

(v) The statement, "The potency of this drug cannot be assured for longer than 60 days after the container is first opened for compounding a prescription".

(vi) The statements, "For use only in extemporaneous prescription compounding. Not for manufacturing use".

(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 the batch for potency, loss on drying, pH, residue on ignition, and identity.

(ii) Samples required: A 0.5-gram portion for each 5,000 packages in the batch, but in no case less than 10 such portions. Each such portion shall be collected at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in 2 milliliters of sterile distilled water for each 5 milligrams of weighed sample. Further dilute an aliquot with sufficient 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in §436.200(b) of this chapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 5 milligrams per milliliter.

(5) *Residue on ignition.* Proceed as directed in §436.207(a) of this chapter.

(6) *Identity.* (i) To a solution of 2 milligrams of polymyxin B sulfate in 5 milliliters of water, add 0.5 milliliter of triketohydrindene solution (1:1,000) and 2 drops of pyridine, boil for 1 minute, and cool; a blue color develops; and

(ii) To a solution of 2 milligrams of polymyxin B sulfate in 5 milliliters of water, add 5 milliliters of sodium hydroxide solution (1:10), mix well, and add, dropwise, 5 drops of a cupric sul-

fate solution (1:100) mixing after the addition of each drop; a reddish-violet color is produced.

[39 FR 19115, May 30, 1974, as amended at 46 FR 16684, Mar. 13, 1981; 50 FR 19920, May 13, 1985]

**§ 448.930b Sterile polymyxin B sulfate-benzalkonium chloride urethral lubricant.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile polymyxin B sulfate-benzalkonium chloride urethral lubricant is polymyxin B sulfate and benzalkonium chloride, with one or more suitable and harmless suspending agents, in a suitable and harmless base. It contains, in each gram, 5,000 units of polymyxin B and 330 micrograms of benzalkonium chloride. Its content of polymyxin B is satisfactory if it contains not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. It is sterile. Its pH is not less than 4.0 and not more than 5.5. The polymyxin B sulfate used conforms to the standards prescribed by §448.30a(a)(1), except sterility, pyrogens, and 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 polymyxin B sulfate used in making the batch for potency, pH, loss on drying, residue on ignition, and identity.

(b) The batch for potency, sterility, and pH.

(ii) Samples required:

(a) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch.

(1) For all tests except sterility: A minimum of five immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(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 sample into a high-speed glass blender jar containing 1.0 milliliter polysorbate 80 and sufficient 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) *Sterility*. Proceed as directed in § 436.20(e)(1) of this chapter, except dissolve the ointment as follows: Aseptically transfer a portion of 0.25 gram from each of 10 immediate containers of the drug to 400 milliliters of diluting fluid D in an Erlenmeyer flask. Repeat the procedure on another 10 immediate containers. Swirl the flasks to dissolve the ointment.

(3) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted sample.

[39 FR 19115, May 30, 1974, as amended at 46 FR 16684, Mar. 13, 1981; 50 FR 19920, May 13, 1985]

## PART 449—ANTIFUNGAL ANTIBIOTIC DRUGS

### Subpart A—Bulk Drugs

Sec.

449.1—449.3 [Reserved]

449.4 Amphotericin B.

449.4a Amphotericin B for use in parenteral products.

449.10 Candicidin.

449.20 Griseofulvin.

449.40 Natamycin.

449.50 Nystatin.

### Subpart B—Oral Dosage Forms

449.104 Amphotericin B oral suspension.

449.120 Griseofulvin oral dosage forms.

449.120a Griseofulvin tablets.

449.120b Griseofulvin capsules.

449.120c Griseofulvin oral suspension.

449.120d Griseofulvin (ultramicrosize) tablets.

449.150 Nystatin oral dosage forms.

449.150a Nystatin tablets.

449.150b Nystatin oral suspension.

449.150c Nystatin for oral suspension.

449.150d Nystatin pastilles.

### Subpart C—Injectable Dosage Forms

449.204 Amphotericin B for injection.

### Subpart D—Ophthalmic Dosage Forms

449.340 Natamycin ophthalmic suspension.

### Subpart E [Reserved]

### Subpart F—Dermatologic Dosage Forms

449.504 Amphotericin B dermatologic dosage forms.

449.504a Amphotericin B ointment.

449.504b Amphotericin B cream.

449.504c Amphotericin B lotion.

449.550 Nystatin dermatologic dosage forms.

449.550a Nystatin ointment.

449.550b Nystatin-iodochlorhydroxyquin ointment.

449.550c Nystatin-neomycin sulfate-gramicidin-triamcinolone acetate ointment; nystatin-neomycin sulfate-gramicidin-fludrocortisone acetate ointment.

449.550d Nystatin cream.

449.550e Nystatin-neomycin sulfate-gramicidin-triamcinolone acetate cream.

449.550f Nystatin topical powder.

449.550g Nystatin-neomycin sulfate-gramicidin topical powder.

449.550h Nystatin lotion.

### Subpart G—Vaginal Dosage Forms

449.610 Candicidin vaginal dosage forms.

449.610a Candicidin vaginal ointment.

449.610b Candicidin vaginal tablets.

449.610c Candicidin vaginal capsules.

449.650 Nystatin vaginal dosage forms.

449.650a Nystatin vaginal tablets.

449.650b Nystatin vaginal suppositories.

AUTHORITY: 21 U.S.C. 357.

SOURCE: 39 FR 19134, May 30, 1974, unless otherwise noted.

### Subpart A—Bulk Drugs

## §§ 449.1—449.3 [Reserved]

### § 449.4 Amphotericin B.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Amphotericin B is a yellow to golden-orange powder. It is insoluble in water at pH. 6.0 to 7.0, anhydrous alcohols, esters, ethers, benzene, and toluene. It is soluble in dimethylformamide and dimethylsulfoxide. It is so purified and dried that:

(i) Its potency is not less than 750 micrograms of amphotericin B per milligram on an anhydrous basis.