

Further dilute an aliquot of this solution with distilled water to 1 milligram of cephradine per milliliter (estimated).

(b) *Calculations.* Calculate the cephradine content as follows:

$$\text{Milligrams per tablet} = \frac{A_u \times P_s \times d}{A_s \times 1,000 \times n}$$

where:

- A_u =Absorbance of sample solution;
- P_s =Potency of working standard in micrograms per milligram;
- d =Dilution factor for sample;
- A_s =Absorbance of working standard solution;
- n =Number of tablets in the sample assayed.

(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 described in paragraph (e)(1) of that section.

[45 FR 22919, Apr. 4, 1980, as amended at 50 FR 19919, May 13, 1985]

§ 442.141 Cephradine dihydrate capsules.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cephradine dihydrate capsules are composed of cephradine dihydrate and one or more suitable and harmless lubricants and diluents enclosed in a gelatin capsule. Each capsule contains 250 milligrams or 500 milligrams of cephradine. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cephradine that it is represented to contain. Its moisture content is not more than 11.0 percent. It passes the dissolution test if the quantity Q is 85 percent at 60 minutes. The cephradine dihydrate used conforms to the standards prescribed by § 442.41(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 cephradine dihydrate used in making the batch for potency, mois-

ture, pH, cephalixin content, identity, and crystallinity.

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

(ii) Samples required:

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

(b) The batch: A minimum of 100 capsules.

(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) *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 capsules into a high-speed glass blender jar containing sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute and aliquot of the stock solution with solution 1 to the reference concentration of 10.0 micrograms of cephradine per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii), except prepare the sample solution and calculate the cephradine content as follows:

(a) *Preparation of sample solution.* Blend a representative number of capsules in a high-speed glass blender jar with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of this solution with distilled water to a concentration of 1 milligram of cephradine per milliliter (estimated).

(b) *Calculations.* Calculate the cephradine content as follows:

$$\text{Milligrams per capsule} = \frac{A_u \times P_s \times d}{A_s \times 1,000 \times n}$$

where:

- A_u =Absorbance of sample solution;
- P_s =Potency of working standard in micrograms per milligram;
- d =Dilution factor for sample;
- A_s =Absorbance of working standard solution;
- n =Number of capsules in the sample assayed.

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

(3) *Dissolution*. Proceed as directed in § 436.541 of this chapter, except:

(i) A distance of 2.5 ± 0.2 centimeters should be maintained between the lower edge of the stirring blade and the lowest inner surface of the vessel during test rather than 4.5 ± 0.5 centimeters as specified in paragraph (a) of that section; and

(ii) In lieu of paragraph (d) of that section, use the interpretation described in the United States Pharmacopeia XX dissolution test.

[47 FR 11857, Mar. 19, 1982, as amended at 50 FR 19919, May 13, 1985]

§ 442.154 Cefpodoxime proxetil oral dosage forms.

§ 442.154a Cefpodoxime proxetil tablets.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Cefpodoxime proxetil tablets are composed of cefpodoxime proxetil and one or more suitable and harmless diluents, binders, lubricants, colorings, and coating substances. Each tablet contains cefpodoxime proxetil equivalent to either 100 milligrams or 200 milligrams of cefpodoxime. Its cefpodoxime proxetil content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefpodoxime that it is represented to contain. Its loss on drying is not more than 5 percent. It passes the dissolution test. It passes the identity test. The cefpodoxime proxetil used conforms to the standards prescribed by § 442.54(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 cefpodoxime proxetil used in making the batch for potency, isomer ratio, moisture, and identity.

(B) The batch for content, loss on drying, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefpodoxime proxetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay—(1) Cefpodoxime content*. Proceed as directed in § 442.54(b)(1), preparing the sample solution and calculating the cefpodoxime content as follows:

(i) *Preparation of sample solution*. Obtain the average tablet weight of at least 20 tablets. Grind the tablets using a mortar and pestle. Weigh approximately 660 milligrams into a suitable container. Add 30 milliliters of internal standard solution. Shake for 30 minutes using a horizontal platform shaker or equivalent. Centrifuge for about 10 minutes at 3,000 revolutions per minute until the particulate matter has settled. Withdraw a 1 milliliter aliquot of the supernatant and dilute with 9 milliliters of dilution solvent. The sample solutions are stable for at least 48 hours. Refrigeration is not recommended.

(ii) *Calculations*. Calculate the cefpodoxime content as follows:

$$\text{Milligrams of cefpodoxime per tablet} = \left(R_{sam} / R_{std} \right) \times \left(W_{std} / W_{sam} \right) \times \left(F_1 / F_3 \right) \times F_2 \times F_4 \times P$$

where:

R_{sam} = Ratio of cefpodoxime proxetil peaks area (sum of both epimers) to the internal standard peak area in the sample preparation;

R_{std} = Ratio of cefpodoxime proxetil peaks

area (sum of both epimers) to the internal standard peak area in the standard preparation;

W_{std} = Weight of cefpodoxime proxetil reference standard, in milligrams;

W_{sam} = Weight of sample, in milligrams;