

solutions in the following manner: Dissolve approximately 100 milligrams each of the sample and standard in a 100-milliliter volumetric flask containing 50 milliliters of absolute methyl alcohol, and dilute to volume with absolute methyl alcohol. Transfer a 2-milliliter aliquot to a 100-milliliter volumetric flask, and dilute to volume with 1 percent potassium phosphate buffer,

pH 6.0, as listed in § 436.101(a)(1) of this chapter. Using a suitable spectrophotometer equipped with a 1-centimeter cell, immediately determine the absorption of each solution at 475 nanometers with the blank containing the same proportion of solution 1 and methyl alcohol as the sample and standard solutions. Calculate the absorptivity as follows:

$$\text{Percent relative absorptivity} = \frac{\text{Absorbance of sample} \times \text{milligrams standard} \times (100 - m_1)}{\text{Absorbance of standard} \times \text{milligrams sample} \times (100 - m_2)} \times 100$$

where:

$m_1$ =percent moisture in standard;  
 $m_2$ =percent moisture in sample.

(6) *Identity*. Proceed as directed in § 436.211 of this chapter, using the sample preparation method described in paragraph (b)(3) of that section, except use a 4 percent solution of the sample in chloroform and 0.1-millimeter matched absorption cells.

(7) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

[39 FR 19166, May 30, 1974, as amended at 50 FR 19921, May 13, 1985]

**§ 455.80a Sterile spectinomycin hydrochloride.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile spectinomycin hydrochloride is the pentahydrated dihydrochloride salt of decahydro-4a, 7, 9-trihydroxy-2-methyl-6,8-bis(methylamino)4H-pyrano[2,3-b][1,4]benzodioxin-4-one. It is so purified and dried that:

(i) Its spectinomycin content is not less than 603 micrograms per milligram. If it is packaged for dispensing, its spectinomycin content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of spectinomycin that it is represented to contain.

(ii) Its microbiological activity is not less than 603 micrograms of spectinomycin per milligram.

(iii) It is sterile.

(iv) It is nonpyrogenic.

(v) [Reserved]

(vi) It contains no depressor substances.

(vii) Its moisture content is not less than 16 percent nor more than 20 percent.

(viii) Its pH is an aqueous solution containing 10 milligrams per milliliter is not less than 3.8 nor more than 5.6. If it is packaged for dispensing, when reconstituted as directed in the labeling, its pH is not less than 4.0 nor more than 7.0.

(ix) It passes the identity test.

(x) Its residue on ignition is less than 1 percent.

(xi) It is crystalline.

(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 the batch for spectinomycin content, microbiological activity, sterility, pyrogens, depressor substances, moisture, pH, identity, residue on ignition, and crystallinity.

(ii) Samples required:

(a) If the batch is packaged for repackaging or for use in the manufacture of another drug:

(1) For all tests except sterility: eight packages, each containing approximately 300 milligrams and two containing not less than 3 grams.

(2) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(b) If the batch is packaged for dispensing:

(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) *Spectinomycin content (vapor phase chromatography)*. Proceed as directed in § 436.307 of this chapter; and also, if the batch is packaged for dispensing prepare the sample for assay as follows: Reconstitute the vial as directed in the labeling. Then using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single dose container, or if the labeling specifies the amount of spectinomycin content in a given volume of the resultant preparation remove an accurately measured representative portion from the container. Dilute the sample with water to a concentration equivalent to about 20 milligrams per milliliter of spectinomycin. Transfer 1.0 milliliter of the diluted sample to a 25-milliliter glass-stoppered Erlenmeyer flask and dry by lyophilization. Proceed as directed in § 436.307(d)(1)(ii) of this chapter. Calculate the spectinomycin content as follows:

$$\text{Milligrams of spectinomycin per dose} = \frac{R_u \times W_s \times D \times f}{R_s}$$

where:

Area of spectinomycin sample peak (at a retention time equal to that observed for the spectinomycin standard)

$$R_u = \frac{\text{Area of spectinomycin sample peak (at a retention time equal to that observed for the spectinomycin standard)}}{\text{Area of internal standard peak}}$$

$$R_s = \frac{\text{Area of the spectinomycin standard peak}}{\text{Area of internal standard peak}}$$

$W_s$ =Weight of the spectinomycin working standard in milligrams;

$D$ =Dilution of the spectinomycin dose;

$f$ =Potency of the spectinomycin working standard in milligrams of spectinomycin per milligram.

(2) *Microbiological activity (microbiological turbidimetric assay)*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient sterile distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 30.0 micrograms of spectinomycin per milliliter (estimated).

(3) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(4) *Pyrogens*. Proceed as directed in § 436.32(a) of this chapter, using a solution containing 50 milligrams of spectinomycin base per milliliter.

(5) [Reserved]

(6) *Depressor substances*. Proceed as directed in § 436.35 of this chapter.

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

(8) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter, except, if it is packaged for dispensing, use the suspension obtained after reconstituting the drug as directed in the labeling.

(9) *Identity test*. Proceed as directed in § 436.211 of this chapter, using the method described in paragraph (b)(2) of that section.

(10) *Residue on ignition*. Proceed as directed in § 436.207 of this chapter, using the method described in paragraph (b) of that section.

(11) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

[39 FR 19166, May 30, 1974, as amended at 46 FR 60568, Dec. 11, 1981; 50 FR 19921, May 13, 1985]

#### § 455.82a Sterile sulbactam sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Sterile sulbactam sodium is sodium (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4 dioxide. It is so purified and dried that:

(i) Its sulbactam potency is not less than 886 micrograms and not more than 941 micrograms per milligram on an anhydrous basis.