

(i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.

(b) The name and quantity of each active ingredient contained in the drug.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

(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 chlortetracycline hydrochloride used in making the batch for potency, loss on drying, pH, crystallinity, and identity.

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The chlortetracycline hydrochloride used in making the batch: 10 packages, each containing approximately 60 milligrams.

(b) The batch: A minimum of five immediate containers:

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §436.106 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.01*N* hydrochloric acid and shake well. Allow the layers to separate. Remove the acid layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of 0.01*N* hydrochloric acid. Combine the extractives in a suitable volumetric flask and dilute to volume with 0.01*N* hydrochloric acid. Further dilute an aliquot with sterile distilled water to the reference concentration of 0.06 microgram of chlortetracycline hydrochloride per milliliter (estimated).

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

[43 FR 11172, Mar. 17, 1978, as amended at 50 FR 19920, May 13, 1985]

§ 446.542 Meclocycline sulfosalicylate cream.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Meclocycline sulfosalicylate cream contains meclocycline sulfosalicylate in a suitable and harmless cream base. Each gram contains meclocycline sulfosalicylate equivalent to 10 milligrams of meclocycline. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of meclocycline that it is represented to contain. The meclocycline sulfosalicylate used conforms to the standards prescribed by §446.42(a)(1).

(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 meclocycline sulfosalicylate used in making the batch for potency, moisture, pH, and crystallinity.

(b) The batch for potency.

(ii) Samples required:

(a) The meclocycline sulfosalicylate used in making the batch: 10 packages, each containing approximately 300 milligrams.

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

(b) *Tests and methods of assay; potency.* Use either of the following methods; however, the results obtained from the high-pressure liquid chromatography method shall be conclusive.

(1) *Microbiological turbidimetric assay.* Proceed as directed in §436.106 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a high-speed glass blender jar containing sufficient 0.01*N* methanolic hydrochloric acid (solution 13) to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 0.06 microgram of meclocycline per milliliter (estimated).

(2) *High-pressure liquid chromatography.* Proceed as directed in

§ 436.329 of this chapter, except, prepare the working standard and sample solution and calculate the meclocyline content as follows:

(i) *Preparation of standard solution.* Accurately weigh an amount of working standard equivalent to approximately 25 milligrams of meclocyline into a 50-milliliter volumetric flask. Dissolve and dilute to volume with methanol and mix. Transfer exactly 2.0 milliliters of this solution to a 100-milliliter volumetric flask, dilute to volume with mobile phase, and mix.

(ii) *Preparation of sample solution.* Accurately weigh approximately 0.4 to 0.7 gram of sample into a 50-milliliter glass-stoppered centrifuge tube. Add 20 milliliters of methanol and 20 milliliters of 0.025*N* sulfuric acid. Disperse the sample thoroughly by a combination of ultrasonic/vortexing and shak-

ing by hand. Shake for 15 minutes on a wrist action shaker. Quantitatively transfer the contents of the centrifuge tube into a 50-milliliter volumetric flask. Rinse the centrifuge tube with two 5-milliliter portions of methanol and add to the flask. Dilute to volume with methanol and mix. Transfer a portion of the content of the volumetric flask into an appropriate-sized centrifuge tube. Centrifuge for 5 minutes at 2,000 revolutions per minute. Transfer 5.0 milliliters of this solution into a 50-milliliter volumetric flask and dilute to volume with mobile phase and mix. Filter this solution through a 0.5 micrometer filter. Inject the filtrate onto the column as described in § 436.329(e) of this chapter.

(iii) *Calculations.* Calculate the meclocyline content as follows:

$$\text{Meclocyline content of cream in percent} = \frac{A \times 2 \times \text{milligrams of working standard} \times \text{Potency of working standard in micrograms per milligram}}{B \times 100 \times \text{milligrams of sample}}$$

where:

A=Area or peak height of the sample peak (at a retention time equal to that observed for the standard);

B=Area or peak height of the standard peak.

[46 FR 3837, Jan. 16, 1981; 46 FR 21361, Apr. 10, 1981, as amended at 47 FR 22515, May 25, 1982; 50 FR 1504, Jan. 11, 1985]

§ 446.567 Oxytetracycline hydrochloride dermatologic forms. hydro dosage

§ 446.567a [Reserved]

§ 446.567b Oxytetracycline hydrochloride-polymyxin B sulfate topical ointment. hydro dosage

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride-polymyxin B sulfate topical ointment is oxytetracycline hydrochloride and polymyxin B sulfate in a suitable and harmless ointment base. Each gram contains oxytetracycline hydrochloride equivalent to 30 milligrams of oxytetracycline and polymyxin B sulfate equivalent to 10,000 units of polymyxin B. Its oxytetra-

cycline content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of oxytetracycline that it is represented to contain. Its polymyxin B sulfate content is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of units of polymyxin B that it is represented to contain. Its moisture content is not more than 1 percent. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67(a)(1). The polymyxin B sulfate conforms to the standards prescribed by § 448.30(a)(1).

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5(a)(3) of this chapter, each package shall bear on its label or labeling as hereinafter indicated, the following:

(i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.

(b) The name and quantity of each active ingredient contained in the drug.