

the flask for 5 minutes. Dilute to volume and mix well. Transfer a 5-milliliter aliquot of the stock solution to a 50-milliliter glass-stoppered centrifuge tube. (The solution will be slightly turbid.) Add 15 milliliters of phosphate-citrate buffer and 20 milliliters of 4-methyl-2-pentanone to the tube. Stopper the tube and shake it for 10 seconds. Centrifuge at 2,000 revolutions per minute to separate the phases. Remove about 15 milliliters of the upper phase and proceed as directed in § 436.300(e) of this chapter.

(ii) *Calculations.* Calculate the carbenicillin content (potency) of the tablets as follows:

$$\text{Milligrams of carbenicillin per tablet} = \frac{(\text{Degrees of rotation of sample solution} \times \text{weight of working standard} \times \text{average tablet weight} \times 100 \times \text{micrograms of carbenicillin in each milligram of the working standard})}{(\text{Degrees of rotation of working standard} \times \text{weight of sample} \times 25 \times 1,000)}$$

where:

100 and 25=The volume of the sample and working standard solutions, respectively;

1,000=Factor to correct micrograms to milligrams.

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

(3) *Identity.* Proceed as directed in § 436.301 of this chapter, preparing the sample as follows: Using a mortar and pestle, grind a representative number of tablets into a fine powder. Dissolve a weighed amount of this powder in sufficient extraction solvent (described in § 436.301(b)(1) of this chapter) to give 10 milligrams of carbenicillin per milliliter. Shake the mixture for 5 minutes and promptly dilute an aliquot in extraction solvent to obtain a final concentration of 1 milligram carbenicillin per milliliter.

(4) *Disintegration time.* Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(2) of that section.

[39 FR 18976, May 30, 1974, as amended at 50 FR 19919, May 13, 1985]

§ 440.115 Cloxacillin sodium monohydrate oral dosage forms.

§ 440.115a Cloxacillin sodium monohydrate capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cloxacillin sodium monohydrate capsules are composed of cloxacillin sodium and one or more suitable and harmless diluents and lubricants. Each capsule contains cloxacillin sodium monohydrate equivalent to 125 milligrams, 250 milligrams, or 500 milligrams of cloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cloxacillin that it is represented to contain. Its moisture content is not more than 5 percent. The cloxacillin sodium monohydrate used conforms to the standards prescribed by § 440.15(a)(1).

(2) *Labeling.* In addition to the labeling requirements of § 432.5 of this chapter, this drug shall be labeled "cloxacillin sodium capsules".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The cloxacillin sodium monohydrate used in making the batch for potency, moisture, pH, cloxacillin content, identity, and crystallinity.

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The cloxacillin sodium monohydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay—(1) Potency—(i) Sample preparation.* Place a representative number of capsules into a high-speed glass blender jar containing sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes.

(ii) *Assay procedure.* Use either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(a) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 5 micrograms of cloxacillin per milliliter (estimated).

(b) *Iodometric assay.* Proceed as directed in § 436.204 of this subchapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this subchapter.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59861, Nov. 22, 1977; 50 FR 19919, May 13, 1985]

§ 440.115b Cloxacillin sodium monohydrate for oral solution.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cloxacillin sodium monohydrate for oral solution is a mixture of sodium cloxacillin with one or more suitable and harmless colorings, flavorings, buffer substances, and preservatives. When reconstituted as directed in the labeling, each milliliter contains the equivalent of 25 milligrams or 50 milligrams of cloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cloxacillin that it is represented to contain. Its moisture content is not more than 1 percent. When reconstituted as directed in its labeling, its pH is not less than 5.0 nor more than 7.5. The cloxacillin sodium monohydrate used conforms to the standards prescribed by § 440.15(a)(1).

(2) *Labeling.* In addition to the labeling requirements of § 432.5 of this chapter, this drug shall be labeled “cloxacillin sodium for oral solution”.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The cloxacillin sodium monohydrate used in making the batch

for potency, moisture, pH, cloxacillin content, identity, and crystallinity.

(b) The batch for potency, moisture, and pH.

(ii) Samples required:

(a) The cloxacillin sodium monohydrate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay—(1) Potency—(i) Sample preparation.* Reconstitute the sample as directed in the labeling. Dilute an accurately measured representative aliquot of the sample with sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration.

(ii) *Assay procedures.* Use either of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(a) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 5 micrograms of cloxacillin per milliliter (estimated).

(b) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(2) *Moisture.* Proceed as directed in § 436.201 of this subchapter.

(3) *pH.* Proceed as directed in § 436.202 of this subchapter, using the drug reconstituted as directed in its labeling.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59861, Nov. 22, 1977; 43 FR 9800, Mar. 10, 1978; 50 FR 19919, May 13, 1985]

§ 440.117 Cyclacillin oral dosage forms.

§ 440.117a Cyclacillin tablets.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cyclacillin tablets are composed of cyclacillin with one or more suitable and harmless diluents, lubricants, colorings, and disintegrants. Each tablet contains 250 or 500 milligrams of cyclacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of