

milliliter of cefprozil (estimated). Filter through a 0.45 micron filter prior to injection into the chromatographic system.

(i) *Calculations.* Calculate the cefprozil content as follows:

$$\frac{\text{Milligrams of cefprozil (Z) or cefprozil (E) per 5 milliliters of sample}}{\text{Milligrams of cefprozil (Z)/5 mL sample}} = \frac{A_u \times P_s \times d \times 5}{A_s \times 1,000 \times V} + \frac{\text{Milligrams of cefprozil (E)/5 mL sample}}{\text{Milligrams of cefprozil (E)/5 mL sample}}$$

where:

A_u = Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s = Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the cefprozil (Z) or the cefprozil (E) working standard;

P_s = Cefprozil (Z) or cefprozil (E) activity in the cefprozil (Z) or the cefprozil (E) working standard solution in micrograms per milliliter;

d = Dilution factor of the sample; and

V = Volume of sample taken in milliliters.

(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 constituted as directed in the labeling.

(4) *Identity*—(i) *High Performance liquid chromatography.* Using the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the responses of the active ingredients must be within 2 percent of the retention times for the responses of the corresponding reference standards.

(ii) *Thin layer chromatography.* Proceed as directed in § 436.368 of this chapter.

[58 FR 26661, May 4, 1993]

Subpart C—Injectable Dosage Forms

§ 442.208 Cefamandole nafate for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefamandole nafate for injection is a dry mixture of cefamandole nafate and one or more suitable and harmless buffering agents. The

cefamandole nafate may be isolated in the manufacture of cefamandole nafate for injection. Its cefamandole content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefamandole that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 3.0 percent. Its pH is not less than 6.0 and not more than 8.0. If isolated, the cefamandole nafate used conforms to the standards prescribed by § 442.8a(a)(1). If the cefamandole nafate is not isolated, the potency of the dry mixture is not less than 810 micrograms and not more than 1,000 micrograms of cefamandole per milligram on an anhydrous basis when corrected for sodium carbonate; and the dry mixture gives a positive identity test.

(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) If isolated, the cefamandole nafate used in making the batch for cefamandole content, moisture, pH, and identity.

(b) The batch for cefamandole content, sterility, pyrogens, moisture, and pH. In addition, if the cefamandole nafate is not isolated, results of tests and assays on the dry mixture for potency and identity.

(ii) Samples required:

(a) For all tests except sterility: A minimum of 10 immediate containers, unless the cefamandole nafate is not isolated, a minimum of 15 immediate containers.

(b) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefamandole content.* Proceed as directed in § 436.324 of this chapter, preparing the sample solution and calculating the cefamandole content as follows:

(i) *Sample preparation.* Reconstitute the sample as directed in the labeling.

If it is represented as a single dose container, remove all of the withdrawable contents with a suitable hypodermic needle and syringe. If the labeling specifies the amount of cefamandole content in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Further dilute an aliquot of this solution with distilled water to obtain a concentration of 2.0 milligrams of cefamandole per milliliter (estimated). Transfer 5 milliliters of this solution to a 50-milliliter volumetric flask, add 30 milliliters of pH 2.3 buffer, dilute to volume with distilled water, and mix. In addition, if the

cefamandole nafate is not isolated, prepare the sample solution as described in §436.324(d) of this chapter. Determine the sodium carbonate content as follows: Dissolve an accurately weighed portion of the dry mixture, approximately 1.0 gram, with approximately 100 milliliters of distilled water. Titrate with 0.2*N* hydrochloric acid. Determine the end-point potentiometrically to the first equivalent using a glass calomel combination electrode. Each milliliter of 0.2*N* hydrochloric acid is equivalent to 21.2 milligrams of sodium carbonate.

(ii) *Calculations*—(a) Calculate the cefamandole content as follows:

$$\text{Milligrams of cefamandole} = \frac{A \times \text{Potency of working} \times \text{standard in micrograms} \times f}{B \times 50 \times 1,000}$$

$\frac{\text{Milligrams of cefamandole} \times \text{working standard.}}{\text{Potency of working standard. per milligram}}$

where:

A=The peak height of the sample;

B=The peak height of the working standard; and

f=The dilution factor of the sample.

(b) If the cefamandole nafate is not isolated in the manufacture of cefamandole nafate for injection, calculate the micrograms of cefamandole per milligram of sample as described in §436.324(f) of this chapter. The micrograms per milligram of cefamandole is corrected for sodium carbonate content and moisture content.

(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 50 milligrams of cefamandole 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 per milliliter, except determine the pH 30 min-

utes after preparation of the sample solution.

(7) *Identity*. Proceed as directed in §436.323 of this chapter.

[44 FR 20665, Apr. 6, 1979, as amended at 47 FR 42099, Sept. 24, 1982; 50 FR 19919, May 13, 1985]

§ 442.209 Cefamandole sodium for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Cefamandole sodium for injection is a dry mixture of cefamandole sodium and one or more suitable and harmless buffering agents. Its cefamandole content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefamandole that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 3.0 percent. Its pH is not less than 6.0 and not more than 8.5. The cefamandole sodium used conforms to the standards prescribed by §442.9a(a)(1).

(2) *Labeling*. It shall be labeled in accordance with the requirements of §432.5 of this chapter.