U.S. FOOD & DRUG ADMINISTRATION

U.S. Food and Drug Administration

Final Administrative Order (OTC000022)

Over-the-Counter Monograph M008: Antidiarrheal Drug Products for Over-the-Counter Human Use (Posted April 4, 2022)

I. Summary

Over-the-Counter Monograph M008: Antidiarrheal 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

[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.

conditions of use for a drug described in section 505G(a)(1) or (2) and that represents the most 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 April 17, 2003 (68 FR 18869 at 18881), FDA issued a final OTC monograph under the procedure in part 330, establishing conditions under which OTC antidiarrheal drug products are generally recognized as safe and effective (GRASE). This final OTC monograph was codified in 21 CFR part 335 and subsequently amended twice, first by a final rule making a technical correction on June 26, 2003 (68 FR 37963), and then by a final rule issued on May 12, 2004 (69 FR 26301).

Accordingly, this final order for OTC antidiarrheal products incorporates the requirements of the final monograph for OTC antidiarrheal drug products issued under part 330, as codified in part 335 as of March 27, 2020, with technical amendments.

III. Final Administrative Order

Over-the-Counter Monograph M008:

Antidiarrheal Drug Products for Over-the-Counter Human Use

Part A—General Provisions

Sec.
M008.1 Scope
M008.3 Definitions

Part B—Active Ingredients

M008.10 Antidiarrheal active ingredients

Part C—Labeling

M008.50 Labeling of antidiarrheal drug products

SOURCE: 68 FR 18881, April 17, 2003, unless otherwise noted.

Part A—General Provisions

§ M008.1 Scope

An over-the-counter antidiarrheal drug product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this OTC monograph and each general condition established in 21 CFR 330.1.

§ M008.3 Definitions

As used in this OTC monograph:

(a) Antidiarrheal. A drug that can be shown by objective measurement to treat or control (stop) the symptoms of diarrhea.

(b) Diarrhea. A condition characterized by increased frequency of loose, watery stools (three or more daily) during a limited period (24 to 48 hours), usually with no identifiable cause.

(c) Travelers' diarrhea. A subset of diarrhea occurring in travelers that is most commonly caused by an infectious agent.

[68 FR 18881, Apr. 17, 2003, as amended at 69 FR 26302, May 12, 2004]

Part B—Active Ingredients

§ M008.10 Antidiarrheal active ingredients

The active ingredient of the product consists of any one of the following when used within the dosage limits established for each ingredient in § M008.50(d):

(a) Bismuth subsalicylate.

(b) Kaolin.

Part C—Labeling

§ M008.50 Labeling of antidiarrheal drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug, if any, and identifies the product either as an "antidiarrheal" or "for diarrhea."

(b) Indications. The labeling of the product states, under the heading "Use," one or more of the phrases listed in § M008.50(b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M008.50(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)).

(1) For products containing bismuth subsalicylate identified in § M008.10(a). The labeling states [select one of the following: "controls" or "relieves"] [select one or both of the following: "diarrhea" or "travelers' diarrhea"]. If both "diarrhea" and "travelers' diarrhea" are selected, each shall be preceded by a bullet in accordance with 21 CFR 201.66(b)(4) and (d)(4) and the heading "Uses" shall be used.

(2) For products containing kaolin identified in § M008.10(b). The labeling states "helps firm stool within 24 to 48 hours".

(3) Additional indications

(i) When any additional indications are used, the heading "Uses" shall be used and each listed use shall be preceded by a bullet in accord with 21 CFR 201.66(b)(4).

(ii) In addition to the indication in § M008.50(b)(1), one or both of the following may be used for products containing bismuth subsalicylate in § M008.10(a): "[bullet] reduces number of bowel movements" "[bullet] helps firm stool".

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

(1) For products containing any ingredient identified in § M008.10.

(i) "Do not use if you have [bullet] bloody or black stool".

(ii) "Ask a doctor before use if you have [bullet] fever [bullet] mucus in the stool".

(2) For products containing bismuth subsalicylate identified in § M008.10(a).

(i) The following shall appear in accordance with 21 CFR 201.66(c)(5)(ii).

(A) The Reye's syndrome warning in 21 CFR 201.314(h).

(B) "Allergy alert: Contains salicylate. Do not take if you are [bullet] allergic to salicylates (including aspirin), [bullet] taking other salicylate products".

(ii) "Do not use if you have [bullet] an ulcer [bullet] a bleeding problem".

(iii) "Ask a doctor or pharmacist before use if you are taking any drug for [bullet] anticoagulation (thinning the blood) [bullet] diabetes [bullet] gout [bullet] arthritis".

(iv) "When using this product, a temporary, but harmless, darkening of the stool and/or tongue may occur".

(v) "Stop use and ask a doctor if [bullet] symptoms get worse [bullet] ringing in the ears or loss of hearing occurs [bullet] diarrhea lasts more than 2 days".

(3) For products containing kaolin identified in § M008.10(b).

(i) "Ask a doctor or pharmacist before use if you are taking any other drugs. Try to use at least 3 hours before or after taking any other drugs."

(ii) "Stop use and ask a doctor if [bullet] symptoms get worse [bullet] diarrhea lasts more than 2 days".

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

(1) For products containing any ingredient identified in § M008.10. The labeling states "[bullet] drink plenty of clear fluids to help prevent dehydration caused by diarrhea".

(2) For products containing bismuth subsalicylate identified in § M008.10(a). The labeling states "[bullet] adults and children 12 years and over:" 525 milligrams "every 1/2 to 1 hour, or" 1,050 milligrams "every hour as needed [bullet] do not exceed" 4,200 milligrams "in 24 hours [bullet] use until diarrhea stops but not more than 2 days [bullet] children under 12 years: ask a doctor".

(3) For products containing kaolin identified in § M008.10(b). The labeling states "[bullet] adults and children 12 years and over:" 26.2 grams "after each loose stool [bullet] continue to take every 6 hours until stool is firm but not more than 2 days [bullet] do not exceed" [262 grams] "in 24 hours [bullet] children under 12 years of age: ask a doctor".

(e) Products that meet the criteria established in 21 CFR 201.66(d)(10). The information described in 21 CFR 201.66(c) shall be printed in accordance with the following specifications.

(1) The labeling shall meet the requirements of 21 CFR 201.66(c) except that the information in § 201.66(c)(3) may be omitted, and the information in §§ 201.66(c)(5) and (c)(6) may be presented as follows:

(i) The words "Contains salicylate." may be omitted from the warning in § M008.50(c)(2)(i)(B).

(ii) The subheading "When using this product" in § M008.50(c)(2)(iv) may be omitted.

(iii) The words "continue to" may be omitted from the directions in § M008.50(d)(3).

(2) The labeling shall be printed in accordance with the requirements of 21 CFR 201.66(d) except that any requirements related to 21 CFR 201.66(c)(3) and the bullet in the warning in 21 CFR 335.50(c)(1)(i) may be omitted.

[68 FR 18881, Apr. 17, 2003, as amended at 69 FR 26302, May 12, 2004]