

B =Absorptivity of amphotericin B standard at 282 nanometers;

a =Absorptivity of nystatin standard at 304 nanometers;

b =Absorptivity of amphotericin B standard at 304 nanometers;

S_1 =Absorbance of sample at 282 nanometers;

S_2 =Absorbance of sample at 304 nanometers;

W_s =Weight of sample in grams (on an anhydrous basis).

(3) [Reserved]

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

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

(6) *Identity.* Using the solutions prepared as described in paragraphs (b)(2)(ii), (iii), and (iv) of this section, record the absorption spectrum from 320 to 240 nanometers. Then dilute these solutions (1+9) with methyl alcohol and record the absorption spectrum from 400 to 320 nanometers. The sample exhibits absorption peaks at identical wavelengths with that of the amphotericin B standard. Depending on the amphotericin A content of the sample, a peak may occur at 304 nanometers.

[39 FR 19115, May 30, 1974, as amended at 46 FR 16684, Mar. 13, 1981; 49 FR 2242, Jan. 19, 1984; 50 FR 19920, May 13, 1985]

§ 449.4a Amphotericin B for use in parenteral products.

(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.

(ii) It contains not more than 5 percent of amphotericin A.

(iii) [Reserved]

(iv) Its loss on drying is not more than 5.0 percent.

(v) It contains not more than 0.5 percent residue on ignition.

(vi) It passes the identity test.

(2) *Labeling.* In addition to the labeling prescribed by § 432.5(b) of this chap-

ter, each package shall bear on its label the statements "Store below 10° C." and "Protect from light and moisture".

(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 the batch for potency, amphotericin A content, loss on drying, residue on ignition, and identity.

(ii) Samples required on the batch: 10 packages, each containing not less than 500 milligrams.

(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 sufficient dimethylsulfoxide to give a stock solution of convenient concentration. Further dilute with dimethylsulfoxide to give a concentration of 20 micrograms of amphotericin B per milliliter (estimated). Dilute an aliquot 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).

(2) *Amphotericin A content.* Proceed as directed in § 449.4(b)(2).

(3) [Reserved]

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

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

(6) *Identity.* Proceed as directed in § 449.4(b)(7).

[39 FR 19134, May 30, 1974, as amended at 49 FR 2243, Jan. 19, 1984; 50 FR 19920, May 13, 1985]

§ 449.10 Candicidin.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Candicidin is a brown to yellow powder. It is sparingly soluble in water; very slightly soluble in ethyl alcohol, butyl alcohol, and acetone. It is so purified and dried that:

(i) Its potency is not less than 1,000 micrograms of candicidin per milligram on an anhydrous basis.

(ii) Its loss on drying is not more than 4 percent.

(iii) Its pH is not less than 8.0 nor more than 10.0 in a 1 percent aqueous suspension.

(iv) Its ultraviolet absorption spectrum is characteristic of a conjugated heptaene and is qualitatively the same as that of the candicidin working standard.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5(b) 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 the batch for potency, loss on drying, pH, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve a portion of the sample in sufficient dimethylsulfoxide to yield an estimated concentration of 1,000 micrograms of candicidin activity per milliliter. Further dilute an aliquot with sterile distilled water to the reference concentration of 0.06 microgram of candicidin activity per milliliter (estimated).

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

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using a 1 percent aqueous suspension.

(4) *Identity—(i) Preparation of aqueous alcohol solution.* Prepare an aqueous alcohol solution by mixing 53 volumes of ethyl alcohol and 47 volumes of water.

(ii) *Preparation of standard solution.* Grind a small portion of the candicidin working standard to a fine powder with a mortar and pestle. Accurately weigh an amount equivalent to 20,000 micrograms of candicidin activity and transfer it to a 100-milliliter volumetric flask. Add about 50 milliliters of the aqueous alcohol solution and shake to effect complete dissolution. Bring to volume with the aqueous alcohol solution and mix well. Transfer a 25-milliliter aliquot to a 100-milliliter volumetric flask and bring to volume with the aqueous alcohol solution. This solution contains 50 micrograms of candicidin activity per milliliter.

(iii) *Preparation of sample solution.* Proceed as directed in paragraph (b)(4)(ii) of this section.

(iv) *Procedure.* Using a suitable recording spectrophotometer, record the absorption spectra of the standard solution and the sample solution between the wavelengths of 330 and 410 nanometers with the aqueous alcohol solution as the reference solution. Compare the absorption spectra of the standard solution and the sample solution. They should exhibit absorption maxima and minima at the same wavelengths, which are approximately 342, 359, 378, and 397 nanometers for the maxima and 348, 366, and 390 nanometers for the minima.

[39 FR 19134, May 30, 1974, as amended at 44 FR 30333, May 25, 1979; 49 FR 2243, Jan. 19, 1984]

§ 449.20 Griseofulvin.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Griseofulvin is a microsize, white to pale-cream compound with the following chemical name: 7-chloro-2',4,6-trimethoxy-6' β -methylspiro[benzofuran-2(3*H*),1'-[2]cyclohexene]-3,4'-dione. It is so purified and dried that:

(i) Its griseofulvin content is not less than 900 micrograms and not more than 1,050 micrograms of griseofulvin per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 1.0 percent.

(iv) Its melting point, after drying, is not less than 217° C. and not more than 224° C.

(v) Its specific rotation in dimethylformamide at 25° C. is not less than +348° and not more than +364°.

(vi) Its ultraviolet absorption spectrum in methyl alcohol compares qualitatively with that of the griseofulvin reference standard.

(vii) Its residue on ignition is not more than 0.2 percent.

(viii) Its heavy metals content is not more than 25 parts per million.

(ix) Its specific surface area is not less than 1.3 and not more than 1.7 square meters per gram.

(x) It is crystalline.