

minutes. Dilute an aliquot with sufficient dimethylformamide to give a stock solution containing 400 units of nystatin per milliliter (estimated). Remove and dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

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

[39 FR 19134, May 30, 1974, as amended at 50 FR 19920, May 13, 1985]

§ 449.150c Nystatin for oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin for oral suspension is a dry powder consisting of nystatin, and suitable and harmless suspending substances, preservatives, diluents, colorings, and flavorings. When the suspension is prepared as directed in its labeling, each milliliter contains 100,000 units of nystatin. Its potency is satisfactory if it is not less than 90 percent and not more than 140 percent of aliquot of the stock solution and further the number of units of nystatin that it is represented to contain. The pH of the reconstituted drug is not less than 4.9 and not more than 5.5. Its moisture content is not more than 7.0 percent. The nystatin used conforms to the standards prescribed by § 449.50(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 the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

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

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each consisting of 300 milligrams.

(b) The batch: A minimum of five 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: Reconstitute the drug as directed in the labeling. Blend an appropriate aliquot in a high-speed glass blender for 3 to 5 minutes, using sufficient dimethylformamide to give a convenient concentration. Dilute an aliquot with sufficient dimethylformamide to give a stock solution containing 400 units of nystatin per milliliter. Further dilute an aliquot with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

(2) *Moisture.* Using the dry powder, proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the suspension after reconstituting as directed in the labeling.

[39 FR 19134, May 30, 1974, as amended at 50 FR 19920, May 13, 1985]

§ 449.150d Nystatin pastilles.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin pastilles are composed of nystatin with suitable diluents, binders, buffers, colorings, and flavorings. Each pastille contains nystatin equivalent to 200,000 units of nystatin. Its potency is satisfactory if it contains not less than 90 percent and not more than 125 percent of the number of units of nystatin that it is represented to contain. The pH in an aqueous solution is not less than 5.0 and not more than 7.5. It disintegrates within 90 minutes. The nystatin used conforms to the standards prescribed by § 449.50(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 the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The batch for potency, pH, and disintegration time.

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

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

(b) The batch: A minimum of 36 pastilles.

(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 a representative number of pastilles into a high-speed glass blender jar containing 100 milliliters of sterile distilled water. Blend for 18 to 20 minutes. Add 400 milliliters of dimethylformamide and continue blending for an additional 10 minutes. Remove an aliquot and add sufficient 80 percent dimethylformamide so that upon final dilution with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter, the concentration of dimethylformamide will be 4 percent.

(2) *pH*. Dissolve 1 pastille in 100 milliliters of distilled water at 37 °C, cool, and proceed as directed in § 436.202 of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the method described in paragraph (e)(4) of that section.

[52 FR 4617, Feb. 13, 1987; 52 FR 7741, Mar. 12, 1987, as amended at 55 FR 11584, Mar. 29, 1990]

Subpart C—Injectable Dosage Forms

§ 449.204 Amphotericin B for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Amphotericin B for injection is a dry mixture containing in each immediate container 50 milligrams of amphotericin B, 41 milligrams of sodium desoxycholate, and suitable buffering substances. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of amphotericin B that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 8.0 percent. Its pH in an aqueous solution containing 10 milligrams of amphotericin B per milliliter is not less than 7.2 and not more than 8.0. The amphotericin B used conforms

to the standards prescribed by § 449.4a(a)(1).

(2) *Labeling*. In addition to the labeling requirements prescribed by § 432.5 of this chapter, each package shall bear on its label and labeling the following statement: “For intravenous infusion in hospitals only”.

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

(i) Results of tests and assays on:

(a) The amphotericin B used in making the batch for potency, amphotericin A content, loss on drying, pH, residue on ignition, and identity.

(b) The batch for potency, sterility, pyrogens, loss on drying, and pH.

(ii) Samples required:

(a) Amphotericin B used in making the batch: 10 packages, each containing approximately equal portions of not less than 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 10 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: Reconstitute as directed in the labeling. Then using a suitable syringe and hypodermic needle, remove all of the withdrawable contents if the container is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with sufficient dimethylsulfoxide to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with dimethylsulfoxide to a concentration of 20 micrograms of amphotericin B per milliliter (estimated). Remove an aliquot of this solution and dilute with 0.2M potassium phosphate buffer, pH 10.5 (solution 10), to the reference concentration of 1.0 microgram of amphotericin B per milliliter (estimated).