarding manufacturer-sponsored assistance programs that CMS require insurance companies to remove any reference in their policies regarding cost-sharing assistance, and stated that the health plan should not have knowledge of transactions that are between the patient and manufacturer.

Response: This comment requests action that is outside the scope of the rule.

Comment: One commenter requested clarification on whether the Bona Fide Service Fee test would apply and whether CMS views the portion of the pharmacy reimbursement that is in excess of the wholesaler acquisition cost as a price concession to the pharmacy. The commenter requested CMS to clarify if, for example, if it is determined that payers typically reimburse pharmacies wholesale acquisition cost plus 12.5 percent, whether the pharmacy reimbursement for free good programs would be excluded from AMP and best price up to that threshold.

Response: This comment is outside the scope of this rule.

After consideration of the comments received, we are finalizing the proposed rule without modification, but delaying the effective date of this final policy. While the effective date of this rule is March 1, 2021, this final policy will not be effective until January 1, 2023. This will give manufacturers time to implement a system that helps them track their programs to ensure the manufacturer assistance is being passed through to the patient in full, and no other entity is receiving any price concessions. To be clear, we are providing a later effective date by which manufacturers will have to ensure that their cost sharing assistance is being passed through to the patient in full in order to exempt any such program assistance from the calculation of best price and AMP.

E. Authorized Generic Drugs (§§ 447.502, 447.504, 447.506)

The Continuing Appropriations Act of 2020, and Health Extenders Act of 2019 (Health Extenders Act) made changes to section 1927(k) of the Act, revising how manufacturers calculate the AMP for a COD for which the manufacturer permits an authorized generic to be

sold. That is, the law requires that manufacturers that approve, allow, or otherwise permit any drug to be sold under the manufacturer's own NDA approved under section 505(c) of the FDCA are no longer permitted to include those sales of these drugs in the calculation of AMP.

Specifically, section 1603 of Health Extenders Act, entitled "Excluding Authorized Generic Drugs from Calculation of Average Manufacturer Price for Purposes of the Medicaid Drug Rebate Program; Excluding Manufacturers from Definition of Wholesaler," amended:

- Section 1927(k)(1)(C) of the Act to replace the term "inclusion" with "exclusion" in the title and further amended paragraph (k)(1)(C) to state that, in the case of a manufacturer that approves, allows, or otherwise permits any drug of the manufacturer to be sold under the manufacturer's NDA approved under section 505(c) of the FDCA, such term shall be *exclusive* of the average price paid for such drug by wholesalers for drugs distributed to retail community pharmacies (emphasis added).

- The definition of wholesaler at section 1927(k)(11) of the Act to remove references to manufacturers from the definition of wholesaler.

The amendments to section 1927 of the Act authorized under section 1603 of the Health Extenders Act are effective October 1, 2019. Therefore, manufacturers must reflect the changes to the calculation of their AMPs for rebate periods beginning October 1, 2019 (reported to CMS no later than 30 days after the end of the rebate period). Furthermore, in accordance with § 447.510(b), manufacturers have 12 quarters from the quarter in which the data were due to revise AMP, if necessary.

In accordance with the statutory amendments to section 1927(k)(1)(C) and (k)(11) of the Act described in this rule, we proposed to revise §§ 447.502, 447.504, and 447.506 as they apply to AMP and authorized generic sales as follows:

- We proposed to revise § 447.502 to change the definition of wholesaler to reflect the revised statutory definition of wholesaler at section 1927(k)(11) of the Act. Specifically, we proposed to revise the definition of wholesaler by removing any reference to "manufacturer(s)" consistent with the changes to the definition of wholesaler made by section 1603(b) of the Health Extenders Act. We proposed the term "wholesaler" to mean a drug wholesaler that is engaged in wholesale distribution of prescription drugs to retail

community pharmacies, including but not limited to repackers, distributors, own-label distributors, private-label distributors, jobbers, brokers, warehouses (including distributor's warehouses, chain drug warehouses, and wholesale drug warehouses), independent wholesale drug traders, and retail community pharmacies that conduct wholesale distributions.

- Since the definition of wholesaler at section 1927(k)(11) of the Act no longer includes manufacturers, we further proposed to remove from the list of sales, nominal price sales, and associated discounts, rebates, payments or other financial transactions included in AMP, sales to other manufacturers who act as wholesalers for drugs distributed to retail community pharmacies at § 447.504(b)(2). The nominal price sales, and associated discounts, rebates, payments or other financial transactions included in AMP in accordance with § 447.504(d) (AMP for 5i drugs that are not generally dispensed through retail community pharmacies) do not change because the statute at section 1927(k)(1)(C) of the Act only speaks to authorized generic sales from the manufacturer to wholesalers that distribute to retail community pharmacies.

- We proposed to revise § 447.506, which provides specific requirements to manufacturers regarding the treatment of authorized generic drug sales when determining AMP and best price. For purposes of those calculations, the current regulation defines primary manufacturer as the manufacturer that holds the NDA of the authorized generic drug and the secondary manufacturer as the manufacturer that is authorized by the primary manufacturer to sell the drug, but does not hold the NDA.

The regulation further requires that the primary manufacturer must include in its calculation of AMP its sales of authorized generic drugs that have been sold or licensed to a secondary manufacturer, acting as a wholesaler for drugs distributed to retail community pharmacies, or when the primary manufacturer holding the NDA sells directly to a wholesaler. The Health Extenders Act revised the definition of wholesaler at section 1927(k)(11) of the Act by removing "manufacturer" and revised the determination of AMP at section 1927(k)(1)(C) of the Act by replacing the term "inclusion" with "exclusion" in the title and further amended paragraph (C) to state, in the case of a manufacturer that approves, allows, or otherwise permits any drug of the manufacturer to be sold under *the manufacturer's* NDA approved under section 505(c) of the FFDCA, such term

shall be *exclusive* of the average price paid for such drug by wholesalers for drugs distributed to retail community pharmacies. Therefore, we proposed to revise § 447.506(b) to replace the word "Inclusion" with "Exclusion" in the first sentence and replace the second sentence in its entirety to state that the primary manufacturer (as defined at § 447.506(a)) must exclude from its calculation of AMP any sales of authorized generic drugs to wholesalers for drugs distributed to retail community pharmacies when reporting the AMP of the brand name drug.

More specifically, we proposed that a separate AMP is determined for the brand drug, which shall be exclusive of any authorized generic sales, and a separate AMP shall be generated for the authorized generic. As discussed in the June 2020 proposed rule, typically, an authorized generic is a product that a manufacturer (primary manufacturer) allows another manufacturer (secondary manufacturer) to sell under the primary manufacturer's FDA-approved NDA but under a different NDC number. The authorized generic is typically the primary manufacturer's brand product offered at a lower price point. Primary manufacturers may sell the authorized generic product to the secondary manufacturer they are allowing to sell an authorized generic of their brand product, and such sales are commonly referred to as transfer sales. Primary manufacturers have included those transfer sales in the determination of the brand product's AMP. Under the amendments made to section 1927 of the Act, a primary manufacturer that sells the authorized generic version of the brand drug to the secondary manufacturer can no longer include the price of the transfer sale of the authorized generic to the secondary manufacturer in its calculation of AMP for the brand product. The exclusion of these transfer sales from the primary manufacturer's brand drug AMP will likely result in higher AMPs for the brand drugs and a potential increase to a manufacturer's Medicaid drug rebates to states. To assist manufacturers, we provided guidance in Manufacturer Release #111 and Manufacture Release #112.²² In turn, we received inquiries as to what is meant by "In the case of a manufacturer that approves, allows, or otherwise permits any drug of the manufacturer to be sold under *the manufacturer's* NDA approved under section 505(c) of the FFDCA, such term shall be *exclusive* of the average price paid for such drug by wholesalers for

drugs distributed to retail community pharmacies." Specifically, we received questions regarding when a primary manufacturer itself, or an affiliate of the manufacturer is also producing the authorized generic, and whether, such a case, constitutes "a case of a manufacturer that approves, allows, or otherwise permits" the drug to be sold under the manufacturer's NDA, such that the exclusion applies. And if not, whether the primary manufacturer may include the average price paid for the authorized generic when calculating AMP for the brand drug. We believed that irrespective of the relationship between the manufacturer of the brand drug, and the manufacturer of the authorized generic, if the primary manufacturer "approves, allows, or otherwise permits" the drug to be sold under the primary manufacturer's NDA, then the AMP for the brand should be calculated separately from (not include) the sales of the authorized generic. That is, it would not matter whether the manufacturer being approved, allowed, or otherwise permitted to sell the drug under the primary manufacturer's NDA was the same, affiliated or non-affiliated.

Therefore, we interpret section 1927(k)(1)(C) of the Act, which provides that in the case of a manufacturer that approves, allows, or otherwise permits any of its drugs to be sold under the same NDA, the AMP for that brand drug shall be exclusive of the average price paid for such drug by wholesalers for drugs distributed to retail community pharmacies, to mean a separate AMP should be calculated for each drug product—that is, one AMP for the brand drug, and one AMP for the authorized generic product, and the AMP for the brand drug should always exclude sales of the authorized generic product, including transfer sales of the brand name drug to the manufacturer of the authorized generic, as the definition of wholesaler no longer includes a manufacturer. Thus, a manufacturer's sales to manufacturers who act as wholesalers can no longer be included in AMP. This includes a situation when it is the same manufacturer making both the brand name drug and authorized generic, or if the drugs are being manufactured by different, but affiliated manufacturers or even non-affiliated manufacturers. We proposed a policy that applies irrespective of a specific brand manufacturer's sales arrangement.

The amendments made by section 1603 of the Health Extenders Act were effective October 1, 2019. Therefore, manufacturers are required to reflect the changes to the calculation of their AMPs for rebate periods beginning October 1,

²² <https://www.medicaid.gov/prescription-drugs/downloads/mfr-rel-112.pdf>.

2019 (reported to CMS no later than 30 days after the end of the rebate period). Furthermore, in accordance with § 447.510(b), manufacturers have 12 quarters from the quarter in which the data were due to revise AMP, if necessary.

We received the following comments on our proposed policies regarding authorized generic drugs (§§ 447.502, 447.504, 447.506).

Comment: A few commenters supported the proposed regulations regarding how manufacturers should calculate AMP for authorized generic drugs. Several commenters supported the proposed regulations that manufacturers must calculate separate AMPs for their brand drug and authorized generic. One commenter noted the proposed regulation should reduce manufacturer anti-competitive strategies and another noted the proposal successfully addresses one of the ways that authorized generics create marketplace distortions that hurt patients. One commenter supported the proposed approach that this exclusion apply irrespective of whether the authorized generic is sold by an affiliated or unaffiliated manufacturer, or the nature of the sales arrangement.

Response: We appreciate the commenters support, and are finalizing the proposals consistent with the changes made by the Continuing Appropriations Act of 2020, and Health Extenders Act of 2019 (Health Extenders Act) to section 1927(k) of the Act with one modification relative to the regulatory definition of secondary manufacturer.

Comment: A few commenters supported the exclusion of sales, nominal price sales, and associated discounts, rebates, payments, or other financial transactions included in AMP from other manufacturers who act as wholesalers for drugs distributed to retail community pharmacies.

Response: We appreciate the support for this proposal. Since the definition of wholesaler at section 1927(k)(11) of the Act no longer includes manufacturers, we are removing from the list of sales, nominal price sales, and associated discounts, rebates, payments or other financial transactions included in AMP, sales to other manufacturers who act as wholesalers for drugs distributed to retail community pharmacies at § 447.504(b)(2). The nominal price sales, and associated discounts, rebates, payments or other financial transactions included in AMP in accordance with § 447.504(d) (AMP for 5i drugs that are not generally dispensed through retail community pharmacies) do not change because the statute at section

1927(k)(1)(C) of the Act only speaks to authorized generic sales from the manufacturer to wholesalers that distribute to retail community pharmacies.

Comment: A few commenters did not support the proposed regulations that would prohibit manufacturers from blending the brand name AMP and the AMP of the authorized generic in certain situations. For example, one commenter stated that the Health Extenders Act that created the statutory prohibition of the blending of brand name and authorized generic AMPs did not amend the Medicaid drug rebate statute provisions which require the calculation of Medicaid URAs at the drug, dosage form, and strength level. As a result, because the brand product and authorized generic share the same drug, dosage form, and strength, the commenter believes that the provision regarding the calculation of the AMP at the drug, dosage form, and strength level also supports blending of AMPs where the same manufacturer sells both. (The URA for a dosage form and strength of drug for a quarter is calculated using the drug's AMP as one of the inputs.)

Another commenter did not support the proposed regulations requiring the calculation of separate AMPs in certain situations, and stated the statutory AMP exclusion for authorized generics applies only in cases when a manufacturer "approves, allows, or otherwise permits any drug of the manufacturer to be sold under the manufacturer's [NDA]". The commenter further indicated that as a result, the requirement to calculate separate AMPs cannot apply where there is no secondary manufacturer. A few commenters did not support CMS' proposal to exclude sales of authorized generics from the AMP calculation of the brand drug when these products are sold without the involvement of a "secondary" manufacturer, and stated that the text and history of the Medicaid rebate statute support blending of the AMPs in this circumstance.

Response: We do not agree with the commenters that the statutory text continues to support the blending of the authorized generic sales and brand sales when calculating AMP in certain situations. As described above, and in Manufacturer Releases #111 and #112, section 1603 of the Health Extenders Act made changes to section 1927(k) of the Act, revising how manufacturers calculate the AMP for a COD for which the manufacturer approves, allows or otherwise permits the COD of the manufacturer to be sold under the manufacturer's NDA. That is,

manufacturers that approve, allow, or otherwise permit any drug to be sold under the manufacturer's own NDA approved under section 505(c) of the FFDCAs shall no longer include those sales in the calculation of the brand name AMP, which includes authorized generic sales.

We have also interpreted this provision regarding the inability of manufacturers to further blend AMPs to apply beyond authorized generic cases to other situations in which a manufacturer approves, allows or otherwise permits the COD to be sold under the manufacturers' NDA. For example, with respect to a manufacturer's importation of drugs under Section 801 of the FFDCAs, we issued manufacturer release #114 guidance on September 25, 2020, in which we interpreted that when a manufacturer approves, allows or otherwise permits a drug imported under an NDA to also be sold under the same NDA, then the manufacturer would not be permitted to blend the AMPs of the drug sold in the United States, with the drug that the manufacturer imports which is sold under the same NDA.

With regard to comments suggesting the exclusion not being applicable to situations where both the brand drug and authorized generic drug are approved, allowed, or permitted to sold under the same NDA by the "same manufacturer", irrespective of the relationship between the manufacturer of the brand drug, and the entity permitted to sell the authorized generic, if the primary manufacturer "approves, allows, or otherwise permits" any drug to be sold under the primary manufacturer's NDA, then the AMP for the brand should be calculated separately from (exclude) the sales of the other drug or drugs that are being sold under that NDA, in this case, an authorized generic. That is, it would not matter whether the manufacturer or entity (that is, the secondary manufacturer) being approved, allowed, or otherwise permitted to sell the drug under the primary manufacturer's NDA was the same, affiliated or non-affiliated from the primary manufacturer as explained further below.

As discussed in the proposed rule (85 FR 37300), after we issued Manufacturer Releases #111 and #112, we received inquiries as to what is meant by "In the case of a manufacturer that approves, allows, or otherwise permits any drug of the manufacturer to be sold under the manufacturer's NDA approved under section 505(c) of the FFDCAs, such term shall be exclusive of the average price paid for such drug by wholesalers for

drugs distributed to retail community pharmacies.” Specifically, we received questions regarding when a primary manufacturer itself, or an affiliate of the manufacturer is also producing the authorized generic, and whether, such a case, constitutes “a case of a manufacturer that approves, allows, or otherwise permits” the drug to be sold under the manufacturer’s NDA, such that the exclusion applies. And if not, whether the primary manufacturer may include the average price paid for the authorized generic when calculating AMP for the brand drug.

In Manufacturer release #112, we advised that, until we issue a regulation in final, when a manufacturer approves, allows, or otherwise permits any of its drugs to be sold under the same NDA, a separate AMP should be calculated for each drug product—that is, one AMP for the brand drug, and one AMP for the authorized generic product, and the AMP for the brand drug should exclude sales of the authorized generic product. We also advised that such situation includes both when a manufacturer is the same for both the brand drug and authorized generic version and the situation when the drugs are being manufactured by different, but affiliated companies. For example, the manufacturer making the authorized generic might be a subsidiary of the brand name company, or the two might simply have a corporate or business relationship.

To support this view, we note that the title of section 1603 of the Health Extenders Act amending section 1927(k)(1) and (k)(11) of the Act is “Excluding Authorized Generic Drugs from Calculation of Average Manufacturer Price for Purposes of the Medicaid Drug Rebate Program,” and section 1603(a)(1) specifically amended the statutory provision at section 1927(k)(1) by striking “INCLUSION” and “inclusive” and inserting “EXCLUSION” and “exclusive.” The statute did not previously, nor was it later amended to distinguish among the different business or corporate relationships, if any, that might exist among the manufacturer of the brand name drug and the entity that that manufacturer approves, allows, or otherwise permits to sell such drug under the same NDA. It simply indicates that the AMP calculation for the brand drug shall be exclusive of (shall not include) the average price paid (sales) of the drug the manufacturer is permitting to be sold under its NDA.

For these reasons, we are also finalizing this rule by not distinguishing among the business or corporate relationships between the companies,

such as whether they are subsidiaries, affiliates, or have corporate relationships. However, based on the comments we received, we are amending the current definition of secondary manufacturer found at § 447.506(a) to clarify this point, and are removing the phrase at the end of the definition, “but does not hold the NDA.” As noted above, the statute neither before amendment or after distinguishes among the different business or corporate relationships, if any, that might exist among the manufacturer of the brand name drug and the entity that that manufacturer approves, allows, or otherwise permits to sell such drug under the same NDA. And this is likely because in some cases, the primary and secondary manufacturers are one in the same; that is, one manufacturer who holds the NDA makes and markets both the brand name drug and the authorized generic. This regulatory modification will clarify that regardless of the relationship that exists between the primary and secondary manufacturer, that the sales of the authorized generic cannot be blended with the sales of the brand name drug.

Comment: One commenter stated that the AMP for the brand product should still include the price of the authorized generic drug as removing the authorized generic will lead to increasing the price of the brand name medication.

Response: We did not make any proposals related to drug launch prices, have no control over how those are set, and remind the commenter that there is the inflation rebate penalty in the Medicaid drug rebate program for manufacturers that increase prices faster than inflation (CPI-U) on their drugs. This should serve as a disincentive to manufacturers to increase prices faster than inflation.

Moreover, we do not believe that the exclusion of the sales of the authorized generic from the calculation of the brand AMP should increase the price of the brand name drug, as the calculation of the AMP by a manufacturer is done solely to report the AMP value used by CMS to calculate the unit rebate amount for states to bill manufacturers for rebates. While the AMP of the brand name drug will likely increase if the manufacturer can no longer include the sales of the authorized generic, it should not affect the sales price of the brand name drug in the marketplace.

For these reasons, we are finalizing the policy that manufacturers cannot blend the sales of the AMPs for the brand name drug sold under the NDA and the sales of any other drug sold under the NDA, regardless of the

relationships between the entities selling the drugs.

After consideration of the comments received, we are finalizing our proposals at §§ 447.502, 447.504 and 447.506 as modified, which includes a clarifying revision to the definition of secondary manufacturer as noted above.

F. Medicaid Drug Rebates (MDR) (§ 447.509)

Manufacturers that participate in the MDRP are required to pay rebates for CODs that are dispensed to Medicaid patients. The rebates are calculated based on formulas described in section 1927(c) of the Act. As described in section I. of the June 2020 proposed rule, the BBA 2015 made revisions to the statutory rebate formula for CODs other than single source or innovator multiple source drugs. That is, section 602 of BBA 2015, amended section 1927(c)(3) of the Act to require that manufacturers pay additional rebates on their CODs other than single source or innovator multiple source drugs (non-innovator multiple source (N) drugs) when the AMP of the N drug increases at a rate that exceeds the rate of inflation. The amendments made by section 602 of BBA 2015 were effective beginning with the January 1, 2017 quarter (that is, first quarter of 2017). The implementation of these amendments was discussed in Manufacturer Release 97 and Manufacturer Release 101.

Prior to the enactment of BBA 2015, the basic quarterly URA calculation for N drugs was equal to 13 percent of a drug’s quarterly AMP. However, section 602(a) of BBA 2015 amended section 1927(c)(3) of the Act by adding an inflation-based additional rebate requirement to the URA for N drugs, which is similar to the additional rebate applied to single source (S) and innovator multiple source (I) drugs.

To calculate the additional rebate portion of the URA calculation for N drugs, section 602(a) of BBA 2015 amended section 1927 of the Act to establish a base AMP or base date AMP value for N drugs based, in part, upon each N drug’s market date. In general, for N drugs marketed on or before April 1, 2013, the base date AMP is equal to the third quarter of 2014 and the Base CPI-U is the CPI-U for September 2014. For N drugs marketed after April 1, 2013, the base date AMP is equal to the AMP for the fifth full calendar quarter after which the drug is marketed as a drug other than a single source or innovator multiple source drug and the base CPI-U is equal to the CPI-U for the last month of the base AMP quarter.

We proposed to revise § 447.509 to codify the rebate formulas in regulation. Specifically, we proposed to revise paragraph (a)(6) to distinguish the basic rebate for N drugs from this additional rebate. In addition, we proposed to add paragraph (a)(7) to expressly include the additional rebate calculation for N drugs. We proposed that in addition to the basic rebate under paragraph (a)(6), for each dosage form and strength of a N drug, the rebate amount will increase by an amount equal to the product of the following: The total number of units of such dosage form and strength paid for under the state plan in the rebate period, and the amount, if any, by which the AMP for the dosage form and strength of the drug for the period exceeds the base date AMP for such dosage form and strength, increased by the percentage by which the consumer price index for all urban consumers (United States city average) for the month before the month in which the rebate period begins exceeds such index associated with the base date AMP of the drug. We also proposed to add paragraph (a)(8) to capture that the total rebate amount for noninnovator multiple source drugs is equal to the basic rebate amount plus the additional rebate amount, if any.

In addition to the proposed regulatory changes related to section 602 of BBA 2015 amendments noted in this rule, we also proposed to amend § 447.509 at:

- Paragraph (a)(5) to specify that in no case will the total rebate amount exceed 100 percent of the AMP of the single source or innovator multiple source drug; and
- By adding paragraph (a)(9) to specify that in no case will the total rebate amount exceed 100 percent of the AMP of the noninnovator multiple source drug.
- We also added to paragraph (a)(7)(ii)(B) to state that the base date AMP has the meaning of AMP set forth in section 1927(c)(2)(A)(ii)(II), (c)(2)(B) and (c)(3)(C) of the Act as the regulation did not provide a specific definition of base date AMP for calculating the additional rebate. We believe it is reasonable to include this in regulation to provide further clarity for manufacturers and states with regard to the calculation of the additional rebate, and to ensure the appropriate product data and pricing information is submitted to CMS.

We received the following comments on Medicaid drug rebates (MDR) (§ 447.509).

Comment: A few commenters supported the proposed changes to the calculation for non-innovator multiple source drugs, single source drugs, or

innovator multiple source drugs to ensure manufacturers of authorized generic drugs do not take advantage of monopoly situations, and increase prices beyond the rate of inflation.

Response: The proposed changes were made to conform to changes made by section 602 of the BBA 2015 to section 1927(c)(3) of the Act which requires that manufacturers pay additional rebates on their non-innovator multiple source (N) drugs if the AMPs of an N drug increase at a rate that exceeds the rate of inflation. It is not clear what the commenter meant by the statement that these proposed changes would ensure that manufacturers of authorized generics do not take advantage of monopoly situations. Authorized generics are considered innovator multiple source drugs as they are sold under a manufacturer's NDA, and an existing inflation penalty applies to such drugs under section 1927(c)(2) of the Act.

Comment: Several commenters do not support the proposed changes to the inflation rebate or the inclusion of an additional rebate for N drugs. A few commenters noted the additional rebate for non-innovators multiple source drugs (N drugs) would be a disincentive to manufacturers from participating in Medicaid and 340B programs.

Response: While we appreciate the commenters expressing their concerns, the proposed revisions to § 447.509, conform with the changes made by section 602 of the BBA 2015 to section 1927(c)(3) of the Act, which require that manufacturers pay additional rebates on their N drugs if the AMPs of an N drug increase at a rate that exceeds the rate of inflation. This provision of BBA 2015 was effective beginning with the January 1, 2017 quarter, or in other words, beginning with the URAs that are calculated for the January 1, 2017 quarter. Since that date, we have not noticed a decline in manufacturers participating in either the Medicaid program or 340B program.

Comment: One commenter noted the proposed methodology for calculating the basic rebate and the additional rebate could result in a “double discount” in situations where products with a price increase that is greater than inflation would also now have to pay an inflation rebate. This commenter recommended rather than add the two rebate components together, a manufacturer should be permitted to sum the total net of the duplicate portion of the rebates.

Response: We believe the commenter is noting that the basic rebate for a non-innovator multiple source drug may already reflect a higher rebate due to

price increases on that non-innovator drug resulting in a higher AMP and therefore, the additional rebate duplicates, to some extent, an already increased basic rebate (due to the increase in the AMP). There is no statutory basis to allow for the type of rebate calculation proposal that the commenter is suggesting. We note that section 602 of the BBA of 2015 added section 1927(c)(3) of the Act, which requires that manufacturers pay, in addition to a basic rebate, an additional rebate for their N drugs if the AMPs of an N drug increase at a rate that exceeds the rate of inflation. This provision of BBA 2015 was effective beginning with the January 1, 2017 quarter, or in other words, beginning with the URAs that are calculated for the January 1, 2017 quarter.

After consideration of the public comments received, we are finalizing the proposed changes (described in this section (II.F. of this final rule)) made to § 447.509 without modification.

Additionally, please refer to section II.C.2. of this final rule for a description of other changes we are finalizing to § 447.509 as they relate to drugs that are line extensions.

G. Requirements for Manufacturers (§ 447.510)

In accordance with section 1927(b)(3) of the Act and the terms of the NDRA, manufacturers are required to report pricing information to CMS on a timely basis or face a penalty. Current regulations at § 447.510 implement the manufacturer price reporting requirements including the timing of revisions to pricing data. The current regulation at § 447.510(b)(1) requires that the revision to pricing data be made within the 12 quarters from which the data were due, unless it meets one of the exceptions in paragraphs (b)(1)(i) through (v).

As discussed in section II.B. of the June 2020 proposed rule, VBP has evolved into a possible option for states and manufacturers to help manage drug expenditures. Many VBP arrangements or pay-over-time models may be better suited for periods longer than 12 quarters, and manufacturers entering into such arrangements may need to adjust AMPs and best prices beyond the 12 quarters because the evidence-based or outcomes-based measures are being measured beyond a period of 12 quarters or a final installment payment is being made outside of the 12 quarters. With this evolution it has become apparent that certain manufacturer reporting requirements could be viewed as an impediment to adopting VBP arrangements. For instance, under

current regulations, a manufacturer would not be able to account for any adjustments to prices that may occur outside of the 12 quarters because of VBP arrangements (or even pay-over-time models), as required.

The definition of AMP at section 1927(k)(1)(B)(ii) of the Act, indicates that any other discounts, rebates, payments or other financial transactions that are received by, paid by, or passed through to retail community pharmacies shall be included in AMP for a COD. The special rules in section 1927(c)(1)(C)(ii) of the Act define best price to be inclusive of cash discounts, free goods that are contingent on any purchase requirement, volume discounts and rebates. Since manufacturers are required to report AMP and best price that capture these statutory required financial transactions, including such financial transactions (for example, rebates, incremental payments) that are a result of VBP arrangements or pay-over-time models, and such pricing structures may be designed to result in transactions taking place outside of the 3-year window, we proposed to add § 447.510(b)(1)(vi) to specify an additional exception to the 12-quarter rule to account for the unique nature of VBP arrangements and pay-over-time models. Specifically, we proposed that the manufacturer may make changes outside of the 12-quarter rule as a result of a VBP arrangement when the outcome must be evaluated outside of this 12-quarter period.

We received the following comments on requirements for manufacturers (§ 447.510).

Comment: Many commenters supported the extension of the price reporting period for VBP arrangements beyond the current 12-quarter restatement window. One commenter noted this will improve the reporting of net prices. Another commenter supported the extension because they noted limiting an outcome measurement to less than the historical 12-quarter maximum, regardless of the clinical data associated with a given treatment, might jeopardize the usefulness of a VBP arrangement.

Response: We appreciate the support for the exception to the 12-quarter restatement window and are finalizing the regulation at § 447.510(b)(1)(vi) as proposed.

Comment: Several commenters provided recommendations for allowing adjustments outside of the 12-quarter window or requested further modifications to CMS' proposals in this section. Specifically, commenters recommended that CMS consider a specific length of the time for the

restatement period of AMP and best price for therapies subject to VBP arrangements, such as 5 or 10 years. In addition, commenters requested that CMS address the impact of the amended restatement period on the traditional AMP smoothing methodology. Finally some commenters requested that manufacturers be able to make such restatements in the same way that they can make restatements within the 12-quarter window, that is, without any need for approval by CMS.

Response: This final regulation adds an exception to the 12-quarter rule that allows a manufacturer to request revisions to price reporting (including quarterly AMP and best price reporting) that exceed 12 quarters from which the data was due when the change is a result of a VBP arrangement and the outcome must be evaluated outside of the 12-quarter period. We do not agree with the suggestion that we consider adding a specific length of time for the applicability of the exception outside of the 12 quarters, because our intent is to provide necessary flexibilities understanding the various VBP arrangements will be designed with different protocols, outcomes and timeframes.

For example, there may be a 5-year lag time between the time that a drug is first administered to a patient and the evaluation period for that patient's VBP arrangement. After that, there may be several years of prior period pricing adjustments based on the data that are generated from VBP program's patient results which may affect the pricing data being reported that had already been reported for the initial 5-year period. Manufacturers that use a VBP-based bundled sales approach would also be expected to revise their pricing metrics as additional data are compiled from the VBP arrangement, and make adjustments to AMP and BP, with the ability to make such adjustments outside the 12-quarter reporting window.

We also note that there are currently five exceptions listed at § 447.510(b) to the 12 quarter price reporting rule, and none of these exceptions are time limited. For example, there are currently no time limits on manufacturer requests for changes related to the initial submission of a product (§ 447.510(b)(1)(ii)) or due to a change in drug category or market date (§ 447.510(b)(1)(i)). We do not see a need, therefore, to place a time limit of manufacturer reporting outside the 12 quarter rule regarding VBP arrangements.

We would implement this new exception to the 12-quarter rule in the

same manner that we are currently processing requests from manufacturers for other exceptions. That is, the manufacturer would submit its request to us to describe the change they want to make with supporting documentation. If the change is permissible, we will notify the manufacturer that they can make the change in the current reporting system, and then the manufacturer would be able to certify that change.

With respect to permitting revisions to the pricing data under a VBP arrangement, the regulations require manufacturers to request, and for the agency to determine whether or not to "reopen" the MDRP for revised pricing outside of the 12 quarters based upon the manufacturer's request and whether it meets an exception at § 447.510(b)(1)(i) through (v). The same practice will apply to this new exception at § 447.510(b)(1)(vi). We will not permit manufacturers to restate pricing data in excess of 12 quarters in MDRP without the manufacturer submitting its request to us.

Comment: A few commenters requested that CMS consider the implications of changes to drug pricing information outside the 12-quarter period on the MDRP and 340B ceiling price calculations.

Response: Price calculations for 340B drugs are made by the Health Resources Services Administration (HRSA) and are based on the pricing data reported to the MDRP each calendar quarter. In accordance with section 340B(a)(1) of the Public Health Service Act, the 340B Ceiling Price and Civil Monetary Penalty final rule defines the 340B ceiling price as calculated as the AMP from the preceding calendar quarter for the smallest unit of measure minus the URA and will be calculated using six decimal places (82 FR 1210). Any retrospective changes to MDRP pricing metrics also affect 340B ceiling prices as the inputs to the ceiling prices would also change. Thus, any changes to MDRP pricing metrics, whether within the 12-quarter adjustment period or outside the 12-quarter adjustment period could affect the 340B ceiling price for the calendar quarter. We would expect manufacturers to make adjustments to their 340B ceiling prices as they have done in the past consistent with any changes to the MDRP pricing metrics.

Comment: A commenter noted the proposal could create a misalignment of discounts and sales volumes in the AMP calculation due to the longer time frame over which patient outcomes will be measured and rebates paid. This commenter recommended CMS engage

commenters to discuss potential solutions to execute through future guidance or rulemaking on a parallel time frame to the effective date of this final rule.

Response: We thank the commenter for this important observation. It is not clear the extent to which “misalignments” may occur within AMP calculation as a result of discounts and sales volume under a VBP approach. However, we expect that the ability of manufacturers to request an adjustment of pricing metrics outside the 12 quarter window for VBP-related changes will give manufacturers and payers more flexibility in structuring VBP arrangements as they would know that there could be a longer timeframe for evaluation. This could encourage the use of these programs, which would help increase their use in commercial plans, as well as their use by Medicaid.

Comment: A few commenters requested clarification on specific operational details and implications on the VBP arrangements exception provided in § 447.510(b)(1)(vi). These commenters requested that CMS should consider that out-year payments in VBP approaches do not need to adjust for the time value of money and that the restatement of Best Price should not be necessary as part of a VBP arrangement since the Best Price would have already been reported.

A few commenters requested clarification of how the proposal would address pay-over-time arrangements. One commenter requested clarification on how the proposal would allow for pay-over-time arrangements, specifically, when resetting Best Price more than three years after administration of the drug, and what would qualify as the product’s Best Price until the benchmark is met and Best Price is reset, especially as each installment payment may stretch across multiple rebate reporting periods and recommended CMS allow for an annuity payment in the case of one-time therapies/gene-therapies.

Response: We recognize that it will be a challenge for CMS to evaluate and address the impact of every VBP arrangement on government pricing as part of this final rule because there is no standard or “one-size” fits all approach to manufacturer VBP arrangements. For example, manufacturers may pay adjustments to payers in the form of rebates if a drug does not work as intended, choose to require payers to pay in installments as the drug meets intended outcomes, or pay premiums to third parties to “warrant” their drug products, which would allow a manufacturer to pay the health care

costs incurred by a payer as a result of the failure of a particular therapy. All these approaches (and more) may require different calculations to determining best price and AMP, and reporting these figures in MDRP.

We note that some manufacturers that are using a “pay-over-time” model that does not involve a VBP component may contract with an intermediary to receive full payment for the drug and thus report it in the manufacturer’s AMP when reporting their pricing metrics. That is, the payer makes “pay-over-time” payments to the intermediary, and the intermediary makes full payment to the manufacturer so the manufacturer can report the full sale in the quarter in which the drug was administered or dispensed so as not to affect their AMP reporting. The “best price” for the quarter would also be reported. However, to the extent that future rebates or discounts adjust the AMP or “best price”, adjustments would have to be reported as they would under a non pay-over-time model. Finally, because pay-over-time arrangements do not necessarily have an outcomes component and simply allow payers to pay for high cost drugs over a period of time, these types of pay-over-time arrangements would not be subject to the exception at § 447.510(b)(1)(vi) because there is no outcomes related to the pay-over-time payments, and the exception applies only in cases when the VBP arrangement involves an outcome that must be evaluated outside of the 12-quarter period.

We will need to remain flexible as additional VBP design structures come to the market. This being the case, we will consider issuing operational guidance to assist manufacturers in the reporting of AMP and best price and to the extent there is no guidance specific to a manufacturer’s VBP arrangement, manufacturers may continue to make reasonable assumptions consistent with statute and regulation regarding the determination of best price and AMP.

Comment: Several commenters did not support the proposed rule providing for an additional exception to the generally applicable 12-quarter reporting rule for certain VBP arrangements. A few commenters noted this would create additional burden on states and fiscal agents to manually review rebates and credits. One commenter noted price reporting requirements for performance-based contracts and annuities with terms greater than 12 quarters are unclear and may cause administrative burden to revise.

Response: We understand and appreciate the comment, as retrospective changes to price reporting can create burdens to states and manufacturers. However, we expect that prior period adjustments resulting from rebates or discounts paid under a VBP program could be made in the same manner as traditional prior period adjustments; that is, through changes to the URA that are sent to states by CMS, and paid by or paid to manufacturers.

Comment: One commenter noted the proposal created opportunity for drug makers to game the system and recommended CMS more clearly define requirements drug makers will need to abide by under the new VBP rules to avoid future gaming.

Response: We appreciate the commenter’s concerns. Manufacturers can offer VBP programs to payers under various approaches, such as a “bundled sales” approach or a multiple best price approach. These programs must comply with the VBP arrangement definition that we are finalizing in this final regulation in order for a manufacturer to avail itself of the regulatory flexibilities we are finalizing in this regulation.

As has been the case with the MDRP program since its inception, manufacturers are responsible for following all applicable laws, and regulations, including entering into and having in effect a national drug rebate agreement which memorializes these requirements. Such responsibilities will include complying with these new regulations relating to VBP approaches, as applicable. Manufacturers continue to be permitted to make reasonable assumptions where necessary, and remain responsible for documenting and retaining those assumptions as provided at § 447.510(f). Manufacturers will remain subject to enforcement actions, such as CMPs, for false reporting of product and pricing information. In addition, we are delaying the effective date of the multiple best price VBP approach to January 1, 2022. We will provide additional guidance should it be necessary to both protect the integrity of the MDRP, as well as help assure a smooth implementation of the VBP arrangement regulatory flexibilities that will be available under this final regulation.

After consideration of the comments received, we are finalizing the proposed rule without modification.

H. Requirements for States (§ 447.511)

Section 1927(b)(2)(A) of the Act requires that states be held responsible to report to each manufacturer not later than 60 days after the end of each rebate period and in a form consistent with a

standard reporting format established by the Secretary, information on the total number of units of each dosage form and strength and package size of each COD dispensed after December 31, 1990, for which payment was made under the plan during the period, including such information reported by each Medicaid MCO, and shall promptly transmit a copy of such report to the Secretary. The accuracy and timeliness of this SDUD report is important for the MDRP, other programs, and legislative efforts including, but not limited to:

- Actuarial and cost impact projections of legislative or regulatory changes to the MDRP;
- The calculation of Medicaid's portion of the branded prescription drug fee specified at section 9008 of the Affordable Care Act); and
- Ongoing audits that demonstrate that some states still fail to bill rebates for physician-administered drugs (PADs), although it has been 13 years since the requirement began.

States are required to send invoices (CMS-R-144 Medicaid Drug Rebate Invoice) to each manufacturer in the MDRP for which payment was made on behalf of the state and federal government for the manufacturers' drugs, or in the case of MCOs (including PHIPs and PHAPs), drugs dispensed to a beneficiary in a rebate period. States are required to send a copy of their SDUD (a summary report of their invoice utilization data) to CMS each quarter. If a state makes an adjustment to a rebate invoice, the state is required to send an updated SDUD to us in the same reporting period in which the manufacturer received the adjustment.

We have found that some states do not have sufficient edits in place to detect, reject and investigate SDUD outliers, which may distort the rebate amounts due by manufacturers. This results in states overbilling manufacturers and generating disputes on rebate invoices; imposing resource burdens on manufacturers, states, CMS, and other MDRP partners, as well as interrupting the payment of rebates to states and CMS. Many states seemingly fail to implement needed system edits to identify such disputes prior to billing manufacturers. Although both overbilling and underbilling must be disputed, manufacturers often neglect to dispute instances of rebate underbilling.

We have also found that many states do not send the same SDUD to CMS as they transmit to manufacturers. In fact, some states send us "pre-edited" SDUD, while the manufacturer's rebate invoice contains edited data. These practices do not comply with section 1927(b)(2)(A)

of the Act and § 447.511(b), which require that states submit the same SDUD to us on a quarterly basis that they transmit to the manufacturers. As we move to implement new systems, we expect to put in place data error screening to better reject or alert identified potential inaccuracies to SDUD. States should also be improving current systems and planning updates to future systems to better identify and correct inaccurate SDUD before reporting to manufacturers and CMS.

Accurate reporting of SDUD to CMS is important for a number of reasons that extend beyond the MDR program. We remind states and manufacturers that the state submission of utilization data to us for purposes of the MDR program is also available on our public website (<https://www.medicaid.gov/medicaid/prescription-drugs/state-drug-utilization-data/index.html>), and is reviewed and utilized by various entities (that is, IRS, OIG). State Release 177 (July 21, 2016) (<https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/state-releases/state-rel-177.pdf>) addresses "Non-Compliant State Drug Utilization Data Reporting to CMS."

We are now providing additional information to assist states in more accurately reporting SDUD to us. SDUD should only contain utilization data on NDCs that are eligible for both FFP and for rebates under the CMS rebate program. Therefore, SDUD reporting should not include an NDC that is not a COD and not eligible for rebates, even though it may be covered by a state as a prescribed drug and eligible for FFP.

States should identify and exclude utilization of those drugs whose NDCs are:

- Paid for with only state funds;
- Not representative of CODs (for example, eligible for FFP as a prescribed drug but not eligible for rebates);
- Prohibited from receiving FFP (for example, COD status 05 and 06, drugs for erectile dysfunction or sexual dysfunction for which there is no other FDA-approved indication); and
- For units utilized for 340B claims prior to submitting their utilization data to CMS.

After an SDUD file is successfully processed by CMS, the system generates a Utilization Discrepancy Report (UDR) that lists edits and alerts that were triggered when the SDUD file was processed. The UDR is routed back to the state via the EFT process and should be received within 2 days of submitting the SDUD file to CMS. While states should review each UDR in its entirety for data issues, certain data edits should

be scrutinized more closely as they may affect state rebate billing. These error and alert messages include:

- NDC's COD Status indicates a less-than-effective drug;
- NDC has been terminated for more than 4 quarters;
- Labeler code is terminated for the submitted quarter/year combination;
- Labeler code does not participate in the MDR program;

As states evaluate whether submitted SDUD should be revised, they should also evaluate whether their CMS-64-R reports require revision because they included costs for drugs that do not qualify for FFP. States may find additional helpful information in the Medicaid Drug Rebate Data Guide for States that is located in the "Documents" section of DDR.

To better hold states accountable for their data integrity and to mitigate the effects of inaccurate and untimely SDUD, we proposed to revise § 447.511. Specifically, we proposed to revise paragraph (a) to specify that any subsequent updates or changes in the data on the CMS-R-144 must be included in the state's utilization data submitted to CMS. We also proposed to revise paragraph (b) to state that, on a quarterly basis, the state must submit drug utilization data to CMS, which will be the same information as submitted to the manufacturers on the CMS-R-144, as specified in § 447.511(a). In addition, to conform to the statutory requirement at section 1927(b)(2)(A) of the Act, we proposed to add in regulatory text that the state data submission will be due no later than 60 days after the end of each rebate period. In the event that a due date falls on a weekend or federal holiday, the submission will be due on the first business day following that weekend or federal holiday. We also proposed that any adjustments to submitted data would be transmitted to the manufacturer and CMS in the same reporting period.

We also proposed to add § 447.511(d) to specify that the state data must be certified by the state Medicaid director (SMD), the deputy state Medicaid director (DSMD), or an individual other than the SMD or DSMD, who has authority equivalent to an SMD or DSMD or an individual with the directly delegated authority to perform the certification on behalf of the individuals noted in this rule.

We also proposed to add § 447.511(e) to specify the state data certification language that must be included in the submission. That is, each data submission by a state must include the following certification language:

I hereby certify, to the best of my knowledge, that the state's data submission is complete and accurate at the time of this submission, and was prepared in accordance with the state's good faith, reasonable efforts based on existing guidance from CMS, section 1927 of the Act and applicable federal regulations. I further certify that the state has transmitted data to CMS, including any adjustments to previous rebate periods, in the same reporting period as provided to the manufacturer. Further, the state certifies that it has applied any necessary edits to the data for both CMS and the manufacturer to avoid inaccuracies at both the NDC/line item and file/aggregate level. Such edits are to be applied in the same manner and in the same reporting period to both CMS and the manufacturer.

We received the following comments on our proposed changes to the requirements for states (§ 447.511).

Comment: One commenter requested clarification as to whether a fiscal agent Rebate Analyst (that is, a contractor) can be delegated the authority from the SMD or DSMD to certify the quarterly file transfer.

Response: The proposed rule specified that the authority to certify may also be delegated to an individual who is authorized to perform the certification on behalf of the SMD or DSMD, and does not limit or restrict a state's ability to delegate the certification function to a fiscal intermediary or contractor. Ultimately, it is the state's responsibility to ensure that the data submitted to CMS complies with the applicable statutory and regulatory requirements and is certified as required.

After consideration of the comments, we are finalizing the proposed rule without modification. However, since CMS will need to develop a collection instrument to address these requirements, we are delaying the effective date of this provision until January 1, 2022.

I. State Plan Requirements, Findings and Assurances (§ 447.518)

Traditionally, states have utilized the SRA pathway to secure additional rebates over and above the federal rebate required of manufacturers participating in the MDRP. To do so, the Secretary must authorize a state to enter directly into these agreements with a manufacturer in accordance with section 1927(a)(1) of the Act. In accordance with section 1927(a)(1) of the Act, we require states to submit a SPA for a SRA which includes a template of the SRA providing the framework for the agreement the state

has with the manufacturer. A CMS-authorized SRA provides the parameters the state and manufacturer agree upon regarding the supplemental rebates, including that such rebates are at least as large as the rebates required by the federal government.

To make new and innovative drugs more available to Medicaid patients, states are permitted to use a SRA pathway to negotiate VBP agreements with manufacturers that are intended to be financially beneficial for Medicaid. As with a traditional SRAs, these VBP SRAs must be financially advantageous for states, but may also include an evidence or outcomes-based measure linked to the rebate. As with any other SRA, states are required to seek a SPA approval for a VBP SRA in accordance with section 1927(a)(1) of the Act. Through the SRA SPA process, a state, when approved by CMS, can enter into VBP SRAs directly with manufacturer(s) for both FFS and MCO (including PHIPs and PHAPs) COD claims. Under the SRA VBP arrangement, the state may need to set up processes to report the results of the evidence or outcomes-based measures of the patient back to the manufacturer. This could require the state to take on additional responsibilities and expense to eventually collect a rebate, such as tracking the patient, collecting data on the patient (such as the results of evidence or outcomes-based measures) or providing services to the patient.

We understand that more states want to develop their own VBP arrangements, but states want to better understand the challenges, resources and costs to structure these programs and make them successful. In addition, given that we have a significant interest in the success of these innovative VBP programs, as well as the nature of the drugs that are subject to these agreements, we have an interest in helping evaluate these programs' effectiveness. To accomplish this, we want to create a mechanism to exchange information about state VBP programs. This approach is consistent with section 1902(a)(30)(A) of the Act which requires that methods and procedures be established relating to the utilization of, and the payment for, care and services available under the plan (including but not limited to utilization review plans) as may be necessary to safeguard against unnecessary utilization of such care and services and to assure that payments are consistent with efficiency, economy, and quality of care.

Therefore, in accordance with section 1902(a) of the Act, we proposed that states provide to us specific data elements associated with these CMS-

authorized VBP SRAs to ensure that payments associated with Medicaid patients receiving a drug under a VBP structure are consistent with efficiency, economy, and quality of care. To that end, we proposed adding § 447.518(d)(1) and (2) to specify that a state participating in a CMS-authorized supplemental rebate VBP arrangement report data as specified on a yearly basis, and within 60 days of the end of each year, including the following data elements:

- State.
- National Drug Code(s) (for the drugs covered under the VBP arrangement).
- Product's FDA list name
- Number of prescriptions.
- Cost to the state to administer VBP arrangement (for example, systems changes, tracking outcomes, etc.).
- Total savings generated by the supplemental rebates due to VBP arrangement.

We invited comments on this approach and were particularly interested in understanding from the states those issues regarding the burden that such a proposal might create, and from all commenters on whether the data elements being collected are appropriate and useful to meet the goals of the proposal that we have described in this rule.

We received the following comments on state plan requirements, findings and assurances (§ 447.518).

Comment: A few commenters did not support the proposed changes to the state plan requirements section regarding VBP data requirements and recommended CMS clarify that states do not need to seek approval via a SPA to enter into VBP arrangements, whether based upon manufacturer arrangements with commercial payers or on their own. However, one commenter agreed that states should not be able to implement such substantial shifts (for example VBP arrangements) in their operations without federal approval.

Response: We understand that there may have been confusion over the breadth of our proposal. This new state reporting requirement will apply only to the information and data generated under the CMS-authorized VBP SRAs that states enter into with manufacturers under CMS approved templates. Therefore, we are revising the proposed changes to § 447.518(d)(1) and (2) (in this final rule at § 447.518(d)(2) and (3)) to make it clear that the data be specific only to CMS-authorized supplemental rebate agreements. As noted above, several state Medicaid programs already have CMS-authorized supplemental rebate agreements that provide a template for them to enter into VBP

agreements with manufacturers. These specific agreements allow the rebates that are negotiated with the manufacturers to be exempt from best price as found under our regulations at § 447.505(c)(7). We will continue to require that states seek approval of these types of SRAs through the SPA process.

States will not need to seek CMS approval for entering into a VBP agreement with a manufacturer under the new multiple best price approach. Nor will states have to report to CMS any information or data generated under these arrangements. We would expect that states and manufacturers would have to enter into a separate agreement under a multiple best price arrangement to indicate their intent to meet the manufacturer's requirements (for example, patient testing, patient tracking). Should the manufacturer and state negotiate additional rebates over and above those that are offered under the VBP arrangement reported to CMS, then the state would have to do that under a CMS authorized VBP SRA to exempt those prices from "best price."

We refer readers to the description of current policy related to state utilization of SRAs as a pathway to securing additional rebates over and above the federal rebate required of manufacturers participating in the MDRP in the proposed rule (85 FR 37302 and 37303), and past guidance regarding SRAs and SPA requirements, which is available at <https://www.medicaid.gov/federal-policy-guidance/downloads/smd091802.pdf> and <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/mfr-releases/mfr-rel-099.pdf>.

Comment: Several commenters supported the proposed changes for states to seek a SPA prior to implementing changes to SRAs. One commenter noted the SPA requirements improve the MDRP and allow those states that have an interest to adopt the same types of agreements that manufacturers have entered into with commercial payers.

Response: We are not revising the state plan requirements related to the SPA process for submission of SRAs. However, we are adding a new requirement relating to the conditions for the approval of such CMS authorized VBP SRAs such that states provide us with certain information relative to the operation and results of the VBP program so that we may evaluate the effectiveness of the programs and share the information with other states. We proposed that states provide to us specific data elements associated with VBP SRAs to ensure that payments

associated with Medicaid patients receiving a drug under a VBP structure are consistent with efficiency, economy, and quality of care.

Comment: One commenter noted these requirements improve transparency relevant to the effectiveness of VBP arrangements as part of a state's SRA, but expressed concern that this approach could affect Medicaid MCOs from negotiating between states and pharmaceutical manufacturers.

Response: We agree that the proposed requirements to collect data regarding a state's VBP SRA arrangement may impact Medicaid MCO negotiations with states and manufacturers to the extent the state and the Medicaid MCO have agreed to include Medicaid managed care enrollees in the state's VBP SRA arrangements. If the Medicaid managed care enrollees are part of the state's VBP SRA arrangement, the state and Medicaid MCO will likely need to establish responsibilities regarding the collection and reporting of data so that states meet the data collection requirements set forth in this final rule.

Comment: A few commenters provided additional recommendations to the proposed changes to § 447.518(d) for CMS' consideration. One commenter recommended that CMS develop a federal framework for state Medicaid agencies to design and implement a VBP arrangement, including expanding the existing SRA requirements to better enable state VBP arrangements. Another commenter recommended CMS require VBP arrangements to include minimum and maximum and expected rebates, such as a high cost drug threshold to avoid impact to Preferred Drug List classes and SRAs.

Response: We have an interest in helping states ensure they understand and evaluate these programs' effectiveness. To accomplish this, we proposed the collection of specific data elements to exchange information about state VBP programs, and in the event this information reveals federal involvement is needed we may address it in the future. We believe our proposal is consistent with section 1902(a)(30)(A) of the Act which provides that a state plan must provide, in part, such methods and procedures relating to the utilization of, and the payment for, care and services available under the plan (including but not limited to utilization review plans) as may be necessary to safeguard against unnecessary utilization of such care and services and to assure that payments are consistent with efficiency, economy, and quality of care.

Comment: A few commenters agreed with the proposed state reporting requirements and offered additional recommendations to CMS. One commenter recommended additional reporting elements, including identifying the drugs under the VBP arrangement, the number of prescriptions, and the costs and savings attributed to the arrangement, and the number of beneficiaries covered under a VBP arrangement. One commenter recommended states report to CMS the average net price paid per unit and per prescription of each drug in a state's VBP arrangement.

Response: We appreciate the support for the proposed data elements and appreciate the suggestions for additional reporting elements. We are finalizing the regulation as proposed, which includes a requirement for the state to identify the specific drug by NDC, the product FDA list name, and the number of prescriptions, and cost and savings attributed to the VBP arrangement. Further instructions regarding the instrument for collection of these data elements will be provided in guidance. We are not finalizing a requirement for the state to report the number of beneficiaries covered under a particular VBP arrangement, as reporting of a low number of participants may lead to privacy concerns. As for the recommendation to require the reporting of the net price paid per unit and per prescription of each drug, we are not accepting this recommendation as this data element relates to a manufacturer's proprietary drug pricing information.

Comment: A few commenters had concerns about consistency of state reporting and requested further guidance or modifications to the proposed data. Specifically, a commenter recommended CMS provide guidance to states to ensure the accuracy and consistency of state calculations of the required elements. Another commenter recommended CMS mandate that states provide claims-level data as a means of ensuring the accuracy of their calculations and reporting.

Response: We intend to prepare a collection instrument which will allow states to report consistent data. If necessary, we will provide additional guidance as states submit reporting obligations. We will not require state collection and reporting of claims-level data at the federal level. However, a state may review its own claims-level data related to the VBP arrangement to further analyze Medicaid beneficiary impact and overall Medicaid program impact at the state level.

Comment: One commenter noted VBP arrangements may involve measuring outcomes over months or years so reporting that would take place annually may fail to provide an accurate measure of the total savings.

Response: We agree that measuring outcomes may take place over a period longer than a year and annual reporting may not result in a full picture of what savings can be generated by a VBP arrangement. Therefore, we are requesting that the data collected and reported in the annual report be cumulative so that the annual report provides the data elements that are requested, and that the final report on the VBP program is generated within 60 days after the final year of the VBP time period. Therefore, we are revising the regulation at § 447.518(d)(2) and (3) to provide that a state participating in a VBP arrangement approved under a CMS authorized SRA report the required data (including cumulative data to date) found at paragraphs (d)(3)(i) through (vi) within 60 days of the end of each year also include cumulative data.

Comment: One commenter did not support the proposed state VBP reporting requirements and recommended CMS implement reporting requirements at a later date.

Response: These reporting requirements will be effective January 1, 2022. This will give states time to prepare to submit this information to us.

Comment: Several commenters disagreed with the proposed state reporting requirements citing their belief that they will disclose proprietary information between the manufacturer, PBM, and state. These commenters recommended CMS clarify that the actual terms and conditions of the contracts would not be subject to full disclosure.

Response: We do not believe the data elements that will be collected in accordance with this final rule will disclose proprietary information. The reporting requirements do not include a state's reporting of actual terms and conditions of the contracts between the state, manufacturer(s), and PBMs.

Comment: A few commenters recommended CMS establish clear guidance regarding how states should calculate savings in a VBP SRA arrangement and how states should calculate the administrative expenses of entering into a VBP SRA arrangement. Another commenter noted the data element requiring states to report the total savings generated by the supplemental rebate due to the VBP may underestimate savings due to failure to account for rebates that have

yet to be paid. One commenter requested clarification on how CMS intends to utilize these annual state reports to evaluate VBP SRA arrangements.

Response: We are finalizing the proposal to require the data elements specified in the proposed rule and will provide further instructions regarding the collection of these data elements in guidance. Given the fact that each VBP arrangement has distinct measures and cost strategies, a one size fits all approach to calculating savings will be a challenge to state Medicaid programs. As stated in the preamble to the proposed rule, these annual reports from states will give CMS and states a better understanding of the challenges, resources and costs to structure these programs and make them successful. To accomplish this, we believe this collection will assist states in evaluating information about savings generated by state supplemental rebates received under VBP arrangements.

Comment: One commenter supported the proposed data elements required to be reported by states to CMS, although noted that many VBP arrangements may show little-to-no economic value in the beginning especially during a multi-year arrangement.

Response: We appreciate the support for the collection of the data elements. The reporting of these data elements will hopefully guide us and the states that choose to participate in VBP arrangements as to whether participating in such arrangements bring economic value to Medicaid.

For the reasons stated above, we are finalizing the policy that states that enter into VBP agreements with manufacturers under a CMS-authorized supplemental rebate agreement template must report to us within 60 days of the end of each calendar year, on the data described in the regulation, including cumulative data to date, regarding the operation and parameters of their VBP arrangements. Thus, for the reasons discussed in the proposed rule (82 FR 37302 and 37303) and after consideration of the comments received we are finalizing the regulations as proposed with modification to 447.518(d) by making it clear that only VBP arrangements approved under a CMS-authorized SRA must submit the data described and "including cumulative data to date" in the regulatory text. Furthermore, while we proposed to revise § 447.518(d)(1) and (2), we are redesignating these sections as § 447.518(d)(2) and (3) in this final rule. This section will not be effective until January 1, 2022 to allow time for

CMS to generate a collection instrument to collect the state's information.

J. Drug Utilization Review (DUR) Program and Electronic Claims Management System for Outpatient Drug Claims (§§ 456.700 Through 456.725), Managed Care Standard Contract Requirements and Requirements for MCOs, PIHPs, or PAHPs That Provide CODs (§ 438.3(s))

Section 1004 of the SUPPORT Act requires states to implement certain opioid-specific DUR standards within their FFS and managed care programs. These requirements supplement preexisting DUR standards under section 1927(g) of Act. In Medicaid, DUR involves the structured, ongoing review of healthcare provider prescribing, pharmacist dispensing, and patient use of medication. DUR involves a comprehensive review of patients' prescription and medication data and dispensing to help ensure appropriate medication decision-making and positive patient outcomes. Potentially inappropriate prescriptions, unexpected and potentially troublesome patterns, data outliers, and other issues can be identified when reviewing prescriptions through prospective DUR or retrospective DUR activities. In Prospective DUR, the screening of prescription drug claims occurs to identify problems such as therapeutic duplication, drug-disease contraindications, incorrect dosage or duration of treatment, drug allergy and clinical misuse or abuse prior to dispensing of the prescription to the patient. Retrospective DUR involves ongoing and periodic examination and reviews of claims data to identify patterns of inappropriate use, fraud, abuse, or medically unnecessary care, and facilitates corrective action when needed. Often times, these activities are synergistic; information gleaned through retrospective DUR claim reviews can be used to shape effective safety edits that can be implemented through prospective DUR, better enabling prescribers and dispensers to investigate prescription concerns prior to dispensing the medication to the patient. From prospective alerts (which can incorporate information from the beneficiary's claims data), potential issues can be identified to help promote the appropriate prescription and dispensing of outpatient drugs to beneficiaries. DUR programs play a key role in helping health care systems understand, interpret, and improve the prescribing, administration, and use of medications.

Section 1902 of the Act, as amended by section 1004 of the SUPPORT Act,

requires states to implement safety edits and claims review automated processes for opioids as DUR requirements. We interpret “safety edits” to refer to the prospective DUR review specified in section 1927(g)(2)(A) of the Act. These prospective safety edits provide for identifying potential problems at point of sale (POS) to engage both patients and prescribers about identifying and mitigating possible opioid misuse, abuse, and overdose risk at the time of dispensing. The POS safety edits provide real-time information to the pharmacist prior to the prescription being dispensed to a patient, but do not necessarily prevent the prescription from being dispensed. When a safety edit is prompted, the pharmacist receives an alert and may be required as dictated by good clinical practice and predetermined standards determined by the state, to take further action to resolve the issue flagged by the alert before the prescription can be dispensed.²³ A claims review automated process, which we interpret to refer to as a retrospective DUR review as defined in section 1927(g)(2)(B) of the Act, provides for additional examination of claims data to identify patterns of fraud, abuse, gross overuse, or inappropriate or medically unnecessary care. Retrospective reviews often involve reviews of patient drug and disease history generated from claims data after prescriptions have been dispensed to the beneficiary. For many retrospective reviews, in an effort to promote appropriate prescribing and utilization of medications, claims data is evaluated against state determined criteria on a regular basis to identify recipients with drug therapy issues, enabling appropriate action to be taken based on any issues identified. After these reviews, prescribers often have the opportunity to review prescriptions and diagnosis history and make changes to therapies based on the retrospective review intervention. Retrospective claims reviews provide access to more comprehensive information relevant to the prescriptions and services that are being furnished to beneficiaries and better enable and encourage prescribers and dispensers to minimize opioid risk in their patients, and assure appropriate pain care.

Many of the proposed safety edits and reviews described in the June 2020 proposed rule were designed to implement requirements outlined in the

SUPPORT Act. The purpose of these safety edits and claims reviews is to prompt prescribers and pharmacists to conduct additional safety reviews to determine if the patient’s opioid use is appropriate and medically necessary. Provisions to address antipsychotic utilization in children and fraud and abuse requirements were also included in the SUPPORT Act and are measures designed to enhance appropriate utilization of medication. In the proposed rule, we recognized that the SUPPORT Act provides considerable flexibility for states to specify particular parameters of the safety edits, claims review automated processes, program for monitoring use of antipsychotic medications in children, and process for identifying fraud and abuse. Additionally, we acknowledged that many states already have effective DUR processes and other controls in place, and that section 1902(oo)(1)(E) of the Act (as added by section 1004 of the SUPPORT Act) clarified that states may meet new opioid-related requirements with such safety edits, claims review automated processes, programs, or processes as were in place before October 1, 2019. However, to ensure a consistent baseline of minimum national standards for these DUR activities, while preserving appropriate flexibility for the states to determine their particular parameters and implementation, we explained our belief that it is necessary under our authority to implement section 1927(g) of the Act, to ensure that prescriptions are appropriate, medically necessary, and not likely to result in adverse medical results, to codify in regulation the proposed safety edits, claims review automated processes, program for monitoring antipsychotic medications in children, and fraud and abuse process requirements as described in the June 2020 proposed rule. Accordingly, we proposed provisions to implement opioid-related requirements established in the SUPPORT Act and further implement requirements under section 1927(g) of the Act, in an effort to reduce prescription-related fraud, misuse and abuse.

In addition to codifying the SUPPORT Act requirements, we proposed additional minimum DUR standards in the June 2020 proposed rule that states would be required to implement as part of their DUR programs. Specifically, section 1927 of the Act provides for drug use review programs for CODs to ensure that prescriptions (1) are appropriate, (2) are medically necessary, and (3) are not likely to result in adverse medical results. Accordingly, under our

authority to implement section 1927(g) of the Act and consistent with the goals of the SUPPORT Act to ensure the appropriate use of prescription opioids, we proposed minimum standards for DUR reviews related to medication assisted treatment (MAT) and identification of beneficiaries who could be at high risk of opioid overdose for consideration of co-prescription or co-dispensing of naloxone.

We also sought comments on potential additional standards that we might implement through future rulemaking, to ensure minimally adequate DUR programs that help ensure prescribed drugs are appropriate, medically necessary, and not likely to result in adverse medical results. We interpreted adverse medical results to include medication errors or medical adverse events, reactions and side effects. We noted our anticipation that any such additional standards would be clinically based and scientifically valid and developed with state collaboration, standards development organizations, and entities that support Medicaid DUR programs, and would help ensure all states have established a reasonable and appropriate DUR program. Such proposed standards would align with current clinical guidelines and could address the following: Maintaining policies and systems to assist in preventing over-utilization and under-utilization of prescribed medications, establishing quality assurance measures and systems to reduce medication errors and adverse drug interactions, and improving medication compliance and overall well-being of beneficiaries. We also noted that we would consider other mechanisms to encourage states to adopt additional DUR standards in a timely manner to respond to new and emerging issues in drug use, as the rulemaking process can be a lengthy process. For example, we are considering issuing possible future suggested “best practices” or guidance for states in advance of and in anticipation of rulemaking. We sought comments on the best processes for collaboratively developing future minimum DUR standards and sought comments from states and other commenters on potential approaches.

The early signs of the opioid crisis emerged years ago, with groundwork for the crisis being laid in the late 1990s, when providers began to prescribe opioid analgesics at greater rates, which led to widespread misuse and abuse of both prescription and illegal opioids. After what the CDC characterizes as a “first wave” of opioid deaths, a second wave followed in 2010, involving heroin, with a third wave beginning in

²³ Prada, Sergio. (2019). Comparing the Medicaid Prospective Drug Utilization Review Program Cost-Savings Methods Used by State Agencies in 2015 and 2016. American Health and Drug Benefits. 12–7–12.

2013 involving overdoses from synthetic opioids.²⁴ CDC data indicate that from 1999 through 2017, almost 400,000 people died in the United States from an overdose involving any opioid, including prescription and illicit opioids.²⁵ In 2018, there were an additional 67,367 drug overdose deaths in the United States. The age-adjusted rate of overdose deaths decreased by 4.6 percent from 2017 (21.7 per 100,000) to 2018 (20.7 per 100,000). Opioids—mainly synthetic opioids (other than methadone)—are currently the main driver of drug overdose deaths. Opioids were involved in 46,802 overdose deaths in 2018 (69.5 percent of all drug overdose deaths)²⁶ and two out of three (67.0 percent) opioid-involved overdose deaths involved synthetic opioids.²⁷

In a 2016 informational bulletin titled, “Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction,”²⁸ CMS issued guidance to states to outline how to help curb the opioid crisis, and in 2019, guidance was issued on how states can use statutory authority to expand the treatment of pain through complementary and integrative approaches.²⁹ Section 6032 of the SUPPORT Act has directed HHS to collaborate with the Pain Management Best Practices Inter-Agency Task Force (PMTF) to develop an action plan on payment and coverage in Medicare and Medicaid for acute and chronic pain, and substance use disorders (SUDs), informed by a RFI and a public meeting held at CMS in September, 2019.³⁰ The action plan is related to CMS’s Fighting

the Opioid Crisis Roadmap, which describes our three-pronged approach to managing pain using a safe and effective range of treatment options that rely less on prescription opioids, expanding treatment for opioid use disorder (OUD), and using data to target prevention efforts and identify fraud and abuse.³¹

In 2018, the SUPPORT Act was passed as part of a bipartisan effort to address the opioid crisis, as well as the treatment of pain. The practice of chronic pain management and the opioid crisis have influenced one another as each has evolved in response to different influences and pressures. At the same time CMS seeks to implement these requirements, we want to ensure Medicaid beneficiaries with chronic pain can work with their health care providers to optimize function, quality of life, and productivity while minimizing risks for opioid misuse and harm such as addiction and overdose.³² Therefore, we discussed in the June 2020 proposed rule that we considered appropriate approaches through which we could collaboratively develop future minimum DUR standards with involvement from states and other commenters, taking into account the need for administrative flexibility and adequate time for operational implementation, which could be implemented more quickly to respond to public health crises that may arise in the future on a more rapid timeframe. We also considered posting DUR recommendations on our website or through guidance to states to allow quick dissemination of the information.

1. Minimum Standards for DUR Programs Under the SUPPORT Act and Section 1927 of the Act

In § 456.703, we proposed to redesignate paragraph (h) as paragraph (i) and to add a new paragraph (h), specifying minimum standards for DUR programs. The proposed minimum standards in § 456.703(h)(1), discussed in greater detail in this rule, would implement the amendments made by section 1004 of the SUPPORT Act and section 1927(g) of the Act and are intended to help ensure DUR programs continue to adapt and improve the quality of pharmaceutical care provided to beneficiaries in the face of evolving healthcare guidelines and technology practices.

We proposed the provisions in this rule for implementation of requirements in the SUPPORT Act³³ consistent with section 1927(g) of the Act. The proposed safety edits and claim reviews were intended to help protect beneficiaries from serious potential consequences of overutilization, including misuse, abuse, overdose, and increased side effects. In addition to the risk of overutilization and diversion, we noted that opioids can have side effects including respiratory depression, confusion, tolerance, and physical dependence.³⁴

The CDC has recommended, in 2016 guidance,³⁵ that primary care providers prescribing to adults in outpatient settings consider non-pharmacologic therapy and non-opioid pharmacologic therapy as the first-line treatment for chronic pain.³⁶ The CDC guideline defines chronic pain as “pain continuing or expected to continue for greater than 3 months or past the time of normal tissue healing.” Regarding chronic pain, CDC states clinicians should use caution when initiating prescribing opioids at any dosage, and should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day.³⁷ Caution is also recommended in prescribing opioids for acute pain, noting that long-term opioid use often begins with treatment of acute pain; when opioids are prescribed for non-traumatic, non-surgical acute pain, primary care clinicians should prescribe the lowest effective dose for the shortest duration possible—usually 3 days or less is sufficient and more than 7 days will

²⁴ “Understanding the Epidemic.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 19 Dec. 2018, <https://www.cdc.gov/drugoverdose/epidemic/index.html>.

²⁵ “Understanding the Epidemic.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 19 Dec. 2018, www.cdc.gov/drugoverdose/epidemic/index.html.

²⁶ Hedegaard H, Miniño AM, Warner M. Drug Overdose Deaths in the United States, 1999–2018. pdf icon NCHS Data Brief, no. 356. Hyattsville, MD: National Center for Health Statistics. 2020.

²⁷ Wilson N, Kariisa M, Seth P, et al. Drug and Opioid-Involved Overdose Deaths—United States, 2017–2018. MMWR Morb Mortal Wkly Rep 2020; 69:290–297.

²⁸ “Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction.” CMCS Informational Bulletin available at www.medicare.gov/federal-policy-guidance/downloads/CIB-02-02-16.pdf.

²⁹ “Medicaid Strategies for Non-Opioid Pharmacologic and Non-Pharmacologic Chronic Pain Management.” CMCS Informational Bulletin at <https://www.medicare.gov/sites/default/files/federal-policy-guidance/downloads/cib022219.pdf>.

³⁰ “Request for Information for the Development of a CMS Action Plan to Prevent Opioid Addiction and Enhance Access to Medication-Assisted Treatment.” CMCS request for information available at <https://www.cms.gov/About-CMS/Story-Page/Opioid-SUPPORT-Act-RFI.pdf>.

³¹ “CMS Roadmap: Fighting the Opioid Crisis.” Available at <http://www.cms.gov/About-CMS/Agency-Information/Emergency/Downloads/Opioid-epidemic-roadmap.pdf>.

³² Pain Management Best Practices Inter-Agency Task Force. “Pain Management Best Practices.” Available at <https://www.hhs.gov/sites/default/files/pmtf-final-report-2019-05-23.pdf>.

³³ <https://www.congress.gov/115/bills/hr6/BILLS-115hr6enr.pdf>.

³⁴ “CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 29 Aug. 2017, <https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/r6501e1er.pdf>.

³⁵ “CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 18 Mar. 2016, https://www.cdc.gov/mmwr/volumes/65/rr/r6501e1.htm?CDC_AA_refVal=https://www.cdc.gov/mmwr/volumes/65/rr/r6501e1er.html.

³⁶ Dowell, D., Haegerich, T.M., Chou, R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States 2016, *Morbidity and Mortality Weekly Report* March 18, 2016; 65(1) [Accessed February 11, 2019 at <https://www.cdc.gov/mmwr/volumes/65/rr/r6501e1.htm>].

³⁷ “CDC Guidelines for Prescribing Opioids for Chronic Pain.” Available at https://www.cdc.gov/drugoverdose/pdf/guidelines_at-a-glance-a.pdf.

rarely be needed.³⁸ Non-pharmacologic therapies pose minimal risks, and many of these treatments, when available and accessible—such as exercise therapy, physical therapy, and cognitive behavioral therapy (CBT)—have been shown to effectively treat chronic pain associated with some conditions.³⁹ For example, exercise therapy can be effective in treating moderate pain associated with lower back pain, osteoarthritis, and fibromyalgia in some patients.⁴⁰

In 2019, HHS' PMTF issued its report to HHS and Congress, *the Pain Management Best Practices Inter-Agency Task Force Report*, on best practices for the treatment of acute and chronic pain. The CDC has identified 50 million adults in the United States with chronic daily pain,⁴¹ and the National Institutes of Health (NIH) states that chronic daily pain cost the nation between \$560 billion and \$635 billion annually.^{42 43} The PMTF final report emphasizes a person-centered approach to pain care that includes the use of individualized, multimodal treatment based on an effective pain treatment plan, and the PMTF identified and described five broad treatment categories: Medications; restorative therapies; interventional approaches; behavioral approaches; and complementary and integrative health that can be used through multidisciplinary care. In its report, the PMTF recognized that there have been “unintended consequences that have resulted following the release of the CDC guideline in 2016, which are due

in part to misapplication or misinterpretation of the guideline, including forced tapers and patient abandonment”⁴⁴ and noted the “CDC has also published a pivotal article in the *New England Journal of Medicine* on April 24, 2019, specifically reiterating that the CDC guideline has been, in some instances, misinterpreted or misapplied.”⁴⁵ HHS recently issued the Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics, to assure proper tapering and discontinuation of long-term opioids, in part to avoid harms and encourage person-centered care that is tailored to the specific needs and unique circumstances of each pain patient,⁴⁶ in addition to the CMS-issued guidance to states in 2016 and 2019 to both outline how to help curb the opioid crisis and provide guidance to states that want to expand care for the treatment of pain.^{47 48}

Accordingly, we proposed to add § 456.703(h)(1)(i) to include minimum standard requirements as described in the June 2020 proposed rule, with the detailed design and implementation specifications left to the state's discretion to meet state-specific needs. We noted that the purpose of these proposed safety edits (specifically, safety edits to implement state-defined limits on initial prescription fill days' supply for patients not currently receiving opioid therapy, quantity, duplicate fills, and early refills) and reviews is to further implement section 1927(g) of the Act to prevent and reduce the inappropriate use of opioids and potentially associated adverse medical events to sufficiently address the nation's opioid overdose epidemic, consistent with the provisions under section 1004 of the SUPPORT Act.

When implementing the SUPPORT Act, we proposed the following safety edits in § 456.703(h)(1)(i) in addition to

a comprehensive opioid claims review automated retrospective review process where trends witnessed in safety edits can be reviewed and investigated. We noted that these reviews would allow subsequent appropriate actions to be taken as designed by the states.

a. Opioid Safety Edits Including Initial Fill Days' Supply for Opioid-Naïve Beneficiaries, Quantity, Therapeutically Duplicative Fills, and Early Refill Limits

The SUPPORT Act requires states to have in place prospective safety edits (as specified by the state) for subsequent fills for opioids and a claims review automated process (as designed and implemented by the state) that indicates when an individual enrolled under the state plan (or under a waiver of the state plan) is prescribed a subsequent fill of opioids in excess of any limitation that may be identified by the state.⁴⁹ As discussed in detail in this rule, consistent with the SUPPORT Act and DUR requirements under section 1927(g)(2)(A) of the Act, we proposed that state-identified limitations must include state-specified restrictions on initial prescription fill days' supply for patients not currently receiving opioid therapy; quantity limits for initial and subsequent fills, therapeutically duplicative fills, and early fills on opioids prescriptions; and a claims review automated process that indicates prescription fills of opioids in excess of these limitations to provide for the ongoing periodic reviews of opioids claim data and other records to identify patterns of fraud, abuse, excessive utilization, or inappropriate or medically unnecessary care, or prescribing or billing practices that indicate abuse or excessive utilization among physicians, pharmacists and individuals receiving Medicaid benefits. To further implement section 1927(g)(1) of the Act, and consistent with section 1004 of the SUPPORT Act, we proposed to require these safety edits to reinforce efforts to combat the nation's opioid crisis and ensure DUR opioid reviews are consistent with current clinical practice. We noted that these proposed safety edits were intended to protect Medicaid patients from serious consequences of overutilization, including overdose, dangerous interactions, increased side effects and additive toxicity (additive side effects). In addition, we noted that overutilization of opioids may serve as an indication of uncontrolled disease

³⁸ Dowell, D., Haegerich, T.M., Chou, R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States 2016, *Morbidity and Mortality Weekly Report* March 18, 2016; 65(1) [Accessed February 11, 2019 at <https://www.cdc.gov/mmwr/volumes/65/rr/r6501e1.html>].

³⁹ For a review of the evidence base for CBT, see Ehde D.M., Dillworth, T.M. and Turner, J.A. 2014. Cognitive-Behavioral Therapy for Individuals with Chronic Pain: Efficacy, Innovations, and Directions for Research. *American Psychologist*, 69(2); 153–166.

⁴⁰ Additional information on non-opioid treatments for chronic pain are available at https://www.cdc.gov/drugoverdose/pdf/nonopioid_treatments-a.pdf.

⁴¹ “Managing Chronic Pain.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 18 Dec. 2019, www.cdc.gov/learnmore/feelbetter/programs/chronic-pain.htm.

⁴² Gaskin, Darrell J. “The Economic Costs of Pain in the United States.” *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.*, U.S. National Library of Medicine, 1 Jan. 1970, www.ncbi.nlm.nih.gov/books/NBK92521/.

⁴³ “Prevalence of Chronic Pain and High-Impact Chronic Pain among Adults—United States, 2016.” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 16 Sept. 2019, www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm.

⁴⁴ Additional information on non-opioid treatments for chronic pain are available at https://www.cdc.gov/drugoverdose/pdf/nonopioid_treatments-a.pdf.

⁴⁵ Dowell D, Haegerich TM, Chou R. No shortcuts to safer opioid prescribing. *N Engl J Med* 2019; 380: 2285–2287.

⁴⁶ HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. Oct. 2019, www.hhs.gov/opa/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf.

⁴⁷ “Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction.” CMCS Informational Bulletin available at www.medicaid.gov/federal-policy-guidance/downloads/CIB-02-02-16.pdf.

⁴⁸ “Medicaid Strategies for Non-Opioid Pharmacologic and Non-Pharmacologic Chronic Pain Management.” CMCS Informational Bulletin at <https://www.medicaid.gov/federal-policy-guidance/downloads/cib022219.pdf>.

⁴⁹ Section 1902(o)(1)(A)(i)(I) of the Act, as added by section 1004 of the SUPPORT Act.

and the need of increased monitoring and coordination of care.

i. Limit on Days' Supply for Opioid Naïve Beneficiaries

To further implement section 1927(g)(1) of the Act, and consistent with section 1004 of the SUPPORT Act, we proposed to require states to establish safety edit limitations on the days' supply for an initial prescription opioid fill for beneficiaries who have not filled an opioid prescription within a defined time period to be specified by the state. In most cases, "Days Supply" is calculated by dividing the dispensed quantity of medication by the amount of the medication taken by the patient in one day per the prescriber's instructions. "Days' Supply" means how many days the supply of dispensed medication will last. This limit would not apply to patients currently receiving opioids and is meant for beneficiaries who have not received opioids within this specified time period (as defined and implemented by the state). The patients who have not received opioids within a specified timeframe are referred to as opioid naïve and would be subjected to the days' supply limit on the opioid prescription. While the SUPPORT Act mentions limits on subsequent fills of opioids, consistent with section 1927(g) of the Act, we proposed this edit on initial fills of opioids to help avoid excessive utilization by opioid naïve beneficiaries, with its attendant risk of adverse effects.

The CDC guideline recommends that opioids prescribed for acute pain in outpatient primary care settings to adults generally should be limited to 3 days or fewer, and more than a 7 days' supply is rarely necessary.⁵⁰ Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred and should be considered by practitioners and patients prior to treatment with opioids.⁵¹ Clinical evidence cited by the CDC review found that opioid use for acute pain is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use. An expected physiologic response in patients exposed to opioids for more than a few days is physical dependence and the chances of long-term opioid use begin to increase after just 3 days of use

⁵⁰ "CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 29 Aug. 2017. <https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/r6501e1er.pdf>.

⁵¹ Ibid.

and rise rapidly thereafter.⁵² The CDC guideline mentions that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply would minimize the number of pills available for unintentional or intentional diversion.⁵³

As discussed in the June 2020 proposed rule, long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.⁵⁴ Limiting days for which opioids are prescribed for opioid naïve patients could minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms and help prevent opioid dependence, the risk of which is associated with the amount of opioid initially prescribed.⁵⁵

On state DUR surveys, many states indicated they already have initial fill limitations in place describing the limitations of 100 dosage units or a 34-day supply. Initial opioid analgesic prescriptions of less than or equal to 7 days' duration appear sufficient for many pain patients seen in primary care settings.⁵⁶ We noted that, in its 2019 clarification of the guideline, the CDC noted that it was "intended for primary care clinicians treating chronic pain for patients 18 and older, and examples of misapplication include applying the guideline to patients in active cancer treatment, patients experiencing acute sickle cell crises, or patients experiencing post-surgical pain." States can consider the current CDC guideline and other clinical guidelines when

⁵² Shah A., Hayes C.J., Martin B.C. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use—United States, 2006–2015. *Morbidity and Mortality Weekly Report* 2017; 66:265–269 [Accessed February 11, 2019 at <http://dx.doi.org/10.15585/mmwr.mm6610a1>].

⁵³ Ibid.

⁵⁴ "CDC Guideline for Prescribing Opioids for Chronic Pain." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, https://www.cdc.gov/drugoverdose/pdf/guidelines_at-a-glance-a.pdf.

⁵⁵ Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017; 66(10):265–269. doi: 10.15585/mmwr.mm6610a1.

⁵⁶ "Days' Supply of Initial Opioid Analgesic Prescriptions and Additional Fills for Acute Pain Conditions Treated in the Primary Care Setting—United States, 2014 | MMWR." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, <https://www.cdc.gov/mmwr/volumes/68/wr/mm6806a3.htm>.

implementing initial fill limitations, being mindful of the context in which such guidelines are written (for example, acute pain, chronic pain, treatment setting, population, etc.).

The CDC guideline states primary care clinicians should assess benefits and harms of opioids with patients early on when starting opioid therapy for chronic pain and regularly when escalating doses and continue to evaluate therapy with patients on an ongoing basis. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioid therapy. Consistent with the foregoing clinical recommendations, we proposed to require states to implement safety edits aligned with clinical guidelines alerting the dispenser at the POS when an opioid prescription is dispensed to an opioid naïve patient that exceeds a state-specified days' supply limitation. In consideration of clinical recommendations to limit opioid use to the shortest possible duration and to assess the clinical benefits and harms of opioid treatment on an ongoing basis, we believe this safety edit is necessary to assure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse events, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed in § 456.703(h)(1)(i)(A) to require states to implement a days' supply limit when an initial opioid prescription is dispensed to a patient not currently receiving ongoing therapy with opioids.

ii. Opioid Quantity Limits

To further implement section 1927(g)(1) of the Act and section 1004 of the SUPPORT Act, we proposed to require states establish safety edits to require states establish safety edits to implement quantity limits on the number of opioid units to be used per day, as identified by the state. We proposed that states take clinical indications and dosing schedules into account when establishing quantity limits to restrict the quantity of opioids per day to ensure dose optimization and to minimize potential for waste and diversion. While the SUPPORT Act mentions quantity limits on subsequent fills of opioids, under section 1927(g) of the Act, we proposed this edit to apply for initial and subsequent fills of opioids to avoid excessive utilization, with its attendant risk of adverse effects.

We proposed that the quantity limits would be required to take into account both dosage and frequency, to allow for

dose optimization of pills, capsules, tablets, etc. (“pills”) and limit the supply of opioids being dispensed. Dose optimization is a method to consolidate the quantity of medication dispensed to the smallest amount required to achieve the desired daily dose and regimen. Dosage optimization seeks to prospectively identify patients who have been prescribed multiple pills per day of a lower strength medication meant to be taken together to achieve higher dose, when a higher strength of medication already is available, and provides clinicians a tool to switch these patients to a regimen that is an equivalent daily dose given as a single pill (or a smaller quantity of pills). Performing this intervention with medications that are available in multiple strengths, with comparable pricing among these strengths, can yield significant drug cost savings. In addition, dose-optimization simplifies dosing schedules, decreases pill burdens, improves treatment compliance and limits the number of excess units available for diversion.⁵⁷ We noted that the proposed safety edit would allow most patients to achieve pain relief while minimizing patient pill burdens and unnecessary unused opioids.⁵⁸ When implementing this edit, we noted that we would expect states to also consider current opioid guidelines, clinical indications, and dosing schedules of opioids to ensure prescriptions are appropriate, medically necessary, and not likely to result in adverse events.

Decreasing the initial amount prescribed will lower the risk that patients develop an addiction to these drugs and transition to chronic use or misuse.⁵⁹ A survey of adults in Utah estimated that in the previous 12 months, 1 in 5 state residents were prescribed an opioid medication and 72 percent had leftover pills and nearly three-quarters of those with leftover pills kept them.⁶⁰ Leftover medications are an important source of opioids that are misused or diverted.⁶¹ We believe that decreasing the initial amount

prescribed will lower the risk that patients develop OUD.⁶²

Prescribing opioids using lowest dosage at fewest possible units dispensed based on product labeling, and matching duration to scheduled reassessment, helps reduce the quantity of unused, leftover opioid pills. Additionally, clinicians should continue to evaluate benefits and harms of continued ongoing therapy with opioid patients every 3 months or more frequently.⁶³ As discussed in the June 2020 proposed rule, if benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.⁶⁴ In circumstances when beneficiaries are already opioid dependent, providers should consider initiating a treatment program, such as medication-assisted treatment (MAT) and/or behavioral counseling. State Medicaid programs already cover MAT, and as of October 2020, states are required cover MAT drugs and services as a mandatory benefit. We encourage states to consider the situation of opioid-dependent beneficiaries in designing and implementing quantity limits in their comprehensive DUR programs, to minimize any possibility of harm.

In consideration of clinical recommendations to limit opioid units to the fewest number possible and to assess the clinical benefits and harms of opioid treatment on an ongoing basis, we believe this safety edit is necessary to assure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse events, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(i)(B) that states be required to implement quantity limits on opioids prescriptions (both initial and subsequent fills) to help identify abuse, misuse, excessive utilization, or inappropriate or medically unnecessary care.

iii. Therapeutic Duplication Limitations

To further implement section 1927(g)(1) of the Act and section 1004 of the SUPPORT Act, we proposed to require states to establish safety edits to alert the dispenser to potential therapeutic duplication before a prescription is filled for an opioid product that is in the same therapeutic class as an opioid product currently being prescribed for the beneficiary. Prescriptions for multiple opioids and multiple strengths of opioids increase the supply of opioids available for diversion and abuse, as well as the opportunity for self-medication and dose escalation.⁶⁵ Some patients, especially those living with multiple chronic conditions, may consult multiple physicians, which can put them at risk of receiving multiple medications in the same therapeutic class for the same diagnosis.⁶⁶ In some instances, the side-effects produced by overmedication, due to the duplication of prescriptions within the same therapeutic class, are more serious than the original condition.⁶⁷ We proposed to require this opioid safety edit to help avoid inappropriate or unnecessary therapeutic duplication when simultaneous use of multiple opioids is detected.

In consideration of clinical recommendations to use caution in combining opioids and to limit opioid use to only when necessary while assessing clinical benefits and harms of opioid treatment on an ongoing basis, we believe this safety edit is necessary to assure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(i)(C) that states must implement safety edits for therapeutically duplicative fills for initial and subsequent prescription fills on opioid prescriptions and identify suspected abuse, misuse, excessive utilization, or inappropriate or medically unnecessary care.

iv. Early Fill Limitations

To further implement section 1927(g)(1) of the Act and section 1004 of the SUPPORT Act, we proposed to

⁵⁷ Calabrese D. Baldinger S., Dose Optimization Intervention Yields Significant Drug Cost Savings. <https://www.jmcp.org/doi/pdf/10.18553/jmcp.2002.8.2.146>.

⁵⁸ Daoust R. Limiting Opioid Prescribing. *JAMA*. 2019; 322(2):170–171. doi:10.1001/jama.2019.5844.

⁵⁹ http://www.cdc.gov/drugoverdose/pdf/hhs_prescription_drug-abuse_report_09.2013.pdf.

⁶⁰ *Ibid*.

⁶¹ “FDA Patient Education Campaign Targets Opioid Diversion, Disposal.” Available at <https://patientengagementhit.com/news/fda-patient-education-campaign-targets-opioid-diversion-disposal>.

⁶² Opioid Use during the Six Months After an Emergency Department Visit for Acute Pain: A Prospective Cohort Study. Friedman, Benjamin W. et al. *Annals of Emergency Medicine*, Volume 0, Issue 0.

⁶³ Dowell, Deborah, et al. “CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016.” *JAMA*, U.S. National Library of Medicine, 19 Apr. 2016, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6390846/>.

⁶⁴ Frieden TR, Houry D. Reducing the Risks of Relief—The CDC Opioid-Prescribing Guideline. *N Engl J Med*. 2016; 374(16):1501–1504. doi: 10.1056/NEJMp1515917.

⁶⁵ Manchikanti, Laxmaiah, et al. “Opioid Epidemic in the United States.” *Pain Physician*, U.S. National Library of Medicine, July 2012, www.ncbi.nlm.nih.gov/pubmed/22786464.

⁶⁶ *Ibid*.

⁶⁷ “Therapeutic Duplication.” *Journal of the American Medical Association*, vol. 160, no. 9, 1956, p. 780., doi:10.1001/jama.1956.02960440052016.

require that states establish safety edits to alert the dispenser before a prescription is filled early for an opioid product, based on the days' supply provided at the most recent fill or as specified by the state. As discussed in the June 2020 proposed rule, these early fill edits on opioids are intended to protect beneficiaries from adverse events associated with using an opioid medication beyond the prescribed dose schedule and to help minimize the opioid supply available for diversion.

In consideration of clinical recommendations to limit opioid use to only when necessary and as prescribed, we believe this safety edit is necessary to assure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(i)(D) that states must implement early fill safety alerts on opioid prescriptions to identify abuse, misuse, excessive utilization, or inappropriate or medically unnecessary care.

b. Maximum Daily Morphine Milligram Equivalent (MME) Limits

Section 1004 of the SUPPORT Act requires state DUR programs to include safety edit limits (as specified by the state) on the maximum daily morphine equivalent that can be prescribed to an individual enrolled under the state plan (or under a waiver of the state plan) for treatment of chronic pain (as designed and implemented by the state) that indicates when an individual enrolled under the plan (or waiver) is prescribed the morphine equivalent for such treatment in excess of any threshold identified by the state.⁶⁸ Accordingly, to further implement section 1927(g)(1) of the Act and section 1004 of the SUPPORT Act, we proposed that states must include in their DUR programs safety edit limitations identified by the state on the maximum daily MME for treatment of chronic pain and a claims review automated process, discussed in this rule in connection with paragraph (h)(1)(iii), that indicates when an individual is prescribed an MME in excess of these limitations.

Section 1004 of the SUPPORT Act specifically addresses MME limitations in the context of chronic pain.

According to the CDC, acute pain (as distinct from chronic pain) usually occurs suddenly and usually has a known cause, like an injury, surgery, or

infection. For example, acute pain can be caused from a wisdom tooth extraction, a surgery, or a broken bone after an automobile accident. Acute pain normally resolves as your body heals. Chronic pain, on the other hand, can last weeks, months or years—past the normal time of healing.⁶⁹ Regarding chronic pain, CDC states clinicians should use caution when prescribing opioids at any dosage, and should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day.⁷⁰ With the proposal to require maximum daily MME limits, we did not mean to suggest rapid discontinuation of opioids already prescribed at higher dosages.

The MME/day metric is often used as a gauge of the overdose potential of the amount of opioid that is being given at a particular time.⁷¹ Calculating the total daily dosage of opioids helps identify patients who may benefit from closer monitoring, reduction or tapering of opioids, prescribing of naloxone, or other measures to reduce risk of overdose. The opioid MME levels discussed in the June 2020 proposed rule typically would not be clinically appropriate for acute, short term pain; moreover, if the prescription were for acute pain, given the risks associated with high acute doses (in particular, respiratory risks), we believe that this limitation also would be appropriate to ensure appropriateness, medical necessity, and avoidance of adverse events. Accordingly, we proposed to require states to establish MME threshold amounts for implementation regardless of whether the prescription is for treatment of chronic or acute pain. We explained this proposal in preamble to the proposed rule (85 FR 37309) but made a technical error in the proposed regulation text, which was erroneously limited to prescriptions “for treatment of chronic pain.”

We also noted that the proposed prospective safety edit must include a MME threshold amount to meet statutory requirements, to assist in identifying patients at potentially high clinical risk who may benefit from closer monitoring and care coordination. Calculation of MMEs is

⁶⁹ “Opioids for Acute Pain.” Centers for Disease Control and Prevention, available at <https://www.cdc.gov/drugoverdose/pdf/patients/Opioids-for-Acute-Pain-a.pdf>.

⁷⁰ “CDC Guidelines for Prescribing Opioids for Chronic Pain.” Available at https://www.cdc.gov/drugoverdose/pdf/guidelines_at-a-glance-a.pdf.

⁷¹ Ibid.

used to assess the total daily dose of opioids, taking into account the comparative potency of different opioids and frequency of use. The calculation to determine MMEs includes drug strength, quantity, days' supply and a defined conversion factor unique to each drug.⁷² Patients prescribed higher opioid dosages are at higher risk of overdose death.⁷³ Calculating the total MME daily dose of opioids can help identify patients who may benefit from closer monitoring, reduction or tapering of opioids, prescribing of naloxone, or other measures to reduce risk of overdose.⁷⁴ HHS's Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics⁷⁵ is also a valuable resource for considering how best to taper and/or discontinue usage in a thoughtful manner, consistent with best clinical practices. We noted that HHS does not recommend opioids be tapered rapidly or discontinued suddenly due to the significant risks of opioid withdrawal, unless there is a life-threatening issue confronting the individual patient. FDA issued a safety announcement on tapering in April 2019 noting concerns about safely decreasing or discontinuing doses of opioids in patients who are physically dependent after hearing reports about serious harm.⁷⁶

When determining MME threshold amounts, states are reminded that clinical resources, including, for example, the CDC guideline,⁷⁷ recommend caution when prescribing opioids for chronic pain in certain circumstances, and recommend that primary care practitioners reassess evidence of individual benefits and risks when increasing doses and

⁷² Calculating Total Daily Dose of Opioids For Safer Dosage. Centers for Disease Control and Prevention, available at https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf.

⁷³ Guideline for Prescribing Opioids for Chronic Pain. www.cdc.gov/drugoverdose/pdf/guidelines_at-a-glance-a.pdf.

⁷⁴ Ibid.

⁷⁵ https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf.

⁷⁶ “FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering.” Food and Drug Administration. Available at <https://www.fda.gov/drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes>.

⁷⁷ Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *MMWR Recomm Rep* 2016; 65(No. RR–1):1–49. DOI: <http://dx.doi.org/10.15585/mmwr.rr6501e1>. https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fmmwr%2Fvolumes%2F65%2Frr%2Frr6501e1er.htm.

⁶⁸ Section 1902(o)(1)(A)(i)(II) of the Act, as added by section 1004 of the SUPPORT Act.

subsequently, justifying decisions by thoroughly documenting the clinical basis for prescribing in the patient's medical record.⁷⁸ As noted, it is important to be cognizant that the CDC guideline states the dosage thresholds referenced therein pertain solely to opioids used to treat chronic pain in primary care settings and that these thresholds, as recommended by the CDC, do not represent hard limits for opioid prescriptions.⁷⁹

In consideration of clinical recommendations and to assess the clinical benefits and harms of opioid treatment on an ongoing basis, we believe the proposed safety edit is necessary to assure at risk individuals are receiving appropriate treatment that is not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(ii) that states be required to implement safety edits that indicate when an individual enrolled under the plan (or waiver) is prescribed the morphine equivalent for such treatment in excess of the MME dose limitation identified by the state.

c. Automated Claims Reviews for Opioids

To further implement section 1927(g) of the Act and section 1004 of the SUPPORT Act, we proposed that states must have in place a claims automated review process (as designed and implemented by the state) that indicates when an individual enrolled under the state plan (or under a waiver of the state plan) is prescribed opioids in excess of proposed limitations identified by the state. In these ongoing, comprehensive reviews of opioid claim data, states should continuously monitor opioid prescriptions, including overrides of safety edits by the prescriber or dispenser on initial fill days' supply for opioid naïve patients, quantity limits, therapeutically duplicative fills, early refills and maximum daily MME limitations on opioids prescriptions.

These opioid claim reviews are necessary to allow states to continually monitor opioid prescriptions beneficiaries are receiving and determine and refine future potential prospective DUR safety edits, based on

the findings of the claims reviews. Information obtained through retrospective DUR claim reviews can be used to shape effective safety edits that can be implemented through prospective DUR, better enabling prescribers and dispensers to investigate prescription concerns prior to dispensing the medication to the patient. Through ongoing monitoring and observation of trends over time, these reviews will allow for regular updates to safety edits in an evolving pain treatment landscape.

Accordingly, we proposed at § 456.703(h)(1)(iii) that states must conduct retrospective claims review automated processes that indicate prescription fills in excess of the prospective safety edit limitations specified by the state under paragraph (h)(1)(i) or (ii) to provide for the ongoing review of opioid claims data to identify patterns of fraud, misuse, abuse, excessive utilization, inappropriate or medically unnecessary care, or prescribing or billing practices that indicate abuse or provision of inappropriate or medically unnecessary care among prescribers, pharmacists and individuals receiving Medicaid benefits. We explained that, in addition to opioid claims data, we also intended for states to consider incorporating other available records to provide for the ongoing periodic reviews of opioids claim data and other records (including but not limited to prescription histories, diagnoses, medical records, and prescription drug monitoring program (PDMP) files, when available), in their retrospective claims review automated processes order to identify patterns of fraud, misuse, abuse, excessive utilization, or inappropriate or medically unnecessary care, or prescribing or billing practices that indicate abuse or excessive utilization among physicians, pharmacists and individuals receiving Medicaid benefits.

d. Concurrent Utilization Reviews

Section 1902 of the Act, as amended by the SUPPORT Act, requires states to have an automated process for claims review (as designed and implemented by the state) that monitors when an individual enrolled under the state plan (or under a waiver of the state plan) is concurrently prescribed opioids and benzodiazepines or opioids and antipsychotics.⁸⁰ This requirement is consistent with the requirement in section 1927(g)(1)(A) of the Act that state DUR programs must assure that prescriptions are appropriate, medically

necessary, and not likely to result in adverse medical results.

Clinically, through the use of retrospective automated claim reviews, concurrent use of opioids and benzodiazepines and opioids and antipsychotics, as well as potential complications resulting from other medications concurrently being prescribed with opioids, can be reduced. In the proposed rule, we reminded states that the requirement for a retrospective automated claims review added by section 1004 of the SUPPORT Act does not preclude the state from also establishing a prospective safety edit system to provide additional information to patients and providers at the POS about concurrent utilization alerts.⁸¹ In addition, the state could use the authorities under section 1927 of the Act to subject these patients to appropriate utilization management techniques. We reminded states that section 1927(g)(1) of the Act also currently supports including other potentially harmful opioid interactions as additional prospective or retrospective reviews in state DUR programs, such as opioids and central nervous system (CNS) depressants, including alcohol or sedatives. We noted that we fully support states including such additional opioid interactions or contraindications in prospective or retrospective DUR reviews as part of a comprehensive DUR program.

In consideration of clinical recommendations to limit opioids interactions with certain other drugs, including benzodiazepines and antipsychotics, and to assess the clinical benefits and harms of opioid treatment on an ongoing basis, we believe the retrospective reviews we proposed to require are necessary to help ensure at-risk individuals are receiving appropriate treatment that is not likely to result in adverse medical results, and otherwise to accomplish purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(iv)(A) and (B) that states be required to implement a claims review automated process that monitors when an individual is concurrently prescribed opioids and benzodiazepines; or opioids and antipsychotics.

i. Opioid and Benzodiazepines Concurrent Fill Reviews

In 2016, FDA added a boxed warning to prescription opioid analgesics, opioid-containing cough products, and

⁷⁸ Dowell, Deborah, et al. "CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016." JAMA, U.S. National Library of Medicine, 19 Apr. 2016, <https://www.ncbi.nlm.nih.gov/pubmed/26977696>.

⁷⁹ Staff, News. "CDC Clarifies Opioid Guideline Dosage Thresholds." AAFP Home, 12 Jan. 2018, www.aafp.org/news/health-of-the-public/20180112cdcopioidclarify.html.

⁸⁰ Section 1902(o)(1)(A)(i)(III) of the Act, as added by section 1004 of the SUPPORT Act.

⁸¹ See section 1902(o)(1)(A)(iii) of the Act, as added by section 1004 of the SUPPORT Act.

benzodiazepines with information about the serious risks associated with using these medications concurrently.⁸² The CDC guideline recommends that clinicians avoid prescribing benzodiazepines concurrently with opioids whenever possible. Benzodiazepines may be abused for recreational purposes by some individuals, with some opioid overdoses also involving opioids and benzodiazepines or other substances, such as alcohol.⁸³

Studies show that people concurrently using both drugs are at higher risk of visiting the emergency department or being admitted to a hospital for a drug-related emergency.⁸⁴ Due to the heightened risk of adverse events associated with the concurrent use of opioids and benzodiazepines, physicians should avoid the initial combination of opioids and benzodiazepines by offering alternative approaches.⁸⁵ This review would alert providers when these drugs have been prescribed concurrently to assist in avoiding and mitigating associated risks.

ii. Opioid and Antipsychotic Concurrent Fill Reviews

This alert is supported by FDA's boxed warning of increased risk of respiratory and CNS depression with concurrent use of opioid and CNS depressants such as antipsychotics or sedatives, including extreme sleepiness, slowed or difficult breathing, unresponsiveness or the possibility that death can occur.⁸⁶ Patients concurrently prescribed opioid and antipsychotic drugs can benefit from increased coordination of care. Additionally,

⁸² Office of the Commissioner. "Drug Safety Communications—FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning." *U.S. Food and Drug Administration Home Page*, Office of the Commissioner, <https://www.fda.gov/media/99761/download>.

⁸³ Jones, Jermaine D, et al. "Polydrug Abuse: a Review of Opioid and Benzodiazepine Combination Use." *Drug and Alcohol Dependence*, U.S. National Library of Medicine, 1 Sept. 2012, www.ncbi.nlm.nih.gov/pmc/articles/PMC3454351/.

⁸⁴ Forum, Addiction Policy. "Sedative Use Disorder." *Addiction Policy Forum*, <https://www.addictionpolicy.org/sedative-use-disorder>.

⁸⁵ "Reduce Risk of Opioid Overdose Deaths by Avoiding and Reducing Co-Prescribing Benzodiazepines." MLN Matters Number: SE19011. Available at <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE19011.pdf>.

⁸⁶ Office of the Commissioner. "Drug Safety Communications—FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning." *U.S. Food and Drug Administration Home Page*, Office of the Commissioner, <https://www.fda.gov/media/99761/download>.

improving treatment of comorbid mental disorders is an important consideration when trying to reduce the overall negative impacts of pain. As the PMTF report noted, "the occurrence of pain and behavioral health comorbidities, including depression, post-traumatic stress disorder, and SUDs, is well documented, and it is established that psychosocial distress can contribute to pain intensity, pain-related disability, and poor response to chronic pain treatment."⁸⁷ Evidence indicates that optimizing mental health and pain treatment can improve outcomes in both areas for patients seen in primary and specialty care settings. Untreated psychiatric conditions may increase the risk of both unintentional and intentional medication mismanagement, OUD, and overdose.⁸⁸ Given the intersection between psychiatric/psychological symptoms and chronic pain, it is important that the behavioral health needs of patients with pain are appropriately and carefully evaluated and treated with the concurrent physical pain problem.⁸⁹ As such, beneficiaries who are concurrently prescribed both opioids and antipsychotics should be considered from a health system or policy perspective when addressing their treatment.⁹⁰ A patient's unique presentation and circumstances should be considered when prescribing opioids and antipsychotics. This review would encourage coordination of care for patients taking antipsychotic and opioid medications concurrently.

e. Other Considerations

Consistent with section 1902(o)(1)(A)(iii) of the Act, as added by section 1004 of the SUPPORT Act, the provisions proposed to be implemented in § 456.703(h)(1) would not prohibit states from designing and implementing an automated claims review process that provides for other processes for the prospective or retrospective review of claims. Furthermore, none of these proposed provisions would prohibit the exercise of clinical judgment by a provider regarding the best or most appropriate care and treatment for any patient.

We encouraged states to develop prospective and retrospective drug

⁸⁷ Pain Management Best Practices Inter-Agency Task Force. "Pain Management Best Practices." Available at <https://www.hhs.gov/sites/default/files/pmtf-final-report-2019-05-23.pdf>.

⁸⁸ Ibid.

⁸⁹ Ibid.

⁹⁰ Davis, Matthew A., et al. "Prescription Opioid Use among Adults with Mental Health Disorders in the United States." *The Journal of the American Board of Family Medicine*, vol. 30, no. 4, 2017, pp. 407–417, doi:10.3122/jabfm.2017.04.170112.

reviews that are consistent with medical practice patterns in the state to help meet the health care needs of the Medicaid patient population. In doing so, we encouraged states to utilize, for example, the 2016 CDC guideline⁹¹ for primary care practitioners on prescribing opioids in outpatient settings for chronic pain.

To avoid abrupt opioid withdrawal, we noted that prior authorization may be necessary for patients who will need clinical intervention to taper off high doses of opioids to minimize potential symptoms of withdrawal and manage their treatment regimen, while encouraging pain treatment using non-pharmacologic therapies and non-opioid medications, where available and appropriate.

When implementing these requirements, we encouraged states to offer education and training and to provide consistent messaging across all healthcare providers. We noted that education and training of all providers on new opioid-related provisions and on the treatment of acute and chronic pain and behavioral health issues related to pain, would help minimize workflow disruption and ensure beneficiaries have access to their medications in a timely manner.

The following is a summary of the comments we received on these proposed minimum standards for DUR programs and under the SUPPORT Act and section 1927 of the Act, and our responses.

Comment: Some commenters expressed support for the availability of the CDC guideline for Prescribing Opioids for Chronic Pain, and approved of our references to the guideline as being a possible resource for states to use in developing their state DUR programs. Other commenters stated a belief that the guideline has been misapplied and is inherently flawed and may result in unintended consequences.

Response: The CDC guideline is intended to help providers determine when and how to prescribe opioids for chronic pain, and also when and how to use nonopioid and nonpharmacologic options that can be effective with less risk. The guideline was developed to help ensure that primary care clinicians work with their patients to consider all safe and effective treatment options for chronic pain management. Some providers have misinterpreted the application of this document, and CDC

⁹¹ "CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 29 Aug. 2017, <https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/r6501e1er.pdf>.

released a clarification in April 2019 in response.⁹² As discussed in the proposed rule and this final rule, the CDC Guideline for Prescribing Opioids for Chronic Pain is one of many clinical guidelines states can consult when implementing DUR safety edits and automated claims review. Section 1004 of the SUPPORT Act amends section 1902 of the Act to include a new paragraph (a)(85), requiring the state plan to provide that the state is in compliance with the new DUR requirements. This statutory provision, as well as the provisions of this final rule, give authority to the states to develop, specify and implement important parameters for these edits and reviews, as determined by the state. In our experience from reviewing the annual FFS and MCO DUR reports, available on www.Medicaid.gov, states typically consult multiple authoritative clinical resources and guidelines when designing and implementing their DUR programs.

Comment: Several commenters suggested that CMS establish uniform opioid-related limits or reporting requirements across Medicare Part D and all Medicaid programs instead of allowing Medicaid programs to create unique policies for the relevant state, and require state Medicaid safety edits to be no more restrictive than those implemented in Medicare.

Response: We appreciate the comments in reference to establishing consistency in DUR activities between Medicaid and Medicare; however, requirements for DUR in Medicare are not within the scope of this rulemaking. Additionally, it is important to remember that while Medicare is a federally-operated program, Medicaid is primarily a state-run program. The amendments made by section 1004 of the SUPPORT Act make clear that Congress intended for states to have considerable discretion in determining how to implement opioid-related DUR measures in their state Medicaid programs.

Comment: Several commenters recommended the promotion of non-pharmacological pain management strategies for OUD and suggested CMS promote integrated care models to include counseling, behavioral therapies and physical rehabilitation. Other commenters suggested additional non-pharmacological pain management strategies to include osteopathic principles, including physical therapy, acupuncture, chiropractic care, over-

the-counter medications and occupational therapy to improve self-management of pain conditions with the goal of reducing pain, improving function, increasing self-efficacy, and improving quality of life.

Response: We appreciate the suggestions regarding alternative non-pharmacologic therapy and agree that there can be an appropriate clinical role for therapies such as those suggested by the commenters. Several related CMS resources include, but are not limited to, the CMS Roadmap Strategy To Fight The Opioid Crisis, June 2020;⁹³ the CMS Opioid Misuse Strategy, January 2017;⁹⁴ the Medicaid Strategies for Non-Opioid Pharmacologic and Non-Pharmacologic Chronic Pain Management, February 2019;⁹⁵ and Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction, January 2016.⁹⁶ These resources provide additional information on Medicaid authorities that states may use for coverage of non-opioid pharmacologic and non-pharmacologic pain management therapies, highlight some preliminary strategies used by several states, and include other useful resources to help states.

Comment: Several commenters expressed concern that the proposed rule would give too much autonomy to the states for determining days' supply for opioid naïve beneficiaries, and quantity, therapeutic duplication and early refill limits. Several commenters also opined that leaving the determination of quantity limits up to the states' discretion will evolve into a highly heterogeneous set of state requirements. Other commenters encouraged alignment and consistency in state DUR programs nationwide, and suggested that CMS should direct state Medicaid agencies to consult existing resources to come into compliance with the proposed requirements, if finalized.

Response: We disagree with the commenters that the proposed policies give too much discretion to the states. In accordance with and the amendments made by section 1004 of the SUPPORT Act, states are required to implement safety edits (as specified by the state) for subsequent fills for opioids and a claims

review automated process (as designed and implemented by the state) that indicates when an individual enrolled under the state plan (or under a waiver of the state plan) is prescribed a subsequent fill of opioids in excess of any limitation that may be identified by the state. We are finalizing our proposal to implement these provisions, and to further implement section 1927(g) of the Act, by requiring states to specify quantity, days' supply, therapeutic duplication, and early fill safety alerts on opioids prescriptions, the specific parameters of which will be left to the states' discretion to establish minimum standards. We believe these state-established parameters will be effective in helping identify abuse, misuse, excessive utilization, or inappropriate or medically unnecessary care. We encourage states to consult existing resources on safe and appropriate opioid prescribing. We recognize there are many national guidelines and resources available to the states. These include, but are not limited to, guidance issued by associations such as the Pharmacy Quality Alliance (PQA), National Committee for Quality Assurance (NCQA), National Quality Forum (NQF); and federal agencies including, but limited to, the Agency for Healthcare Research and Quality (AHRQ), the Substance Abuse and Mental Health Services Administration, and the CDC. In our experience from reviewing the annual FFS and MCO DUR reports, available on www.Medicaid.gov, states typically consult multiple authoritative clinical resources and guidelines when designing and implementing their DUR programs. We agree with commenters who suggested that the proposed policies would result in varying implementations across state DUR programs. However, we believe this variation was specifically contemplated by Congress in enacting the relevant provisions of the SUPPORT Act, and is fully consistent with the overall structure of the Medicaid program, which gives states flexibility to design and administer their programs. Additionally, the flexibility afforded to states will help enable them to ensure the establishment of minimum standards relevant to their state circumstances and beneficiary populations.

Comment: One commenter suggested adopting the models found in the Virginia Medicaid Addiction and Recovery Treatment Services program and the Vermont Blueprint for Health when implementing opioid safety edits.

Response: States can evaluate these and other models when designing and

⁹³ <https://www.cms.gov/About-CMS/Agency-Information/Emergency/Downloads/Opioid-epidemic-roadmap.pdf>.

⁹⁴ <https://www.cms.gov/Outreach-and-Education/Outreach/Partnerships/Downloads/CMS-Opioid-Misuse-Strategy-2016.pdf>.

⁹⁵ <https://www.medicaid.gov/sites/default/files/federal-policy-guidance/downloads/cib022219.pdf>.

⁹⁶ <https://www.medicaid.gov/sites/default/files/Federal-Policy-Guidance/Downloads/cib-02-16.pdf>.

⁹² <https://www.cdc.gov/media/releases/2019/s0424-advises-misapplication-guideline-prescribing-opioids.html>.

implementing their DUR programs. States have the flexibility to employ techniques and standards from existing state models, or develop their own, in compliance with the requirements of this final rule.

Comment: One commenter stated that CMS is applying a “one-size-fits-all algorithm and policies that do not take individual patient’s [sic] needs into account” when suggesting opioid safety edits.

Response: We disagree with the commenter. Consistent with the SUPPORT Act and section 1927(g) of the Act, under the policies in this final rule, states have autonomy to implement safety edits as determined by the state, in consideration of state-specific circumstances and the needs of the state’s Medicaid population. For example, we are not prescribing a national limit on the quantity of opioids that may be prescribed or dispensed to a beneficiary, only that each state must determine a limit and implement a safety edit that, if exceeded, would trigger an alert and opportunity for appropriate clinical intervention prior to dispensing. Similarly, we are not establishing a specific national MME limit, but consistent with the statutory requirement added by the SUPPORT Act, we are requiring states to determine an MME limit and implement a safety edit to trigger an alert if it is exceeded. Safety edits provide an opportunity for identifying potential problems at the pharmacy POS before the prescription is dispensed to the individual, which creates an opportunity for engagement between pharmacists, prescribers and patients to identify and mitigate possible opioid misuse, abuse, and overdose risk. POS safety edits provide real-time information to the pharmacist prior to the prescription being dispensed to a patient; however, they do not necessarily prevent the prescription from being dispensed. When a safety edit is prompted, the pharmacist receives an alert and may be required, as dictated by predetermined standards established by the state, to take further action to resolve the issue prior to the prescription being dispensed.

Comment: One commenter requested that CMS require states, when implementing these opioid safety edit requirements, to offer education and training and to provide consistent messaging across all healthcare providers, and noted that coordination between all stakeholders is key to successful policy and DUR program implementation for opioid safety edits.

Response: Based on CMS’ Annual DUR Survey, it is apparent that states have implemented a majority of these

proposed safety edits already. We agree with the commenter’s suggestion that states provide education and training on their DUR programs generally and regarding opioid utilization review initiatives specifically to providers in the state. Currently, states are required to carry out an educational program with respect to their DUR programs, as specified in section 1927(g)(2)(D) of the Act. We believe states generally are providing consistent messaging to their providers through educational mechanisms that include, but are not limited to, state website postings, bulletins and newsletters, educational seminars, and toolkits, as needed and appropriate to promote effective provider education and training.

Comment: A few commenters urged consideration of flexible policies to accommodate the needs of provider groups, such as emergency physicians, and special patient populations, such as cancer survivors and patients with sickle cell disease, through the use of evidence-based, nationally-recognized, and population specific prescribing guidelines. These commenters suggested CMS direct state Medicaid agencies to consult existing resources on safe and appropriate opioid prescribing.

Response: We appreciate the commenters concerns, and believe that the structure of the final regulation will continue to give states flexibility in designing their DUR programs to meet the needs of certain providers, such as emergency physicians and oncologists, and certain special populations, such as cancer and sickle cell patients and those in chronic pain. Consistent with the requirements of section 1004 of the SUPPORT Act, the states will determine and implement specifications for their DUR programs. As discussed below in this final rule, states have the option to exclude certain populations from these opioid-related DUR requirements. Nationally-recognized guidelines and resources are also available to the states and providers. Organizations that have developed relevant materials include, but are not limited to, the PQA, NCQA, NQF, and federal agencies including, but not limited to AHRQ, SAMHSA, and the CDC. We encourage states to consult existing resources on safe and appropriate opioid prescribing. In our experience from reviewing the annual FFS and MCO DUR reports, available on www.Medicaid.gov, states typically consult multiple authoritative clinical resources and guidelines when designing and implementing their DUR programs. Therefore, we are finalizing our proposal to allow flexibility in designing implementing the opioid-

related DUR parameters under § 456.703(h).

Comment: A few commenters encouraged CMS to gather data on the impact of the proposed opioid safety edits across race and ethnicity as studies have found that although the rate of drug-related deaths is highest among non-Hispanic whites, patients who are African American and Hispanic are less likely to receive any pain medication and more likely to receive lower doses of pain medication, despite higher pain scores.

Response: In implementing statutory requirements added by the SUPPORT Act and in section 1927(g) of the Act, this final rule is intended to improve the clinical use of opioids in all beneficiaries, regardless of race or ethnicity, to promote improved quality of life. As we have noted, the states operate their DUR programs under federal guidelines and are responsible for using their DUR data to improve the use of medications in the Medicaid population. We believe that the use of these new opioid-related safety edits will help identify for states and health care professionals both those patients who might be taking too many opioids, or taking opioids in circumstances where their use could be medically inappropriate or likely to result in adverse medical events. States also retain flexibility to implement opioid and non-opioid related safety edits and claims reviews that are designed to help ensure that patients suffering from pain are receiving adequate treatment. As described in the proposed rule and elsewhere in this final rule, the states through their DUR programs are required to retrospectively review claims and provide feedback to prescribers through the required program of educational interventions, see § 456.711. The retrospective review process helps to identify patterns in prescribing and dispensing which can then be used by states in designing interventions to help improve the overall use of these medications.

In addition, to support these state level activities, CMS collects information through collaboration with various CMS components and Department partners to develop and implement initiatives to improve data collection, analysis and reporting by race, ethnicity, primary language, disability, and gender, as well as other characteristics that have been associated with health disparities. We have formulated objectives to disseminate information, identify vulnerabilities and collaborate with states and external organizations on health disparities, to include data collection and strategies for

achieving health equity. Resources, including federal and state initiatives, can be accessed on *Medicaid.gov*.⁹⁷ Through collaboration with other CMS, Departmental, and external entities, we hope to determine and correlate claims data to assess impact of the newly required safety edits in the future.

Comment: One commenter expressed concern that utilization management in certain patient populations risks discriminating on the basis of disability, depending on what “utilization management techniques” the state may adopt in its implementation of the proposed requirements for opioid-related safety edits and automated claims reviews.

Response: Nothing in the proposed rule or this final rule is intended to interfere with the providers’ clinical decision-making or with the provider-patient relationship. The final rule continues to allow providers to make clinical decisions based on each patient’s specific situation and relevant clinical principles. Section 1557 of the Affordable Care Act⁹⁸ provides that an individual shall not, on the grounds prohibited under Title VI of the Civil Rights Act of 1964 (Title VI), 42 U.S.C. 2000d *et seq.* (race, color, national origin), Title IX of the Education Amendments of 1972 (Title IX), 20 U.S.C. 1681 *et seq.* (sex), the Age Discrimination Act of 1975 (Age Act), 42 U.S.C. 6101 *et seq.* (age), or Section 504 of the Rehabilitation Act of 1973 (Section 504), 29 U.S.C. 794 (disability), be excluded from participation in, be denied the benefits of, or be subjected to discrimination under, any health program or activity, any part of which is receiving federal financial assistance, or under any program or activity that is administered by an Executive Agency or any entity established under Title I of the Act or its amendments. States have many years of experience applying utilization management techniques in the context of their Medicaid DUR programs, with the enactment of the DUR provisions of the Omnibus Budget Reconciliation Act (OBRA) of 1990. The safety edits are intended to help protect Medicaid patients from serious consequences of overutilization, including overdose, dangerous interactions, increased side effects and additive toxicity. Safety edits provide for identifying potential problems at pharmacy POS to engage both patient and provider in identifying and

mitigating possible opioid misuse, abuse, and overdose risk at the time of dispensing which ultimately assists the provider in making appropriate clinical decisions. States will continue to have flexibility in design, development and implementation of safety edits and respective claims review as specified in section 1004 of the SUPPORT Act.

Comment: One commenter suggested that the proposed rule could create disparities in care between individuals who are and who are not Medicaid beneficiaries, if similar safety edits and claims reviews, specifically including early refill limits, are not established for non-Medicaid beneficiaries.

Additionally, one commenter suggested states could build in appropriate flexibilities and exceptions to allow for extenuating circumstances.

Response: Implementing safety edits and claims reviews, including for early refill limits, is beyond the scope of this rulemaking with respect to individuals who are not Medicaid beneficiaries. The non-Medicaid population is not addressed by the relevant provisions of the SUPPORT Act and section 1927 of the Act that we are implementing through this rulemaking. We proposed and are finalizing early fill limitations at § 456.703(h)(1)(i)(D) to apply with respect to Medicaid beneficiaries. However, we agree that there is no reason that the standards of care or protocols for the dispensing of prescription opioids should vary between individuals solely on the basis of the individual’s status as a Medicaid beneficiary (or not). Nothing in the SUPPORT Act or section 1927(g) of the Act prohibits states from considering and implementing more broadly applicable requirements for opioid-related safety edits.

Consistent with the provisions in section 1004 of the SUPPORT Act allowing states considerable discretion in their design and implementation of opioid-related safety edits, and with similar flexibility available for states in operating their DUR programs under section 1927(g) of the Act, this final rule affords states flexibility in designing and implementing required safety edits in the manner the state determines would be best adapted to the circumstances in the state, including the particular needs of the state’s Medicaid beneficiaries. This flexibility extends to the manner in which the state’s design and implementation account for potential extenuating circumstances, including emergency situations and the situations of beneficiaries being treated for particular conditions such as acute or chronic pain. We agree that safety edits should be implemented in a way

that is sufficiently flexible to ensure that medically appropriate care is not withheld from beneficiaries in such circumstances, and agree that safety edits generally should be designed to avoid harm. States are encouraged to apply national guidelines and best practices to inform their design and implementation of the required safety edits before implementing any safety edit to ensure coordinated and undisruptive patient care.

Comment: One commenter suggested that states that have existing initial prescription fill limits should be encouraged to align with CMS’s initial fill limits.

Response: We do not specify a prescription fill limit for opioid drugs or other Medicaid reimbursed drugs; however, consistent with the SUPPORT Act and DUR requirements under section 1927(g) of the Act, we proposed and are finalizing at § 456.703(h)(1)(i) that states must establish state-identified prospective safety edits that must include limitations on initial prescription fill days’ supply for patients not currently receiving opioid therapy; quantity limits for initial and subsequent fills, therapeutically duplicative fill limits, and early fill limits on opioids prescriptions. To further implement section 1927(g)(1) of the Act, and consistent with section 1004 of the SUPPORT Act, we proposed and are finalizing this rule to require states to establish safety edit limitations on the days’ supply for an initial prescription opioid fill for beneficiaries who have not filled an opioid prescription within a defined time period to be specified by the state. This limit would not apply to patients currently receiving opioids and is meant for beneficiaries who have not received opioids within this specified time period (as defined and implemented by the state). The patients who have not received opioids within this state-specified timeframe are referred to as opioid naïve and would be subjected to the days’ supply limit on the opioid prescription initial fill, as defined and implemented by the state. While the SUPPORT Act requires state-specified limits on subsequent fills of opioids, pursuant to section 1927(g) of the Act, we proposed and are finalizing this rule with edits on initial fills of opioids to help avoid excessive utilization by opioid naïve beneficiaries, with its attendant risk of adverse effects.

Comment: Some commenters requested that CMS modify parts of the proposed opioid safety edits regarding the limit on days’ supply for opioid naïve beneficiaries, specifically that CMS remove language relating to initial

⁹⁷ <https://www.medicaid.gov/medicaid/quality-of-care/quality-improvement-initiatives/quality-of-care-health-disparities/index.html>.

⁹⁸ <https://www.hhs.gov/sites/default/files/ppacon.pdf>.

prescribing as they claim it goes beyond the statute and could be harmful to certain patient groups. Other commenters stated that evidence for strict duration limits is insufficient to support state laws currently in place and that limitations may harm patients with chronic illnesses and injuries. These commenters expressed their belief that states should not implement a days' supply limit that is less than 7 days, and in exceptional circumstances, should allow for a longer supply. A few commenters requested that states build in exceptions for emergencies and extreme situations that could make it possible for patients to receive a needed refill.

Response: We disagree that the proposed requirement that states establish opioid initial fill days' supply limits, which we are finalizing in § 456.703(h)(1)(i)(A), exceeds our statutory authority. As we discussed in the proposed rule, although the amendments made by section 1004 of the SUPPORT Act only require states to establish safety edits (and a claims review automated process) to identify subsequent fills of opioids in excess of any limitation that may be identified by the state, pursuant to our authority under section 1927(g) of the Act, we proposed and are finalizing a requirement to apply limitations to initial fills, as well. In consideration of clinical recommendations to limit opioid use to the shortest possible duration and to assess the clinical benefits and harms of opioid treatment on an ongoing basis, this safety edit is necessary to help ensure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse events, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and section 1004 of the SUPPORT Act. Accordingly, we proposed and are finalizing this rule at § 456.703(h)(1)(i)(A) to require states to implement a days' supply limit when an initial opioid prescription is dispensed to a patient not currently receiving ongoing therapy with opioids. The safety edit requirements under this final rule authorize states to not only design and implement the specific parameters of the safety edits based on existing state-specific criteria, but also allow states to consider all relevant factors in designing and implementing their state-specific limitations, such as the particular needs and circumstances of patients with chronic illnesses or injuries. States are encouraged to consult national guidelines when determining, specifying and implementing any safety edit (to include

initial days supply) to ensure appropriate, coordinated patient care and minimize any unnecessary disruption to such care. States are also encouraged to evaluate specific needs that may arise in particular care settings in the state, such as in emergency departments and other acute treatment facilities; in vulnerable populations, such as chronically ill or disabled patients; and in other relevant state programs and initiatives, such as those for managing patients receiving medication-assisted treatment, when considering whether exceptional circumstances could mean that a particular implementation of a days' supply limit may adversely affect patient care.

We note that, under section 1927(d)(5) of the Act, states are required to provide for the dispensing of at least a 72-hour supply of a covered outpatient drug (COD), within 24 hours, in an emergency situation. This statutory requirement helps ensure timely access to needed medications, including when a beneficiary may require an opioid prescription in an emergency situation. Section 1927(d)(5)(B) of the Act ensures that a beneficiary can obtain an emergency supply until the prescriber or pharmacist is able to obtain prior authorization approval for the drug, if such approval is required.

Comment: Some commenters did not support CMS' proposal to require safety edits on initial prescription fill days' supply for patients not currently receiving opioid therapy, quantity, duplicate fills, and early refills to prevent and reduce the inappropriate use of opioids and potentially associated adverse medical events. One commenter noted that "strict limits on opioid prescription may be counterproductive by increasing opioid dependence and failing to effectively address the need for SUD and OUD treatment." The commenter explained that while quantity and other limits on prescriptions for opioids may lead to a decrease in the supply of opioids, there is no guarantee that it will result in a reduction of opioid-related harm.

Response: Based on the requirements added by section 1004 of the SUPPORT Act and our existing authority under section 1927(g) of the Act, we proposed and are finalizing a requirement that state-identified safety edits must include state-specified limitations on initial prescription fill days' supply for patients not currently receiving opioid therapy, quantity limits, therapeutically duplicative fill limits, and early refill limits. These opioid-related safety edits are intended to protect Medicaid enrollees, to include people with

disabilities who live with chronic pain, from serious consequences of overutilization, including overdose, dangerous interactions, increased side effects and additive toxicity. In addition, overutilization of opioids may serve as an indication of uncontrolled disease and the need of increased monitoring and coordination of care. We believe these safety edits are not counterproductive, in fact these safety edits, as designed and implemented by the state, are necessary to assure that opioid prescriptions are appropriate, medically necessary, and not likely to result in adverse events. Safety edits provide for identifying potential problems at the pharmacy POS to engage both patient and provider in identifying and mitigating possible opioid misuse, abuse, and overdose risk at the time of dispensing, which ultimately assists the provider in making appropriate clinical decisions. Accordingly, we proposed and are finalizing at § 456.703(h)(1)(i)(A) through (D) minimum standards for required safety edits, with the detailed design and implementation specifications left to the state's discretion to meet state-specific needs, to further implement section 1927(g) of the Act and section 1004 of the SUPPORT Act.

Comment: Several commenters recommended that CMS standardize the look-back period for evaluating beneficiaries' opioid medication use in implementing the proposed safety edits and claims reviews, such as considering whether the patient had used opioids within the previous 90 days, as a uniform standard for identifying acute and chronic opioid utilization. Several commenters recommended that we develop guidance on prior authorization standards to avoid abrupt opioid withdrawal.

Response: We did not propose, and are not finalizing, any specific look-back period of time that states must use in their implementation of the required opioid-related safety edits and claims reviews, nor are we developing guidance on prior authorization standards to avoid abrupt opioid withdrawal. However, states may reference guidelines such as the CDC Guideline for Prescribing Opioids for Chronic Pain⁹⁹ and/or the HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of

⁹⁹ https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fmmwr%2Fvolumes%2F65%2Frr%2Frr6501e1er.htm.

Long-Term Opioid Analgesics¹⁰⁰ when designing or implementing these standards to avoid abrupt opioid withdrawal.

Details such as these are left to the states to determine, in consideration of the particular circumstances and needs of beneficiaries in the state. Moreover, we are not aware of authoritative clinical or health policy guidance that suggests a particular length of time for a look-back period for opioid prescription monitoring in patients receiving opioid medications. This time period should be established by the state through consultation with experts, such as their DUR Board.

However, to provide an example of how one state uses a look back period to help avoid possible abuse of short term opioids, Kansas Medicaid requires prior authorization for a patient to obtain another opioid prescription if that patient had already obtained a short term supply of opioids (defined as a quantity of opioids to treat a patient for fewer than 90 days) within the last 4 months.¹⁰¹ The prior authorization allows for the determination of whether the additional course of treatment is medically necessary, given that the patient recently had another course of treatment with opioids during the designated look back period. The Washington State Hospital Association, which has partnered with the Washington State Medical Association, is another resource to consult when developing and implementing state-specific look-back periods in a comprehensive DUR program.¹⁰²

Comment: One commenter noted that a patient may be taking more than one opioid-based medication for long-term opioid therapy for chronic pain (that is, duplicate therapy), and as result, a significant number of safety edit alerts to the pharmacist may result.

Response: The proposed safety edit we are finalizing in this rule for therapeutically duplicative fills is intended to identify and alert to the prescribing and dispensing of the same drug or two or more drugs from the same therapeutic class where periods of drug administration overlap. We acknowledge that there may be patients who are taking multiple opioids to help manage pain, and these situations may result in safety alerts, depending on the

state's implementation of the requirements being finalized in this rule. The alerts are not intended to necessarily limit or deny patients access to a prescribed opioid drug; rather, they are meant to flag for the pharmacist that the beneficiary is taking multiple opioids and that the opportunity should be used to assess the patient's need for the prescribed drugs or possible changes in therapy, including through discussion with the beneficiary and/or the prescriber. Potential effects from taking therapeutically duplicative opioids may include excessive drowsiness, confusion and respiratory distress. Respiratory distress in turn may cause a condition known as hypoxia. Hypoxia can have short- and long-term psychological and neurological effects, including coma, permanent brain damage, or death.¹⁰³ Therefore, we proposed and are finalizing at § 456.703(h)(1)(i)(C) that states must implement safety edits for therapeutically duplicative fills for initial and subsequent prescription fills on opioids prescriptions, to help identify potential abuse, misuse, excessive utilization, or inappropriate or medically unnecessary care.

Comment: One commenter noted that the use of an MME to limit opioid use does not correspond to current CDC guidelines. The commenter further requested CMS postpone finalizing any new MME requirements around the treatment of chronic pain until the new CDC Opioid Workgroup has a chance to convene, consider current evidence and best practices, and issue recommendations.

Response: Section 1004 of the SUPPORT Act requires state DUR programs to include safety edit limits (as specified by the state) on the maximum daily MME that can be prescribed to an individual enrolled under the state plan (or under a waiver of the state plan) for treatment of chronic pain (as designed and implemented by the state) that indicates when an individual enrolled under the plan (or waiver) is prescribed the morphine equivalent for such treatment in excess of any threshold identified by the state. Based on the FFY 2018 Annual DUR Survey, most states were already compliant with having established an MME threshold, and those not having this safety edit in place were aware of the requirement added by section 1004 of the SUPPORT Act, effective October 1, 2019. To note, the newly appointed CDC Opioids Workgroup is actively working to

update the CDC guideline; however, its release is not expected until late 2021, and is hoped to include new recommendations not only for chronic pain management, but for the treatment of acute, short-term pain. To implement the statutory requirement, we proposed and are finalizing at § 456.703(h)(1)(ii) that states must include in their DUR programs safety edit limitations identified by the state on maximum daily MME for treatment of chronic pain and, under § 456.703(h)(1)(iii), a claims review automated process that indicates when an individual is prescribed a MME in excess of these limitations. The application of this required safety edit does not necessarily prevent the prescription from being dispensed, rather, it provides the opportunity to assure clinical appropriateness of therapy.

Comment: One commenter requested CMS emphasize that Morphine Milligram Equivalent (MME) safety edits are not strict limits, and that individual provider decision-making based on the patient's condition will supersede safety edits. Another commenter recommended that CMS policies should allow physicians to make clinical decisions based on each patient's specific circumstances, and not interfere in the provider-patient relationship.

Response: The safety edits required under this final rule are intended to protect Medicaid patients from serious consequences of overutilization, including overdose, dangerous interactions, increased side effects and additive toxicity. These safety edits provide for identifying potential problems at the pharmacy POS to engage both patient and provider in identifying and mitigating possible opioid misuse, abuse, and overdose risk at the time of dispensing, which ultimately assists the prescriber in making appropriate clinical decisions; however, the required safety edits do not necessarily prevent the prescription from being dispensed. When a safety edit is prompted, the pharmacist receives an alert and may be required, as dictated by predetermined standards established by the state, to take further action to resolve the issue prior to the prescription being dispensed. This rule is not intended to interfere with provider-patient relationship or the provider's exercise of clinical judgment. We are finalizing at § 456.703(h)(1)(ii), to require state DUR programs to include prospective safety edit limitations for opioid prescriptions, as specified by the state, on the maximum daily MME for treatment of pain, for initial and subsequent prescription fills.

¹⁰⁰ https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf.

¹⁰¹ https://www.kmap-state-ks.us/Documents/Content/Bulletins/18101%20-%20General%20-%20Opioid_2.1.pdf.

¹⁰² <https://www.wsha.org/quality-safety/projects/opioid-pain-management/opioid-prescribing-reports/>.

¹⁰³ <https://www.drugabuse.gov/publications/drugfacts/prescription-opioids>.

Comment: A few commenters expressed concern that due to variance in tolerance among patients receiving long-term opioid treatment and the risks of opioid tapering, it may not be conceptually possible for states to select an MME limit that uniformly achieves the goal of patient safety or that does not create new risks.

Response: Section 1004 of the SUPPORT Act requires state DUR programs to include safety edit limits (as specified by the state) on the maximum daily MME that can be prescribed to an individual enrolled under the state plan (or under a waiver of the state plan) for treatment of chronic pain (as designed and implemented by the state) that indicates when an individual enrolled under the plan (or waiver) is prescribed the morphine equivalent for such treatment in excess of any threshold identified by the state. We would expect that states typically would not establish MME limits that cannot be overridden, but instead would implement them as a safety edit that, when triggered by a prescription for a beneficiary, would prompt the dispensing pharmacist to review the patient's prescribed therapy. We expect that state implementations of maximum MME limits would include a function for exceptions based on specific patient factors affecting treatment protocol, including opioid dose tapering, as applicable. For example, the safety edit might prompt the pharmacist to more closely review all relevant clinical information about the prescription, counsel the beneficiary about the prescription and solicit from him or her additional information about why the drug has been prescribed, and consult directly with the prescriber to confirm the medical appropriateness of the prescription. If activities such as these result in a determination that the prescription is clinically sound and can be dispensed without modification, then we envision that the pharmacist typically would be able to override the safety edit after appropriately documenting that decision (consistent with any applicable documentation requirements, such as those that may be established by the state or a professional licensure or other governance entity). In this regard, we encourage states to consult existing resources on safe and appropriate opioid prescribing. We recognize there are many national guidelines and resources available to the states. Associations including, but not limited to, the PQA, NCQA, NQF, and federal agencies including AHRQ, SAMHSA, and the CDC can be utilized as existing resources. Therefore, we are

finalizing as proposed this implementing regulation at § 456.703(h)(1)(ii).

Comment: Some commenters suggested removing the word "rapid" from the statement in the CMS proposed rule "we do not mean to suggest rapid discontinuation of opioids already prescribed at higher dosages," as the commenter stated that even slow tapers have resulted in serious harm, which has not been adequately studied. Additionally, commenters noted that withdrawal is one of many risks associated with opioid tapering.

Response: We use the word "rapid" as a commonly referenced term to differentiate tapering regimens and agree withdrawal symptoms may be a risk of opioid tapering, which could potentially occur with slow tapering regimens, also. We do not suggest rapid discontinuation of opioids already prescribed at higher dosages. The maximum daily MME metric is often used as a gauge of the overdose potential of the amount of opioid that is being given at a particular time. Please refer to the HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics¹⁰⁴ for more information.

Comment: Some commenters noted that CMS could develop clearer guidance to ensure that safety edits and automated retrospective claims reviews achieve their intended goals without harming certain patient groups, emphasizing flexibility when applying safety edit thresholds, as well as addressing potential burden placed on physicians whose prescriptions might frequently be flagged due to the nature of their specialty, for example, such as cancer pain specialists, orthopedists or dental providers.

Response: We expect that states will continue to allow prescribers to make the best clinical decisions for patients regarding prescription medications needed to treat the patient's medical condition. The safety edits and automated retrospective claims reviews, as determined and implemented by state, that we are requiring under this final rule, are intended to assist providers in making clinical decisions to augment, not jeopardize patient care and clinical decision-making. We expect that many of the safety edit parameters will be reviewed by the state's DUR Board—which must include physicians and pharmacists, see § 456.716(b)—prior to implementation by the state. We also know that often times, prescribers may not be aware that patients are taking

concomitant drugs that include the same type of active ingredients, such as opioids, and these situations are sometimes only detected at the time that the prescription is filled through a prospective review process, or after the prescription is filled, through a retrospective review process. We view the DUR program as providing an important, positive feedback loop to prescribers and dispensers to assure patient safety and improve therapeutic outcomes.

States will continue to have flexibility in design, development and implementation of safety edits and automated retrospective claims review as specified in section 1004 of the SUPPORT Act and in the provisions of this final rule. We envision that states will consult national guidelines and resources available to develop state policy to provide appropriate flexibility for their providers to ensure prospective safety edits and automated claims reviews will not adversely affect coordinated patient care, but augment clinical decision-making. We recognize there are many national guidelines and resources available to the states. Associations including, but not limited to, the PQA, NCQA, NQF, and federal agencies including AHRQ, SAMHSA, and the CDC can be utilized as existing resources.

Comment: One commenter recommended requiring an additional prospective safety edit to monitor when an individual is concurrently prescribed opioids and either benzodiazepines or antipsychotics.

Response: Under section 1004 of the SUPPORT Act, states are required, as determined and implemented by the state, to establish a retrospective claims review automated process to monitor when an individual is concurrently prescribed opioids, and benzodiazepines or antipsychotics. At the option of the state, the state may also establish prospective safety edits as part of a comprehensive DUR program to monitor for the same. The benefit of prospective safety edits for concurrently-prescribed medications would allow for real-time clinical assessment at the point of dispensing of the prescribed drugs. Additionally, such prospective safety edits could help in the detection of fraud and abuse. State Medicaid DUR programs promote patient safety through state-administered utilization management (UM) tools and systems that interface with the state's claims processing systems. The concurrent prescription monitoring requirement added by section 1004 of the SUPPORT Act is consistent with the requirement in

¹⁰⁴ <https://www.cms.gov/About-CMS/Story-Page/CDCs-Tapering-Guidance.pdf>.

section 1927(g)(1)(A) of the Act that state DUR programs must assure that prescriptions are appropriate, medically necessary, and not likely to result in adverse medical results. Therefore, we proposed and are finalizing this rule at § 456.703(h)(1)(iv)(A) and (B) to require states to establish a retrospective claims review automated process and, at the option of the state, prospective safety edits for concurrently prescribed opioids and benzodiazepines or antipsychotics, as determined and implemented by the state.

Comment: One commenter recommended adding nonbenzodiazepine sedative hypnotics to CMS' proposed minimum DUR requirements for monitoring concurrent prescribing with opioids.

Response: We encourage states to determine whether to adopt safety edits for the prescribing of nonbenzodiazepine sedative hypnotics concurrently with opioids as part of their DUR programs. There are many existing resources available to the states, including but not limited to the PQA, NCQA, NQF, and federal agencies including AHRQ, SAMHSA, and the CDC, that have developed clinical guidance that may be relevant to establishing such safety edits and claims reviews. Neither the SUPPORT Act nor this final rule prohibits states from designing and implementing a prospective safety edit and/or retrospective automated claims review process to monitor for concurrent prescribing of opioids and another drug class, which additional monitoring could support enhanced care and treatment for Medicaid beneficiaries.

Comment: A few commenters encouraged CMS to work with various commenters, including NIH and the NIDA, to develop objective measures of pain and to perform ongoing assessment of the DUR activities to ensure that legitimate patient access to appropriate pain treatment is not negatively impacted.

Response: These activities described by the commenters are not within the scope of this rulemaking; however, we acknowledge the commenters' concern regarding the need for beneficiaries to have access to appropriate pain treatment, and the need to assess whether the pain treatment regimen prescribed is working to alleviate the patient's pain. Currently, we publish states' annual responses to the FFS and MCO DUR surveys on *Medicaid.gov*, including national summary comparison reports collated by CMS. These reports help us conduct state oversight and enable states to review other states' reports and compare their

own DUR program activity to that of other states. In doing so, CMS and states gain visibility into the effectiveness of various DUR efforts and are better able to ensure that legitimate patient access to appropriate pain treatment is not negatively impacted. Additionally, beginning with state-submitted DUR reporting regarding the state's compliance with requirements of this final rule for FFY 2020, as required under amendments made by section 1004 of the SUPPORT Act, we will submit an annual report to Congress (RTC) that includes this state-submitted information to facilitate improved congressional oversight of the implementation of opioid-related DUR requirements. Finally, regarding the comments on developing objective measures of pain, we note that currently available national pain assessment resources include the CMS Clinical Quality Measures (CQMS) Pain Assessment and Follow-Up criteria¹⁰⁵ and the Joint Commission's Pain Assessment and Management Standards.¹⁰⁶

Comment: One commenter noted that the proposed DUR standards should specifically require providers to consider benefits of opioid medication along with risks, and to include patients' goals and priorities in any decisions regarding dosage reduction.

Response: Decisions weighing the benefits and risks of opioid prescription treatment are the purview of the prescriber and the patient. We agree that, generally in medical decision-making, the health care provider and the patient should thoroughly consider the benefits and risks of available treatment options together before arriving at a decision about the patient's care. However, the DUR program can provide systematic feedback to prescribers about their opioid prescribing patterns, as compared to other prescribers, which information can help inform their thinking about their clinical treatment practices.

Comment: One commenter stated that flexibility at all levels of DUR program development and implementation is key to ensuring that patient needs are met.

Response: While states will need to comply with the requirements of the SUPPORT Act and the requirements of this final rule, we agree with the commenter that affording states the flexibility to develop and implement

prospective safety edits and automated claims review processes in this final rule will allow states to ensure patient and provider needs are addressed in an effective DUR program. The flexibilities afforded to the states in this final rule will allow states to establish state-specific DUR standards to suit their circumstances and beneficiary populations. States also have the flexibility to use standards from existing state DUR models, or develop their own, in complying with the requirements of this final rule. We envision states will consult national guidelines and resources issued by public associations such as the PQA, NCQA, NQF; and federal agencies including, but not limited to, the AHRQ, SAMHSA, and the CDC, to develop, implement and potentially enhance their safety edits and claims reviews for an effective and efficient DUR program.

In consideration of the comments received, with a limited exception, we are finalizing as proposed § 456.703(h)(1)(i) through (iv), to require that the state's DUR program must include certain minimum standards for DUR Programs under the SUPPORT Act and section 1927 of the Act. The limited modification to the proposed regulation text concerns the safety edit for MME in § 456.703(h)(1)(ii), which we explained in preamble to the proposed rule that we intended to apply with respect to opioids prescribed for pain, not limited to chronic pain. 85 FR 37309. We made a technical error in the proposed regulation text that limited the applicability of the MME safety edit to opioids prescribed for chronic pain, which we are correcting in this final rule by removing the errant word "chronic" from the regulation text so that the requirement will clearly apply for opioid prescriptions "for treatment of pain," whether chronic or acute.

f. Program To Monitor Antipsychotic Medications in Children

Under section 1004 of the SUPPORT Act, states must have a program (as designed and implemented by the state) to monitor and manage the appropriate use of antipsychotic medications by children enrolled under the state plan (or under a waiver of the state plan), including any Medicaid expansion group for the Children's Health Insurance Program (CHIP).¹⁰⁷ Additionally, states must annually submit information on activities carried out under this program for individuals not more than the age of 18 years old generally, and children in foster care

¹⁰⁵ https://qpp.cms.gov/docs/QPP_quality_measure_specifications/CQM-Measures/2019_Measure_131_MIPSCQM.pdf.

¹⁰⁶ <https://www.jointcommission.org/resources/patient-safety-topics/pain-management-standards-for-accredited-organizations/#a98ee961a3184ec899b62579053a24a7>.

¹⁰⁷ Section 1902(o)(1)(B) of the Act, as added by section 1004 of the SUPPORT Act.

specifically, as part of the annual report submitted to the Secretary under section 1927(g)(3)(D) of the Act, as provided in section 1902(o)(1)(D) of the Act.

Antipsychotic medications are increasingly used for a wide range of clinical indications in diverse populations, including privately and publicly insured youth.¹⁰⁸ Antipsychotics' adverse metabolic effects have heightened concern over growth in prescribing to youth, including off-label prescribing and polytherapy of multiple antipsychotics.¹⁰⁹ Studies have raised concerns regarding the long term safety and effectiveness of antipsychotics in this broadened population. Studies in adults have found that antipsychotics can cause serious side effects and long-term safety and efficacy for off-label utilization is a particular concern in children.¹¹⁰

Some of the most concerning effects include uncontrollable movements and tremors; an increased risk of diabetes; substantial weight gain; elevated cholesterol, triglycerides and prolactin; changes in sexual function; and abnormal lactation.¹¹¹ Children appear to be at higher risk than adults for a number of adverse effects, such as extrapyramidal symptoms and metabolic and endocrine abnormalities. Some studies suggests that antipsychotic treatment may be associated with increased mortality among children and youths and the distal benefit/risk ratio for long-term off-label treatment remains to be determined.^{112 113}

In consideration of clinical recommendations to monitor and manage the appropriate use of antipsychotic medications by children and to assess the clinical benefits and harms of treatment on an ongoing basis, we believe this program is necessary to help ensure children are receiving appropriate treatment that is not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(v) that states be required

to implement programs to monitor and manage the appropriate use of antipsychotic medications by children enrolled under the state plan, including any Medicaid expansion groups for CHIP. We noted that we understand states need considerable flexibility when implementing this program. The proposed provisions were not meant to prohibit the exercise of clinical judgment by a provider regarding the best or most appropriate care and treatment for any patient. We noted that states are expected to work with their pharmacy and therapeutics (P&T) and DUR committees to identify clinically appropriate safety edits and reviews. We recommended states consider expanding DUR programs to include reviews on children for polytherapy (therapy that uses more than one medication), inappropriate utilization or off label utilization.

The following is a summary of the comments we received on the proposed minimum standards for DUR programs for monitoring of antipsychotic medications in children, and our responses.

Comment: Some commenters recommended that CMS further define or identify guidelines for appropriate use of antipsychotics in children and encourage states to align their DUR programs on this particular DUR edit with national clinical practice guidelines.

Response: As outlined in the proposed rule, states are expected to consult with their Medicaid P&T and DUR committees, as well as state mental health and behavioral health professionals, to identify clinically appropriate parameters for the safety edits and reviews required under this final rule. We recommend that states, when developing parameters and criteria to implement appropriate prospective and retrospective DUR oversight for children, also consider specifically the applicability of such criteria for children in potentially vulnerable groups, such as children in foster care and those with disabilities. Some states have developed fact sheets to help communicate recommended strategies for prescribing psychotropic medication to children, including those in foster care and those living with disabilities.¹¹⁴

Resources to consider using include, but are not limited to, the AHRQ–CMS Pediatric Quality Measures Program

(PQMP) fact sheet¹¹⁵ and the SAMHSA guidance on Strategies to Promote Best Practice in Antipsychotic Prescribing for Children and Adolescents.¹¹⁶

After considering the comments received, we are finalizing, as proposed, § 456.703(h)(i)(v), to require states to establish a program to monitor and manage the use of antipsychotic medications by children enrolled under the state plan, including any expansion group for the Children's Health Insurance Program (CHIP). States must annually submit information on activities carried out under this program for beneficiaries not more than the age of 18 years old generally, and children in foster care specifically, as part of the annual report submitted to the Secretary under section 1927(g)(3)(D) of the Act, as provided in section 1902(o)(1)(D) of the Act.

g. Fraud and Abuse Identification

Section 1902(o)(1)(C) of the Act, as added by section 1004 of the SUPPORT Act, provides that states must have a process (as designed and implemented by the state) that identifies potential fraud or abuse of controlled substances by individuals enrolled under the state plan (or under a waiver of the state plan), health care providers prescribing drugs to individuals so enrolled, and pharmacies dispensing drugs to individuals so enrolled. We proposed to implement this requirement at § 456.703(h)(1)(vi); specifically, we proposed that the state's DUR program must include a process to identify potential fraud or abuse of controlled substances by individuals enrolled under the state plan, health care providers prescribing drugs to individuals so enrolled, and pharmacies dispensing drugs to individuals so enrolled.

We intended that the proposed process would operate in a coordinated fashion with other state program integrity efforts. States would have flexibility to define specific parameters for reviews for fraud and abuse, as well as protocols for recommendation, referral, or escalation of reviews to the relevant Program Integrity/Surveillance Utilization Review (SURS) unit, law enforcement, or state professional board, based on patterns discovered through the proposed DUR process. Additionally, we noted that state policy should specify the documentation required when suspected fraud and/or abuse results in a recommendation,

¹⁰⁸ Crystal, Stephen et al. "Broadened use of atypical antipsychotics: safety, effectiveness, and policy challenges." *Health affairs (Project Hope)* vol. 28, 5 (2009): w770–81. doi:10.1377/hlthaff.28.5.w770.

¹⁰⁹ Ibid.

¹¹⁰ Ibid.

¹¹¹ Marder SR, et al. Physical health monitoring of patients with schizophrenia. *Am J Psychiatry*. 2004; 161(8):1334.

¹¹² <https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2717966>.

¹¹³ <https://www.healthline.com/health/consumer-reports-antipsychotics-children#1>.

¹¹⁴ <https://children.wi.gov/Documents/Psychotropic%20Medication%20Prescribing%20for%20Children%20on%20Medicaid.pdf>.

¹¹⁵ https://www.ahrq.gov/sites/default/files/wysiwyg/policymakers/chipra/factsheets/chipra_1415-p011-1-ef_0.pdf.

¹¹⁶ https://store.samhsa.gov/sites/default/files/d7/priv/pep19-antipsychotic-bp_508.pdf.

referral, or escalation for further review, including the findings of any subsequent investigation into the potential deviation from the standard of care. States would be expected to ensure that DUR reviews conducted under the proposed requirement are aligned with all applicable federal requirements, including those specified in in §§ 455.12, 455.13 through 455.21, and 455.23 and section 1902(a)(64) of the Act.

We acknowledged that other initiatives, which many states are already undertaking, could work synergistically with the proposed requirement to help reduce fraud, misuse, and abuse related to opioids. For example, patient review and restriction programs (lock-in programs)¹¹⁷ and PDMPs¹¹⁸ also play an important role in detecting and preventing opioid-related fraud, misuse and abuse. Lock-in programs, also called patient review and restriction or drug management programs, are meant to cut down on “doctor shopping”—the practice of going to several doctors or pharmacies to obtain or fill multiple prescriptions for opioids or other controlled substances for illicit sale or misuse or to support an addiction. Such programs are used primarily to restrict overutilization of medications. Additionally, we noted that programs may require beneficiaries to receive all prescriptions through one pharmacy, have all prescriptions written by one prescriber, receive health care services from one clinical professional, or all three, depending on how the program is designed.¹¹⁹

Section 5042 of the SUPPORT Act requires covered providers who are permitted to prescribe controlled substances and who participate in Medicaid to query qualified PDMPs before prescribing controlled substances to most Medicaid beneficiaries, beginning October 1, 2021. PDMPs are database tools sometimes utilized by government officials and law enforcement for reducing prescription drug fraud, abuse and diversion, but which more frequently can be used to monitor controlled substance use by

healthcare providers including prescribers and pharmacists. PDMPs collect electronically transmitted prescribing and some dispensing data submitted by pharmacies and dispensing practitioners. The data are monitored and analyzed to support states’ efforts in education, research, enforcement and abuse prevention.¹²⁰ Data analytics can help to determine the extent to which beneficiaries are prescribed high amounts of opioids, identify beneficiaries who may be at serious risk of opioid misuse or overdose, and identify prescribers with questionable opioid prescribing patterns for these beneficiaries.¹²¹ ¹²² The process required under the SUPPORT Act and the proposed rule would identify potential fraud or abuse, and can help ensure that state officials and staff implementing the state’s program integrity, PDMP, and DUR functions work collaboratively to identify opportunities for DUR activities to assist in the identification of potential fraud and abuse.

The following is a summary of the comments we received on the proposed minimum standards for DUR programs for fraud and abuse identification processes, and our responses.

Comment: Some commenters urged CMS to work with states to ensure that mechanisms to decrease provider administrative burden are implemented, relative to checking PDMPs, such as allowing PDMP queries and patient history checks to be performed by designated provider staff before patient visits, and the ability for designated provider staff to integrate results into existing electronic health record systems. This would reduce the burden on prescribers to check the PDMP at the time the prescription is written, and reduce patient waiting time. Additionally, some commenters suggested that PDMP interoperability between states would enable more coordinated patient care and better guard against fraud and abuse.

Response: Section 5042 of the SUPPORT Act requires covered providers who are permitted to

prescribe controlled substances and who participate in Medicaid to query qualified PDMPs before prescribing controlled substances to most Medicaid beneficiaries, beginning October 1, 2021. We agree this has the potential to increase administrative burden on the prescriber, and that such increased burden could be minimized if designated provider staff are authorized to check patient history prior to patient visits and if PDMP information is integrated into existing electronic health record systems used by prescribers. We encourage states to educate providers on any best practices identified by the state regarding allocation of staff resources for accessing PDMP information and integrating it into clinical care processes. Furthermore, we agree that direct integration of PDMP information into electronic health record systems has the potential to increase the usefulness of PDMPs and promote improved clinical outcomes while minimizing burdens on clinical staff. The process required under section 5042 of the SUPPORT Act and the fraud and abuse identification process required under this final rule will help identify potential fraud or abuse, and help ensure that state officials and staff implementing the state’s program integrity, PDMP, and DUR functions work collaboratively to identify opportunities for DUR activities to assist in the identification of potential fraud and abuse. Additionally, national initiatives to promote interoperability of PDMPs is being assessed by the Office of National Drug Control Policy (ONDCP) and the CDC.

Comment: Some commenters noted it may be difficult to fully understand a patient’s entire opioid history and use if the patient crosses state lines to receive care, since PDMPs currently are separate, state-specific and non-integrated databases. In many cases, this results in information from one state’s PDMP not being easily accessible to or interoperable with PDMPs in other states.

Response: We acknowledge the commenter’s concern; however, the accessibility and interoperability of PDMPs is not within the scope of this rulemaking. We note that section 1944(a)(1) of the Act, as added by section 5042 of the SUPPORT Act, requires state Medicaid programs, beginning in October 2021, to require covered providers to check a qualified PDMP for a covered individual’s prescription drug history before prescribing a controlled substance. Additionally, the amendments made by section 5042 of the SUPPORT Act incentivize states to enter into

¹¹⁷ “Pharmacy Lock-In Programs Slated For Expanded Use.” OPEN MINDS, www.openminds.com/market-intelligence/executive-briefings/pharmacy-lock-programs-slanted-expanded-use/.

¹¹⁸ Office of National Drug Control Policy. Prescription Drug Monitoring Program. Prescription Drug Monitoring Program, April 2011. <https://www.ncjrs.gov/pdffiles1/ondcp/pdmp.pdf>.

¹¹⁹ “Pharmacy Lock-In Programs Slated For Expanded Use.” OPEN MINDS, www.openminds.com/market-intelligence/executive-briefings/pharmacy-lock-programs-slanted-expanded-use/.

¹²⁰ “Prescription Drug Monitoring Frequently Asked Questions (FAQ): The PDMP Training and Technical Assistance Center.” *Prescription Drug Monitoring Frequently Asked Questions (FAQ)* | The PDMP Training and Technical Assistance Center, www.pdmpassist.org/content/prescription-drug-monitoring-frequently-asked-questions-faq.

¹²¹ Beaton, Thomas. “Preventing Provider Fraud through Health IT, Data Analytics.” *HealthPayerIntelligence*, 5 Oct. 2018, <https://healthpayerintelligence.com/news/preventing-provider-fraud-through-health-it-data-analytics>.

¹²² OIG, *Opioids in Medicare Part D: Concerns about Extreme Use and Questionable Prescribing*, OEI-02-17-00250, July 2017. <https://oig.hhs.gov/oei/reports/oei-02-17-00250.pdf>.

agreements with contiguous states to enable covered providers also to check the PDMPs of such contiguous states by providing 100 percent federal matching funds during fiscal years 2019 and 2020 for design, development, and implementation activities for establishing and connecting qualifying PDMPs.

Comment: Some commenters recommended that dosage alone not be used as an indicator of questionable prescribing when there is no other evidence of fraud or abuse, and that CMS should adopt fraud detection measures that do not compromise individualized care.

Response: We agree that using the dosage of drug being prescribed as a sole indicator for fraud and abuse would not be appropriate, and we encourage states to utilize their flexibility to define the specific parameters to be implemented for the detection of fraud and abuse. We intend that this process should operate in a coordinated manner with other state program integrity efforts. States have flexibility to define specific parameters for review for fraud and abuse and to determine how best to ensure these parameters will not compromise or unduly interfere with patient care. Resources states may consult in determining parameters can be found in established national guidelines such as those issued by the PQA, NCQA, NQF, and federal agencies including AHRQ, SAMHSA, and the CDC.

Comment: One commenter expressed concern with CMS' suggestions that states may implement programs such as provider "lock-in programs" or programs that require beneficiaries to receive all prescriptions through one pharmacy, have all prescriptions written by one prescriber, or receive health care services from one clinical professional, to enhance existing fraud and abuse policies. The commenter noted that such programs may have unintended negative consequences for patients from a continuity of care perspective if patients are required to change their providers or discontinue using certain providers for services that such providers have appropriately provided to them in the past.

Response: We intend that the process for developing and/or enhancing existing fraud and abuse programs should proceed in a coordinated fashion with other state program integrity efforts. Under this final rule, states have flexibility to define specific parameters for reviews for fraud and abuse, as well as protocols for recommendation, referral, or escalation of reviews to the relevant SURS unit, law enforcement, or

state professional board, based on patterns discovered through the state's DUR program. State flexibility in developing and/or enhancing fraud and abuse programs will enable states to mitigate potential negative effects on prescribers' ability to provide coordinated patient care. State parameters should include processes to ensure continuity of care is not adversely affected when developing and implementing new or enhanced fraud and abuse programs. National guidelines such as those issued by the PQA, NCQA, NQF, and federal agencies including AHRQ, SAMHSA, and the CDC can help identify best practices for states to consider in implementing these programs.

In consideration of the comments received, we are finalizing § 456.703(h)(1)(vi) as proposed, to require that the state's DUR program must include a process to identify potential fraud or abuse of controlled substances by individuals enrolled under the state plan, health care providers prescribing drugs to individuals so enrolled, and pharmacies dispensing drugs to individuals so enrolled.

2. Other CMS Proposed Standards

In addition to regulations implementing requirements added by section 1004 of the SUPPORT Act, we proposed additional minimum DUR standards in the June 2020 proposed rule that states would be required to implement as part of their DUR programs at § 456.703(h)(1)(vii). Specifically, under our authority to implement section 1927(g) of the Act and consistent with the goals of the SUPPORT Act to help combat the nation's opioid overdose epidemic, we proposed additional minimum standards related to MAT and identification of beneficiaries who could be at high risk of opioid overdose and should be considered for co-prescription or co-dispensing of naloxone. These additional standards were included to ensure prescribed drugs are: (1) Appropriate; (2) medically necessary; and (3) not likely to result in adverse medical results.

Under the proposed policies, state DUR programs would be required to include prospective safety edit alerts, automatic retrospective claims review, or a combination of these approaches as determined by the state, to identify cases where a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT, and prospective safety edit alerts, automatic retrospective claims review, or a combination of these approaches as

determined by the state to expand appropriate utilization of naloxone. As discussed in the June 2020 proposed rule, we proposed these minimum requirements to further implement section 1927(g) of the Act to prevent and reduce the inappropriate use of opioids and potentially associated adverse medical results, consistent with the provisions under section 1004 of the SUPPORT Act.

a. Medication Assisted Treatment (MAT)

To further implement section 1927(g)(1) of the Act and consistent with section 1004 of the SUPPORT Act, we proposed to require states to establish prospective safety edit alerts, automatic retrospective claims review, or a combination of these approaches as determined by the state, to identify cases where a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT or had an OUD diagnosis within a specified number of days (as determined by the state), without having a new indication to support utilization of opioids (such as a new cancer diagnosis, new palliative care treatment or entry into hospice).

MAT is treatment for SUD that includes addiction treatment and services plus a medication approved by FDA for opioid addiction, detoxification, or maintenance treatment or relapse prevention. Section 1006(b) of the SUPPORT Act defines MAT to include all FDA approved drugs and licensed biological products to treat opioid disorders, as well as counseling services and behavioral therapies for the provision of such drugs and biological products.¹²³ MAT has proven to be clinically effective in treating OUD and significantly reduces the need for inpatient detoxification services.¹²⁴ Medications such as buprenorphine and methadone, in combination with counseling and behavioral therapies, provide a whole-patient approach to the treatment of OUDs.

Using opioid medications during the course of MAT is dangerous from a clinical perspective. Prospective drug safety edits are also designed to identify other prescription and non-prescription medications that are not indicated for use by patients being treated with opioid therapy. For example, an

¹²³ Support for Patients and Communities Act, Section 1006(b). Requirement For State Medicaid Plans To Provide Coverage For Medication-Assisted Treatment.

¹²⁴ "Medication and Counseling Treatment". September 28, 2015. Available at <https://www.samhsa.gov/medication-assisted-treatment/treatment>.

effective prospective DUR program can alert the pharmacist before dispensing that the patient is taking other medications, such as blood pressure or cough and cold medications that might have an additive sedating effect when taken with opioids. These prospective edits are effective only to the extent that the other potential interacting medications are in the patient's prescription record, and not if the patient has obtained them from a non-pharmacy source. That is, the system can only send the alerts to the pharmacist if it includes all the prescription and non-prescription medications being taken by the patient.

We believe states could take effective action to help prevent adverse medical results and possible OUD relapse, and increase coordination of care in patients with a history of OUD. We noted that we understand states need considerable flexibility when implementing these reviews to address complicated patient populations. The proposed prospective safety edits, automatic retrospective claims reviews, or a combination of these approaches, would help identify cases where a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT or has received an OUD diagnosis. Accordingly, we proposed that states would have flexibility to determine which of these DUR approaches the state would implement, including the flexibility to incorporate both into an effective DUR program. State flexibility also would extend to specifying the time period between the prior episode of MAT or OUD diagnosis (or most recent prior episode of MAT or OUD diagnosis) and the subject opioid prescription that, if not met, would trigger the alert (for example, an opioid prescription within 24 months of the end of the most recent episode of MAT would trigger a prospective safety edit). Flexibility could also extend to diagnoses where opioid use after MAT is appropriate without compromising OUD treatment (for example, in end of life care or in cancer patients with severe pain resulting from their disease or that does not respond to alternative pain management options).

In consideration of clinical recommendations to ensure appropriate MAT treatment, and to prevent opioid related abuse and misuse, we believe the proposed prospective safety edits and/or retrospective claim reviews are necessary to assure that prescriptions are appropriate, medically necessary, and not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the

SUPPORT Act. This proposed requirement is authorized by and expected to advance the purposes of section 1927(g) of the Act and is consistent with the purposes of section 1004 of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(vii)(A) that states be required to implement reviews to alert when the beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT for an OUD or has been diagnosed with an OUD, within a timeframe specified by the state, in the absence of a new indication to support utilization of opioids (such as new cancer related pain diagnosis or entry into hospice care). In addition to helping ensure appropriate utilization of medications, we noted that these edits would assist in coordination of care, and potentially in improved treatment of pain.

The following is a summary of the comments we received on these additional minimum standards for DUR programs related to MAT, and our responses.

Comment: One commenter requested clarification as to whether DUR activities are applicable to beneficiaries who receive implantable or injectable formulations of medications for opioid use disorder (MOUD). Additionally, other commenters expressed concern that MOUD dispensed in an Outpatient Treatment Programs (OTPs) or MOUD administered in settings where regulations pertaining to CODs do not apply are vulnerable to adverse reactions that result from concurrent prescribing, particularly for beneficiaries receiving methadone. With respect to OTPs, this concern arises because methadone is generally paid for as part of a single bundled service when used in an OTP, and thus would not be a covered outpatient drug as a result of the limiting definition found at section 1927(k)(3) of the Act; therefore, methadone use may not be detected by DUR systems designed to examine use of covered outpatient drugs.

Response: We interpret the comment regarding MOUD as referring to medications used to treat opioid use disorders, more commonly referred to as medication-assisted treatment (MAT). Medications used in MAT—including methadone, naltrexone, and buprenorphine—are used to treat individuals who have opioid use disorders, such as opioid dependency. Section 1006(b) of the SUPPORT Act amended section 1902(a)(10)(A) of the Act to require state Medicaid plans to include coverage of MAT for OUD for categorically needy populations, added this new required benefit to the

definition of medical assistance at section 1905(a)(29) of the Act, and added a definition of the coverage required under the new benefit at section 1905(ee)(1) of the Act. Section 1905(a)(29) specifies that the new mandatory MAT benefit will be in effect for the period beginning October 1, 2020, and ending September 30, 2025.

CMS interprets section 1905(a)(29) and 1905(ee) of the Act to require that states include as part of this new mandatory benefit all forms of drugs and biologicals that FDA has approved or licensed for MAT to treat OUD. At this time, this includes the drugs methadone, buprenorphine, and naltrexone, as there are no biologicals currently licensed by FDA to treat OUD. Before the new mandatory MAT benefit took effect on October 1, 2020, states covered many of these MAT drugs (for all FDA approved and medically-accepted indications) under the optional benefit for prescribed drugs described at section 1905(a)(12) of the Act.

A statutory change was made to sections 1905(a)(29) and 1905(ee) of the Act by section 2601 of the Continuing Appropriations Act of 2021, and other Extensions Act (Pub. L. 116–159), to specify that the Medicaid drug rebate program (MDRP) requirements in section 1927 of the Act shall apply to any MAT drugs or biologicals used to treat OUD described under the definition of the mandatory benefit at section 1905(ee)(1)(A) of the Act, that are furnished as medical assistance under sections 1905(a)(29) and section 1902(a)(10)(A) of the Act, and are covered outpatient drugs, as that term is defined at section 1927(k)(7) of the Act.

In determining whether such a MAT drug or biological satisfies the definition of a covered outpatient drug, such MAT drugs or biologicals are deemed prescribed drugs for such purposes. More specifically, these amendments ensure that MAT drugs and biologicals covered under the new mandatory benefit are included in the MDRP, make it possible for states to seek section 1927 rebates and apply drug utilization management mechanisms (such as preferred drug lists and prior approval) with respect to these drugs and biologicals, and establish a manufacturer's obligation to pay appropriate rebates and comply with all applicable drug product and drug pricing reporting and payment of rebates with respect to these drugs and biologicals. The change in law is effective as if included in the enactment of the SUPPORT Act, which was October 24, 2018.

To the extent the injectable and implantable drugs used for MOUD

satisfy the definition of a covered outpatient drug, such drugs would be subject to the same DUR edits and activities as other drugs that meet the definition of a covered outpatient drug. That is, states would be expected to include such drugs in the prospective claims edits and retrospective claims analysis that would be applicable to other covered outpatient drugs, and apply any of the opioid safety edits and other required DUR activities to the extent that these MAT drugs were also opioids.

Comment: One commenter encouraged CMS to consider how the proposed DUR approaches complement or otherwise interact with other utilization management strategies, to ensure that states are not unduly restricting access to MOUD.

Response: As noted above, MAT drugs, or medications for opioid use disorders, are covered under a new mandatory MAT benefit, but can also be covered outpatient drugs. MAT drugs that are also covered outpatient drugs can thus be subject to the same utilization management approaches, such as prior authorization, and DUR program safety edits and claims reviews, as can other covered outpatient drugs under section 1927 of the Act. Before the new mandatory MAT benefit took effect on October 1, 2020, MAT drugs were available to patients through the optional prescription drug benefit under section 1905(a)(12) of the Act as covered outpatient drugs, and evidence from state DUR program surveys indicate that these medications were made available by states to Medicaid beneficiaries under the optional benefit. We expect that access to these medications will increase given that they are now covered under the new MAT mandatory benefit.

Comment: A few commenters urged CMS to clearly articulate the requirements for a MAT DUR program.

Response: We are not requiring states to implement a DUR program specific to MAT medications. We proposed to require states to implement prospective safety edits, automatic retrospective claims reviews, or a combination of these approaches, as determined by the state, to identify when a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT for an OUD or has been diagnosed with an OUD, within a timeframe specified by the state, in the absence of a new indication to support utilization of opioids (such as new cancer related pain diagnosis or entry into hospice care). Accordingly, we proposed that states would have flexibility to determine which of these

DUR approaches—prospective, retrospective, or both—the state would implement as part of an effective DUR program to identify these patients. State flexibility also would extend to specifying the time period between the prior episode of MAT or OUD diagnosis (or most recent prior episode of MAT or OUD diagnosis), as well as the identification of specific indications that could support a new opioid prescription (such as new cancer related pain diagnosis or entry into hospice care) and therefore not trigger a safety edit alert and/or retrospective review under the state's implementation. We are finalizing this provision as proposed in § 456.703(h)(1)(vii)(A).

Comment: One commenter supported the proposed minimum standards for MAT but noted that the proposals for prospective safety edit alerts and retrospective claims review may impact 42 CFR part 2 confidentiality protection of those patients with Substance Use Disorder (SUD) patient records. Another commenter suggested that CMS and SAMHSA provide guidance on how the proposed opioid-related DUR requirements should be implemented in a manner that protects beneficiary information consistent with the requirements in part 2; this commenter was specifically concerned that claims data about services beneficiaries receive from part 2 providers might be disclosed to non-part 2 providers without patient consent.

Response: We believe that it is essential for all states to comply with 42 CFR part 2 regulations in order to uphold the confidentiality of patient medication information held by part 2 providers. We further note the potential applicability of state privacy regulations and Health Information Portability and Accountability Act as referenced in the National Association of State Mental Health Program Directors Technical Assistance Coalition's *Compilation of State Behavioral Health Patient Treatment Privacy and Disclosure Laws and Regulations*.¹²⁵ The 42 CFR part 2 regulations serve to protect substance use disorder patient records that are maintained in connection with the performance of part 2 programs (as defined in 42 CFR 2.11). The 42 CFR part 2 regulations have been revised, most recently in 2020, to facilitate better coordination of care activities with providers that are not participating in a part 2 program (considered non-part 2 providers) in response to the opioid epidemic while maintaining patient

confidentiality protections against unauthorized record use and disclosure pursuant to 42 CFR part 2. Section 3221 of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) will require further revisions to part 2. CMS notes that part 2 records may be disclosed under certain conditions with patient consent and under various exceptions to patient consent requirements (for example, 42 CFR 2.53). Because the application of part 2 regulations to specific disclosures may be complex, state programs should consult legal counsel about DUR programs, applicable privacy laws and regulations and disclosure of patient identifying information. A SAMHSA Part 2 Revised Rule Fact Sheet is available for more information.¹²⁶

Comment: One commenter encouraged CMS to provide more examples of when it may be appropriate to prescribe additional opioid medications to patients receiving MAT.

Response: We included examples in the proposed rule focusing on end of life care or for cancer patients with severe pain resulting from their disease or that does not respond to alternative pain management options. We recommend exploring currently approved and accepted clinical practice guidelines to better understand these and other instances when it may be appropriate to prescribe additional opioid medications to patients receiving MAT, such as SAMHSA's publication, *Medication-Assisted Treatment For Opioid Addiction in Opioid Treatment Programs*.¹²⁷

Comment: One commenter suggested that certified registered nurse anesthetists' (CRNAs') approach to pain management may reduce the reliance on opioids as primary pain management as CRNAs manage chronic pain in a compassionate, patient-centered, holistic manner, using a variety of therapeutic, physiological, pharmacological, and interventional modalities. Additionally, this commenter stated that moving from a unimodal approach of using opioid drugs to manage chronic and acute pain to a more patient-centered, multidisciplinary, multimodal opioid-sparing treatment approach optimizes patient engagement in their own pain care which would reduce the risk of patients developing SUDs.

Response: We agree that all of a patient's treating providers working in

¹²⁶ <https://www.hhs.gov/about/news/2020/07/13/fact-sheet-samhsa-42-cfr-part-2-revised-rule.html>.

¹²⁵ <https://www.nasmhpd.org/content/tac-assessment-working-paper-2016-compilation-state-behavioral-health-patient-treatment>.

¹²⁷ <https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Documents/PEP20-02-01-006>.

coordination have a role to play in reducing the reliance on opioids as a primary pain management modality. Section 1006(b) of the SUPPORT Act amended the Social Security Act to include a new MAT Medicaid benefit, and defined that benefit to not only include FDA approved drugs and licensed biological products to treat OUD, but also counseling services and behavioral therapies related to the provision of the drugs and biological products, and thus recognizes that providing these therapies could help to optimize treatment.

Comment: One commenter noted that for chronic pain management, particularly if opioids are prescribed in the treatment, the clinician should discuss the risk of dependence and OUD, as well as enter into a pain management treatment agreement with the patient.

Response: Generally, to the greatest extent possible, clinical decision-making should be undertaken in the context of the relationship between the provider and the patient and should consider nationally recognized clinical best practices relevant to the patient's specific treatment needs. The provider should educate the patient on any prescribed treatment, to include both benefits and potential risks. Resources and guidance issued by public associations such as the PQA, NCQA, NQF; and federal agencies including, but limited to, the AHRQ, SAMHSA, and the CDC are available to support clinical best practices. Additionally, the safety edits required under this final rule can create an opportunity for additional review and patient consultation that could potentially result in a more clinically appropriate approach to treatment to forge a stronger provider/patient relationship. Another tool available to help foster a better a provider/patient relationship could be to employ the use of a pain management agreement (PMA) which allows for the documentation of understanding between a provider and patient. PMAs, when used, provide a means of facilitating care and improving communication between providers and their patients. It is important to note that the PMA is not designed as a contract, but rather a tool that sets forth important information about potential risks, benefits, safeguards, expectations, and patient and provider responsibilities. In the event the patient gets off-course with his or her treatment, the PMA provides a foundation for

discussion as to the potential consequences and solutions.¹²⁸

Comment: One commenter opined that CMS should encourage state Medicaid programs to remove coverage and formulary limits, prior authorization requirements, step therapy requirements, and other administrative burdens or barriers that may inappropriately delay or deny MAT, with respect to all medications approved by FDA for OUD.

Response: MAT is an effective, comprehensive, and evidence-based treatment that is integral to addressing the nation's opioid crisis. Section 1006(b) of the SUPPORT Act amended the Social Security Act to require state Medicaid plans to cover MAT for OUD for the categorically needy populations. Evidence demonstrates that treatment for substance use disorders—including inpatient, residential, and outpatient treatment—is cost-effective compared with no treatment.¹²⁹ Existing Medicaid authorities, as well as new opportunities afforded by the SUPPORT Act, are available to help states expand their SUD service continuum, which can include MAT. Additionally, to increase access to MAT for OUD, section 1006(b) of the SUPPORT Act requires states to provide Medicaid coverage of certain drugs and biological products, and related counseling services and behavioral therapy.¹³⁰ Additionally, states may use utilization management controls to promote the efficient delivery of care and to control costs.

In consideration of comments received, we are finalizing § 456.703(h)(1)(vii)(A) as proposed, to require states to establish approaches to identify cases where a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT or had an OUD diagnosis within a specified number of days, without having a new indication to support utilization of opioids.

¹²⁸ <https://health.rti.gov/publications/guidelines/provider/PatientViolatesPainAgreement.pdf>.

¹²⁹ Office of the Surgeon General, *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. Washington, DC: HHS, November 2016. Chapter 4, Early Intervention, Treatment, and Management of Substance Use Disorders. <https://addiction.surgeongeneral.gov/sites/default/files/surgeon-generals-report.pdf>.

¹³⁰ SUPPORT for Patients and Communities Act section 1006(b), Public Law 115–271 (2018), <https://www.congress.gov/115/plaws/publ271/PLAW-115publ271.pdf>.

b. Coprescribing or Codispensing of Naloxone When a Patient Is at High Risk for Opioid Overdoses

To further implement section 1927(g)(1) of the Act, and consistent with section 1004 of the SUPPORT Act, we proposed and sought comment on requiring states to establish prospective safety edit alerts, automatic retrospective claims review, or a combination of these approaches as determined by the state, to identify beneficiaries who could be at high risk of opioid overdose and should be considered for co-prescription or co-dispensing of naloxone with the goal of expanding appropriate utilization to individuals at risk of opioid overdose. As discussed below, based on comments received, we are modifying the proposal in this final rule by replacing the reference to naloxone with a reference to all FDA-approved opioid antagonist/reversal agents so that the final regulation is broad enough to encompass additional such drugs, should FDA approve any others in the future. An opioid antagonist/reversal agent is a medication designed to rapidly reverse opioid overdose by binding to opioid receptors and reversing the effects of opioids. Opioid antagonist/reversal agents work quickly to restore normal respiration to a person whose breathing has slowed or stopped as a result of an opioid overdose, including both illicit and prescription opioids. However, opioid antagonist/reversal agents only work if a person has opioids in their system; the medication has no effect if opioids are absent.¹³¹ Currently, naloxone is the only FDA-approved opioid antagonist/reversal agent, but it is possible that FDA could approve others in the future.

The prescribing or co-prescribing of an opioid antagonist/reversal agent to patients at elevated risk for opioid overdose or for those who have overdosed on opioids can save lives.¹³² We recommended states consider ways to expand access to, and distribution and use of naloxone, or another opioid antagonist/reversal agent that may be approved in the future, when clinically appropriate.

When implementing this safety edit or review, we noted that states should

¹³¹ "Understanding Naloxone." Harm Reduction Coalition. Available at <https://harmreduction.org/issues/overdose-prevention/overview/overdose-basics/understanding-naloxone/>.

¹³² NEJM Journal Watch: Summaries of and Commentary on Original Medical and Scientific Articles from Key Medical Journals, HHS-recommends-coprescribing-naloxone-with-opioids-high. <https://www.jwatch.org/fw114907/2018/12/20/hhs-recommends-coprescribing-naloxone-with-opioids-high>.

determine standards for identifying individuals at high risk for opioid overdose, such as individuals who have been discharged from emergency medical care following opioid overdose, individuals who use heroin or misuse prescription pain relievers, as well as those who use high-dose opioids for long-term management of chronic pain.¹³³ Before starting and periodically during continuation of opioid therapy, we stated that clinicians should evaluate risk factors for opioid-related harms. When prescribing opioids, the CDC guideline recommends clinicians should incorporate strategies to mitigate opioid risks, including considering offering an opioid antagonist/reversal agent when factors that increase risk for opioid overdose are present, such as history of overdose, history of SUD, higher opioid dosages (≥ 50 MME/day), or concurrent benzodiazepine use.¹³⁴ We noted that we understand states need considerable flexibility when implementing this requirement to address a complex problem and proposed that states would have flexibility to determine which DUR approach the state would implement in an effective DUR program: either or both of prospective safety edits and/or retrospective claims reviews. Further, we proposed that states would have flexibility to determine the particular criteria they would use to identify which beneficiaries may be at high risk of opioid overdose such that they should be considered for co-prescription or co-dispensing of an opioid antagonist/reversal agent.

In consideration of clinical recommendations to expand opioid antagonist/reversal agent use to prevent adverse medical events among those who are prescribed opioids or those who may be at high risk of opioid overdose or who have previously overdosed, we believe this requirement is necessary to ensure that at-risk individuals are receiving appropriate treatment that is not likely to result in adverse medical results, and to accomplish other purposes of the DUR program under section 1927(g) of the Act and of the SUPPORT Act. Accordingly, we proposed at § 456.703(h)(1)(vii)(B) that states be required to implement prospective safety edit alerts, automatic retrospective claims reviews, or a combination of these approaches, as determined by the state, to identify when a beneficiary could be at high risk

of opioid overdose and should be considered for co-prescription or co-dispensing of naloxone. As discussed below, we are modifying this requirement in this final rule to extend to any FDA-approved opioid antagonist/reversal agent. As noted in the proposed rule, we anticipate that this requirement may help expand appropriate utilization of an opioid antagonist/reversal agent, including the facilitation of dispensing to individuals at risk of overdose.

The following is a summary of the comments we received on additional minimum standards for DUR programs with respect to co-prescribing or co-dispensing of naloxone and our responses.

Comment: One commenter suggested expanding the language in the proposed rule to include therapies that are not naloxone-based, suggesting “any FDA-approved opioid antagonist/reversal agent” in the place of naloxone.

Response: We agree with the commenter. The language in our proposed rule referred to naloxone because this is the only FDA approved antagonist/reversal agent at this time. We do understand that other agents may be developed and receive FDA approval within this therapeutic class. We do not want to limit the new safety edit to simply one drug, should another opioid antagonist/reversal agent gain FDA approval in the future; such a limitation would be less effective in accomplishing our goal of promoting the appropriate co-prescribing and co-dispensing of such agents to help mitigate the effects of opioid overdose. To reflect the proactive intent of this rulemaking, we are implementing the commenter’s suggestion to revise the regulation text to refer to “any FDA-approved opioid antagonist/reversal agent.”

Comment: A few commenters encouraged CMS to work with state Medicaid agencies and other commenters to develop recommended best practices for prescribers and pharmacists for communicating with patients about an opioid antagonist/reversal agent. Some commenters recommended that CMS consider approaches to expand education on administering opioid antagonist/reversal agents and in recognizing the signs and symptoms of an overdose.

Response: We agree with the commenters that best practices should be established for providers to educate beneficiaries and their families about opioid antagonist/reversal agents. Currently available relevant materials include the SAMHSA Opioid Overdose

Prevention Toolkit.¹³⁵ This toolkit provides advice for prescribers and beneficiaries and their families. Additionally, the toolkit encourages providers and others to learn about preventing and managing opioid overdose, promoting access to treatment for individuals who have a SUD, expanding access to naloxone, and it encourages prescribers to use PDMPs. This resource could be helpful to providers, including prescribers and pharmacists, in discussing opioid overdose risk and prevention with patients and their families and caregivers.

Comment: Some commenters expressed the belief that pharmacists should be allowed to dispense any FDA-approved opioid antagonist/reversal agent over the counter (OTC) without a prescription and appropriate related indemnification should be extended to pharmacists. One commenter suggested CMS address prescription status, as well as the cost of opioid antagonist/reversal agents as barriers to utilization. Commenters also opined that Good Samaritan laws should be implemented in every state to shield health care personnel and lay persons from liability when administering an opioid antagonist/reversal agent to individuals suspected of opioid overdose.

Response: Although this is not in scope of this rule, most states do allow pharmacists to dispense FDA-approved opioid antagonist/reversal agents. Forty-seven states (94 percent) allow pharmacists to dispense these agents independently or through collaborative practice agreements, standing orders, or other predetermined protocols developed by entities including State Boards of Professional Regulations, Boards of Pharmacy, and/or Boards of Medicine, as applicable.¹³⁶ This allows greater access and less barriers to obtain these agents by patients and/or their family members and caregivers. Additionally, FDA-approved opioid antagonists/reversal agents are available without prior authorization in all states.¹³⁷

Comment: Some commenters suggested standards for healthcare providers who administer naloxone or any FDA-approved opioid antagonist/reversal agent such as educational programs designed to inform providers on proper administration and patient communication.

¹³⁵ <https://store.samhsa.gov/sites/default/files/d7/priv/sma18-4742.pdf>.

¹³⁶ <https://www.medicare.gov/medicaid/prescription-drugs/drug-utilization-review/drug-utilization-review-annual-report/index.html>.

¹³⁷ Ibid.

¹³³ Ibid.

¹³⁴ “CDC Guidelines for Prescribing Opioids for Chronic Pain.” Available at https://www.cdc.gov/drugoverdose/pdf/guidelines_at-a-glance-a.pdf.

Response: We agree that clinical standards for healthcare providers who administer any FDA-approved opioid antagonist/reversal could be useful and that providers should be properly educated on the correct use of drugs in this class, of which naloxone currently is the only one. The SAMHSA Opioid Overdose Prevention Toolkit is a resource available to states, providers, and beneficiaries; it contains helpful information regarding the proper use of naloxone.¹³⁸

In consideration of comments received, with a limited exception, to further implement section 1927(g)(1) of the Act, and consistent with section 1004 of the SUPPORT Act, we are finalizing, as proposed, § 456.703(h)(1)(vii)(B) to require states to establish approaches to identify beneficiaries who could be at high risk of opioid overdose and should be considered for co-prescription or co-dispensing of naloxone. Based on comments received, we are revising the final regulation text in § 456.703(h)(1)(vii)(B) to replace the proposed reference to naloxone with a reference to all FDA-approved opioid antagonist/reversal agents, so that the final regulation is broad enough to encompass additional such drugs, should FDA approve any others in the future.

3. Exclusions

The foregoing DUR requirements added to section 1902(o) of the Act by section 1004 of the SUPPORT Act, which we proposed to implement along with additional related proposals under section 1927(g) of the Act at § 456.703(h)(1)(i) through (h)(1)(vii)(B), do not apply for individuals who are receiving hospice or palliative care or those in treatment for cancer; residents of a long-term care (LTC) facility, a facility described in section 1905(d) of the Act (that is, an intermediate care facility for the intellectually disabled), or of another facility for which frequently abused drugs are dispensed for residents through a contact with a single pharmacy; or other individuals the state elects to treat as exempted from such requirements.

We understand states need considerable flexibility when implementing these safety edits and claims reviews to address complicated patient populations. We noted our expectation that states would consult national guidelines and work with their P&T and DUR committees to identify other clinically appropriate patient

populations for possible exclusion from the safety edits and claims reviews specified in § 456.703(h)(1)(i) through (vii), to avoid impeding critical access to needed medication when managing specific complex disease states.

We proposed to implement this statutory exclusion at § 456.703(h)(2), such that states would not be required to implement the specified DUR requirements for these populations. However, while states are not required to comply with these requirements for these individuals, we clarified, and proposed to codify in the regulation, that states voluntarily may apply the prospective safety edits and claims review automated processes otherwise required under the SUPPORT Act to exempt populations.¹³⁹

The following is a summary of the comments we received on the proposed exclusion standards for DUR programs, and our responses.

Comment: One commenter expressed concern that more information would be needed from the states for the pharmacist and other providers to properly identify beneficiaries who are receiving hospice or palliative care, or who are residents in certain LTC facilities, to ensure exemptions from opioid safety edits and automated claims reviews are correctly applied.

Response: We understand states have multiple patient information systems and data sources available to help identify beneficiaries that are exempt from opioid-related safety edits and/or claims reviews, including their claims systems, PDMPs, and information from the databases of pharmacy benefit managers with which the state (or the state's managed care plans) has contracted to administer COD benefits for beneficiaries. As drug utilization review is performed through claims processing systems, linking to other sources to identify these populations should help states implement their safety edits and claims reviews. Ideally, a comprehensive DUR program that optimizes such system linkages would present safety edit information at the point of care, including to the provider (such as through an EHR system) before the prescription is written and to the pharmacist before it is dispensed. This way, clinical issues can be resolved proactively and the beneficiary will be able to receive his or her clinically-indicated opioid therapy without undue disruption.

We remind states that they should not impose a greater burden on medication access for individuals with disabilities

residing in community-based settings than that applied to similar individuals residing in institutional settings, consistent with the Americans with Disabilities Act (ADA) and the Supreme Court's decision in *Olmstead v. L.C.*, 527 U.S. 581 (1999).

CMS will consider adding additional questions to the annual state and MCO DUR surveys that may help provide additional information on policies relating to patient populations that the state exempts from the opioid-specific DUR requirements, and how states implement such policies.

Comment: One commenter suggested that CMS identify beneficiaries residing in assisted living facilities (ALFs) as a population that would be excluded from these opioid safety edits. Additionally, some commenters recommended that patients with sickle cell disease and cancer survivors should be considered as potential excluded populations. Other commenters requested that we delete from the regulatory exemption text proposed at § 456.703(h)(2) the following sentence: "While States are not required to apply these requirements for these individuals, States may elect to do so," due to the commenters' belief that the statement is inconsistent with the clear expression of the Congress that the specified groups should be exempt from the DUR requirements.

Response: Under this final rule, states have flexibility to determine additional populations to exclude from the application of the required opioid-related safety edits and claims reviews. This includes the flexibility to exclude, for example, patients with sickle cell disease or cancer survivors. Additionally, we proposed to codify in the regulation, that states voluntarily may apply prospective safety edits and claims review automated processes, as well as the program for monitoring antipsychotic use in children and the process for identifying potential fraud or abuse of controlled substances that are otherwise required under the SUPPORT Act to otherwise exempt populations. As stated, this is not a requirement; however, we believe beneficiaries in the excluded populations would benefit from the safety edits and claims reviews and other measures otherwise required under this final rule, to help ensure their opioid-related treatment is clinically appropriate and their risk of opioid-related harm is minimized. For example, beneficiaries in the excluded populations would also benefit from safety edits and reviews being finalized in this rule to help avert unintended therapeutic duplication and drug interactions, which would be more

¹³⁸ <https://store.samhsa.gov/sites/default/files/d7/priv/sma18-4742.pdf>.

¹³⁹ Section 1902(o)(3) of the Act, as added by section 1004 of the SUPPORT Act.

likely to be missed if the beneficiaries were not subject to opioid-related safety edits and claims reviews. States would benefit from subjecting as broad a population as possible to opioid-related safety edits and claims reviews, too, as comprehensive data collection better ensures all populations are accounted for when further developing the DUR program and making other policy decisions. States that opt not to exclude otherwise excluded beneficiaries from the activities required under § 456.703(h)(1)(i) through (vii) would do so under the authority of section 1927(g) of the Act, not the amendments made by the SUPPORT Act. Furthermore, as discussed above, the safety edits and claims reviews required under this final rule are not intended to prevent any beneficiary from receiving clinically appropriate prescribed treatment, but rather, to help ensure their prescribed treatment is appropriate and medically necessary.

Comment: One commenter requested clearer guidance to ensure that safety edits and retrospective claims reviews, if voluntarily implemented by the state for otherwise exempt populations, achieve their intended goal without harming these excluded patients.

Response: This final rule is intended to ensure that certain patient and clinical information is provided to prescribers and pharmacists to help ensure that beneficiaries who take opioids are taking them correctly and are not unnecessarily subjected to increased potential for clinical harm. State flexibility to voluntarily implement safety edits and claims reviews on otherwise excluded patient populations should help ensure coordinated patient care and avoid harm that could be associated with excessive or otherwise inappropriate use of opioids. We encourage states to consult nationally-recognized guidelines when implementing these safety edits, including but not limited to those issued by PQA, NCQA, NQF, and federal agencies such as AHRQ, SAMHSA, and the CDC.

In consideration of the comments received, we are finalizing § 456.703(h)(2) as proposed, specifying that the requirements in § 456.703(h)(1)(i) through (vii) do not apply with respect to individuals receiving hospice or palliative care or treatment for cancer; individuals who are residents of long-term care facilities, intermediate care facilities for the intellectually disabled, or facilities that dispense frequently abused drugs through a contract with a single pharmacy; or other individuals the state elects to exempt. While states are not

required to apply these requirements with respect to these individuals, states may elect to do so, pursuant to section 1927(g) of the Act.

4. Managed Care Requirements

Pursuant to section 1902(o)(1)(A)(ii) of the Act, as added by section 1004 of the SUPPORT Act, states also must ensure that their contracts with MCOs under section 1903(m) of the Act and MCEs under section 1905(t)(3) of the Act require that the MCOs or MCEs have safety edits, an automated review processes, a program to monitor antipsychotic medications in children, and fraud and abuse identification requirements as described in the June 2020 proposed rule for individuals eligible for medical assistance under the state plan (or waiver of the state plan) who are enrolled with the entity, subject to the exclusions of individuals specified in section 1902(o)(1)(C) of the Act. We noted that states must include these DUR provisions in managed care contracts by October 1, 2019. Although the foregoing provisions added by the SUPPORT Act address only MCOs and MCEs in the managed care context, we proposed also to extend these requirements to contracts with PAHPs and PIHPs under our authority in section 1902(a)(4) of the Act, under which existing PIHP and PAHP requirements are authorized. Thus, as proposed, states would be required to include PAHPs and PIHPs when uniformly implementing the updates and requirements specified in amendments made by section 1004 of the SUPPORT Act for all Medicaid managed care programs, regardless of whether the services are covered through a contract with an MCO, MCE, PIHP, or PAHP.

As required by section 1004 of the SUPPORT Act, each Medicaid MCO and MCE within a state must also operate a DUR program that complies with specified requirements. We proposed to define MCEs in § 438.2 to have the meaning given to the term under section 1932(a)(1)(B) of the Act, which defines the term to mean a Medicaid MCO, as defined in section 1903(m)(1)(A), that provides or arranges for services for enrollees under a contract pursuant to section 1903(m) of the Act, or a primary care case manager, as defined in section 1905(t)(2) of the Act. Managed care regulations at § 438.3(s)(4) require Medicaid managed care DUR programs in which an MCO, PIHP, or PAHP contracts to provide coverage for CODs to operate consistently with section 1927(g) of the Act and part 456, subpart K, and that state contracts must be updated to include these requirements.

We proposed to amend the regulation at § 438.3(s) introductory text and (s)(4) and (5) to require that MCEs comply with the requirements in section 1902(o)(1)(A) of the Act as implemented in these proposed regulations, similar to MCOs, PIHPs, and PAHPs.

Although no comments were received, we are not finalizing our proposed definition of managed care entities and MCE in § 438.2 and we are finalizing amendments to § 438.3(s) introductory text and (s)(4) and (s)(5) replacing all proposed references to MCE to “PCCM” in the final version of § 438.2(s) to implement our proposal that PCCMs be added to the list of managed care plans that must comply with § 438.3(s)(4) and (5). Because MCO and PCCM are already defined terms, we believe it would be simpler and less potentially confusing to add a reference to PCCM in each of the amended provisions, rather than define MCE as a new term that would only group two already-defined entity types. No substantive change in meaning from the proposal is intended by this change in the final rule.

5. State Plan Amendment (SPA) Requirements

Section 1004 of the SUPPORT Act amended the state plan requirements in section 1902 of the Act to include a new paragraph (a)(85), which requires the state plan to provide that the state is in compliance with the new drug review and utilization requirements set forth in section 1902(o) of the Act, as also added by the SUPPORT Act. The SUPPORT Act also requires all states to implement these requirements by October 1, 2019, and to submit an amendment to their state plan no later than December 31, 2019, consistent with the SPA requirements in 42 CFR part 430, subpart B, to describe how the state addresses these provisions in the state plan. States are also expected to give appropriate tribal notification, as required, if applicable. Guidance regarding state plan amendment requirements was issued to states in a CMS informational bulletin in August 2019.¹⁴⁰ In the proposed rule, we noted that, if the proposed provisions implementing section 1004 of the SUPPORT Act and section 1927(g) of the Act were finalized, then an additional SPA potentially could be needed to ensure that state plans are in compliance with the applicable final regulations. We stated that we would

¹⁴⁰ <https://www.medicare.gov/federal-policy-guidance/downloads/cib080519-1004.pdf>.

expect to provide related guidance in connection with any final rule.

The following is a summary of the comments we received on SPA requirements, and our responses.

Comment: One commenter noted that CMS is proposing a number of minimum DUR standards that restate the requirements of the SUPPORT Act, with which states have already submitted state plan amendments to comply. This commenter noted that states should be required to follow their approved state plans, which the state can seek to further amend based on best practices in medicine. This commenter also opined that CMS is overstepping its authority to regulate by proposing to prescribe other DUR practices in regulation beyond those that are included in the SUPPORT Act.

Response: We agree with the commenter that all states have submitted state plan amendments to comply with the amendments made by section 1004 of the SUPPORT Act, and all have been approved. Additionally, the state plan must be amended as necessary so that it accurately and comprehensively describes how the state complies with the requirements added to section 1902 of the Act by section 1004 of the SUPPORT Act, as well as the requirement in section 1902(a)(54) of the Act that a state plan that includes coverage of CODs must comply with the applicable requirements of section 1927 of the Act.

We do not believe that we have exceeded our statutory authority with respect to the proposed requirements, which we are finalizing as discussed elsewhere in this final rule, for safety edits and claims reviews beyond those that are expressly required pursuant to amendments made by the SUPPORT Act. To further implement section 1927(g)(1) of the Act, which requires that a state DUR program assures that covered outpatient drugs are appropriate, medically necessary, and not likely to result in adverse events, and consistent with section 1004 of the SUPPORT Act, we proposed to require states to establish several new safety edits and/or claims reviews. Specifically, these requirements are: To develop prospective safety edit alerts, automatic retrospective claims review, or a combination of these approaches as determined by the state to identify cases where a beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for MAT or had an OUD diagnosis; and where beneficiaries who could be at high risk of opioid overdose should be considered for co-prescription or co-dispensing of any FDA-approved opioid

antagonist/reversal agent. This final rule affords states flexibility in designing and implementing required safety edits and claims reviews in the manner the state determines would be best adapted to the circumstances in the state, including the particular needs of the state's Medicaid beneficiaries. These requirements implement section 1927 of the Act, and while consistent with them, do not directly implement amendments made by section 1004 of the SUPPORT Act.

6. Reporting Requirements

Consistent with section 1927(g)(3)(D) of the Act, we require each state Medicaid agency to submit to us an annual report on the operation of its Medicaid DUR program. Under § 456.712(a), the state must require the DUR Board to prepare and submit, on an annual basis, a report to the state Medicaid agency. Under § 456.712(b), each state Medicaid agency must in turn submit this report to us, as well as specified additional information, including but not limited to descriptions of the nature and scope of the state's prospective and retrospective DUR programs, detailed information on the specific DUR criteria and standards in use, a description of the actions taken to ensure compliance with predetermined standards requirements in § 456.703, a summary of the educational interventions used and an assessment of their effect on quality of care, and an estimate of the cost savings generated as a result of the DUR program. We have compiled state FFS Medicaid DUR annual reports since 1995 and have published them on *Medicaid.gov* since 2012. Since 2016, § 438.3(s)(4) requires any MCO, PIHP or PAHP that covers CODs to operate a DUR program that complies with section 1927(g) of the Act and 42 CFR part 456, subpart K, as though these requirements applied to the MCO, PIHP, or PAHP instead of the state, including requirements related to annual DUR reporting. Given the commercial nature of many MCEs, incorporation of information posted to *Medicaid.gov* provides new considerations with regard to public disclosure of information received by CMS.

In an effort to share and encourage innovative and collaborative practices, we also proposed to publish all information received in annual DUR reports from FFS and managed care programs on a CMS website. We proposed to add new paragraph (c) to § 456.712 to provide that all FFS and managed care DUR reports received by CMS under § 456.712(b) and, as applicable, under § 438.3(s), will be

publicly posted on a website maintained by CMS for the sharing of reports and other information concerning Medicaid DUR programs.

The following is a summary of the comments we received on the proposed minimum standards for DUR program reporting requirements, and our responses.

Comment: One commenter recommended CMS provide a standardized template for Medicaid MCOs reporting DUR program information, to help ease administrative burdens.

Response: CMS does currently provide a standardized template for Medicaid MCOs to complete. In response to section 1004 of the SUPPORT Act, revised and additional survey questions have been incorporated to the annual MCO survey to address recently enacted provisions. Reports can be accessed on *www.Medicaid.gov*.¹⁴¹

In consideration of comments received, CMS is finalizing § 456.712(c) as proposed, to provide that all FFS and managed care DUR reports received by CMS under § 456.712(b) and, as applicable, pursuant to § 438.3(s), will be publicly posted on a website maintained by CMS for the sharing of these reports and other information concerning Medicaid DUR programs.

III. Collection of Information Requirements

Under the Paperwork Reduction Act of 1995, we are required to provide 30-day notice in the **Federal Register** and solicit public comment before a collection of information requirement is submitted to the Office of Management and Budget (OMB) for review and approval. With respect to the PRA and this section of the preamble, collection of information is defined under 5 CFR 1320.3(c) of the PRA's implementing regulations.

To fairly evaluate whether a collection of information should be approved by OMB, section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995 requires that we solicit comment on the following issues:

- The need for the collection of information and its usefulness in carrying out the proper functions of our agency.
- The accuracy of our estimate of the information collection burden.
- The quality, utility, and clarity of the information to be collected.
- Recommendations to minimize the information collection burden on the

¹⁴¹ <https://www.medicaid.gov/medicaid/prescription-drugs/drug-utilization-review/drug-utilization-review-annual-report/index.html>.

affected public, including automated collection techniques.

Our June 2020, proposed rule (85 FR 37286) solicited public comment on each of these issues for our proposed information collection requirements, burden estimates, and assumptions. PRA-related comments were received for ICR #1 Regarding State Plan Requirements, Findings, and

Assurances and ICR #3 Regarding the Payment of Claims 18. Summaries of the public comments and our response can be found below under the respective ICR. We did not receive any PRA-related comments for ICR #2 Regarding Requirements for States.

A. Wage Estimates

To derive average costs, we used data from the U.S. Bureau of Labor Statistics' May 2018 National Occupational Employment and Wage Estimates (http://www.bls.gov/oes/current/oes_nat.htm). Table 3 presents the mean hourly wage, the cost of fringe benefits and overhead (calculated at 100 percent of salary), and the adjusted hourly wage.

TABLE 3—NATIONAL OCCUPATIONAL EMPLOYMENT AND WAGE ESTIMATES

Occupation title	Occupation code	Mean hourly wage (\$/hr)	Fringe benefits and overhead (\$/hr)	Adjusted hourly wage (\$/hr)
Chief Executives	11-1011	93.20	93.20	186.40
Data Entry and Information Processing Workers	43-9020	17.52	17.52	35.04
General Operations Manager	11-1021	59.15	59.15	118.30

We are adjusting our employee hourly wage estimates by a factor of 100 percent since fringe benefits and overhead costs vary significantly from employer to employer, and because methods of estimating these costs vary widely from study to study.

Nonetheless, we believed that doubling the hourly wage to estimate total cost is a reasonably accurate estimation method.

Revised Wage and Cost Estimates: While our proposed rule's costs were based on BLS's May 2018 wages, this

final rule's cost estimates are based on BLS's more recent May 2019 wages. Changes to BLS' mean hourly wage figures are presented in the Table 4.

TABLE 4—COMPARISON OF PROPOSED AND FINAL RULE MEAN WAGE DATA

Occupation title	Occupation code	CMS-2482-P: May 2018 (\$/hr)	CMS-2482-F: May 2019 (\$/hr)	Difference (\$/hr)
Chief Executives	11-1011	96.22	93.20	-3.02
Data Entry and Information Processing Workers	43-9020	17.05	17.52	+0.47
General Operations Manager	11-1021	59.56	59.15	-0.41

B. Information Collection Requirements (ICRs)

1. ICRs Regarding State Plan Requirements, Findings, and Assurances (§ 447.518(d)(2) and (3))

The following changes will be submitted to OMB for approval under control number 0938-1385(CMS-10722).

Under section 1902(a)(30)(A) the Act, we are granted the authority to require that methods and procedures be established by states relating to the utilization of, and the payment for, care and services available under the state plan process (including but not limited to utilization review plans) as may be necessary to safeguard against unnecessary utilization of such care and services and to assure that state payments to providers of Medicaid services are consistent with efficiency, economy, and quality of care.

To that end, as part of the state plan approval process relative to the CMS authorized VBP SRA, we are finalizing new reporting requirements that would

affect the 51 state Medicaid programs (the 50 states and the District of Columbia). Specifically, a state participating in CMS authorized supplemental rebate VBP arrangements will be required to report data described in § 447.518(d)(2) and (3) on an annual basis within 60 days of the end of each year, as well as cumulative data if a CMS authorized SRA VBP program ended in that year. The reported data must include: The state name; NDC(s) (for drugs covered under the CMS authorized SRA VBP); product FDA list name; number of prescriptions; cost to the State to administer the CMS authorized SRA VBP (for example: Systems changes, tracking evidence or outcomes-based measures, etc.); and the total savings generated by the supplemental rebate due to the CMS-authorized SRA VBP. The reporting requirements will be applicable to both FFS and MCO COD claims.

We estimate it would take an additional 6 hours at \$118.30/hr for a general operations manager to collect the SRA VBP drug utilization

information when due annually (we will choose the quarter in which the annual data will be due), and submit the report to CMS. In aggregate we estimate an ongoing annual burden of 306 hours (6 hr/report × 1/year × 51 respondents) at a cost of \$36,200.60 (306 hr × \$118.30/hr).

Other than our adjusted costs as discussed above under Wage Estimates, our proposed requirements and burden estimates are being finalized in this rule without change.

Comment: Several commenters raised concerns about the proposed data reporting requirements for states participating in CMS-authorized SRA VBP arrangements and the burden it may place on state Medicaid agencies, such as additional administrative expenses. A few commenters noted that if more CMS-authorized SRA VBP contracts are signed between manufacturers and state Medicaid agencies, the administrative burden may become too great for current state Medicaid staff and require additional resources, such as additional staff,

system changes, and physical office space. Another commenter suggested that CMS delay finalizing the proposal for states to provide CMS specific data elements associated with CMS-authorized VBP SRAs to ensure that the data elements can be easily collected and would not unintentionally create additional administrative burden to state Medicaid agencies in collecting and reporting the data elements.

Response: This final regulation does not require that states participate in CMS authorized VBP SRAs with manufacturers, or any other VBP arrangement. Rather, this regulation addresses the challenges faced by manufacturers and states regarding the impact of the VBP arrangements on MDRP price reporting obligations and the regulatory challenges that may impede manufacturers and payer progress in structuring and implementing VBP arrangements. However, we recognize that states may encounter administrative burden associated with CMS-authorized SRA VBP arrangements. This is one of the reasons that we have requested that states provide specific data elements associated with participating in VBP arrangements via CMS-authorized SRAs, so that we can determine how we can help states reduce these burdens, which may facilitate their contracting with manufacturers.

2. ICRs Regarding Requirements for States (§ 447.511(b), (d) and (e))

The following changes will be submitted to OMB for approval under control number 0938–0582 (CMS–R–144). Subject to renewal, the control number is currently set to expire on June 30, 2023.

Under § 447.511(b) states, territories, and the District of Columbia will be required to ensure by certification that the quarterly rebate invoices sent to manufacturers that participate in the MDRP no later than 60 days after the end of each rebate period via CMS–R–144 (Quarterly Medicaid Drug Rebate Invoice), mirrors the data sent to us. This rule does not impose any changes to the CMS–R–144 form.

Under § 447.511(d) states will be required to certify that their SDUD meets the requirements specified under § 447.511(e) via a certification statement. We believe the certification will not impose a significant burden as we will provide systems access to state certifiers to log in once per quarter to certify their SDUD report. Certifiers

would have to apply for a CMS user ID and password, and keep current with required annual computer-based training, as current state staff with access to our systems must do. To comply with the certification requirements, states must already have system edits in place to find and correct SDUD outliers prior to reporting to manufacturers and CMS.

We estimate it would take 5 hours at \$186.40/hr for the State Medicaid Director, Deputy State Medicaid Director, another individual with equivalent authority, or an individual with directly delegated authority from one of the above to obtain current CMS systems access. In aggregate we estimate a one-time system ID/password access burden of 280 hours (5 hr × 56 respondents) at a cost of \$52,192 (280 hr × \$186.40/hr).

We also estimate an additional annual burden of 2 hours (or 30 minutes/quarter) at \$186.40/hr for a chief executive to certify such data and to add the state data certification language in their submission. In aggregate we estimate an annual burden of 112 hours (2 hr × 56 respondents) at a cost of \$20,877 (112 hr × \$192.44/hr).

Other than our adjusted costs as discussed above under Wage Estimates, our proposed requirements and burden estimates are being finalized in this rule without change.

3. ICRs Regarding the Payment of Claims (§ 433.139(b)(2), (b)(3)(i), and (b)(3)(ii)(B))

The following changes will be submitted to OMB for approval under control number 0938–1265 (CMS–10529). Subject to renewal, the control number is currently set to expire on April 30, 2021. It was last approved on June 10, 2019, and remains active.

This final rule would implement provisions of BBA 2018 which includes several provisions that modify COB and TPL in both statute and regulation related to special treatment of certain types of care and payment in Medicaid and Children's Health Insurance Program Reauthorization Act of 2009 (CHIPRA) (Pub. L. 111–3, enacted February 4, 2009). Section 53102 of BBA 2018 amended the TPL provision at section 1902(a)(25) of the Act. Effective February 9, 2018, section 53102(a)(1) of the BBA 2018 amended section 1902(a)(25)(E) of the Act to require states to cost avoid claims for prenatal care for pregnant women including labor and delivery and postpartum care,

and to allow the state Medicaid agency 90 days instead of 30 days to pay claims related to medical support enforcement services, as well as requiring states to collect information on TPL before making payments. Effective April 18, 2019, section 7 of the MSIAA amended section 1902(a)(25)(E) of the Act to allow 100 days instead of 90 days to pay claims related to medical support enforcement services, as well as requiring all states, the District of Columbia, and the territories (56 respondents) to collect information on TPL before making payments.

Additionally, effective October 1, 2019, section 53102(a)(1) of the Bipartisan Budget Act of 2018 amended section 1902(a)(25)(E) of the Act, to require a state to make payments without regard to third party liability for pediatric preventive services unless the state has made a determination related to cost-effectiveness and access to care that warrants cost avoidance for 90 days.

Under the authority in section 1902(a)(25)(A) of the Act, our regulations at part 433, subpart D, establishes requirements for state Medicaid agencies to support the COBs effort by identifying TPL. Section 433.139(b)(2), (b)(3)(i), and (b)(3)(ii)(B) detail the exception to standard COB cost avoidance by allowing pay and chase for certain types of care, as well as the timeframe allowed prior to Medicaid paying claims for certain types of care. Title XIX of the Act requires state Medicaid programs to identify and seek payment from liable third parties, before billing Medicaid.

We estimate it would take 1 hour at \$35.040/hr for a data entry/information processing worker to collect information on TPL and report that information to CMS on CMS–64 (approved by OMB under the aforementioned OMB control number and CMS ID number) on a quarterly basis. In aggregate we estimate an annual burden of 224 hours (1 hr/response × 4 responses/year × 56 respondents) at a cost of \$8,550 (224 hr × \$35.04/hr).

Other than our adjusted costs as discussed above under Wage Estimates, our proposed requirements and burden estimates are being finalized in this rule without change.

C. Summary of Finalized Requirements and Annual Burden Estimates

Table 5 sets out our annual burden estimates.

TABLE 5—SUMMARY OF ANNUAL REQUIREMENT AND BURDEN

Section under title 42 of the CFR	Number of respondents	Total responses (per year)	Time per response (hours)	Total time (hours)	Labor rate (\$/hr)	Total cost (\$)	OMB control number (CMS ID No.)
§ 447.518(d)(1) and (2).	51	51	6	306	118.30	36,200	0938–1385 (CMS–10722)
§ 447.511	56	56	5	280	186.40	52,192	0938–0582 (CMS–R–144)
§ 447.518(d) (1) and (2).	51	51	6	306	18.3	36,200	0938–1385 (CMS–10722)
§ 447.511	56	224	0.5	112	186.40	20,877	0938–0582 (CMS–R–144)
§ 433.139(b)(2), (b)(3)(i), and (b)(3)(ii)(B).	56	224	1	224	35.04	7,849	0938–1265 (CMS–10529)
Total	56	555	Varies	922	Varies	117,118	n/a

IV. Regulatory Impact Statement

A. Statement of Need

This final rule will implement:

- Changes to section 1927 of the Act;
- Statutory changes from the Medicaid Services Investment and Accountability Act of 2019 (Pub. L. 116–16, enacted April 18, 2019), BBA 2018 and the Affordable Care Act;
- Section 602 of BBA 2015, which amended section 1927(c)(3) of the Act;
- Section 2501(d) of the Affordable Care Act, which added section 1927(c)(2)(C) of the Act;
- Section 1927(b)(2)(A) of the Act requiring states to report to each manufacturer not later than 60 days after the end of each rebate period;
- Changes and additions to sections 1902 and 1927(g)(1) of the Act as set forth by section 1004 of the SUPPORT Act;
- Title XIX of the Act and section 7 of the Medicaid Services Investment and Accountability Act of 2019 amending section 1902(a)(25)(E) of the Act (§ 433.139(b)(2), (b)(3)(i), and (b)(3)(ii)(B)); and
- Changes made by section 1603 of Public Law 116–59, the Continuing Appropriations Act, 2020, and Health Extenders Act of 2019 (Health Extenders Act), which amended sections 1927(k)(1) and 1927(k)(11) of the Act.

B. Overall Impact

We have examined the impact of this rule as required by Executive Order 12866 on Regulatory Planning and Review (September 30, 1993), Executive Order 13563 on Improving Regulation and Regulatory Review (January 18, 2011), the Regulatory Flexibility Act (RFA) (September 19, 1980, Pub. L. 96–354), section 1102(b) of the Act, section 202 of the Unfunded Mandates Reform Act of 1995 (March 22, 1995; Pub. L. 104–4), Executive Order 13132 on Federalism (August 4, 1999) and Executive Order 13771 on Reducing Regulation and Controlling Regulatory Costs (January 30, 2017).

Executive Orders 12866 and 13563 direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). A regulatory impact analysis (RIA) must be prepared for major rules with economically significant effects (\$100 million or more in any 1 year). A regulatory impact analysis (RIA) must be prepared for major rules with economically significant effects (\$100 million or more in any 1 year). We believe that this rule does reach the economic threshold and thus is considered a major rule.

We received the following comments regarding the impact of this rule:

Comment: A few commenters disagreed with CMS’ conclusion that the proposed rule did not reach the necessary threshold for economically significant effects (of \$100 million or more in any 1 year), and therefore, did not require a regulatory impact analysis. The commenters noted that the proposed changes to best price, line extension, drug rebate payments, drug pricing reporting requirements, and DUR would greatly impact state Medicaid agencies and manufacturers and would meet the financial threshold for a regulatory impact analysis. A few commenters suggested that CMS conduct a regulatory impact analysis prior to publication of a final rule or withdraw the proposed rule in order to conduct a regulatory impact analysis.

Several commenters expressed concern that the proposed rule does not include an impact analysis of the proposed changes on state Medicaid programs or Medicaid program spending specific to the proposed changes or potential decreases to the Medicaid manufacturer rebate amounts and increase to Medicaid drug costs. The commenters requested CMS analyze the proposed changes to best price

reporting and how it may impact state Medicaid programs. One commenter also requested that CMS provide financial impact estimates on states’ rebates due to their belief that this will ensure transparency and provide states adequate time to address budget shortfalls created from the proposed rule. A few commenters expressed concern that CMS did not conduct an impact analysis of the proposed VBP-related regulations on the U.S. healthcare system.

Response: For the following reasons, we agree with the commenters that a regulatory impact analysis is necessary. The projections below are based on the assumptions and projections for Medicaid expenditures in the President’s FY 2021 Budget. As with any projections of health care spending and changes to health care regulations, these projections are uncertain and impacts could be higher or lower than projected here. In addition, these projections do not account for any impacts related to COVID–19, which has had a major impact on health care spending and coverage in 2020.

- *Implementation of Minimum DUR Standards:* The requirement under section 1927 of the Act to provide for DUR (prospective and retrospective) for CODs to assure that prescriptions (1) are appropriate, (2) are medically necessary, and (3) are not likely to result in adverse medical results, is longstanding. Under our authority to implement section 1927(g) of the Act and the SUPPORT Act, to ensure the appropriate use of prescription opioids, the minimum standards for DUR in this final regulation, including standards related to MAT and co-prescribing or co-dispensing of any FDA-approved opioid antagonist/reversal agent, have already been adopted by state Medicaid programs as reflected in our most recent

DUR survey.¹⁴² Therefore, such DUR standards and the addition of minimum standards as set forth under this rule will not have a substantial impact on state Medicaid programs. Furthermore, these standards establish a baseline for minimally adequate DUR programs that help ensure prescribed drugs are appropriate, medically necessary, and not likely to result in adverse medical results, which ultimately may result in savings to the states and Federal government.

• *Line Extension and New*

Formulation: Since the line extension provision came into effect on January 1, 2010, manufacturers have been making reasonable assumptions as to the meaning of line extension at section 1927(c)(2)(C) of the Act, and where appropriate, have been permitted to use such reasonable assumptions in their determination of whether their drug qualifies as a line extension. Thus, manufacturers have been applying the alternative rebate calculation approach for ten years to determine their rebate obligations for drugs that are line extensions. The economic impact of the new policies for line extensions would be dependent on the change in the number of drugs that are reported to us as line extensions, the differences between the standard rebate amount and the alternative rebate amount that is calculated for that line extension drug, and that the impact of the new policies on the incentives to bring new formulations of existing drugs to market

that represented true advancements in treatment of particular conditions.

Notably, only 1.5 percent of all drugs that are reported to the Medicaid Drug Rebate Program (MDRP), or 408 drugs, are currently classified by their manufacturer as a line extension. This reporting is based on the manufacturer making its own reasonable assumptions that the new formulation of their drug is a line extension.

With respect to innovation, we also note that since we added a specific indicator in the Drug Data Reporting (DDR) system in 2016 for manufacturers to self-identify drugs that are line extensions, the rate at which the number of line extension drugs reported has been relatively stable, but increasing, thereby providing evidence that the line extension policies in existence have not resulted in a sharp change in the number of line extensions brought to market by manufacturers. For example, in 2016, 320 line extensions were reported to us, 360 in 2017, 373 in 2018, 389 in 2019, and 397 in 2020.

We have reviewed the impacts of the final regulatory definition of line extension on Medicaid drug rebates. The final rule clarifies the definition of “line extension” drugs. Drugs classified as line extensions are subject to an alternative rebate. The additional rebate amounts under the alternative rebate are collected entirely by the federal government. To calculate this impact, we determined which drugs were likely to be classified as line extensions under the definition in this final rule. We

reviewed the top 100 drugs by total spending (from data in the second quarter of 2020 in the MDR), and then identified which of those drugs would be defined as line extension drugs under the definition in the final rule. There were 17 drugs identified of the top 100 that would likely be classified as line extensions, which would not now be currently classified as line extensions under the statutory definition of line extension.

We then calculated the alternative rebate per unit for these drugs (defined as the inflationary or additional rebate divided by the AMP for the original drug, multiplied by the AMP of the line extension drug). Note that only 6 of the 17 drugs had alternative rebates that were higher than the standard rebate. For these 6 drugs, the rebates would increase by 6.5 percent and reduce spending net of rebates by 19.3 percent. We estimate that this would represent an increase of about 1.1 percent on rebates for the top 100 drugs, while decreasing net drug spending by 3.3 percent. We extrapolated the estimates on these drugs to the impact on all Medicaid drug spending. This assumes that the number of drugs classified as line extensions under the new regulatory definition of line extension, and the relative impacts on those drugs for the rest of the brand-name drug market is comparable to the top 100 drugs; it is possible that the impact on the rest of the drug market could be greater than or less than we have estimated here.

	Total spending	Total rebates	Net spending	Change in rebates due to line extension definition	Percentage change in rebates	Percentage change in net spending
Top 100 drugs	\$25,265	\$18,894	\$6,371	\$209	1.1	-3.3
Top 100 drugs identified as line extensions	4,295	3,212	1,083	209	6.5	-19.3
All drug spending	86,017	39,802	46,215	381	1.0	-0.8

The table below shows the projected impacts by fiscal year in millions of dollars.

Lower bound	2021	2022	2023	2024	2025	2021–2025
Federal government	-\$400	-\$430	-\$460	-\$490	-\$520	-\$2,300
State government	0	0	0	0	0	0
Total	-400	-430	-460	-490	-520	-2,300

There are several caveats to the estimates. First, the estimates do not

assume any impact on future drug pricing or new line extension

introduction changes. It is possible manufacturers might reconsider future

¹⁴² <https://www.medicaid.gov/medicaid/prescription-drugs/downloads/2019-dur-ffs-summary-report.pdf>.

drug launch strategies (including pricing and formulations) in light of this change. Second, we have not considered if there might be impacts on state supplemental rebate agreements that states negotiate directly with manufacturers. It is possible that there are some drugs for which states have some supplemental rebates that could be affected by the line extension rebates. Finally, the estimates rely on an analysis of a limited number of drugs; however, these drugs do represent a substantial share of Medicaid prescription drug spending (about 29 percent of prescription drug spending, and about 37 percent of brand-name prescription drug spending). The impact on the drugs affected could be significant, but given the small number of drugs affected, the overall impact may be smaller as a percentage of total spending. Depending on the final number of drugs determined to be line extensions and the relative increase in the rebates for those drugs, the actual impact could be greater than or less than estimated here.

We also note with respect to comments on the proposed definition of line extension and new formulation that there would be a negative impact on manufacturers' incentive to continue to innovate, that we refined the final definitions to limit the scope of drugs that are new formulations, and thereby subject to the alternative rebate calculation relative to our proposed definitions.

As previously stated, the proposed definitions included combination drugs and drugs approved with a new indication; however, we are not finalizing those changes. We believe that the exclusion of combination drugs and drugs that obtain new indications from the final definition of line extension will help ensure that we have maintained incentives for manufacturers to bring such advances to the market, such as new HIV drugs, or new uses for drugs that could be used to treat COVID-19.

Finally, the amount of additional rebate amounts that may be due from manufacturers as a result of the new regulatory definition of line extension are a function of the net change in the number of drugs that may be considered a line extension, as well as the difference between the standard rebate calculated on the line extension drug and the alternative rebate calculation, as noted above. The existence of a line

extension drug does not categorically result in a higher URA for a line extension of a drug, as there are many factors that enter into the URA calculation. As previously noted, one of the most important factors in the calculation is the inflation-based rebate that is applied to the initial brand name listed drug for the rebate quarter being calculated. Regardless of the price of the line extension drug, if the initial brand name listed drug did not increase in price in excess of the rate of inflation, then the alternative rebate calculation for the line extension should not result in a higher URA than the standard calculation for the drug that is a line extension. That is, if a manufacturer's price increases over the years have been within the CPI-U, then there is reduced chance that they will be subject at all to the alternative rebate calculation.

- *VBP Arrangements and Changes to Best Price and Manufacturer Reporting requirements:* As stated previously, this final regulation makes revisions to the determination of best price and AMP and manufacturer reporting requirements to address the regulatory challenges that manufacturers, states and private payers encounter when considering the development and implementation of VBP arrangements. The changes made by this regulation ensure that the regulatory framework is sufficient to support such arrangements and to promote transparency, flexibility, and innovation in drug pricing without undue administrative burden on states and manufacturers. They also clarify certain already-established policies to assist manufacturers and states in participating in VBP arrangements in a manner that is consistent with the law and maintains the integrity of the MDRP.

The change being finalized in this rule, which provides for the reporting of multiple best prices pursuant to a VBP arrangement (which meets the definition of VBP arrangement, also being finalized in this rule), is the most significant from a policy perspective, and could result in an increased use of VBP among commercial payers, and thus Medicaid programs. The estimated impacts of these VBP arrangements under the final rule are significantly uncertain. Primarily, this is due to lack of experience with such arrangements and the fact that the impacts will be highly dependent on the interest of states and manufacturers to enter into such arrangements.

As of 2020, there are only 9 such state arrangements of which we are aware, and we do not have data or estimates on the impact of these arrangements. Moreover, the impact will depend on 3 factors: (1) How many states would take up such arrangements; (2) how many drugs and which drugs would be covered under these arrangements; and (3) the nature of these arrangements (for example, what will be the terms for payment and coverage of drugs under these arrangements). These are all unknowable at this time.

In an attempt to estimate the possible impacts of such arrangements, we have estimated a range of impacts. At the upper bound of impacts on the federal government and the states, we estimate the impact would be 0. In these circumstances, it could be a combination of (1) no states or manufacturers enter into these VBP arrangements and (2) while states and manufacturers enter into VBP arrangements, these do not reduce net prescription drug spending.

At the lower bound (on impacts on the federal government and the states), we have estimated that there could be some savings. We made the following assumptions: (1) Half of states would enter into VBP arrangements; (2) states would enter into arrangements with 50 percent of the top 100 drugs as measured by price per unit; and (3) these arrangements would reduce net spending on these drugs by 50 percent.

Based on data from the Medicaid Drug Rebate (MDR) database from 2020, we estimate that these drugs account for about \$1.1 billion in spending and about \$320 million in net drug spending (net of rebates) in 2020. Using the assumptions described above, this would reduce net drug spending by \$40 million in 2020 (\$24 million federal share, \$16 million state share). This would represent about a 7,000 percent increase in the number of such arrangements, and it assumes a significant reduction in spending on the drugs under these arrangements. Therefore, we believe it is more likely the actual impact would be smaller than the lower bound of the estimates (that is, it would generate fewer savings for the federal government and the states).

The tables below shows the projected impacts by fiscal year in millions of dollars at the lower bound and upper bound.

Lower bound	2021	2022	2023	2024	2025	2021–2025
Federal government	–\$25	–\$26	–\$27	–\$29	–\$30	–\$137

Lower bound	2021	2022	2023	2024	2025	2021–2025
State government	-17	-17	-18	-19	-20	-91
Total	-42	-43	-45	-48	-50	-228

Upper bound	2021	2022	2023	2024	2025	2021–2025
Federal government	\$0	\$0	\$0	\$0	\$0	\$0
State government	0	0	0	0	0	0
Total	0	0	0	0	0	0

We note that the policy finalized in this rule permitting manufacturers to report multiple best price points pursuant to a VBP arrangement, still requires a manufacturer to report a non-VBP best price. Thus, a key consideration for states would be determining whether the expected savings achieved by participation in the VBP arrangement (in excess of the non-VBP rebate that they would receive) would outweigh any additional administrative costs that might occur as a result of participating in the VBP arrangement itself, for example, costs associated with tracking patients' outcomes. Thus, states that decide not to participate in multiple best price VBP arrangements will continue to receive a Medicaid drug rebate that is based upon a non-VBP best price as reported by the manufacturer.

Encouraging the use of VBP arrangements by permitting manufacturers to report multiple best price points also alleviates burdens on states to submit a SPA to enter into their own CMS-authorized SRAs in order to participate in VBP arrangements with manufacturers. That is because this approach allows states to take advantage of the approaches made available to commercial payers. Thus, the administrative burden of participating in VBP arrangements through the submission of a CMS-authorized SRA is no longer required unless a state wants to negotiate its own VBP arrangements with manufacturers. However, there will be costs to states and manufacturers of tracking patients, and engaging with health care professionals to track and evaluate outcomes of these VBP arrangements.

With respect to the additional administrative costs to states of participating in a VBP arrangement resulting in the reporting of multiple best price points, we will use existing operational mechanisms to make states aware of such manufacturer VBP arrangements that have been reported to us. We will provide additional unit rebate amounts that states can earn under these programs through quarterly

file transfers that we currently provide each quarter, which will happen through the Medicaid Drug Rebate (MDR) system that will become fully functional in July, 2021.

Finally, it is possible that the increased use of VBP arrangements as a result of the new flexibilities provided in this regulation will encourage manufacturers to increase launch prices of new therapies to payers in an attempt to compensate for the additional rebates that they may have to give these payers under a VBP arrangement. This regulation does not control the launch prices of new drugs, and such is beyond the scope of this rulemaking, or our ability to assess economic impact.

However, we expect that commercial payers will negotiate rebates and price concessions under VBP arrangements with manufacturers for high cost therapies, and that states will consider whether to take advantage of such arrangements if offered to the states by the manufacturers based on those prices. Notably, the ability of manufacturers to set high launch prices for new expensive gene and cells therapies are facilitated by the fact that these therapies are usually used to treat a small number of patients and often do not have therapeutic competitors. This lack of competition limits the ability of payers in the marketplace to manage the prices of drugs without therapeutic competitors.

We would expect that commercial payers would, as they do now for drugs that are not provided for under a VBP arrangement, negotiate as aggressively as they could, and Medicaid programs would be able to take advantage of such negotiations. States that thought they could obtain better price concessions from a manufacturer under a VBP arrangement could do so by themselves by using a CMS-authorized SRA.

- *Assuring Pass Through of Manufacturer Patient Assistance:* We heard from patient groups expressing concerns that, while the value of manufacturer cost sharing assistance programs is rapidly eroding due to PBM accumulator programs, and that patients

were paying more out of pocket for their drugs, the implementation of the pass through assurance policy in the proposed rule would lead manufacturers to reduce or eliminate these programs. Commenters contended that our proposal could result in great economic harm to patients who would have to spend more for the drugs, or go without if they are unable to afford them. We offer the following impact analysis of the finalized policy we are adopting in this regulation.

First, we view the required “pass through” of manufacturer’s cost sharing assistance to patients as a condition of exclusion from AMP and best price as a program integrity issue relating to the MDRP. Manufacturers have a legal obligation to certify each quarter that their AMPs and best prices are calculated accurately based on the inclusions and exclusions permitted based on law and regulation. This is not new policy, but long-standing policy. Moreover, rebates to states should reflect the discounts that manufacturers provide to best price eligible entities, whether they are provided directly or indirectly.

While we do not require manufacturers to provide us with documentation regarding their AMP or best price calculations, they should maintain records regarding such calculations, including any reasonable assumptions that they use in making such calculations. Should they be audited by OIG or DOJ, manufacturers would likely have to provide such documentation, including any documentation regarding their treatment of patient assistance programs in the calculation of their AMP and best price. Under this final policy, we will not be requiring manufacturers to provide us with any additional documentation regarding the assurance that the patient assistance is passed through, but they should maintain such documentation in their records. However, we understand that there may be additional costs to manufacturers of modifying their patient assistance programs if necessary, working with their business partners,

and keeping records of such pass through assurance, to ensure compliance with the regulations.

Second, we also understand through discussions with manufacturers, patient groups, and from information included in publicly-available reports, studies, and documents, that PBM accumulator programs are growing in number and quickly eroding the value of the manufacturer assistance programs for patients. As a result, there is significant tension between manufacturers and payers regarding copay assistance, with patients caught in the middle.

According to a February 2019 survey of 43 payer/health plan decision makers (representing over 80 million lives), nearly 60 percent of respondents are targeting limiting manufacturer commercial copay assistance, up from 40 percent in 2018. That same report found that the drug categories targeted for limiting copay assistance by payers include rheumatoid arthritis drugs, high cholesterol drugs, and hepatitis drugs, with the HIV drug category and orphan drug category on the horizon.¹⁴³

Another study noted that as of early 2018, approximately 60 percent of covered commercial lives were under payers that had already implemented a copay accumulator program, whereas an additional approximately 30 percent of covered commercial lives were encompassed by plans projected to implement such a program in 2019 and beyond.¹⁴⁴ This study also noted that manufacturers are concerned about these accumulator programs because of the lack of transparency regarding how the associated cost sharing is being used in practice, and manufacturers' inability to determine the impact on their public financial statements. As a result, many are considering changing the design of their programs to prepaid debit cards and/or rebate refunds provided directly to patients. Thus, manufacturers already appear to be considering changes to these programs for various reasons.

Additionally, another recent survey of large employers found that 30 percent implemented a copay accumulator program for 2019, and 21 percent were considering implementing them in 2020 or 2021.¹⁴⁵ Yet, another recent employer survey found that 54 percent of respondents did not credit third party

copay assistance programs toward patient deductibles.¹⁴⁶ Thus, based on these studies, it seems clear that as the value of these patient assistance programs to patients continues to erode, and the economic benefits to health plans increase, given that the health plans' spending on drugs for a patient decreases.

CMS has had long standing policy under § 447.505(b) that best price includes all prices, including applicable discounts, rebates, or other transactions that adjust prices either directly or indirectly to the best price eligible entity. Therefore, states and the Federal government may be eligible for additional rebates which they are now not earning if the value of these patient assistance programs is accruing to the health plans, which are best price eligible entities, and the plan's best price is the one that has to be reported to us by the manufacturer for that drug for the quarter because it is the lowest price available.

Accordingly, the provisions in the final regulation are a clarification to the existing exclusions to best price and AMP by stating that manufacturers must ensure their manufacturer assistance programs pass on the full value of discounts to the consumer and that the pharmacy, agent, or other entity (in this case, the commercial insurer) does not receive any price concession. Since this is a clarification to an existing requirement, we believe manufacturers will take the steps necessary (if they have not already done so) to ensure the exclusion of their manufacturer assistance programs will apply appropriately to their calculations and determinations of AMP and best price.

We also believe that there are potential future economic and health care consequences to patients that will result if these copay accumulator programs are not reformed and restructured. That is because the benefit of the manufacturer cost sharing assistance is increasingly not accruing to the patient, potentially impeding their ability to obtain their medications. As a result, a patient's out-of-pocket costs for medications in a health plan with accumulators can be thousands of dollars, due largely to plans with coinsurance and deductibles.¹⁴⁷ This factor could have an impact on patients' accessibility to medications, medication adherence, and thus long term health.

For example, a recent study found that following implementation of a copay accumulator program, in which patients with autoimmune disease had to pay a higher percentage of drug costs, a significant share of these patients either reduced or discontinued the use of autoimmune specialty drugs.¹⁴⁸ Thus, the PBM accumulator program, which can increase patient out of pocket costs for drugs, could potentially lead to higher overall health care spending in private plans, as well as eventually in Medicare and Medicaid. Recognizing this potential increase in spending, several states have also taken action to ban these accumulator programs in certain health care plans.¹⁴⁹

Finally, we understand that some manufacturers may eliminate, reduce, or restructure their programs as a result of this policy, which could result in increased medication costs to some patients. However, patient assistance programs serve as important marketing tools for manufacturers to start a patient on a therapy, and to promote and maintain adherence once patients are taking their medications. We are hopeful that manufacturers will not eliminate these programs under this policy, but will work with their current partners to reform or restructure the programs as has been stated in public documents, or find another mechanism to provide the assistance. We believe that any changes manufacturers may make to their assistance programs may be in response to multiple factors, such as corporate integrity issues, including shareholder concerns about how this cost sharing is being used; continued patient demand for this assistance given the increasing costs of new drugs; and the need to respond to competition from other manufacturers.

As we noted above in our responses to comments regarding this issue, we believe that the current prescription claims processing system—which consists of switches, manufacturer cost sharing assistance brokers, PBMs, and pharmacies, among others—can be used to help assure manufacturer compliance with the requirement that patient cost sharing assistance is being passed through to the patient. There are also other entities in the marketplace that manufacturers already work with to ensure compliance with Federal laws and regulations such as third party vendors and switches. These companies can help manufacturers comply with various Federal laws regulations relating

¹⁴³ Rolling Back the Tide: Deploying a Consultative Approach to Tackle the Growing Expansion of Copay Accumulators, Xcenda, February 2019.

¹⁴⁴ Pharmacy Times, Co-pay Accumulator Programs: Behind the Controversy, Lee Feigert Pharm.D, July 22, 2019.

¹⁴⁵ Large Employers 2018 Health Plan Design Survey, Washington DC, National Business Group on Health, 2018.

¹⁴⁶ Trends in Specialty Drug Benefits. Plano, TX: Pharmacy Benefits Management Institute, 2018.

¹⁴⁷ CMS Maximizers are Displacing Accumulators—But CMS Ignores how Payers Leverage Patient Support, Drug Channels, May 19, 2020.

¹⁴⁸ Impact of Copay Accumulator Adjustment Programs on Specialty Drug Adherence, American Journal of Managed Care, Vol 25 No 7, July 2019.

¹⁴⁹ See 148.

to patient copay assistance programs by reducing possible government sanctions, and improve compliance efforts in a real time manner.

Given the existence of the electronic infrastructure in place that manufacturers are already using with these partners in applying and tracking patient assistance; the competitive nature of manufacturers with respect to marketing their drugs to patients, and wanting them to continue to take them; and the 2-year time frame before the effective date of this policy, we believe that manufacturers will both retain their cost sharing assistance programs, as well as continue to be able to meet their legal obligations under section 1927 of the Act to ensure that manufacturer patient assistance accrues to the patient.

However, we recognize that there may be impact to patients as a result of some period of time when manufacturers may modify or restructure their patient assistance programs such they are able to track the pass through of patient assistance and fulfill their legal obligations under section 1927 of the Act.

Comment: A few commenters noted that CMS did not analyze the impact of the proposed changes in the rule on Medicare prices and the 340B drug discount program. One commenter suggested that failure to consider these potential impacts could potentially make the proposed rule “susceptible to claims that the rules were arbitrary and capricious for failing to consider an important aspect of the problem.”

Response: This rule makes no changes to either the pricing program under 340B of the PHSA or Medicare Part B payment policies. Furthermore, we do not believe we have failed to consider the impacts on these programs because we believe the changes made by this final rule will not have a significant impact on best price, AMP or Medicaid drug rebates that would impact either Medicare Part B payment allowances or 340B pricing. That is, because manufacturers will continue to be required to report a non-VBP best price when reporting multiple best prices generated from a VBP arrangement, and that non-VBP best price will be used to calculate the 340B ceiling price.

The bundled sale approach’s impact on best price will be minimal since it is permitting the manufacturer to allocate the discounts or price concessions as a result of a VBP arrangement across a bundled sale, thus spreading out the discounts over multiple units in the bundled sale. This approach to a bundled sale is already being adopted by manufacturers using reasonable assumptions, and we do not expect that

codifying this practice in regulatory text will significantly reduce the best price to the point it increases the Medicaid drug rebate which may impact 340B pricing.

The RFA requires agencies to analyze options for regulatory relief of small entities. For purposes of the RFA, small entities include small businesses, nonprofit organizations, small pharmaceutical manufacturers participating in the MDRP, and small governmental jurisdictions. Most hospitals and most other providers and suppliers are small entities, either by nonprofit status or by having revenues of less than \$8.0 million to \$41.5 million in any 1 year. Individuals and states are not included in the definition of a small entity. We are not preparing an analysis for the RFA because we have determined, and the Secretary certifies, that this final rule will not have a significant economic impact on a substantial number of small entities.

In addition, section 1102(b) of the Act requires us to prepare an RIA if a rule may have a significant impact on the operations of a substantial number of small rural hospitals. This analysis must conform to the provisions of section 604 of the RFA. For purposes of section 1102(b) of the Act, we define a small rural hospital as a hospital that is located outside of a Metropolitan Statistical Area for Medicare payment regulations and has fewer than 100 beds. We are not preparing an analysis for section 1102(b) of the Act because we have determined, and the Secretary certifies, that this final rule with comment period will not have a significant impact on the operations of a substantial number of small rural hospitals.

Section 202 of the Unfunded Mandates Reform Act of 1995 also requires that agencies assess anticipated costs and benefits before issuing any rule whose mandates require spending in any 1 year of \$100 million in 1995 dollars, updated annually for inflation. In 2020, that threshold is approximately \$156 million. This rule will have no consequential effect on state, local, or tribal governments or on the private sector.

Executive Order 13132 establishes certain requirements that an agency must meet when it issues a proposed rule (and subsequent final rule) that imposes substantial direct compliance costs on state and local governments, preempts state law, or otherwise has federalism implications. Since this regulation does not impose any substantial direct compliance costs on state or local governments, preempt state law, or otherwise have federalism

implications, the requirements of Executive Order 13132 are not applicable.

Executive Order 13771 (January 30, 2017) requires that the costs associated with significant new regulations “to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations.”

In accordance with the provisions of Executive Order 12866, this regulation was reviewed by the Office of Management and Budget.

List of Subjects

42 CFR Part 433

Administrative practice and procedure, Child support, Claims, Grant programs—health, Medicaid, Reporting and recordkeeping requirements.

42 CFR Part 438

Grant programs—health, Medicaid, Reporting and Recordkeeping requirements.

42 CFR Part 447

Accounting, Administrative practice and procedure, Drugs, Grant programs—health, Health facilities, Health professions, Medicaid, Reporting and recordkeeping requirements, Rural areas.

42 CFR Part 456

Administrative practice and procedure, Drugs, Grant programs—health, Health facilities, Medicaid, Reporting and recordkeeping requirements.

For the reasons set forth in the preamble, the Centers for Medicare & Medicaid Services amends 42 CFR chapter IV as set forth below:

PART 433—STATE FISCAL ADMINISTRATION

- 1. The authority citation for part 433 is revised to read as follows:

Authority: 42 U.S.C. 1302.

- 2. Section 433.139 is amended by—
 - a. Removing and reserving paragraph (b)(2); and
 - b. Revising paragraphs (b)(3)(i) and (b)(3)(ii)(B).

The revisions read as follows:

§ 433.139 Payment of claims.

* * * * *

(b) * * *

(3) * * *

(i) The claim is for preventive pediatric services, including early and periodic screening, diagnosis and treatment services provided for under part 441, subpart B, of this chapter, that are covered under the State plan; or

(ii) * * *

(B) For child support enforcement services beginning February 9, 2018, the provider certifies that before billing Medicaid, if the provider has billed a third party, the provider has waited 100 days from the date of the service and has not received payment from the third party.

* * * * *

PART 438—MANAGED CARE

■ 3. The authority citation for part 438 continues to read as follows:

Authority: 42 U.S.C. 1302.

■ 4. Section 438.3 is amended by revising paragraphs (s) introductory text and (s)(4) and (5) to read as follows:

§ 438.3 Standard contract requirements.

* * * * *

(s) *Requirements for MCOs, PCCMs, PIHPs, or PAHPs that provide covered outpatient drugs.* Contracts that obligate MCOs, PCCMs, PIHPs, or PAHPs to provide coverage of covered outpatient drugs must include the following requirements:

* * * * *

(4) The MCO, PCCM, PIHP, or PAHP must operate a drug utilization review program that complies with the requirements described in section 1927(g) of the Act and part 456, subpart K, of this chapter, as if such requirement applied to the MCO, PCCM, PIHP, or PAHP instead of the State.

(5) The MCO, PCCM, PIHP, or PAHP must provide a detailed description of its drug utilization review program activities to the State on an annual basis.

* * * * *

PART 447—PAYMENTS FOR SERVICES

■ 5. The authority citation for part 447 continues to read as follows:

Authority: 42 U.S.C. 1302 and 1396r–8.

■ 6. Section 447.502 is amended—
 ■ a. In the definition of “Bundled sale” by adding paragraph (3);

■ b. By adding the definition of “CMS-authorized supplemental rebate agreement” in alphabetical order;
 ■ c. By revising the definitions of “Innovator multiple source drug”, “Multiple source drug”, and “Single source drug”;

■ d. By adding the definitions of “Value-based purchasing (VBP) arrangement” in alphabetical order; and

■ e. By revising the definition of “Wholesaler”.

The additions and revisions read as follows:

§ 447.502 Definitions.

* * * * *

Bundled sale * * *

(3) Value-based purchasing (VBP) arrangements may qualify as a bundled sale.

* * * * *

CMS-authorized supplemental rebate agreement means an agreement that is approved through a state plan amendment (SPA) by CMS, which allows a state to enter into single and/or multi-state supplemental drug rebate arrangements that generate rebates that are at least as large as the rebates set forth in the Secretary’s national rebate agreement with drug manufacturers. Revenue from these rebates must be paid directly to the state and be used by the state to offset a state’s drug expenditures resulting in shared savings with the Federal Government.

* * * * *

Innovator multiple source drug means a multiple source drug, including an authorized generic drug, that is marketed under a new drug application (NDA) approved by FDA, unless the Secretary determines that a narrow exception applies (as described in this section). It also includes a drug product marketed by any cross-licensed producers, labelers, or distributors operating under the NDA and a covered outpatient drug approved under a biologics license application (BLA), product license application (PLA), establishment license application (ELA) or antibiotic drug application (ADA).

* * * * *

Multiple source drug means, for a rebate period, a covered outpatient drug, including a drug product approved for marketing as a non-prescription drug that is regarded as a covered outpatient drug under section 1927(k)(4) of the Act, for which there is at least 1 other drug product which meets all of the following criteria:

(1) Is rated as therapeutically equivalent (under the FDA’s most recent publication of “Approved Drug Products with Therapeutic Equivalence Evaluations” which is available at <http://www.accessdata.fda.gov/scripts/cder/ob/>).

(2) Except as provided at section 1927(k)(7)(B) of the Act, is pharmaceutically equivalent and bioequivalent, as defined at section 1927(k)(7)(C) of the Act and as determined by FDA.

(3) Is sold or marketed in the United States during the period.

* * * * *

Single source drug means a covered outpatient drug, including a drug product approved for marketing as a

non-prescription drug that is regarded as a covered outpatient drug under section 1927(k)(4) of the Act, which is produced or distributed under a new drug application approved by the FDA, including a drug product marketed by any cross-licensed producers or distributors operating under the new drug application unless the Secretary determines that a narrow exception applies (as described in this section), and includes a covered outpatient drug that is a biological product licensed, produced, or distributed under a biologics license application approved by the FDA.

* * * * *

Value-based purchasing (VBP) arrangement means an arrangement or agreement intended to align pricing and/or payments to an observed or expected therapeutic or clinical value in a select population and includes, but is not limited to:

(1) Evidence-based measures, which substantially link the cost of a covered outpatient drug to existing evidence of effectiveness and potential value for specific uses of that product; and/or

(2) Outcomes-based measures, which substantially link payment for the covered outpatient drug to that of the drug’s actual performance in patient or a population, or a reduction in other medical expenses.

Wholesaler means a drug wholesaler that is engaged in wholesale distribution of prescription drugs to retail community pharmacies, including but not limited to repackers, distributors, own-label distributors, private-label distributors, jobbers, brokers, warehouses (including distributor’s warehouses, chain drug warehouses, and wholesale drug warehouses), independent wholesale drug traders, and retail community pharmacies that conduct wholesale distributions.

■ 7. Section 447.502 is further amended, effective January 1, 2022, by—

■ a. Adding the definitions of “Line extension” and “New formulation” in alphabetical order; and

■ b. Revising the definition of “Oral solid dosage form”.

The additions and revision read as follows:

§ 447.502 Definitions.

* * * * *

Line extension means, for a drug, a new formulation of the drug, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary).

* * * * *

New formulation means, for a drug, a change to the drug, including, but not

limited to: an extended release formulation or other change in release mechanism, a change in dosage form, strength, route of administration, or ingredients.

* * * * *

Oral solid dosage form means, an orally administered dosage form that is not a liquid or gas at the time the drug enters the oral cavity.

* * * * *

§ 447.504 [Amended]

■ 8. Section 447.504 is amended by removing paragraph (b)(2) and redesignating paragraph (b)(3) as paragraph (b)(2).

■ 9. Section 447.504 is further amended, effective January 1, 2023, by revising paragraphs (c)(25) through (29) and paragraphs (e)(13) through (17) to read as follows:

§ 447.504 Determination of average manufacturer price.

* * * * *

(c) * * *

(25) Manufacturer coupons to a consumer redeemed by the manufacturer, agent, pharmacy or another entity acting on behalf of the manufacturer, but only to the extent that the manufacturer ensures the full value of the coupon is passed on to the consumer and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession.

(26) Manufacturer-sponsored programs that provide free goods, including but not limited to vouchers and patient assistance programs, but only to the extent that the manufacturer ensures: the voucher or benefit of such a program is not contingent on any other purchase requirement; the full value of the voucher or benefit of such a program is passed on to the consumer; and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession.

(27) Manufacturer-sponsored drug discount card programs, but only to the extent that the manufacturer ensures the full value of the discount is passed on to the consumer and the pharmacy, agent, or the other AMP-eligible entity does not receive any price concession.

(28) Manufacturer-sponsored patient refund/rebate programs, to the extent that the manufacturer ensures that the manufacturer provides a full or partial refund or rebate to the patient for out-of-pocket costs and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession.

(29) Manufacturer copayment assistance programs, to the extent that the manufacturer ensures the program

benefits are provided entirely to the patient and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession

* * * * *

(e) * * *

(13) Manufacturer coupons to a consumer redeemed by the manufacturer, agent, pharmacy or another entity acting on behalf of the manufacturer, but only to the extent that the manufacturer ensures the full value of the coupon is passed on to the consumer and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession

(14) Manufacturer-sponsored programs that provide free goods, including, but not limited to vouchers and patient assistance programs, but only to the extent that the manufacturer ensures: the voucher or benefit of such a program is not contingent on any other purchase requirement; the full value of the voucher or benefit of such a program is passed on to the consumer; and the pharmacy, agent, or other AMP-eligible entity does not receive any price concession.

(15) Manufacturer-sponsored drug discount card programs, but only to the extent that the manufacturer ensures the full value of the discount is passed on to the consumer and the pharmacy, agent, or the other AMP-eligible entity does not receive any price concession.

(16) Manufacturer-sponsored patient refund/rebate programs, to the extent that the manufacturer ensures the manufacturer provided a full or partial refund or rebate to the patient for out-of-pocket costs and the pharmacy agent, or other AMP-eligible entity does not receive any price concession.

(17) Manufacturer copayment assistance programs, to the extent that the manufacturer ensures the program benefits are provided entirely to the patient and the pharmacy agent, or other AMP-eligible entity does not receive any price concession

* * * * *

■ 10. Section 447.505 is amended—

■ a. Effective January 1, 2022, in paragraph (a), by revising the definition of “Best price”;

■ b. Effective March 1, 2021, by revising paragraph (d)(3).

The revisions read as follows:

§ 447.505 Determination of best price.

(a) * * *

Best price means, for a single source drug or innovator multiple source drug of a manufacturer (including the lowest price available to any entity for an authorized generic drug), the lowest price available from the manufacturer

during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States in any pricing structure (including capitated payments) in the same quarter for which the AMP is computed. If a manufacturer offers a value-based purchasing arrangement (as defined at § 447.502) to all states, the lowest price available from a manufacturer may include varying best price points for a single dosage form and strength as a result of that value based purchasing arrangement.

* * * * *

(d) * * *

(3) The manufacturer must adjust the best price for a rebate period if cumulative discounts, rebates, or other arrangements subsequently adjust the prices available, to the extent that such cumulative discounts, rebates, or other arrangements are not excluded from the determination of best price by statute or regulation.

■ 11. Section 447.505 is amended, effective January 1, 2023, by revising paragraphs (c)(8) through (12) to read as follows:

§ 447.505 Determination of best price.

* * * * *

(c) * * *

(8) Manufacturer-sponsored drug discount card programs, but only to the extent the manufacturer ensures that the full value of the discount is passed on to the consumer and the pharmacy, agent, or other entity does not receive any price concession.

(9) Manufacturer coupons to a consumer redeemed by a consumer, agent, pharmacy, or another entity acting on behalf of the manufacturer; but only to the extent the manufacturer ensures that the full value of the coupon is passed on to the consumer, and the pharmacy, agent, or other entity does not receive any price concession.

(10) Manufacturer copayment assistance programs, to the extent that the manufacturer ensures the program benefits are provided entirely to the patient and the pharmacy, agent, or other entity does not receive any price concession.

(11) Manufacturer-sponsored patient refund or rebate programs, to the extent that the manufacturer ensures the manufacturer provides a full or partial refund or rebate to the patient for out-of-pocket costs and the pharmacy, agent, or other entity does not receive any price concession.

(12) Manufacturer-sponsored programs that provide free goods, including but not limited to vouchers

and patient assistance programs, but only to the extent that the manufacturer ensures the voucher or benefit of such a program is not contingent on any other purchase requirement; the full value of the voucher or benefit of such a program is passed on to the consumer; and the pharmacy, agent, or other entity does not receive any price concession.

* * * * *

- 12. Section 447.506 is amended—
- a. In paragraph (a) by revising the definition of “Secondary manufacturer of an authorized generic drug”; and
- b. By revising paragraph (b).

The revisions read as follows:

§ 447.506 Authorized generic drugs.

(a) * * *

Secondary manufacturer of an authorized generic drug means a manufacturer that is authorized by the primary manufacturer to sell the drug.

(b) *Exclusion of authorized generic drugs from AMP by a primary manufacturer.* The primary manufacturer must exclude from its calculation of AMP any sales of authorized generic drugs to wholesalers for drugs distributed to retail community pharmacies when reporting the AMP of the brand name drug of that authorized generic drug.

* * * * *

- 13. Section 447.509 is amended—
- a. Revising paragraph (a)(5);
- b. In paragraph (a)(6) introductory text, by removing word “rebate” and adding in its place the phrase “basic rebate”; and
- c. By adding paragraphs (a)(7), (8), and (9).

The revision and additions read as follows:

§ 447.509 Medicaid drug rebates (MDR).

(a) * * *

(5) *Limit on rebate.* In no case will the total rebate amount exceed 100 percent of the AMP of the single source or multiple source innovator drug.

* * * * *

(7) *Additional rebate for noninnovator multiple source drugs.* In addition to the basic rebate described in paragraph (a)(6) of this section, for each dosage form and strength of a noninnovator multiple source drug, the rebate amount will be increased by an amount equal to the product of the following:

- (i) The total number of units of such dosage form and strength paid for under the State plan in the rebate period.
- (ii) The amount, if any, by which:
 - (A) The AMP for the dosage form and strength of the drug for the period exceeds the base date AMP for such dosage form and strength, increased by

the percentage by which the consumer price index for all urban consumers (United States city average) for the month before the month in which the rebate period begins exceeds such index associated with the base date AMP of the drug.

(B) The base date AMP has the meaning of AMP set forth in sections 1927(c)(2)(A)(ii)(II), 1927(c)(2)(B) and 1927(c)(3)(C) of the Act.

(8) *Total rebate.* The total rebate amount for noninnovator multiple source drugs is equal to the basic rebate amount plus the additional rebate amount, if any.

(9) *Limit on rebate.* In no case will the total rebate amount exceed 100 percent of the AMP for the noninnovator multiple source drug.

* * * * *

- 14. Section 447.509 is further amended, effective January 1, 2022, by—

- a. By revising paragraphs (a)(4)(ii) introductory text;
- b. By redesignating paragraph (a)(4)(iii) as paragraph (a)(4)(iv); and
- c. Adding a new paragraph (a)(4)(iii).

The revision and addition read as follows:

§ 447.509 Medicaid drug rebates (MDR).

(a) * * *

(4) * * *

(ii) In the case of a drug that is a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form, the rebate obligation for the rebate periods beginning on October 1, 2018 through December 31, 2021 is the amount computed under paragraphs (a)(1) through (3) of this section for such new drug or, if greater, the amount computed under paragraph (a)(1) of this section plus the product of all of the following:

* * * * *

(iii) In the case of a drug that is a line extension of a single source drug or an innovator multiple source drug, provided that the initial single source drug or innovator multiple source drug is an oral solid dosage form, the rebate obligation for the rebate periods beginning on and after January 1, 2022 is the amount computed under paragraphs (a)(1) through (3) of this section for such new drug or, if greater, the amount computed under paragraph (a)(1) of this section plus the product of all of the following:

- (A) The AMP of the line extension of a single source drug or an innovator multiple source drug.
- (B) The highest additional rebate (calculated as a percentage of AMP) under this section for any strength of the

original single source drug or innovator multiple source drug.

(C) The total number of units of each dosage form and strength of the line extension product paid for under the State plan in the rebate period (as reported by the State).

* * * * *

- 15. Section 447.510 is amended by adding paragraph (b)(1)(vi) to read as follows:

§ 447.510 Requirement for manufacturers.

* * * * *

(b) * * *

(1) * * *

(vi) The change is a result of a VBP arrangement, as defined in § 447.502, requiring the manufacturer to make changes outside of the 12-quarter rule in this paragraph (b), when the outcome must be evaluated outside of the 12-quarter period.

* * * * *

- 16. Section 447.511 is amended, effective January 1, 2022—
- a. In paragraph (a) introductory text, by removing the phrase “following data:” and adding in its place the phrase “following data and any subsequent changes to the data fields on the CMS–R–144 Medicaid Drug Rebate Invoice form:”;

- b. By revising paragraph (b); and
- c. By adding paragraphs (d) and (e).

The revision and additions read as follows:

§ 447.511 Requirements for States.

* * * * *

(b) *Data submitted to CMS.* On a quarterly basis, the State must submit drug utilization data to CMS, which will be the same information as submitted to the manufacturers on the CMS–R–144, as specified in paragraph (a) of this section. The state data submission will be due no later than 60 days after the end of each rebate period. In the event that a due date falls on a weekend or Federal holiday, the submission will be due on the first business day following that weekend or Federal holiday. Any adjustments to previously submitted data will be transmitted to the manufacturer and CMS in the same reporting period.

* * * * *

(d) *State data certification.* Each data submission in this section must be certified by one of the following:

- (1) The State Medicaid Director (SMD);
- (2) The Deputy State Medicaid Director (DSMD);
- (3) An individual other than the SMD or DSMD, who has authority equivalent to an SMD or DSMD; or

(4) An individual with the directly delegated authority to perform the certification on behalf of an individual described in paragraphs (d)(1) through (3) of this section.

(e) *State data certification language.* Each data submission by a state must include the following certification language: "I hereby certify, to the best of my knowledge, that the state's data submission is complete and accurate at the time of this submission, and was prepared in accordance with the state's good faith, reasonable efforts based on existing guidance from CMS, section 1927 of the Act and applicable Federal regulations. I further certify that the state has transmitted data to CMS, including any adjustments to previous rebate periods, in the same reporting period as provided to the manufacturer. Further, the state certifies that it has applied any necessary edits to the data for both CMS and the manufacturer to avoid inaccuracies at both the NDC/line item and file/aggregate level. Such edits are to be applied in the same manner and in the same reporting period to both CMS and the manufacturer."

■ 17. Section 447.518 is amended, effective January 1, 2022, by—
■ a. Redesignating the text of paragraph (d) as paragraph (d)(1); and
■ b. Adding paragraphs (d)(2) and (3).
The additions read as follows:

§ 447.518 State plan requirements, findings, and assurances.

* * * * *
(d) * * *

(2) A State participating in VBP arrangements approved under a CMS-authorized supplemental rebate agreement (SRA) must report data described in paragraph (d)(3) of this section on an annual basis.

(3) Within 60 days of the end of each year, the State must submit all of the following data, including cumulative data to date:

- (i) State.
- (ii) National drug code(s) (for drugs covered under the CMS-authorized VBP SRA).
- (iii) Product's FDA list name.
- (iv) Number of prescriptions.
- (v) Cost to the State to administer the CMS-authorized VBP SRA (for example, systems changes, tracking outcomes, etc.).
- (vi) Total savings generated by the supplemental rebate due to the CMS-authorized VBP SRA.

PART 456—UTILIZATION CONTROL

■ 18. The authority citation for part 456 is revised to read as follows:

Authority: 42 U.S.C. 1302.

- 19. Section 456.703 is amended by—
■ a. Redesignating paragraph (h) as paragraph (i); and
■ b. Adding a new paragraph (h).
The addition reads as follows:

§ 456.703 Drug use review programs.

* * * * *

(h) *Minimum standards for DUR programs*—(1) *Minimum standards.* In operating their DUR programs, States must include the following minimum standards:

(i) Prospective safety edit limitations for opioid prescriptions, as specified by the State, on:

(A) Days' supply for patients not currently receiving opioid therapy for initial prescription fills;

(B) Quantity of prescription dispensed for initial and subsequent prescription fills;

(C) Therapeutically-duplicative initial and subsequent opioid prescription fills; and

(D) Early refills, for subsequent prescription fills.

(ii) Prospective safety edit limitations for opioid prescriptions, as specified by the State, on the maximum daily morphine milligram equivalent for treatment of pain, for initial and subsequent prescription fills.

(iii) A retrospective claims review automated process that indicates prescription fills of opioids in excess of the prospective safety edit limitations specified by the state under paragraph (h)(1)(i) or (ii) of this section to provide for the ongoing review of opioid claims data to identify patterns of fraud, abuse, excessive utilization, inappropriate or medically unnecessary care, or prescribing or billing practices that indicate abuse or provision of inappropriate or medically unnecessary care among prescribers, pharmacists and individuals receiving Medicaid benefits.

(iv) A retrospective claims review automated process and, at the option of the State, prospective safety edits that monitor when an individual is concurrently prescribed opioids and:

- (A) Benzodiazepines; or
- (B) Antipsychotics.

(v) A program to monitor and manage the appropriate use of antipsychotic medications by children enrolled under the State plan, including any Medicaid expansion groups for the Children's Health Insurance Program (CHIP).

(vi) A process to identify potential fraud or abuse of controlled substances by individuals enrolled under the State plan, health care providers prescribing drugs to individuals so enrolled, and

pharmacies dispensing drugs to individuals so enrolled.

(vii) Prospective safety edits, retrospective claims review automated processes, or a combination of these approaches as determined by the State, to identify when:

(A) A beneficiary is prescribed an opioid after the beneficiary has been prescribed one or more drugs used for Medication Assisted Treatment (MAT) of an opioid use disorder or has been diagnosed with an opioid use disorder, within a timeframe specified by the State, in the absence of a new indication to support utilization of opioids (such as new cancer diagnosis or entry into hospice care); and

(B) A beneficiary could be at high risk of opioid overdose and should be considered for co-prescription or co-dispensing of any FDA-approved opioid antagonist/reversal agent.

(2) *Exclusion.* The requirements in paragraphs (h)(1)(i) through (vii) of this section do not apply with respect to individuals receiving hospice or palliative care or treatment for cancer; individuals who are residents of long-term care facilities, intermediate care facilities for the intellectually disabled, or facilities that dispense frequently abused drugs through a contract with a single pharmacy; or other individuals the State elects to exempt. While States are not required to apply the requirements in paragraphs (h)(1)(i) through (vii) with respect to these individuals, States may elect to do so.

* * * * *

■ 20. Section 456.712 is amended by adding paragraph (c) to read as follows:

§ 456.712 Annual report.

* * * * *

(c) *Public availability.* All fee-for-service (FFS) and managed care DUR reports received by CMS under paragraph (b) of this section and, as applicable, pursuant to § 438.3(s) of this chapter, will be publicly posted on a website maintained by CMS for the sharing of reports and other information concerning Medicaid DUR programs.

Dated: November 30, 2020.

Seema Verma,
Administrator, Centers for Medicare & Medicaid Services.

Dated: December 11, 2020.

Alex M. Azar II,
Secretary, Department of Health and Human Services.

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