

§ 201.320

21 CFR Ch. I (4–1–13 Edition)

(b) Any drug products for human use containing a water-soluble gum, hydrophilic gum, or hydrophilic mucilloid as an active ingredient in an oral dosage form when marketed in a dry or incompletely hydrated form as described in paragraph (a) of this section are misbranded within the meaning of section 502 of the Federal Food, Drug, and Cosmetic Act unless their labeling bears the following warnings (under the subheading “Choking”) and directions:

“‘Choking’ [highlighted in bold type]: Taking this product without adequate fluid may cause it to swell and block your throat or esophagus and may cause choking. Do not take this product if you have difficulty in swallowing. If you experience chest pain, vomiting, or difficulty in swallowing or breathing after taking this product, seek immediate medical attention;” and

“‘Directions’ [highlighted in bold type]:” (Select one of the following, as appropriate: “Take” or “Mix”) “this product (child or adult dose) with at least 8 ounces (a full glass) of water or other fluid. Taking this product without enough liquid may cause choking. See choking warning.”

(c) After February 28, 1994, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce, or any such drug product that is repackaged or relabeled after this date regardless of the date the product was manufactured, initially introduced, or initially delivered for introduction into interstate commerce, that is not in compliance with this section is subject to regulatory action.

[58 FR 45201, Aug. 26, 1993, as amended at 64 FR 13292, Mar. 17, 1999; 72 FR 14674, Mar. 29, 2007]

§ 201.320 Warning statements for drug products containing or manufactured with chlorofluorocarbons or other ozone-depleting substances.

(a)(1) All drug products containing or manufactured with chlorofluorocarbons, halons, carbon tetrachloride, methyl chloride, or any other class I substance designated by the Environmental Protection Agency (EPA) shall, except as provided in para-

graph (b) or (c) of this section, bear the following warning statement:

Warning: Contains [or Manufactured with, if applicable] [insert name of substance], a substance which harms public health and the environment by destroying ozone in the upper atmosphere.

(2) The warning statement shall be clearly legible and conspicuous on the product, its immediate container, its outer packaging, or other labeling in accordance with the requirements of 40 CFR part 82 and appear with such prominence and conspicuousness as to render it likely to be read and understood by consumers under normal conditions of purchase.

(b)(1) For prescription drug products for human use, the following alternative warning statement may be used:

NOTE: The indented statement below is required by the Federal government’s Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFC’s) [or name of other class I substance, if applicable]:

This product contains [or is manufactured with, if applicable] [insert name of substance], a substance which harms the environment by destroying ozone in the upper atmosphere.

Your physician has determined that this product is likely to help your personal health. USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR PHYSICIAN. If you have any questions about alternatives, consult with your physician.

(2) The warning statement shall be clearly legible and conspicuous on the product, its immediate container, its outer packaging, or other labeling in accordance with the requirements of 40 CFR part 82 and appear with such prominence and conspicuousness as to render it likely to be read and understood by consumers under normal conditions of purchase.

(3) If the warning statement in paragraph (b)(1) of this section is used, the following warning statement must be placed on the package labeling intended to be read by the physician (physician package insert) after the “How supplied” section, which describes special handling and storage conditions on the physician labeling:

NOTE: The indented statement below is required by the Federal government’s Clean

Air Act for all products containing or manufactured with chlorofluorocarbons (CFC's) [or name of other class I substance, if applicable]:

WARNING: Contains [or Manufactured with, if applicable] *[insert name of substance]*, a substance which harms public health and the environment by destroying ozone in the upper atmosphere.

A notice similar to the above WARNING has been placed in the information for the patient [or patient information leaflet, if applicable] of this product under the Environmental Protection Agency's (EPA's) regulations. The patient's warning states that the patient should consult his or her physician if there are questions about alternatives.

(c)(1) For over-the-counter drug products for human use, the following alternative warning statement may be used:

NOTE: The indented statement below is required by the Federal government's Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFC's) [or other class I substance, if applicable]:

WARNING: Contains [or Manufactured with, if applicable] *[insert name of substance]*, a substance which harms public health and environment by destroying ozone in the upper atmosphere.

CONSULT WITH YOUR PHYSICIAN OR HEALTH PROFESSIONAL IF YOU HAVE ANY QUESTION ABOUT THE USE OF THIS PRODUCT.

(2) The warning statement shall be clearly legible and conspicuous on the product, its immediate container, its outer packaging, or other labeling in accordance with the requirements of 40 CFR part 82 and appear with such prominence and conspicuousness as to render it likely to be read and understood by consumers under normal conditions of purchase.

(d) This section does not replace or relieve a person from any requirements imposed under 40 CFR part 82.

[61 FR 20100, May 3, 1996]

§ 201.323 Aluminum in large and small volume parenterals used in total parenteral nutrition.

(a) The aluminum content of large volume parenteral (LVP) drug products used in total parenteral nutrition (TPN) therapy must not exceed 25 micrograms per liter ($\mu\text{g/L}$).

(b) The package insert of LVP's used in TPN therapy must state that the

drug product contains no more than 25 $\mu\text{g/L}$ of aluminum. This information must be contained in the "Precautions" section of the labeling of all large volume parenterals used in TPN therapy.

(c) Except as provided in paragraph (d) of this section, the maximum level of aluminum present at expiry must be stated on the immediate container label of all small volume parenteral (SVP) drug products and pharmacy bulk packages (PBPs) used in the preparation of TPN solutions. The aluminum content must be stated as follows: "Contains no more than ___ $\mu\text{g/L}$ of aluminum." The immediate container label of all SVP's and PBP's that are lyophilized powders used in the preparation of TPN solutions must contain the following statement: "When reconstituted in accordance with the package insert instructions, the concentration of aluminum will be no more than ___ $\mu\text{g/L}$." This maximum level of aluminum must be stated as the highest of:

(1) The highest level for the batches produced during the last 3 years;

(2) The highest level for the latest five batches, or

(3) The maximum historical level, but only until completion of production of the first five batches after July 26, 2004.

(d) If the maximum level of aluminum is 25 $\mu\text{g/L}$ or less, instead of stating the exact amount of aluminum as required in paragraph (c) of this section, the immediate container label may state: "Contains no more than 25 $\mu\text{g/L}$ of aluminum." If the SVP or PBP is a lyophilized powder, the immediate container label may state: "When reconstituted in accordance with the package insert instructions, the concentration of aluminum will be no more than 25 $\mu\text{g/L}$."

(e) The package insert for all LVP's, all SVP's, and PBP's used in TPN must contain a warning statement. This warning must be contained in the "Warnings" section of the labeling. The warning must state:

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly