

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the ointment in a separatory funnel containing 50 milliliters of reagent-grade petroleum ether. Shake until dissolved. Wash with four separate washings of a 4:1 mixture of methyl alcohol and distilled water. Combine the washings and bring to volume with the methyl alcohol-water solution in a volumetric flask. Further dilute with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *Moisture*. Proceed as directed in §436.201 of this chapter.

[39 FR 19149, May 30, 1974, as amended at 49 FR 5097, Feb. 10, 1984; 49 FR 47829, Dec. 7, 1984; 50 FR 47214, Nov. 15, 1985]

§452.510b Erythromycin topical solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Erythromycin topical solution contains in each milliliter 15.0 or 20.0 milligrams of erythromycin. It may also contain one or more suitable and harmless solvents, surfactants, buffer substances, diluents, and perfumes. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of erythromycin that it is represented to contain. If it contains 15.0 milligrams of erythromycin per milliliter, its moisture content is not more than 5.0 percent. If it contains 20.0 milligrams of erythromycin per milliliter, its moisture content is not more than 8.0 percent, except if it contains acetone, its moisture content is not more than 2.0 percent. The erythromycin used conforms to the standards prescribed by §452.10(a)(1), except heavy metals.

(2) *Packaging*. In addition to the requirements of §432.1 of this chapter, it may either be dispensed on individually packaged pledgets, each individual pledget containing 0.8 milliliter of

erythromycin topical solution, or in a jar containing 60 pledgets. The jar contains 0.8 milliliter of erythromycin topical solution per pledget. Although the pledgets in the jar are not individually packaged, the drug is uniformly distributed throughout the pledgets. The erythromycin topical solution used on the pledgets contains 20 milligrams of erythromycin per milliliter.

(3) *Labeling*. It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(4) *Requests for certification; samples*. In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The erythromycin used in making the batch for potency, moisture, pH, residue on ignition, identity, and crystallinity.

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The erythromycin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 6 immediate containers.

(b) *Tests and methods of assay*. If the erythromycin topical solution is dispensed on a pledget, express the contents of a representative number of pledgets into a suitable container to obtain a volume of sample adequate to perform each assay described in paragraph (b)(1) and (2) of this section.

(1) *Potency*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion of the sample and dilute with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *Moisture*. Proceed as directed in §436.201 of this chapter, except if the

sample contains acetone, in lieu of Solvent A, use a mixture of pyridine and methanol (1:1).

[46 FR 2995, Jan. 13, 1981, as amended at 48 FR 51293, Nov. 8, 1983; 49 FR 374, Jan. 4, 1984; 50 FR 1504, Jan. 11, 1985; 50 FR 19921, May 13, 1985; 50 FR 20204, May 15, 1985; 54 FR 47352, Nov. 14, 1989; 54 FR 50472, Dec. 6, 1989]

§ 452.510d Erythromycin-benzoyl peroxide topical gel.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Erythromycin-benzoyl peroxide topical gel is erythromycin packaged in combination with a suitable and harmless gel containing benzoyl peroxide and one or more suitable dispersants, stabilizing agents, perfumes, and wetting agents. When reconstituted as directed in the labeling, each gram contains 30 milligrams of erythromycin and 50 milligrams of benzoyl peroxide. The erythromycin content is satisfactory if it contains not less than 90 percent and not more than 125 percent of the number of milligrams of erythromycin that it is represented to contain. The benzoyl peroxide content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the milligrams of benzoyl peroxide that it is represented to contain. The erythromycin used conforms to the standards prescribed by § 452.10(a)(1), except with respect to heavy metals.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The erythromycin used in making the batch for potency, moisture, pH, residue on ignition, identity, and crystallinity.

(b) The batch for erythromycin content and benzoyl peroxide content.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(a) The erythromycin used in making the batch: 5 packages, each containing approximately 100 milligrams.

(b) The batch: A minimum of 8 containers.

(b) *Tests and methods of assay—(1) Erythromycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Reconstitute the sample as directed in the labeling. Place an accurately weighed representative portion of the constituted product into a high-speed glass blender jar containing 0.5 milliliter of polysorbate 80 and sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *Benzoyl peroxide content.* Reconstitute the sample as directed in the labeling. Place an accurately weighed representative portion (about 2.5 grams) of the constituted product into a tared 250-milliliter glass-stoppered flask. Add 50 milliliters of glacial acetic acid and 20 milliliters of methylene chloride. Stopper and shake vigorously to disperse the gel. Add 1.0 milliliter phenylsulfide, swirl, stopper, and allow to stand at room temperature for 2 minutes. Purge the flask with nitrogen for 3 seconds. Add 5 milliliters for freshly prepared saturated sodium iodide solution, stopper, and swirl to mix. Let stand in the dark for 30 minutes. Add 50 milliliters of previously boiled and cooled distilled water and titrate the liberated iodine with 0.1N sodium thiosulfate, adding starch T.S. near the endpoint. Perform a blank determination and correct the sample titer. Each milliliter of 0.1N sodium thiosulfate is equivalent to 12.11 milligrams of benzoyl peroxide. Calculate the benzoyl peroxide content as follows:

$$\text{Percent benzoyl peroxide} = \frac{V_u \times \text{Normality of sodium thiosulfate} \times 12.11}{\text{Sample weight in grams}}$$

where:

V_u = Milliliters of sodium thiosulfate used in the titration of the sample minus the milliliters of sodium thiosulfate used in the titration of the sample blank.

[49 FR 47485, Dec. 5, 1984; 49 FR 49090, Dec. 18, 1984; 49 FR 49449, Dec. 20, 1984, as amended at 55 FR 11584, Mar. 29, 1990]