U.S. Food and Drug Administration

Final Administrative Order (OTC000020)

Over-the-Counter Monograph M027:
Orally Administered Menstrual Drug Products for Over-the-Counter Human Use
(Posted December 16, 2021)

I. Summary

Over-the-Counter Monograph M027: Orally Administered Menstrual Drug Products 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 November 16, 1988 (53 FR 46194 at 46201), FDA published a tentative final monograph under the procedure in part 330, that would establish conditions under which OTC orally administered menstrual drug products are generally recognized as safe and effective (GRASE) (see also technical correction on January 18, 1989 (54 FR 2039)).

Accordingly, this final order for OTC orally administered menstrual drug products incorporates the requirements of the tentative final monograph for OTC orally administered menstrual drug products issued under part 330 as proposed in the *Federal Register* on November 16, 1988 (53 FR 46194), and as amended on January 18, 1989 (54 FR 2039), with technical amendments.

III. Final Administrative Order

Over-the-Counter Monograph M027:
Orally Administered Menstrual Drug Products for Over-the-Counter Human Use

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SOURCE: 53 FR 46201, Nov. 16, 1988, unless otherwise noted.

Part A—General Provisions

§ M027.1 Scope

An over-the-counter (OTC) menstrual 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.

§ M027.3 Definitions

As used in this OTC monograph:

(a) Diuretic. A drug that increases the excretion of water.

(b) Menstrual period. The period of time from onset to stoppage of cyclic, physiologic uterine bleeding which (in the absence of pregnancy) normally recurs, usually at approximately 4-week intervals.

(c) Menstruation. The monthly flow of blood from the genital tract of women.

(d) Premenstrual period. The period of time approximately 1 week before onset of menstruation.

(e) Premenstrual syndrome. A recurrent symptom complex that begins during the week prior to menstruation and usually disappears soon after the onset of the menstrual flow. This symptom complex consists predominately of edema; lower abdominal pain (including cramps); breast tenderness; headache; abdominal bloating; fatigue; and feelings of depression, irritability, tension, and anxiety.

Part B—Active Ingredients

§ M027.12 Diuretic active ingredients

The active ingredients of the product consist of the following within the dosage limits established for each ingredient in § M027.52(d):

(a) Acidifying diuretic. Ammonium chloride.

(b) Xanthine diuretics.

(1) Caffeine.

(2) Pamabrom.

§ M027.20 Permitted combinations of active ingredients

The following combinations are permitted provided each active ingredient is present within the established dosage limits and the product is labeled in accordance with § M027.60.

(a) Any analgesic identified in § M013.10 of OTC Monograph M013 or any combination of analgesics identified in § M013.20(a) of OTC Monograph M013 and any diuretic identified in § M027.12.

(b) Ammonium chloride identified in § M027.12(a) with any one ingredient identified in § M027.12(b).

Part C—Labeling

§ M027.52 Labeling of orally administered menstrual drug products containing diuretic ingredients identified in § M027.12

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

(b) Indications. The labeling of the product states, under the heading "Uses," any of the phrases listed in § M027.52(b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M027.52(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 the relief of temporary water-weight gain, bloating, swelling, and/or full feeling associated with the premenstrual and menstrual periods."

(2) In addition to the indication in § M027.52(b)(1), products containing caffeine identified in § M027.12(b)(1) may also contain the following indication: "For the relief of fatigue associated with the premenstrual and menstrual periods."

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

(1) For products containing ammonium chloride identified in § M027.12(a).

(i) "Do not use if you have kidney or liver disease."

(ii) "This drug may cause nausea, vomiting, and gastrointestinal distress."

(2) For products containing caffeine identified in § M027.12(b)(1). "The recommended dose of this product contains about as much caffeine as a cup of coffee. Limit the use of caffeine-containing medications, foods, or beverages while taking this product because too much caffeine may cause nervousness, irritability, sleeplessness, and occasionally rapid heart rate."

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

(1) For products containing ammonium chloride identified in § M027.12(a). Adult oral dosage is 1 gram three times a day for no longer than 6 days.

(2) For products containing caffeine identified in § M027.12(b)(1). Adult oral dosage is 100 to 200 milligrams every 3 to 4 hours while symptoms persist.

(3) For products containing pamabrom identified in § M027.12(b)(2). Adult oral dosage is 50 milligrams four times a day, not to exceed 200 milligrams per day.

§ M027.60 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 indications sections of the applicable OTC monographs, unless otherwise stated in § M027.60(b). Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M027.60(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 the permitted combinations identified in § M027.20(a). "For the temporary relief of minor aches and pains and temporary water-weight gain, bloating, swelling, and full feeling associated with the premenstrual and menstrual periods."

(2) For the permitted combinations identified in § M027.20(a) that contain caffeine identified in § M027.12(b)(1) the following indication may be used as an alternative to the one identified in § M027.60(b)(1). "For the temporary relief of minor aches and pains and temporary water-weight gain, bloating, swelling, full feeling, and fatigue associated with the premenstrual and menstrual periods."

(c) Warnings. The labeling of the product states, under the heading "Warning," 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 of administration 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. For example, an appropriate direction for a tablet containing 25 milligrams pamabrom and 325 mg aspirin would be "Two tablets every 4 to 6 hours not to exceed 8 tablets per day."