

$$\text{Percent methicillin} = \frac{\text{Absorbance of sample} \times \text{weight of working standard} \times \text{volume of sample solution} \times \text{percent methicillin in working standard}}{\text{Absorbance of standard} \times \text{weight of sample} \times \text{volume of standard solution}}$$

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

(9) *Identity*. Using the sample solution prepared as described in paragraph (b)(7) of this section, determine the absorbancies at the absorption maximum at 280 nanometers and at the absorption minimum at 264 nanometers. The ratio of the two

<sup>A280/A264</sup>

should be not less than 1.30 and not more than 1.45.

[39 FR 18976, May 30, 1974, as amended at 40 FR 15089, Apr. 4, 1975; 42 FR 59858, Nov. 22, 1977; 50 FR 19918, May 13, 1985]

**§ 440.37a Sterile mezlocillin sodium monohydrate.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Sterile mezlocillin sodium monohydrate is the monohydrate sodium salt of (2*S*, 5*R*, 6*R*)-3,3-dimethyl-6-[(*R*)-2-[3-(methylsulfonyl)-2-oxo-1-imidazolidine-carboxamido]-2-phenylacetamido]-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid. It is so purified and dried that:

(i) It contains not less than 838 micrograms and not more than 978 micrograms of mezlocillin per milligram on an anhydrous basis. If it is packaged for dispensing, its mezlocillin content is not less than 90 percent and not more than 115 percent of the number of milligrams of mezlocillin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 6.0 percent.

(vi) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 4.5 and not more than 8.0.

(vii) The specific rotation in an aqueous solution containing 10 milligrams

of mezlocillin per milliliter at 25° C is 185°±10°.

(viii) It gives a positive identity test for mezlocillin.

(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, specific rotation, and identity.

(ii) Samples required:

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

(1) For all tests except sterility: 10 packages, each containing approximately 300 milligrams; and 5 packages, each containing approximately 1 gram.

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

(b) If it is packaged for dispensing:

(1) For all tests except sterility: A minimum of 15 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*. Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay*. Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except:

(a) *Buffer*. In lieu of the buffer described in § 442.40(b)(1)(ii)(b)(2) of this chapter, use the buffer prepared as follows: Dissolve 200 grams of primary standard tris (hydroxymethyl) aminomethane in sufficient distilled water to make 1 liter. Filter before use.

(b) *Preparation of working standard solution*. Dissolve and dilute an accurately weighed portion of the

mezlocillin working standard with sufficient distilled water to obtain a concentration of 2.0 milligrams of mezlocillin per milliliter.

(c) *Preparation of sample solution.* Dissolve an accurately weighed portion of the sample with sufficient distilled water to obtain a stock solution of convenient concentration; also, if packaged for dispensing, reconstitute as directed in the labeling using distilled water in lieu of the reconstituting fluid. 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 potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to a concentration of 2.0 milligrams of mezlocillin per milliliter (estimated).

(d) *Calculations—(1)* Calculate the mezlocillin content in micrograms per milligram as follows:

$$\text{Micrograms of mezlocillin per milligram of sample} = \frac{A_u \times P_a}{A_s \times W_u}$$

where:

- $A_u$ =Absorbance of sample solution;
- $P_a$ =Potency of working standard solution in micrograms per milliliter;
- $A_s$ =Absorbance of working standard solution;
- $W_u$ =Milligrams of sample per milliliter of sample solution.

(2) Calculate the mezlocillin content of the single-dose vial as follows:

$$\text{Milligrams of mezlocillin per single-dose vial} = \frac{A_u \times P_a \times d}{A_s \times 1,000}$$

where:

- $A_u$ =Absorbance of sample solution;
- $P_a$ =Potency of working standard solution in micrograms per milliliter;
- $A_s$ =Absorbance of working standard solution;
- $d$ =Dilution factor of the sample.

(3) Calculate the mezlocillin content of the multiple-dose vial as follows:

$$\text{Milligrams of mezlocillin per multiple-dose vial} = \frac{A_u \times P_a \times d}{A_s \times 1,000 \times n}$$

where:

- $A_u$ =Absorbance of sample solution;
- $P_a$ =Potency of working standard solution in micrograms per milliliter;
- $A_s$ =Absorbance of working standard solution;
- $d$ =Dilution factor of the sample;
- $n$ =Volume of sample solution assayed.

(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)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(b) of this chapter, using a solution containing 100 milligrams of mezlocillin 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 100 milligrams of mezlocillin per milliliter.

(7) *Specific rotation.* Dilute an accurately weighed sample with sufficient distilled water to obtain a concentration of approximately 10 milligrams of mezlocillin per milliliter. Proceed as directed in §436.210 of this chapter, using a 1-decimeter polarimeter tube.

(8) *Identity.* Proceed as directed in §436.311 of this chapter, diluting the sample with distilled water to a concentration of 4 milligrams of mezlocillin per milliliter, except:

(i) Use the mezlocillin working standard and dilute with distilled water to a concentration of 4 milligrams of mezlocillin per milligram;

(ii) In lieu of the ninhydrin spray solution, after the plate is dried with a current of warm air, expose the plate to iodine vapors for about 30 seconds; and

(iii) Mezlocillin has an  $R_f$  value of about 0.67.

[46 FR 58298, Dec. 1, 1981, as amended at 50 FR 19918, 19919, May 13, 1985]

**§ 440.41 Nafcillin sodium monohydrate.**

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