

the number of milligrams of cyclacillin that it is represented to contain. Its moisture content is not more than 5 percent. The tablets disintegrate within 15 minutes. It gives a positive identity test for cyclacillin. The cyclacillin used conforms to the standards prescribed by § 440.17(a)(1).

(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:

(a) The cyclacillin used in making the batch for potency, moisture, pH, cyclacillin content, concordance, crystallinity, and identity.

(b) The batch for potency, moisture, disintegration time, and identity.

(ii) Samples required:

(a) The cyclacillin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay*—(1) *Potency.* Use any 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: Place a representative number of tablets into a high-speed glass blender jar with sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of cyclacillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, preparing the sample solution as follows: Place a representative number of tablets in a high-speed glass blender jar and add sufficient distilled water to give a convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot with distilled water to the prescribed concentration.

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

working standard and sample solutions and calculate the potency of the sample as follows:

(a) *Preparation of working standard solution.* Dissolve and dilute an accurately weighed portion of the cyclacillin working standard in sufficient distilled water to obtain a concentration of 1.25 milligrams of cyclacillin per milliliter.

(b) *Preparation of sample solution.* Place one tablet into a high-speed glass blender jar and add sufficient distilled water to obtain a concentration of 1.25 milligrams of cyclacillin per milliliter. Blend for 3 to 5 minutes. Filter, if necessary.

(c) *Calculations.* Calculate the cyclacillin content in milligrams per tablet as follows:

$$\text{Milligrams of cyclacillin per 5 milliliters of sample} = \frac{A_u \times P_a \times d}{A_s \times 1,000}$$

where:

A_u =Absorbance of sample solution;

P_a =Potency of working standard in micrograms per milliliter;

A_s =Absorbance of working standard solution;

d =Dilution factor of the sample.

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

(3) *Disintegration time.* Proceed as directed in § 436.212 of this chapter, using the procedure in paragraph (e)(1) of that section, except do not use discs.

(4) *Identity.* Proceed as directed in § 436.327 of this chapter, preparing the sample as follows: Dissolve a representative portion of finely powdered tablets with sufficient 0.1N sodium hydroxide to obtain a solution containing 1 milligram of cyclacillin per milliliter. Allow the sample solution to stand for 15 minutes before using.

[46 FR 2985, Jan. 13, 1981; 46 FR 15880, Mar. 10, 1981, as amended at 50 FR 19919, May 13, 1985]

§ 440.117b Cyclacillin for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cyclacillin for oral suspension is a mixture of cyclacillin with one or more suitable and harmless colorings, flavorings, buffer substances, sweetening ingredients, preservatives,

and suspending agents. When reconstituted as directed in the labeling, it contains either 25 milligrams, 50 milligrams, or 100 milligrams of cyclacillin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cyclacillin that it is represented to contain. Its moisture content is not more than 1.5 percent. When reconstituted as directed in the labeling, its pH is not less than 4.5 and not more than 6.5. It gives a positive identity test for cyclacillin. The cyclacillin used conforms to the standards prescribed by § 440.17(a)(1).

(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:

(a) The cyclacillin used in making the batch for potency, moisture, pH, cyclacillin content, concordance, crystallinity, and identity.

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

(ii) Samples required:

(a) The cyclacillin used in making the batch: 10 packages, each containing approximately 500 milligrams.

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

(b) *Tests and methods of assay—(1) Potency.* Assay for potency by any 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: Reconstitute the drug as directed in the labeling. Place an accurately measured representative portion of the sample into a suitable volumetric flask and dilute to volume with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a convenient concentration. Mix well. Further dilute an aliquot with solution 3 to the reference concentration of 1.0 microgram of cyclacillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, preparing the sample as follows: Reconstitute the drug as directed in the label-

ing. Place an accurately measured representative portion of the sample into an appropriate-sized volumetric flask and dilute to volume with 1 percent potassium phosphate buffer, pH 6.0 (solution 1). Mix well. Further dilute with solution 1 to the prescribed concentration.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except prepare the working standard and sample solutions and calculate the potency of the sample as follows:

(a) *Preparation of working standard solution.* Dissolve and dilute an accurately weighed portion of the cyclacillin working standard in sufficient distilled water to obtain a concentration of 1.25 milligrams of cyclacillin per milliliter.

(b) *Preparation of sample solution.* Reconstitute the sample as directed in the labeling. Place an accurately measured aliquot of the sample into an appropriate-sized volumetric flask and dilute to volume with distilled water to yield a concentration of 1.25 milligrams of cyclacillin per milliliter. Mix well. Filter, if necessary.

(c) *Calculations.* Calculate the cyclacillin content as follows:

$$\frac{\text{Milligrams of cyclacillin per 5 milliliters of sample}}{A_s \times 1,000} = \frac{A_u \times P_a \times d}{A_s \times 1,000}$$

where:

A_u =Absorbance of sample solution;

P_a =Potency of working standard in micrograms per milliliter;

A_s =Absorbance of working standard solution;

d =Dilution factor of the sample.

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

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

(4) *Identity.* Proceed as directed in § 436.327 of this chapter, preparing the sample as follows: Dilute an accurately measured representative portion of the reconstituted suspension with 0.1N sodium hydroxide to obtain a solution containing 1 milligram of cyclacillin

per milliliter. Allow the sample solution to stand 45 minutes before using.

[46 FR 2985, Jan. 13, 1981; 46 FR 15880, Mar. 10, 1981, as amended at 50 FR 19919, May 13, 1985]

§ 440.119 Dicloxacillin sodium monohydrate oral dosage forms.

§ 440.119a Dicloxacillin sodium monohydrate capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Dicloxacillin sodium monohydrate capsules are composed of dicloxacillin sodium monohydrate and one or more suitable diluents and lubricants. Each capsule contains dicloxacillin sodium monohydrate equivalent to 62.5, 125, 250, or 500 milligrams of dicloxacillin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of dicloxacillin that it is represented to contain. The moisture content is not more than 5 percent. The dicloxacillin sodium monohydrate conforms to the requirements of § 440.19(a)(1).

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

(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:

(a) The dicloxacillin sodium monohydrate used in making the batch for potency, moisture, pH, organic chlorine content, free chloride content, crystallinity, and identity.

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The dicloxacillin sodium monohydrate used in making the batch: 10 containers, each containing not less than 500 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 min-

utes. Remove an aliquot and further dilute with solution 1 to the reference concentration of 5.0 micrograms of dicloxacillin per milliliter (estimated) for the microbiological agar diffusion assay and to the prescribed concentration for the iodometric assay.

(ii) *Assay procedure.* Assay for potency by 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.

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

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

[39 FR 18976, May 30, 1974, as amended at 42 FR 59861, Nov. 22, 1977; 43 FR 2393, Jan. 17, 1978; 44 FR 10379, Feb. 20, 1979; 50 FR 19919, May 13, 1985]

§ 440.119b Dicloxacillin sodium monohydrate for oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Dicloxacillin sodium monohydrate for oral suspension is a mixture of dicloxacillin sodium monohydrate with one or more suitable colorings, flavorings, buffer substances, and preservatives. When reconstituted as directed in the labeling, it contains the equivalent of 12.5 or 25 milligrams of dicloxacillin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of dicloxacillin that it is represented to contain. Its moisture content is not more than 2 percent. The pH of the suspension, when reconstituted as directed in the labeling, is not less than 4.5 nor more than 7.5. The dicloxacillin sodium monohydrate used conforms to the requirements of § 440.19(a)(1).

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

(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 assay on: