U.S. FOOD & DRUG ADMINISTRATION

U.S. Food and Drug Administration

Final Administrative Order (OTC000031):

Over-the-Counter Monograph M004: First Aid Antibiotic Drug Products for Over-the-Counter Human Use (Posted May 2, 2023)

I. Summary

Over-the-Counter Monograph M004: First Aid Antibiotic Drug Products for Over-the-Counter Human Use, as set forth in this document, is a final administrative order (final order) deemed by section 505G(b)(8) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h(b)(8)), and effective upon enactment of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), Public Law 116-136, on March 27, 2020.

II. Background

The CARES Act added section 505G of the FD&C Act, which revised the framework for the regulation of over-the-counter (OTC) monograph drug products. Among other things, section 505G of the FD&C Act provides as a baseline status that, as of the date of enactment of the CARES Act, drugs that satisfy certain requirements described in section 505G(a)(1) or (2) are deemed to be generally recognized as safe and effective under section 201(p)(1) of the FD&C Act (21 U.S.C. 321(p)(1)), not a new drug under section 201(p), and not subject to section 503(b)(1) of the FD&C Act (21 U.S.C. 353(b)(1)). To obtain this status, among other things, a drug either must be one that is in conformity with the requirements for nonprescription use of a final monograph issued under part 330 (21 CFR part 330) (except as provided in section 505G(a)(2)),[1] as well as other requirements;[2] or must be one that is (i) classified in category I for safety and effectiveness under a tentative final monograph that is the most recently applicable proposal or determination issued under part 330, and (ii) in conformity with the proposed requirements for nonprescription use of such tentative final monograph and any applicable subsequent determination by the Secretary, as well as other requirements.[3] Other applicable requirements in section 505G(a)(1) of the FD&C Act include conditions or requirements under section 505G(b) of the FD&C Act.

Complementary to the requirements for conformity to tentative final or final monographs described in section 505G(a)(1) and (2) of the FD&C Act, Congress provided that, under section 505G(b)(8) of the FD&C Act, a final monograph or tentative final monograph that establishes conditions of use for a drug described in section 505G(a)(1) or (2) and that represents the most

[1] Section 505G(a)(2) of the FD&C Act is inapplicable here. It establishes the applicable requirements in terms of conformity with a final monograph, for purposes of section 505G(a)(1)(A)(i) of the FD&C Act, for sunscreen drugs subject to section 505G of the FD&C Act.
[2] Section 505G(a)(1)(A) of the FD&C Act.
[3] Section 505G(a)(1)(B) of the FD&C Act.

recently promulgated version of the conditions of use, including as modified, in whole or in part, by any proposed or final rule, is deemed to be a final order. The final order may be amended, revoked, or otherwise modified in accordance with the procedures under section 505G of the FD&C Act. Under section 505G(b)(8)(C) of the FD&C Act, the deemed establishment of a final order is construed to include technical amendments necessary to ensure that the order is appropriately harmonized, in terms of terminology or cross-references, with the applicable provisions of the FD&C Act (and regulations) and any other final orders issued under section 505G of the FD&C Act.

In the *Federal Register* of December 11, 1987 (52 FR 47322), FDA issued a final OTC monograph under the procedure in part 330, establishing conditions under which OTC first aid antibiotic drug products are generally recognized as safe and effective (GRASE) (see also technical correction on December 24, 1987 (52 FR 48792)). This final OTC monograph was codified in 21 CFR part 333, subpart B and subsequently amended by final rules issued on May 25, 1988 (53 FR 18838), March 15, 1990 (55 FR 9722), October 3, 1990 (55 FR 40381), December 5, 1990 (55 FR 50172), November 15, 1996 (61 FR 58472), and January 5, 1999 (64 FR 403).

Accordingly, this final order for OTC first aid antibiotic drug products incorporates the requirements of the final monograph for OTC first aid antibiotic drug products issued under part 330, as codified in part 333, subpart B as of March 27, 2020, with technical amendments.

III. Final Administrative Order

Over-the-Counter Monograph M004:

First Aid Antibiotic Drug Products for Over-the-Counter Human Use

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SOURCE: 52 FR 47322, Dec. 11, 1987, unless otherwise noted.

Part A—General Provisions

§ M004.1 Scope

An over-the-counter (OTC) first aid antibiotic drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this OTC monograph and each of the general conditions established in 21 CFR 330.1.

§ M004.3 Definitions

As used in this OTC monograph:

First aid antibiotic. An antibiotic-containing drug product applied topically to the skin to help prevent infection in minor cuts, scrapes, and burns.

[52 FR 47322, Dec. 11, 1987, as amended at 64 FR 403, Jan. 5, 1999]

Part B—Active Ingredients

§ M004.10 First aid antibiotic active ingredients

The product consists of any of the following active ingredients within the specified concentration established for each ingredient and in the specified dosage form:

(a) Bacitracin ointment containing, in each gram, 500 units of bacitracin in a suitable ointment base.

(b) Bacitracin zinc ointment containing, in each gram, 500 units of bacitracin zinc in a suitable ointment base.

(c) Chlortetracycline hydrochloride ointment containing, in each gram, 30 milligrams of chlortetracycline hydrochloride in a suitable ointment base.

(d) Neomycin sulfate ointment containing, in each gram, 3.5 milligrams of neomycin in a suitable water soluble or oleaginous ointment base.

(e) Neomycin sulfate cream containing, in each gram, 3.5 milligrams of neomycin in a suitable cream base.

(f) Tetracycline hydrochloride ointment containing, in each gram, 30 milligrams of tetracycline hydrochloride in a suitable ointment base.

[52 FR 47322, Dec. 11, 1987, as amended at 53 FR 18838, May 25, 1988; 64 FR 403, Jan. 5, 1999]

§ M004.20 Permitted combinations of active ingredients

The following combinations are permitted provided each active ingredient is present within the established concentration and in the specified dosage form, and the product is labeled in accordance with § M004.60.

(a) Combinations of antibiotic active ingredients.

(1) Bacitracin-neomycin sulfate ointment containing, in each gram, 500 units of bacitracin and 3.5 milligrams of neomycin in a suitable ointment base.

(2) Bacitracin-neomycin sulfate-polymyxin B sulfate ointment containing, in each gram, in a suitable ointment base the following:

(i) 500 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B; or

(ii) 400 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B.

(3) Bacitracin-polymyxin B sulfate topical aerosol containing, in each gram, 500 units of bacitracin and 5,000 units of polymyxin B in a suitable vehicle, packaged in a pressurized container with suitable inert gases.

(4) Bacitracin zinc-neomycin sulfate ointment containing, in each gram, 500 units of bacitracin and 3.5 milligrams of neomycin in a suitable ointment base.

(5) Bacitracin zinc-neomycin sulfate-polymyxin B sulfate ointment containing, in each gram, in a suitable ointment base the following:

(i) 400 units of bacitracin, 3 milligrams of neomycin, and 8,000 units of polymyxin B; or

(ii) 400 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B; or

(iii) 500 units of bacitracin, 3.5 milligrams of neomycin, and 5,000 units of polymyxin B; or

(iv) 500 units of bacitracin, 3.5 milligrams of neomycin, and 10,000 units of polymyxin B.

(6) Bacitracin zinc-polymyxin B sulfate ointment containing, in each gram, 500 units of bacitracin and 10,000 units of polymyxin B in a suitable ointment base.

(7) Bacitracin zinc-polymyxin B sulfate topical aerosol containing, in each gram, 120 units of bacitracin and 2,350 units of polymyxin B in a suitable vehicle, packaged in a pressurized container with suitable inert gases.

(8) Bacitracin zinc-polymyxin B sulfate topical powder containing, in each gram, 500 units of bacitracin and 10,000 units of polymyxin B in a suitable base.

(9) Neomycin sulfate-polymyxin B sulfate ointment containing, in each gram, 3.5 milligrams of neomycin and 5,000 units of polymyxin B in a suitable water miscible base.

(10) Neomycin sulfate-polymyxin B sulfate cream containing, in each gram, 3.5 milligrams of neomycin and 10,000 units of polymyxin B in a suitable vehicle.

(11) Oxytetracycline hydrochloride-polymyxin B sulfate ointment containing, in each gram, 30 milligrams of oxytetracycline and 10,000 units of polymyxin B in a suitable ointment base.

(12) Oxytetracycline hydrochloride-polymyxin B sulfate topical powder containing, in each gram, 30 milligrams of oxytetracycline and 10,000 units of polymyxin B with a suitable filler.

(b) Combinations of first aid antibiotic active ingredients and local anesthetic active ingredients.

(1) Bacitracin ointment containing, in each gram, 500 units of bacitracin and any single generally recognized as safe and effective amine or “caine”-type local anesthetic active ingredient in a suitable ointment base.

(2) Bacitracin-neomycin sulfate-polymyxin B sulfate ointment containing, in each gram, in a suitable ointment base the following:

(i) 500 units of bacitracin, 3.5 milligrams of neomycin, 5,000 units of polymyxin B, and any single generally recognized as safe and effective amine or “caine”-type local anesthetic active ingredient; or

(ii) 400 units of bacitracin, 3.5 milligrams of neomycin, 5,000 units of polymyxin B, and any single generally recognized as safe and effective amine or “caine”-type local anesthetic active ingredient.

(3) Bacitracin-polymyxin B sulfate topical aerosol containing, in each gram, 500 units of bacitracin and 5,000 units of polymyxin B and any single generally recognized as safe and effective amine or “caine”-type local anesthetic active ingredient in a suitable vehicle, packaged in a pressurized container with suitable inert gases.

(4) Bacitracin zinc-neomycin sulfate-polymyxin B sulfate ointment containing, in each gram, in a suitable ointment base the following:

(i) 400 units of bacitracin, 3 milligrams of neomycin, 8,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient; or

(ii) 400 units of bacitracin, 3.5 milligrams of neomycin, 5,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient; or

(iii) 500 units of bacitracin, 3.5 milligrams of neomycin, 5,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient; or

(iv) 500 units of bacitracin, 3.5 milligrams of neomycin, 10,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient.

(5) Bacitracin zinc-polymyxin B sulfate ointment containing, in each gram, 500 units of bacitracin, 10,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient in a suitable ointment base.

(6) Neomycin sulfate-polymyxin B sulfate cream containing, in each gram, 3.5 milligrams of neomycin, 10,000 units of polymyxin B, and any single generally recognized as safe and effective amine or "caine"-type local anesthetic active ingredient in a suitable vehicle.

[52 FR 47322, Dec. 11, 1987; 52 FR 48792, Dec. 24, 1987, as amended at 53 FR 18838, May 25, 1988; 55 FR 9722, Mar. 15, 1990; 55 FR 40381, Oct. 3, 1990; 55 FR 50172, Dec. 5, 1990; 64 FR 403, Jan. 5, 1999]

Part C—Labeling

§ M004.50 Labeling of first aid antibiotic drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug, if any, and identifies the product as a "first aid antibiotic."

(b) Indications. The labeling of the product states, under the heading "Uses," the following: "First aid to help" [select one of the following: "prevent," ("decrease" ("the risk of" or "the chance of")), ("reduce" ("the risk of" or "the chance of")), "guard against," or "protect against"] [select one of the following: "infection," "bacterial contamination," or "skin infection"] "in minor cuts, scrapes, and burns." Other truthful and nonmisleading statements describing only the indications for use that have been established and listed in § M004.50(b) may also be used, as

provided in 21 CFR 330.1(c)(2), subject to the provisions of section 502 of the Federal Food Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 352) relating to misbranding and the prohibition in section 301(d) of the FD&C Act (21 U.S.C. 331(d)) against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the FD&C Act (21 U.S.C. 355(a)).

(c) Warnings. The labeling of the product contains the following warnings under the heading "Warnings":

(1) "For external use only. Do not use in the eyes or apply over large areas of the body. In case of deep or puncture wounds, animal bites, or serious burns, consult a doctor."

(2) For products containing chlortetracycline hydrochloride or tetracycline hydrochloride. "Stop use and ask a doctor if the condition persists or gets worse. Do not use longer than 1 week unless directed by doctor."

(3) For any product containing bacitracin, bacitracin zinc, neomycin, neomycin sulfate, polymyxin B, and/or polymyxin B sulfate. "Stop use and ask a doctor if the condition persists or gets worse, or if a rash or other allergic reaction develops. Do not use if you are allergic to any of the ingredients. Do not use longer than 1 week unless directed by a doctor."

(d) Directions. The labeling of the product contains the following statements under the heading "Directions":

(1) For ointment and cream products. "Clean the affected area. Apply a small amount of this product (an amount equal to the surface area of the tip of a finger) on the area 1 to 3 times daily. May be covered with a sterile bandage."

(2) For powder products. "Clean the affected area. Apply a light dusting of the powder on the area 1 to 3 times daily. May be covered with a sterile bandage."

(3) For aerosol products. "Clean the affected area. Spray a small amount of this product on the area 1 to 3 times daily. May be covered with a sterile bandage."

(e) The word "doctor" may be substituted for the word "physician" in any of the labeling statements in § M004.50.

[52 FR 47332, Dec. 11, 1987, as amended at 61 FR 58472, Nov. 15, 1996]

§ M004.60 Labeling of permitted combinations of active ingredients

Statements of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) Statement of identity. For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC monographs. For a combination drug product that does not have an established name, the labeling of the product states the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC monographs.

(b) Indications. The labeling of the product states, under the heading "Uses," the indication(s) for each ingredient in the combination, as established in the "Uses" sections of the applicable OTC monographs, unless otherwise stated in § M004.60. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M004.60(b) may also be used, as provided in 21 CFR 330.1(c)(2), subject to the provisions of section 502 of the FD&C Act relating to misbranding and the prohibition in section 301(d) of the FD&C Act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the FD&C Act.

(1) For permitted combinations identified in § M004.20(a). The indications in § M004.50 should be used.

(2) For permitted combinations identified in § M004.20(b). In addition to the required indication identified in § M004.50, the labeling of the product may state, under the heading "Uses," the following additional indication: "First aid for the temporary relief of" [select one of the following: "pain," "discomfort," "pain or discomfort" or "pain and itching"] "in minor cuts, scrapes, and burns."

(c) Warnings. The labeling of the product states, under the heading "Warnings," the warning(s) for each ingredient in the combination, as established in the warnings sections of the applicable OTC monographs.

(d) Directions. The labeling of the product states, under the heading "Directions," directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC monographs. When the time intervals or age limitations for administrations of the individual ingredients differ, the directions for the combination product may not exceed any maximum dosage limits established for the individual ingredients in the applicable OTC monograph.