

and purity. Sterile 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) It is sterile.
- (iii) It is nonpyrogenic.
- (iv) [Reserved]
- (v) Its moisture content is not less than 3.5 and not more than 5.0 percent.
- (vi) Its pH in an aqueous solution containing 30 milligrams per milliliter is not less than 4.5 and not more than 7.5.
- (vii) Its oxacillin content is not less than 81.5 percent and not more than 95.0 percent.
- (viii) It is crystalline.
- (ix) 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, sterility, pyrogens, moisture, pH, oxacillin content, crystallinity, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams, plus one package containing approximately 2 grams.

(b) For sterility testing: 20 packages, each containing approximately 600 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) *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 20 milligrams of oxacillin 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 a solution containing 30 milligrams per milliliter.

(7) *Oxacillin content.* Proceed as directed in § 440.49(b)(5).

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

(9) *Identity.* Proceed as directed in § 440.49(b)(7).

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

§ 440.55a Sterile penicillin G benzathine.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Penicillin G benzathine is the *N,N*-dibenzylethylenediamine salt of penicillin G. It is so purified and dried that:

(i) Its potency is not less than 1,090 units and not more than 1,272 units per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not less than 5.0 percent and not more than 8 percent.

(vi) Its pH in a 1:1 mixture of absolute ethyl alcohol and water containing 0.5 milligram per milliliter is not less than 4.0 and not more than 6.5.

(vii) Its penicillin G content is not less than 57.9 percent and not more than 71.6 percent.

(viii) 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 potency, sterility, pyrogens, moisture, pH, penicillin G content, and crystallinity.

(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 600 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Use either of the following methods; however, the results obtained from the iodometric 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 measured representative portion of the sample in sufficient absolute methyl alcohol to give a solution of convenient concentration. Immediately, further dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

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

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, medium F in lieu of medium E, and during the period of incubation shake the tubes at least once daily.

(3) *Pyrogens.* Proceed as directed in §436.32(d) of this chapter, using a solution containing 4,000 units of penicillin G 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, except prepare the sample as follows: Dissolve 50 milligrams of sample with 50 milliliters of absolute ethyl alcohol. Add 50 milliliters of distilled water and mix well.

(7) *Penicillin G content.* Accurately weigh approximately 50 milligrams of the sample, dissolve in absolute methyl alcohol, and dilute to 100 milliliters with absolute methyl alcohol. Treat a portion of the working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and absolute methyl alcohol as the blank, determine the absorbance at 263 nanometers. Calculate the percent penicillin G as follows:

$$\text{Percent penicillin G} = \frac{\text{Absorbance of sample} \times \text{weight in milligrams of standard} \times \text{percent penicillin G in standard}}{\text{Absorbance of standard} \times \text{weight in milligrams of sample}}$$

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

[42 FR 59858, Nov. 22, 1977, as amended at 45 FR 16472, Mar. 14, 1980; 49 FR 6092, Feb. 17, 1984; 50 FR 19918, 19919, May 13, 1985]

§ 440.71 Penicillin V.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Penicillin V is 3,3-dimethyl-7-oxo-6-(2-phenoxyacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 1,525 units nor more than 1,780 units per milligram.

(ii) [Reserved]

(iii) Its moisture content is not more than 2.0 percent.

(iv) Its pH in a saturated aqueous solution is not less than 2.5 and not more than 4.0.

(v) Its penicillin V content is not less than 90 percent and not more than 105 percent.

(vi) It is crystalline.

(2) *Labeling.* In addition to the labeling requirements of §432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement "For