

§ 440.41a Sterile nafcillin sodium monohydrate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile nafcillin sodium monohydrate is the monohydrated sodium salt of 6-(2-ethoxy-1-naphthamido) penicillanic acid. It is so purified and dried that:

- (i) It contains not less than 820 micrograms of nafcillin per milligram.
- (ii) It is sterile.
- (iii) It is nonpyrogenic.
- (iv) [Reserved]
- (v) Its moisture content is not less than 3.5 nor more than 5.3 percent.
- (vi) Its pH in an aqueous solution containing 30 milligrams per milliliter is not less than 5.0 and not more than 7.0.
- (vii) It is crystalline.
- (viii) Its nafcillin content is not less than 82.0 percent.
- (ix) It gives a positive identity test for nafcillin.

(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 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, sterility, pyrogens, moisture, pH, crystallinity, nafcillin content, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

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

(b) *Tests and methods of assay—(1) Potency.* Use any of the following methods: however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 2

micrograms of nafcillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

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

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 80 milligrams of nafcillin per milliliter.

(4) [Reserved]

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

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 30 milligrams per milliliter.

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

(8) *Nafcillin content.* Proceed as directed in § 440.41(b)(6).

(9) *Identity.* The absorption spectrum of the sample determined as directed in paragraph (b)(8) of this section compares qualitatively with that of the nafcillin working standard.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59858, Nov. 22, 1977; 45 FR 16474, Mar. 14, 1980; 45 FR 22921, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§ 440.49 Oxacillin sodium monohydrate.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Oxacillin sodium monohydrate is the monohydrated sodium salt of 5-methyl-3-phenyl-4-isoxazolyl penicillin. It is so purified and dried that:

(i) It contains not less than 815 and not more than 950 micrograms of oxacillin per milligram.

(ii) [Reserved]

(iii) Its moisture content is not less than 3.5 and not more than 5.0 percent.

(iv) Its pH in an aqueous solution containing 30 milligrams per milliliter is not less than 4.5 and not more than 7.5.

(v) Its oxacillin content is not less than 81.5 percent and not more than 95.0 percent.

(vi) It is crystalline.

(vii) It gives a positive identity test for the oxacillin moiety.

(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 potency, moisture, pH, oxacillin content, crystallinity, and identity.

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

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 5.0 micrograms of oxacillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) [Reserved]

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

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using a solution containing 30 milligrams per milliliter.

(5) *Oxacillin content.* Place approximately 60 milligrams of sample, accurately weighed, into a 100-milliliter volumetric flask. Dissolve and fill to volume with distilled water. Pipette a 5.0-milliliter aliquot of the sample solution into a 22- by 200-millimeter test tube, and add 5 milliliters of 10 *N* NaOH. Mix the solution, and place the tube in a boiling water bath for 60 minutes. Cool the tube, carefully add 10 milliliters of 6 *N* HCl, mix, and replace the tube in the boiling water bath for 10 minutes. Position the tube in the bath so that the liquid level in the tube is the same as the liquid level in the bath. After heating, remove the tube from the bath, carefully agitate the contents of the tube, and cool to room temperature. Quantitatively transfer the contents of the tube to a 250-milliliter volumetric flask. Add approximately 200 milliliters of freshly boiled and cooled distilled water, then 4.0 milliliters of 7.5 *N* NH₄OH, and dilute to volume with freshly boiled and cooled distilled water. Treat a sample of the oxacillin working standard in the same manner. Determine the absorbance of the sample and working standard solutions on a suitable spectrophotometer at 235 nanometers against a reagent blank, and calculate as follows:

$$\text{Percent oxacillin} = \frac{\text{Absorbance of sample} \times \text{Weight in milligrams of standard} \times \text{oxacillin content of standard in percent}}{\text{Absorbance of standard} \times \text{Weight in milligrams of sample}}$$

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

(7) *Identity.* Use the sample solution prepared as described in paragraph (b)(5) of this section and record the ultraviolet spectrum between 230 nanometers and 260 nanometers. It

should be basically identical to that of the standard similarly treated.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59858, Nov. 22, 1977; 49 FR 5096, Feb. 10, 1984; 50 FR 19918, 19919, May 13, 1985]

§ 440.49a Sterile oxacillin sodium monohydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality,*