

§ 201.326

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partner is infected, choose another form of birth control”.

(4) “When using this product [in bold type] [optional, bullet] you may get vaginal irritation (burning, itching, or a rash)”.

(5) “Stop use and ask a doctor if [in bold type] [optional, bullet] you or your partner get burning, itching, a rash, or other irritation of the vagina or penis”.

(c) The labeling of this product states under the “Other information” section of the Drug Facts labeling in accordance with § 201.66(c)(7), “[bullet] when used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of catching or spreading HIV, the virus that causes AIDS.

(d) The labeling of this product includes the following statements either on the outside container or wrapper of the retail package, under the “Other information” section of the Drug Facts labeling in accordance with § 201.66(c)(7), or in a package insert:

(1) “[bullet] studies have raised safety concerns that products containing the spermicide nonoxynol 9 can irritate the vagina and rectum. Sometimes this irritation has no symptoms. This irritation may increase the risk of getting HIV/AIDS from an infected partner”.

(2) “[bullet] you can use nonoxynol 9 for birth control with or without a diaphragm or condom if you have sex with only one partner who is not infected with HIV and who has no other sexual partners or HIV risk factors”.

(3) “[bullet] use a latex condom without nonoxynol 9 if you or your sex partner has HIV/AIDS, multiple sex partners, or other HIV risk factors”.

(4) “[bullet] ask a health professional if you have questions about your best birth control and STD prevention methods”.

(e) Any drug product subject to this section that is not labeled as required and that is initially introduced or initially delivered for introduction into interstate commerce after June 19, 2008, is misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352), is a new drug under section 505 of the act (21

U.S.C. 355), and is subject to regulatory action.

[72 FR 71785, Dec. 19, 2007]

§ 201.326 Over-the-counter drug products containing internal analgesic/antipyretic active ingredients; required warnings and other labeling.

(a) *Labeling.* The labeling for all over-the-counter (OTC) drug products containing any internal analgesic/antipyretic active ingredients (including, but not limited to, acetaminophen, aspirin, carbaspirin calcium, choline salicylate, ibuprofen, ketoprofen, magnesium salicylate, naproxen sodium, and sodium salicylate) alone or in combination must bear the following labeling in accordance with §§ 201.60, 201.61, and 201.66.

(1) *Acetaminophen*—(i) *Statement of identity.* The statement of identity appears in accord with §§ 201.61 and 299.4 of this chapter. The ingredient name “acetaminophen” must appear highlighted (e.g., fluorescent or color contrast) or in bold type, be in lines generally parallel to the base on which the package rests as it is designed to be displayed, and be in one of the following sizes, whichever is greater:

(A) At least one-quarter as large as the size of the most prominent printed matter on the principal display panel (PDP), or

(B) At least as large as the size of the “Drug Facts” title, as required in § 201.66(d)(2). The presence of acetaminophen must appear as part of the established name of the drug, as defined in § 299.4 of this chapter. Combination products containing acetaminophen and a nonanalgesic ingredient(s) (e.g., cough-cold) must include the name “acetaminophen” and the name(s) of the other active ingredient(s) in the product on the PDP in accord with this paragraph. Only the name “acetaminophen” must appear highlighted or in bold type, and in a prominent print size, as described in this paragraph.

(ii) *Active Ingredient and Purpose Headings.* The information required under § 201.66(c)(2) and (c)(3) of this chapter must be included under these headings. The information under these headings, but not the headings, may appear highlighted.

(iii) *For products labeled for adults only.* The labeling of the product states the following warnings under the heading “Warnings”:

(A) The liver warning states “Liver warning [heading in bold type]: This product contains acetaminophen. Severe liver damage may occur if you take [bullet] more than [insert maximum number of daily dosage units] in 24 hours, which is the maximum daily amount [optional: ‘for this product’] [bullet] with other drugs containing acetaminophen [bullet] 3 or more alcoholic drinks every day while using this product”. This “Liver” warning must be the first warning under the “Warnings” heading. For products that contain both acetaminophen and aspirin, this “Liver” warning must appear after the “Reye’s syndrome” and “Allergy alert” warnings in § 201.66(c)(5)(ii)(A) and (c)(5)(ii)(B) and before the “Stomach bleeding” warning in paragraph (a)(2)(iii)(A) of this section. If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister card and remain intact and readable when drug product is removed from the blister card. The warning does not need to be included on each blister unit.

(B) “Do not use with any other drug containing acetaminophen (prescription or nonprescription). If you are not sure whether a drug contains acetaminophen, ask a doctor or pharmacist.”

(C) “Ask a doctor before use if you have liver disease”.

(D) “Ask a doctor or pharmacist before use if you are taking the blood thinning drug warfarin” except on the labeling of combination products that contain acetaminophen and NSAID(s).

(iv) *For products labeled only for children under 12 years of age.*

(A) *Warnings.* The labeling of the product states the following warnings under the heading “Warnings”:

(1) The liver warning states “Liver warning [heading in bold type]: This product contains acetaminophen. Severe liver damage may occur if your child takes [bullet] more than 5 doses in 24 hours, which is the maximum daily amount [optional: ‘for this prod-

uct’] [bullet] with other drugs containing acetaminophen”. This “Liver” warning must be the first warning under the “Warnings” heading. If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister card and remain intact and readable when drug product is removed from the blister card. The warning is not required to be included on each blister unit.

(2) “Do not use with any other drug containing acetaminophen (prescription or nonprescription). If you are not sure whether a drug contains acetaminophen, ask a doctor or pharmacist.”

(3) “Ask a doctor before use if your child has liver disease”.

(4) “Ask a doctor or pharmacist before use if your child is taking the blood thinning drug warfarin” except on the labeling of combination products that contain acetaminophen and NSAID(s).

(B) *Directions.* The labeling of the product contains the following information under the heading “Directions”: “this product does not contain directions or complete warnings for adult use” [in bold type].

(v) *For products labeled for adults and children under 12 years of age.* The labeling of the product states all of the warnings in paragraphs (a)(1)(iii)(A), (a)(1)(iii)(B), and (a)(1)(iii)(C) of this section with the following modifications:

(A) The liver warning states “Liver warning [heading in bold type]: This product contains acetaminophen. Severe liver damage may occur if [bullet] adult takes more than [insert maximum number of daily dosage units] in 24 hours, which is the maximum daily amount [optional: ‘for this product’] [bullet] child takes more than 5 doses in 24 hours [bullet] taken with other drugs containing acetaminophen [bullet] adult has 3 or more alcoholic drinks everyday while using this product.” If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister

card and remain intact and readable when drug product is removed from the blister card. The warning is not required to be included on each blister unit.

(B) “Ask a doctor before use if the user has liver disease.”

(C) “Do not use with any other drug containing acetaminophen (prescription or nonprescription). If you are not sure whether a drug contains acetaminophen, ask a doctor or pharmacist.”

(D) “Ask a doctor or pharmacist before use if the user is taking the blood thinning drug warfarin” except on the labeling of combination products that contain acetaminophen and NSAID(s).

(2) *Nonsteroidal anti-inflammatory analgesic/antipyretic active ingredients—including, but not limited to, aspirin, carbaspirin calcium, choline salicylate, ibuprofen, ketoprofen, magnesium salicylate, naproxen sodium, and sodium salicylate.*

(i) *Statement of identity.* The statement of identity appears in accord with §§201.61 and 299.4 of this chapter. The word “(NSAID)” must appear highlighted (e.g., fluorescent or color contrast) or in bold type, be in lines generally parallel to the base on which the package rests as it is designed to be displayed, and be in one of the following sizes, whichever is greater:

(A) At least one-quarter as large as the size of the most prominent printed matter on the PDP, or

(B) At least as large as the size of the “Drug Facts” title, as required in §201.66(d)(2). The word “(NSAID)” must appear as part of the established name of the drug, as defined in §299.4 of this chapter, or after the general pharmacological (principal intended) action of the NSAID ingredient. Combination products containing an NSAID and a nonanalgesic ingredient(s) (e.g., cough-cold) must include the name of the NSAID ingredient and the word “(NSAID)” in accordance with this paragraph, and the name(s) of the other active ingredient(s) in the product on the PDP. Only the word “(NSAID)” needs to appear highlighted or in bold type, and in a prominent print size, as described in this paragraph.

(ii) *Active Ingredient and Purpose Headings.* The information required

under §201.66(c)(2) and (c)(3) of this chapter must be included under these headings. The active ingredient(s) section of the product’s labeling, as defined in §201.66(c)(2), contains the term “(NSAID*)” after the NSAID active ingredient with an asterisk statement at the end of the active ingredient(s) section that defines the term “NSAID” and states “*nonsteroidal anti-inflammatory drug.” The information under these headings may appear highlighted. However, the headings “Active Ingredient” and “Purpose” may not appear highlighted.

(iii) *For products labeled for adults only.* The labeling of the product states the following warnings under the heading “Warnings”:

(A) The stomach bleeding warning states “Stomach bleeding warning [heading in bold type]: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if you [bullet] are age 60 or older [bullet] have had stomach ulcers or bleeding problems [bullet] take a blood thinning (anticoagulant) or steroid drug [bullet] take other drugs containing prescription or nonprescription NSAIDs (aspirin, ibuprofen, naproxen, or others) [bullet] have 3 or more alcoholic drinks every day while using this product [bullet] take more or for a longer time than directed”. This “Stomach bleeding” warning must appear after the “Reye’s syndrome” and “Allergy alert” warnings in §201.66(c)(5)(ii)(A) and (c)(5)(ii)(B). For products that contain both acetaminophen and aspirin, the acetaminophen “Liver” warning in paragraph (a)(1)(iii) of this section must appear before the “Stomach bleeding” warning in this paragraph. If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister card and remain intact and readable when drug product is removed from the blister card. The warning is not required to be included on each blister unit.

(B) “Ask a doctor before use if [bullet] stomach bleeding warning applies to you [bullet] you have a history of stomach problems, such as heartburn

[bullet] you have high blood pressure, heart disease, liver cirrhosis, or kidney disease [bullet] you are taking a diuretic”.

(C) “Stop use and ask a doctor if [bullet] you experience any of the following signs of stomach bleeding:” [add the following as second level of statements: “[bullet] feel faint [bullet] vomit blood [bullet] have bloody or black stools [bullet] have stomach pain that does not get better”].

(iv) *For products labeled only for children under 12 years of age.*

(A) *Warnings.* The labeling of the product states the following warnings under the heading “Warnings”:

(1) The stomach bleeding warning states “Stomach bleeding warning [heading in bold type]: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if your child [bullet] has had stomach ulcers or bleeding problems [bullet] takes a blood thinning (anti-coagulant) or steroid drug [bullet] takes other drugs containing prescription or nonprescription NSAIDs (aspirin, ibuprofen, naproxen, or others) [bullet] takes more or for a longer time than directed”. The “Stomach bleeding” warning must appear after the “Reye’s syndrome” and “Allergy alert” warnings in § 201.66(c)(5)(ii)(A) and (c)(5)(ii)(B). If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister card and remain intact and readable when drug product is removed from the blister card. The warning is not required to be included on each blister unit.

(2) “Ask a doctor before use if [bullet] stomach bleeding warning applies to your child [bullet] child has a history of stomach problems, such as heartburn [bullet] child has not been drinking fluids [bullet] child has lost a lot of fluid due to vomiting or diarrhea [bullet] child has high blood pressure, heart disease, liver cirrhosis, or kidney disease [bullet] child is taking a diuretic”.

(3) “Stop use and ask a doctor if [bullet] child experiences any of the following signs of stomach bleeding:” [add

the following as second level of statements: [bullet] feels faint [bullet] vomits blood [bullet] has bloody or black stools [bullet] has stomach pain that does not get better”].

(B) *Directions.* The labeling of the product contains the following information under the heading “Directions”: “this product does not contain directions or complete warnings for adult use” [in bold type].

(v) *For products labeled for adults and children under 12 years of age.* The labeling of the product states all of the warnings in paragraphs (a)(2)(iii)(A) through (a)(2)(iii)(C) of this section with the following modifications:

(A) The Stomach bleeding warning states “Stomach bleeding warning [heading in bold type]: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if the user [bullet] has had stomach ulcers or bleeding problems [bullet] takes a blood thinning (anti-coagulant) or steroid drug [bullet] takes other drugs containing prescription or nonprescription NSAIDs (aspirin, ibuprofen, naproxen, or others) [bullet] takes more or for a longer time than directed [bullet] is age 60 or older [bullet] has 3 or more alcoholic drinks everyday while using this product”. The “Stomach bleeding” warning must appear after the “Reye’s syndrome” and “Allergy alert” warnings in § 201.66(c)(5)(ii)(A) and (c)(5)(ii)(B). If there is an outer and immediate container of a retail package, this warning must appear on both the outer and immediate containers. If the immediate container is a blister card, the warning must appear on the blister card and remain intact and readable when drug product is removed from the blister card. The warning is not required to be included on each blister unit.

(B) The labeling states “Ask a doctor before use if [bullet] stomach bleeding warning applies to user [bullet] user has history of stomach problems, such as heartburn [bullet] user has high blood pressure, heart disease, liver cirrhosis, or kidney disease [bullet] user takes a diuretic [bullet] user has not been drinking fluids [bullet] user has lost a lot of fluid due to vomiting or diarrhea”.

(C) The labeling states “Stop use and ask a doctor if [bullet] user experiences any of the following signs of stomach bleeding:” [add the following as second level of statements: [bullet] feels faint [bullet] vomits blood [bullet] has bloody or black stools [bullet] has stomach pain that does not get better”].

(b) *New warnings information statement.* The labeling of any drug product subject to this section that is initially introduced or initially delivered for introduction into interstate commerce before or on April 29, 2010, must bear on its PDP, as defined in §201.60, the statement “See new warnings information”. This statement must appear highlighted (e.g., fluorescent or color contrast) or in bold type, be in lines generally parallel to the base on which the package rests as it is designed to be displayed, and be in one of the following sizes, whichever is greater:

(1) At least one-quarter as large as the size of the most prominent printed matter on the PDP, or

(2) At least as large as the size of the “Drug Facts” title, as required in §201.66(d)(2). The new warnings information statement must remain on the PDP of the drug product for at least 1 year from the date the product is initially introduced into interstate commerce.

(c) *Requirements to supplement approved application.* Holders of approved applications for OTC drug products that contain internal analgesic/antipyretic active ingredients that are subject to the requirements of paragraph (a) of this section must submit supplements under §314.70(c) of this chapter to include the required information in the product’s labeling. Such labeling may be put into use without advance approval of FDA provided it includes at least the exact information included in paragraph (a) of this section.

[74 FR 19407, Apr. 29, 2009, as amended at 74 FR 31180, June 30, 2009; 74 FR 61514, Nov. 25, 2009]

§ 201.327 Over-the-counter sunscreen drug products; required labeling based on effectiveness testing.

The following provisions apply to sunscreen products containing aminobenzoic acid, avobenzone, cinoxate,

dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, oxybenzone, padimate O, sulisobenzene, titanium dioxide, trolamine salicylate, or zinc oxide, alone or in combination. The provisions do not apply to sunscreen products marketed under approved new drug applications or abbreviated new drug applications.

(a) *Principal display panel.* In addition to the statement of identity in paragraph (b) of this section, the following labeling shall be prominently placed on the principal display panel:

(1) *Effectiveness claim*—(i) *For products that pass the broad spectrum test in paragraph (j) of this section.* (A) The labeling states “Broad Spectrum SPF [insert numerical SPF value resulting from testing under paragraph (i) of this section]”.

(B) *Prominence.* The Broad Spectrum SPF statement shall appear as continuous text with no intervening text or graphic. The entire text shall appear in the same font style, size, and color with the same background color.

(ii) *For sunscreen products that do not pass the broad spectrum test in paragraph (j) of this section.* The labeling states “SPF [insert numerical SPF value resulting from testing under paragraph (i) of this section]”. The entire text shall appear in the same font style, size, and color with the same background color.

(2) *Water resistance statements*—(i) *For products that provide 40 minutes of water resistance according to the test in paragraph (i)(7)(i) of this section.* The labeling states “Water Resistant (40 minutes)”.

(ii) *For products that provide 80 minutes of water resistance according to the test in paragraph (i)(7)(ii) of this section.* The labeling states “Water Resistant (80 minutes)”.

(b) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the drug as a “sunscreen.”

(c) *Indications.* The labeling of the product states, under the heading “Uses,” the phrases listed in this paragraph (c), as appropriate. Other truthful and nonmisleading statements, describing only the uses that have been established and listed in this paragraph