

(d) *Directions*. The labeling of the product contains the following statement under the heading “Directions”: [optional, bullet] “apply 4 to 5 drops in each affected ear.”

[65 FR 48905, Aug. 10, 2000]

PART 346—ANORECTAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.

346.1 Scope.

346.3 Definitions.

Subpart B—Active Ingredients

346.10 Local anesthetic active ingredients.

346.12 Vasoconstrictor active ingredients.

346.14 Protectant active ingredients.

346.16 Analgesic, anesthetic, and antipruritic active ingredients.

346.18 Astringent active ingredients.

346.20 Keratolytic active ingredients.

346.22 Permitted combinations of anorectal active ingredients.

Subpart C—Labeling

346.50 Labeling of anorectal drug products.

346.52 Labeling of permitted combinations of anorectal active ingredients.

AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

SOURCE: 55 FR 31779, Aug. 3, 1990, unless otherwise noted.

Subpart A—General Provisions

§ 346.1 Scope.

(a) An over-the-counter anorectal drug product in a form suitable for external (topical) or intrarectal (rectal) administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21 unless otherwise noted.

§ 346.3 Definitions.

As used in this part:

(a) *Analgesic, anesthetic drug*. A topically (externally) applied drug that relieves pain by depressing cutaneous sensory receptors.

(b) *Anorectal drug*. A drug that is used to relieve symptoms caused by anorectal disorders in the anal canal, perianal area, and/or the lower rectal areas.

(c) *Antipruritic drug*. A topically (externally) applied drug that relieves itching by depressing cutaneous sensory receptors.

(d) *Astringent drug*. A drug that is applied topically (externally) to the skin or mucous membranes for a local and limited protein coagulant effect.

(e) *External use*. Topical application of an anorectal drug product to the skin of the perianal area and/or the skin of the anal canal.

(f) *Intrarectal use*. Topical application of an anorectal drug product to the mucous membrane of the rectum.

(g) *Keratolytic drug*. A drug that causes desquamation (loosening) and debridement or sloughing of the surface cells of the epidermis.

(h) *Local anesthetic drug*. A drug that produces local disappearance of pain, burning, itching, irritation, and/or discomfort by reversibly blocking nerve conduction when applied to nerve tissue in appropriate concentrations.

(i) *Protectant drug*. A drug that provides a physical barrier, forming a protective coating over skin or mucous membranes.

(j) *Vasoconstrictor*. A drug that causes temporary constriction of blood vessels.

Subpart B—Active Ingredients

§ 346.10 Local anesthetic active ingredients.

The active ingredient of the product consists of any of the following when used in the concentration or within the concentration range established for each ingredient:

- (a) Benzocaine 5 to 20 percent.
- (b) Benzyl alcohol 1 to 4 percent.
- (c) Dibucaine 0.25 to 1 percent.
- (d) Dibucaine hydrochloride 0.25 to 1 percent.
- (e) Dyclonine hydrochloride 0.5 to 1 percent.
- (f) Lidocaine 2 to 5 percent.
- (g) Pramoxine hydrochloride 1 percent.
- (h) Tetracaine 0.5 to 1 percent.

(i) Tetracaine hydrochloride 0.5 to 1 percent.

§ 346.12 Vasoconstrictor active ingredients.

The active ingredient of the product consists of any of the following when used in the concentration or within the concentration range established for each ingredient.

(a) Ephedrine sulfate 0.1 to 1.25 percent.

(b) Epinephrine 0.005 to 0.01 percent.

(c) Epinephrine hydrochloride 0.005 to 0.01 percent.

(d) Phenylephrine hydrochloride 0.25 percent.

§ 346.14 Protectant active ingredients.

(a) The following active ingredients may be used as the sole protectant active ingredient in a product if the ingredient as identified constitutes 50 percent or more by weight of the final product. In addition, the following active ingredients may be used in concentrations of less than 50 percent by weight only when used in combinations in accordance with § 346.22 (a), (b), or (n).

(1) Aluminum hydroxide gel.

(2) Cocoa butter.

(3) Glycerin in a 20- to 45-percent (weight/weight) aqueous solution so that the final product contains not less than 10 and not more than 45 percent glycerin (weight/weight). Any combination product containing glycerin must contain at least this minimum amount of glycerin.

(4) Hard fat.

(5) Kaolin.

(6) Lanolin.

(7) Mineral oil.

(8) Petrolatum.

(9) Topical starch.

(10) White petrolatum.

(b) The following active ingredients may not be used as a sole protectant ingredient but may be used in combination with one, two, or three other protectant active ingredients in accordance with § 346.22 (a), (b), (n), and (o) and with the following limitations:

(1) Calamine not to exceed 25 percent by weight per dosage unit (based on the zinc oxide content of calamine).

(2) Cod liver oil, provided that the product is labeled so that the amount

of the product that is used in a 24-hour period represents a quantity that provides 10,000 U.S.P. units of vitamin A and 400 U.S.P. units of cholecalciferol.

(3) Shark liver oil, provided that the product is labeled so that the amount of the product that is used in a 24-hour period represents a quantity that provides 10,000 U.S.P. units of vitamin A and 400 U.S.P. units of cholecalciferol.

(4) Zinc oxide not to exceed 25 percent by weight per dosage unit.

§ 346.16 Analgesic, anesthetic, and antipruritic active ingredients.

The active ingredient of the product consists of any of the following when used within the concentration range established for each ingredient:

(a) Camphor 0.1 to 3 percent.

(b) Juniper tar 1 to 5 percent.

(c) Menthol 0.1 to 1 percent.

§ 346.18 Astringent active ingredients.

The active ingredient of the product consists of any of the following when used within the concentration range established for each ingredient:

(a) Calamine, within a concentration range of 5 to 25 percent by weight per dosage unit (based on the zinc oxide content of calamine).

(b) Witch hazel, 10 to 50 percent.

(c) Zinc oxide, within a concentration range of 5 to 25 percent by weight per dosage unit.

[55 FR 31779, Aug. 3, 1990, as amended at 59 FR 28767, June 3, 1994]

§ 346.20 Keratolytic active ingredients.

The active ingredient of the product consists of any of the following when used within the concentration range established for each ingredient:

(a) Alcloxa 0.2 to 2 percent.

(b) Resorcinol 1 to 3 percent.

§ 346.22 Permitted combinations of anorectal active ingredients.

(a) Any two, three, or four protectants identified in § 346.14(a) may be combined, except aluminum hydroxide gel in § 346.14(a)(1) and kaolin in § 346.14(a)(5) may not be combined with any ingredient in § 346.14(a) (2), (4), (6), (7), (8) and (10), and (b) (2) and (3), provided that the combined percentage by weight of all protectants in the combination is at least 50 percent of the

§ 346.50

21 CFR Ch. I (4–1–05 Edition)

final product (e.g., 1 gram of a 2-gram dosage unit). Any protectant ingredient included in the combination must be present at a level that contributes at least 12.5 percent by weight (e.g., 0.25 gram of a 2-gram dosage unit), except cod liver oil and shark liver oil. If an ingredient in § 346.14(b) is included in the combination, it must not exceed the concentration limit specified in § 346.14(b).

(b) Any single anorectal ingredient identified in § 346.10, 346.12, 346.16, 346.18, or 346.20 may be combined with up to four protectants in accordance with paragraph (a) of this section.

(c) Any single local anesthetic identified in § 346.10 may be combined with any single vasoconstrictor identified in § 346.12.

(d) Any single local anesthetic identified in § 346.10 may be combined with any single astringent identified in § 346.18.

(e) Any single local anesthetic identified in § 346.10 may be combined with any single keratolytic identified in § 346.20.

(f) Any single vasoconstrictor identified in § 346.12 may be combined with any single astringent identified in § 346.18.

(g) Any single analgesic, anesthetic, and antipruritic identified in § 346.16 may be combined with any single astringent identified in § 346.18.

(h) Any single analgesic, anesthetic, and antipruritic identified in § 346.16 may be combined with any single keratolytic identified in § 346.20.

(i) Any single astringent identified in § 346.18 may be combined with any single keratolytic identified in § 346.20.

(j) Any single local anesthetic identified in § 346.10 may be combined with any single vasoconstrictor identified in § 346.12 and with any single astringent identified in § 346.18.

(k) Any single local anesthetic identified in § 346.10 may be combined with any single astringent identified in § 346.18 and with any single keratolytic identified in § 346.20.

(l) Any single vasoconstrictor identified in § 346.12 may be combined with any single analgesic, anesthetic, and antipruritic identified in § 346.16 and with any single astringent identified in § 346.18.

(m) Any single analgesic, anesthetic, and antipruritic identified in § 346.16 may be combined with any single astringent identified in § 346.18 and with any single keratolytic identified in § 346.20.

(n) Any combination of ingredients listed in paragraphs (c) through (m) of this section may be combined with up to four protectants in accordance with paragraph (a) of this section.

(o) Any product containing calamine for use as a protectant and/or as an astringent and/or containing zinc oxide for use as a protectant and/or as an astringent may not have a total weight of zinc oxide exceeding 25 percent by weight per dosage unit.

Subpart C—Labeling

§ 346.50 Labeling of anorectal drug products.

The labeling of the product contains the following information for anorectal ingredients identified in §§ 346.10, 346.12, 346.14, 346.16, 346.18, and 346.20, and for combinations of anorectal ingredients identified in § 346.22. Unless otherwise specified, the labeling in this subpart is applicable to anorectal drug products for both external and intrarectal use.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as “anorectal (hemorrhoidal),” “hemorrhoidal,” “hemorrhoidal (anorectal) (insert dosage form, e.g., cream, lotion, or ointment).”

(b) *Indications.* The labeling of the product states, under the heading “Indications,” any of the phrases listed in paragraph (b) of this section, as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph, may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) (“For the temporary relief of,” “Gives temporary relief of,” or “Helps

relieve the”) (As an option, select one or both of the following: “local” or “anorectal”) [select one or more of the following: “discomfort,” “itching,” or “itching and discomfort,” followed by: “in the perianal area” or “associated with” (select one or more of the following: “hemorrhoids,” “anorectal disorders,” “inflamed hemorrhoidal tissues,” “anorectal inflammation,” “hemorrhoidal tissues,” or “piles (hemorrhoids).”)]

(2) *Additional indications.* Indications applicable to each active ingredient of the product may be combined to eliminate duplicative words or phrases so that the resulting indication is clear and understandable. In addition to the indication identified in paragraph (b)(1) of this section, the labeling of the product intended for external or intrarectal use may also contain the following indications, as appropriate.

(i) *For products for external use only containing any ingredient identified in § 346.10.* “For the temporary relief of” (select one or more of the following: “pain,” “soreness,” or “burning”).

(ii) *For products containing epinephrine or epinephrine hydrochloride identified in § 346.12 (b) and (c) for external use only, and for products containing ephedrine sulfate or phenylephrine hydrochloride identified in § 346.12 (a) and (d).*

(A) “Temporarily reduces the swelling associated with” (select one of the following: “irritated hemorrhoidal tissue and other anorectal disorders” or “irritation in hemorrhoids and other anorectal disorders”).

(B) “Temporarily shrinks hemorrhoidal tissue.”

(iii) *For products for external use only containing glycerin identified in § 346.14(a)(3) and for products for external and/or intrarectal use containing any protectant identified in § 346.14(a) (2), (4), (6) through (10), and (b) (1) through (4).*

(A) “Temporarily forms a protective coating over inflamed tissues to help prevent drying of tissues.”

(B) “Temporarily protects irritated areas.”

(C) “Temporarily relieves burning.”

(D) “Provides temporary relief from skin irritations.”

(E) “Temporarily provides a coating for relief of anorectal discomforts.”

(F) “Temporarily protects the inflamed, irritated anorectal surface” (select one of the following: “to help make bowel movements less painful” or “from irritation and abrasion during bowel movement”).

(G) “Temporarily protects inflamed perianal skin.”

(H) “Temporarily relieves the symptoms of perianal skin irritation.”

(iv) *For products containing aluminum hydroxide gel identified in § 346.14(a)(1) and for products containing kaolin identified in § 346.14(a)(5).* “For the temporary relief of itching associated with moist anorectal conditions.”

(v) *For products for external use only containing any analgesic, anesthetic, and antipruritic identified in § 346.16.*

(A) “For the temporary relief of” (select one or both of the following: “pain” or “burning”).

(B) “Can help distract from pain.”

(C) “May provide a cooling sensation.”

(vi) *For products for external use only containing witch hazel identified in § 346.18(b), and for products for external use and/or intrarectal use containing calamine or zinc oxide identified in § 346.18 (a) and (c).*

(A) “Aids in protecting irritated anorectal areas.”

(B) “Temporary relief of” (select one or both of the following: “irritation” or “burning”).

(vii) *For products for external use only containing any ingredient identified in § 346.20.* The indication in paragraph (b)(1) of this section applies.

(c) *Warnings.* Warnings applicable to each active ingredient of the product may be combined to eliminate duplicative words or phrases so that the resulting warning is clear and understandable. The labeling of the product contains the following warnings under the heading “Warnings”:

(1) “If condition worsens or does not improve within 7 days, consult a doctor.”

(2) “Do not exceed the recommended daily dosage unless directed by a doctor.”

(3) “In case of bleeding, consult a doctor promptly.”

(4) *For products for external use only.* “Do not put this product into the rectum by using fingers or any mechanical device or applicator.”

(5) *For products for intrarectal use to be used with a special applicator such as a pile pipe or other mechanical device.* “Do not use this product with an applicator if the introduction of the applicator into the rectum causes additional pain. Consult a doctor promptly.”

(6) *For products for external use only containing any local anesthetic identified in § 346.10, menthol identified in § 346.16(c), or resorcinol identified in § 346.20(b).* “Certain persons can develop allergic reactions to ingredients in this product. If the symptom being treated does not subside or if redness, irritation, swelling, pain, or other symptoms develop or increase, discontinue use and consult a doctor.”

(7) *For products containing any vasoconstrictor identified in § 346.12.* (i) “Do not use this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor.”

(ii) “Ask a doctor or pharmacist before use if you are [bullet]¹ presently taking a prescription drug for high blood pressure or depression.”

(iii) *For products containing ephedrine sulfate identified in § 346.12(a).* “Some users of this product may experience nervousness, tremor, sleeplessness, nausea, and loss of appetite. If these symptoms persist or become worse, consult your doctor.”

(8) *For products containing aluminum hydroxide gel identified in § 346.14(a)(1) and for products containing kaolin identified in § 346.14(a)(5).* “Remove petrolatum or greasy ointment before using this product because they interfere with the ability of this product to adhere properly to the skin area.”

(9) *For products for external use only containing resorcinol identified in § 346.20(b).* “Do not use on open wounds near the anus.”

(d) *Directions.* Directions applicable to each active ingredient of the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and un-

derstandable. The labeling of the product contains the following information under the heading “Directions”:

(1) *“Adults:* When practical, cleanse the affected area” (select one or both of the following: “with mild soap and warm water and rinse thoroughly” or “by patting or blotting with an appropriate cleansing pad”). “Gently dry by patting or blotting with toilet tissue or a soft cloth before application of this product.” [Other appropriate directions in this section may be inserted here.] “Children under 12 years of age: consult a doctor.”

(2) *For products for external use only.* “Apply externally to the affected area” (insert appropriate time interval of administration as identified in paragraphs (d)(6), (7), (8), or (9) of this section).

(3) *For products for external use that are pads containing anorectal ingredients.* “Gently apply to the affected area by patting and then discard.”

(4) *For products for intrarectal use that are wrapped suppositories.* “Remove wrapper before inserting into the rectum.”

(5) *For products for intrarectal use that are to be used with a special applicator such as a pile pipe or other mechanical device.* “FOR INTRARECTAL USE: Attach applicator to tube. Lubricate applicator well, then gently insert applicator into the rectum.”

(6) *For products for external use only containing any of the local anesthetics identified in § 346.10; analgesics, anesthetics, and antipruritics identified in § 346.16; or alcloxa or resorcinol identified in § 346.20.* Apply to the affected area up to 6 times daily.

(i) *For products for external use only containing dibucaine or dibucaine hydrochloride identified in § 346.10 (c) and (d).* Apply to the affected area up to 3 or 4 times daily.

(ii) *For products for external use only containing pramoxine hydrochloride identified in § 346.10(g).* Apply to the affected area up to 5 times daily.

(7) *For products containing vasoconstrictors identified in § 346.12.* Apply to the affected area up to 4 times daily.

(8) *For products for external use only containing glycerin identified in § 346.14(a)(3) or witch hazel identified in § 346.18(b), and for products for external*

¹ See § 201.66(b)(4) of this chapter.

and/or intrarectal use containing any protectant identified in § 346.14(a)(1), (2), (4), (5), (6), (7), and (9), and (b)(1), (2), (3), and (4), or any astringent identified in § 346.18(a) and (c). Apply to the affected area up to 6 times daily or after each bowel movement.

(9) *For products containing petrolatum or white petrolatum identified in § 346.14(a)(8) and (10).* Apply liberally to the affected area as often as necessary.

(e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

[55 FR 31779, Aug. 3, 1990, as amended at 59 FR 28767, June 3, 1994; 64 FR 13295, Mar. 17, 1999]

§ 346.52 Labeling of permitted combinations of anorectal active ingredients.

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 established in § 346.50(a). For a combination drug product that does not have an established name, the labeling of the product states the statement of identity established in § 346.50(a).

(b) *Indications.* The labeling of the product states, under the heading "Indications," the indication(s) for each ingredient in the combination, as established in the indications sections of this subpart.

(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 this subpart.

(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 this subpart. 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 drug monograph.

PART 347—SKIN PROTECTANT DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.

347.1 Scope.

347.3 Definitions.

Subpart B—Active Ingredients

347.10 Skin protectant active ingredients.

347.12 Astringent active ingredients.

347.20 Permitted combinations of active ingredients.

Subpart C—Labeling

347.50 Labeling of skin protectant drug products.

347.52 Labeling of astringent drug products.

347.60 Labeling of permitted combinations of active ingredients.

AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

SOURCE: 58 FR 54462, Oct. 21, 1993, unless otherwise noted.

Subpart A—General Provisions

§ 347.1 Scope.

(a) An over-the-counter skin protectant drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21 unless otherwise noted.

§ 347.3 Definitions.

As used in this part:

Astringent drug product. A drug product applied to the skin or mucous membranes for a local and limited protein coagulant effect.

Lip protectant drug product. A drug product that temporarily prevents dryness and helps relieve chapping of the exposed surfaces of the lips; traditionally called "lip balm."