U.S. Food and Drug Administration

Over-the-Counter (OTC) Monograph M001: Antacid Products for Over-the-Counter Human Use (Posted October 14, 2022)[1,2]

Part A—General Provisions

Sec.

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SOURCE: 39 FR 19874, June 4, 1974, unless otherwise noted.

Part A—General Provisions

§ M001.1 Scope

An over-the-counter (OTC) antacid product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each of the following conditions and each of the general conditions established in 21 CFR 330.1.

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[1] Final Administrative Order (OTC000024), effective upon enactment of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), Public Law 116-136, on March 27, 2020.

[2] Section M001.21 of Over-the-Counter Monograph M001 was revised on May 2, 2023 to correct the process for submitting any proposed modification to testing and the data to support it.

Part B—Active Ingredients

§ M001.10 Antacid active ingredients

(a) The active antacid ingredients of the product consist of one or more of the ingredients permitted in § M001.11 within any maximum daily dosage limit established, each ingredient is included at a level that contributes at least 25 percent of the total acid-neutralizing capacity of the product, and the finished product contains at least 5 mEq of acid-neutralizing capacity as measured by the procedure provided in the United States Pharmacopeia (USP) 23/National Formulary (NF) 18[3]. The method established in § M001.20 shall be used to determine the percent contribution of each antacid active ingredient.

(b) § M001.10(a) does not apply to an antacid ingredient specifically added as a corrective to prevent a laxative or constipating effect.

[39 FR 19874, June 4, 1974, as amended at 61 FR 4822, Feb. 8, 1996]

§ M001.11 Listing of specific active ingredients

(a) Aluminum-containing active ingredients:

(1) Basic aluminum carbonate gel.

(2) Aluminum hydroxide (or as aluminum hydroxide-hexitol stabilized polymer, aluminum hydroxide-magnesium carbonate codried gel, aluminum hydroxide-magnesium trisilicate codried gel, aluminum-hydroxide sucrose powder hydrated).

(3) Dihydroxyaluminum aminoacetate and dihydroxyaluminum aminoacetic acid.

(4) Aluminum phosphate gel when used as part of an antacid combination product and contributing at least 25 percent of the total acid-neutralizing capacity; maximum daily dosage limit is 8 grams.

(5) Dihydroxyaluminum sodium carbonate.

(b) Bicarbonate-containing active ingredients: Bicarbonate ion; maximum daily dosage limit 200 mEq for persons up to 60 years old and 100 mEq for persons 60 years or older.

(c) Bismuth-containing active ingredients:

(1) Bismuth aluminate.

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[3] United States Pharmacopeia (USP) 23/National Formulary (NF) 18 (January 1995), is incorporated by reference and is available for inspection at FDA. For further information about inspecting incorporated material, contact druginfo@fda.hhs.gov. Copies may also be available from the publisher, United States Pharmacopeia.

(2) Bismuth carbonate.

(3) Bismuth subcarbonate.

(4) Bismuth subgallate.

(5) Bismuth subnitrate.

(d) Calcium-containing active ingredients: Calcium, as carbonate or phosphate; maximum daily dosage limit 160 mEq calcium (e.g., 8 grams calcium carbonate).

(e) Citrate-containing active ingredients: Citrate ion, as citric acid or salt; maximum daily dosage limit 8 grams.

(f) Glycine (aminoacetic acid).

(g) Magnesium-containing active ingredients:

(1) Hydrate magnesium aluminate activated sulfate.

(2) Magaldrate.

(3) Magnesium aluminosilicates.

(4) Magnesium carbonate.

(5) Magnesium glycinate.

(6) Magnesium hydroxide.

(7) Magnesium oxide.

(8) Magnesium trisilicate.

(h) Milk solids, dried.

(i) Phosphate-containing active ingredients:

(1) Aluminum phosphate; maximum daily dosage limit 8 grams.

(2) Mono- or dibasic calcium salt; maximum daily dosage limit 2 grams.

(3) Tricalcium phosphate; maximum daily dosage limit 24 grams.

(j) Potassium-containing active ingredients:

(1) Potassium bicarbonate (or carbonate when used as a component of an effervescent preparation); maximum daily dosage limit 200 mEq of bicarbonate ion for persons up to 60 years old and 100 mEq of bicarbonate ion for persons 60 years or older.

(2) Sodium potassium tartrate.

(k) Sodium-containing active ingredients:

(1) Sodium bicarbonate (or carbonate when used as a component of an effervescent preparation); maximum daily dosage limit 200 mEq of sodium for persons up to 60 years old and 100 mEq of sodium for persons 60 years or older, and 200 mEq of bicarbonate ion for persons up to 60 years old and 100 mEq of bicarbonate ion for persons 60 years or older. That part of the warning required by 21 CFR 330.1(g), which states, “Keep this and all drugs out of the reach of children” is not required on a product that contains only sodium bicarbonate powder and that is intended primarily for other than drug uses.

(2) Sodium potassium tartrate.

(l) Silicates:

(1) Magnesium aluminosilicates.

(2) Magnesium trisilicate.

(m) Tartrate-containing active ingredients. Tartaric acid or its salts; maximum daily dosage limit 200 mEq (15 grams) of tartrate.

[39 FR 19874, June 4, 1974, as amended at 51 FR 27763, Aug. 1, 1986; 55 FR 19859, May 11, 1990]

§ M001.15 Combination with nonantacid active ingredients

(a) An antacid may contain any generally recognized as safe and effective nonantacid laxative ingredient to correct for constipation caused by the antacid. No labeling claim of the laxative effect may be used for such a product.

(b) (1) Antacid and acetaminophen combinations. See § M013.20(b)(1) of OTC Monograph M013.

(2) Antacid and aspirin combinations. See § M013.20(b)(3) of OTC Monograph M013.

(c) An antacid may contain any generally recognized as safe and effective antiflatulent ingredient if it is indicated for use solely for the concurrent symptoms of gas associated with heartburn, sour stomach, or acid indigestion.

[39 FR 19874, June 4, 1974, as amended at 53 FR 46190, Nov. 16, 1988]

Part C—Testing Procedures

§ M001.20 Determination of percent contribution of active ingredients

To determine the percent contribution of an antacid active ingredient, place an accurately weighed amount of the antacid active ingredient equal to the amount present in a unit dose of the product into a 250-milliliter (mL) beaker. If wetting is desired, add not more than 5 mL of alcohol (neutralized to an apparent pH of 3.5), and mix to wet the sample thoroughly. Add 70 mL of water, and mix on a magnetic stirrer at 300±30 r.p.m. for 1 minute. Analyze the acid-neutralizing capacity of the sample according to the procedure provided in the USP 23/NF 18[4] and calculate the percent contribution of the antacid active ingredient in the total product as follows:

Percent contribution = (Total mEq Antacid Active Ingredient × 100)/(Total mEq Antacid Product).

[61 FR 4823, Feb. 8, 1996]

§ M001.21 Test modifications

The formulation or mode of administration of certain products may require a modification of the USP 23/NF 18[5] acid-neutralizing capacity test. Any proposed modification and the data to support it shall be submitted as a petition in accord with 21 CFR 10.30 or in accord with section 505G(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h(b)).

[61 FR 4823, Feb. 8, 1996]

Part D—Labeling

§ M001.30 Labeling of antacid products

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

(b) Indications. The labeling of the product states, under the heading "Uses," any of the phrases listed in § M001.30(b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M001.30(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 (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

[4] See footnote 3.
[5] See footnote 3.

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 active ingredients identified in §§ M001.11(a) through (j), (k)(2), (l) and (m). "For the relief of" (select any or all of the following: "heartburn," "sour stomach," and/or "acid indigestion") which may be followed by the statement: "and upset stomach associated with" (select one or more of the following, as appropriate: "this symptom," "these symptoms," or "overindulgence in food and drink."))

(2) For products containing sodium bicarbonate as an active ingredient in a dosage form intended to be dissolved in liquid before administration identified in § M001.11(k)(1). "For the relief of" (select any or all of the following: "heartburn," "sour stomach," and/or "acid indigestion") (which may be followed by the statement: "and upset stomach associated with" (select one of the following, as appropriate: "this symptom" or "these symptoms".)) These products may not bear any claims that relate to use for "overindulgence in food and drink."

(c) Warnings. The labeling of the product contains the following warnings, under the heading "Warnings", which may be combined, but not rearranged, to eliminate duplicative words or phrases if the resulting warning is clear and understandable:

(1) "Do not take more than (maximum recommended daily dosage, broken down by age groups if appropriate, expressed in units such as tablets or teaspoonfuls) in a 24-hour period, or use the maximum dosage of this product for more than 2 weeks, except under the advice and supervision of a physician."

(2) For products which cause constipation in 5 percent or more of persons who take the maximum recommended dosage: "May cause constipation."

(3) For products which cause laxation in 5 percent or more of persons who take the maximum recommended dosage: "May have laxative effect."

(4) For products containing more than 5 gm per day lactose in a maximum daily dosage: "Do not use this product except under advice and supervision of a physician if you are allergic to milk or milk products."

(5) For products containing sodium bicarbonate as an active ingredient in a dosage form intended to be dissolved in liquid before administration identified in § M001.11(k)(1), portions of the warning statements must appear in bold print and in capital letters as follows: "STOMACH WARNING: To avoid serious injury, do not take until" (insert product dosage form, e.g., "tablet," "powder") "is completely dissolved. It is very important not to take this product when overly full from food or drink. [first two sentences in bold print and all capital letters] Consult a doctor if severe stomach pain occurs after taking this product."

(d) Drug interaction precaution. The labeling of the product contains the following statement "Ask a doctor or pharmacist before use if you are [bullet][6] presently taking a prescription drug. Antacids may interact with certain prescription drugs."

(e) Directions for use. The labeling of the product contains the recommended dosage, under the heading "Directions", per time interval (e.g., every 4 hours) or time period (e.g., 4 times a day) broken down by age groups if appropriate, followed by "or as directed by a physician."

> (1) The labeling for products containing sodium bicarbonate as an active ingredient in a dosage form intended to be dissolved in liquid before administration identified in § M001.11(k)(1) contains the following additional directions: "Dissolve completely in water" [For effervescent dosage forms add: "and be sure bubbling has stopped"] "before drinking. Do not exceed recommended dose. [second sentence in bold print and all capital letters] See Warnings."

(f) Exemption from the general accidental overdose warning. The labeling for antacid drug products containing the active ingredients identified in §§ M001.11(a), (b), and (d) through (m); permitted combinations of these ingredients provided for in § M001.10; and any of these ingredients or combinations of these ingredients in combination with simethicone (identified in § M002.10 of OTC Monograph M002 and provided for in § M001.15(c)), are exempt from the requirement in 21 CFR 330.1(g) that the labeling bear the general warning statement "In case of accidental overdose, seek professional assistance or contact a poison control center immediately." With the exception of sodium bicarbonate powder products identified in § M001.11(k)(1), the labeling must continue to bear the first part of the general warning in 21 CFR 330.1(g), which states, "Keep this and all drugs out of the reach of children."

(g) The word "doctor" may be substituted for the word "physician" in any of the labeling statements in § M001.30.

[39 FR 19874, June 4, 1974, as amended at 47 FR 38484, Aug. 31, 1982; 51 FR 16266, May 1, 1986; 51 FR 27763, Aug. 1, 1986; 52 FR 7830, Mar. 13, 1987; 55 FR 11581, Mar. 29, 1990; 58 FR 45208, Aug. 26, 1993; 59 FR 5064, Feb. 2, 1994; 59 FR 60556, Nov. 25, 1994; 61 FR 17806, Apr. 22, 1996; 64 FR 13295, Mar. 17, 1999; 69 FR 13734, Mar. 24, 2004]

[6] See 21 CFR 201.66(b)(4).

§ M001.60 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 § M001.60(b). Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M001.60(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 § M001.15(b)(1). The indications in § M013.60(b)(2) of OTC Monograph M013 should be used.

(2) For permitted combinations identified in § M001.15(b)(2). The indications in § M013.60(b)(4) of OTC Monograph M013 should be used.

(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, unless otherwise stated in § M001.60(d). When the time intervals or age limitations for 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.

[53 FR 46190, Nov. 16, 1988]

Part E—Professional Use

§ M001.80 Professional labeling

(a) The labeling of the product provided to health professionals (but not to the general public):

(1) Shall contain the neutralizing capacity of the product as calculated using the procedure set forth in USP 23/NF 18[7] expressed in terms of the dosage recommended per minimum time interval or, if the labeling recommends more than one dosage, in terms of the minimum dosage recommended per minimum time interval.

(2) May contain an indication for the symptomatic relief of hyperacidity associated with the diagnosis of peptic ulcer, gastritis, peptic esophagitis, gastric hyperacidity, and hiatal hernia.

(3) For products containing basic aluminum carbonate gel identified in § M001.11(a)(1)—Indication. "For the treatment, control, or management of hyperphosphatemia, or for use with a low phosphate diet to prevent formation of phosphate urinary stones, through the reduction of phosphates in the serum and urine."

(4) For products containing aluminum identified in § M001.11(a)—Warnings.

(i) Prolonged use of aluminum-containing antacids in patients with renal failure may result in or worsen dialysis osteomalacia. Elevated tissue aluminum levels contribute to the development of the dialysis encephalopathy and osteomalacia syndromes. Small amounts of aluminum are absorbed from the gastrointestinal tract and renal excretion of aluminum is impaired in renal failure. Aluminum is not well removed by dialysis because it is bound to albumin and transferrin, which do not cross dialysis membranes. As a result, aluminum is deposited in bone, and dialysis osteomalacia may develop when large amounts of aluminum are ingested orally by patients with impaired renal function.

(ii) Aluminum forms insoluble complexes with phosphate in the gastrointestinal tract, thus decreasing phosphate absorption. Prolonged use of aluminum-containing antacids by normophosphatemic patients may result in hypophosphatemia if phosphate intake is not adequate. In its more severe forms, hypophosphatemia can lead to anorexia, malaise, muscle weakness, and osteomalacia.

(b) Professional labeling for an antacid-antiflatulent combination may contain the information allowed for health professionals for antacids and antiflatulents.

[39 FR 19874, June 4, 1974. Redesignated and amended at 55 FR 19859, May 11, 1990]

[7] See footnote 3.