Monographs. In the future, OTC *Monographs@FDA* will facilitate the public's ability to submit, search, and view comments and data for proposed and interim final orders.

II. Paperwork Reduction Act of 1995

The proposed order OTC000039 is issued under section 505G(b)(1) of the FD&C Act. Under section 505G(o) of the FD&C Act, the Paperwork Reduction Act of 1995 (Chapter 35 of title 44, United States Code) does not apply to collections of information made under section 505G of the FD&C Act. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required for collections of information, if any, in a final order issued under section 505G that results from this proposed order.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–22649 Filed 12–11–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–N–4732]

Determination That ZANTAC (Ranitidine Hydrochloride) Injection, Equivalent to 25 Milligrams Base/Milliliter, Has Not Been Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that ZANTAC (ranitidine hydrochloride (HCl)) injection, equivalent to (EQ) 25 milligram (mg) base/milliliter (mL), has not been withdrawn from sale for reasons of safety or effectiveness to the extent that the drug can be manufactured or formulated in a manner that satisfies any applicable acceptable intake limit for nitrosamine impurities. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to this drug product, and it will allow FDA to continue to approve ANDAs that refer to the product as long as they meet relevant legal and regulatory requirements, including satisfying any applicable acceptable intake limit for nitrosamine impurities.

FOR FURTHER INFORMATION CONTACT: Robin Fastenau, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6236, Silver Spring, MD 20993–0002, 240–893–4962, *robin.fastenau@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved, and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products With Therapeutic Equivalence Evaluations,'' which is known generally as the ''Orange Book.'' Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, is the subject of NDA 019090, held by Pharmaceutical Associates, Inc. (PAI) Pharma, and initially approved on October 19, 1984. ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL is indicated in some hospitalized patients with pathological hypersecretory conditions or intractable duodenal ulcers, or as an alternative to the oral dosage form for short-term use in patients who are unable to take oral medication.

On March 31, 2020, FDA requested that all manufacturers voluntarily withdraw their ranitidine products from the market because accumulated data showed levels of N-Nitrosodimethylamine (NDMA) above the acceptable daily intake limit in many ranitidine-containing products.[1] This request applied to all ranitidine applicants, including the applicant for ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, NDA 019090. ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, NDA 019090, was withdrawn from sale prior to March 31, 2020. ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, is currently listed in the ''Discontinued Drug Product List'' section of the Orange Book.

After reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, has not been withdrawn for reasons of safety or effectiveness to the extent that the drug can be manufactured or formulated in a manner that satisfies any applicable acceptable intake limit for nitrosamine impurities.

Accordingly, the Agency will continue to list ZANTAC (ranitidine HCl) injection, EQ 25 mg base/mL, in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. FDA will not begin procedures to withdraw approval of approved ANDAs that refer to this drug product. Additional ANDAs for this drug product may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs, including satisfying any applicable acceptable intake limit for nitrosamine impurities.

[1] Nitrosamine impurities in the drug supply are an important public health concern. As explained in the guidance for industry entitled ''Control of Nitrosamine Impurities in Human Drugs'' published September 2024 (available at *https://www.fda.gov/media/141720/download*) (at 4–5), ''Nitrosamine compounds are potent genotoxic agents in several animal species and some are classified as probable or possible human carcinogens by the International Agency for Research on Cancer. They are referred to as *cohort of concern* compounds in the International Council for Harmonisation of Technical Requirements for . . . Human Use (ICH) guidance for industry *M7(R2) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk* (July 2023).'' Many drug products have been found to contain levels of nitrosamines that are unacceptable or require further evaluation. FDA's current understanding is that nitrosamine levels in affected drug products have different causes and may be controlled using different strategies, including formulation design (*i.e.,* adding antioxidants or adding pH adjusters that modify the microenvironment to base or neutral pH) and supplier qualification programs.

If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–22676 Filed 12–11–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–P–1617]

Determination That BACTROBAN (Mupirocin) Nasal Ointment, 2%, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that BACTROBAN (mupirocin) nasal ointment, 2%, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for mupirocin nasal ointment, 2%, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Iris Masucci, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Silver Spring, MD 20993–0002, 301–796–3600, *iris.masucci@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved, and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products With Therapeutic Equivalence Evaluations,'' which is known generally as the ''Orange Book.'' Under FDA regulations, a drug is removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

BACTROBAN (mupirocin) nasal ointment, 2%, is the subject of NDA 050703, held by SmithKline Beecham (Cork) Ltd., Ireland/GlaxoSmithKline (GSK), and was initially approved on September 18, 1995. BACTROBAN nasal ointment, 2%, is indicated for the eradication of nasal colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in adult and pediatric patients (aged 12 years and older) and healthcare workers as part of a comprehensive infection control program to reduce the risk of infection among patients at high risk of MRSA infection during institutional outbreaks of infections with this microorganism.

In a correspondence dated February 9, 2018, GSK notified FDA that BACTROBAN (mupirocin) nasal ointment, 2%, was being discontinued, and FDA moved the drug product to the ''Discontinued Drug Product List'' section of the Orange Book. In a letter dated January 5, 2022, GSK requested withdrawal of NDA 050703 for BACTROBAN (mupirocin) nasal ointment, 2%, under § 314.150(c) (21 CFR 314.150(c)). In the **Federal Register** of August 4, 2025, FDA announced that it was withdrawing approval of NDA 050703 upon request of GSK under § 314.150(c), effective September 3, 2025.

E4 Consulting submitted a citizen petition dated June 24, 2020 (Docket No. FDA–2020–P–1617), under 21 CFR 10.30, requesting that the Agency determine whether BACTROBAN (mupirocin) nasal ointment, 2%, was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that BACTROBAN (mupirocin) nasal ointment, 2%, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that BACTROBAN (mupirocin) nasal ointment, 2%, was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of BACTROBAN (mupirocin) nasal ointment, 2%, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have found no information that would indicate that this drug product was withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list BACTROBAN (mupirocin) nasal ointment, 2%, in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to BACTROBAN (mupirocin) nasal ointment, 2%, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2024–P–2952]

Determination That LUNELLE (Estradiol Cypionate and Medroxyprogesterone Acetate) Injectable, 5 Milligrams/0.5 Milliliter and 25 Milligrams/0.5 Milliliter, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has