

A_s =Area of the cefpiramide peak in the chromatogram of the cefpiramide working standard;

P_s =Cefpiramide activity in the cefpiramide working standard solution in micrograms per milliliter; and

d =Dilution factor of the sample.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in § 436.20(e)(1).

(3) *Pyrogens*. Proceed as directed in § 436.32(b) of this chapter, using a solution containing 50 milligrams of cefpiramide per milliliter.

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

(5) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Identify*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefpiramide working standard.

[55 FR 14242, Apr. 17, 1990]

§ 442.270 Cefmetazole injectable dosage forms.

§ 442.270a Sterile cefmetazole sodium.

The requirements for certification and the tests and methods of assay for sterile cefmetazole sodium packaged for dispensing are described in § 442.70a.

[55 FR 6636, Feb. 26, 1990]

§ 442.270b Cefmetazole sodium injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Cefmetazole sodium injection is a frozen, aqueous, iso-osmotic solution of cefmetazole and sodium citrate. It contains one or more suitable and harmless buffer substances and a tonicity adjusting agent. Each milliliter contains cefmetazole sodium equivalent to 20 milligrams or 40 milligrams of cefmetazole per milliliter. Its cefmetazole content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of cefmetazole that it is represented to contain. It is sterile. It contains not more than 0.2 endotoxin units per milligram. Its pH is not less than 4.2 and not more than 6.2. It

passes the identity test. The cefmetazole used conforms to the standards prescribed by § 442.69(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 cefmetazole used in making the batch for potency, moisture, and identity.

(B) The batch for potency, sterility, bacterial endotoxins, pH, and identity.

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

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

(B) The batch:

(1) For all tests except sterility: A minimum of 12 immediate containers.

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

(b) *Tests and methods of assay*. Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) *Cefmetazole potency*. Proceed as directed in § 442.70a(b)(1), except prepare the sample solution and calculate the cefmetazole content as follows:

(i) *Preparation of sample solution*. Using a suitable hypodermic needle and syringe, remove an accurately measured portion from each container immediately after thawing and reaching room temperature and dilute with mobile phase to obtain a solution containing 500 micrograms of cefmetazole per milliliter (estimated). Prepare the sample solution just prior to its introduction into the chromatograph.

(ii) *Calculation*. Calculate the milligrams of cefmetazole per milliliter of sample as follows:

$$\text{Milligrams of cefmetazole per milliliter} = \frac{A_U \times P_s \times d}{A_s \times 1,000}$$

where:

A_U =Area of the cefmetazole peak in the chromatogram of the - sample (at a retention time equal to that observed for the standard);

A_S =Area of the cefmetazole peak in the chromatogram of the cefmetazole working standard;

P_S =Cefmetazole activity in the cefmetazole working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

(2) *Sterility*. Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Bacterial endotoxins*. Proceed as directed in the United States Pharmacopeia bacterial endotoxins test.

(4) *pH*. Proceed as directed in §436.202 of this chapter, using the undiluted solution.

(5) *Identity*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefmetazole working standard.

[59 FR 12546, Mar. 17, 1994]

PART 443—CARBACEPHEM ANTIBIOTIC DRUGS

Subpart A—Bulk Drugs

Sec.

443.20 Loracarbef.

Subpart B—Oral Dosage Forms

443.120 Loracarbef oral dosage forms.

443.120a Loracarbef capsules.

443.120b Loracarbef for oral suspension.

AUTHORITY: 21 U.S.C. 357.

SOURCE: 58 FR 26667, May 4, 1993, unless otherwise noted.

Subpart A—Bulk Drugs

§443.20 Loracarbef.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity*. Loracarbef is the monohydrate form of (6*R*,7*S*)-7-[(*R*)-2-amino-2-phenylacetamido]-3-chloro-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 960 micrograms and not more than 1,020 micrograms of loracarbef activity per milligram, on an anhydrous basis.

(ii) Its moisture content is not less than 3.5 percent and not more than 6.0 percent.

(iii) The pH of an aqueous slurry containing 100 milligrams per milliliter is not less than 3.5 and not more than 5.5.

(iv) Its specific rotation in an 0.1 *N* HCl solution containing 10 milligrams of loracarbef per milliliter at 25° C is +27° to +33° on an anhydrous basis.

(v) It is crystalline.

(vi) It 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 the batch for loracarbef potency, moisture, pH, specific rotation, crystallinity, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay—(1) Potency*. Proceed as directed in §436.216 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 265 nanometers, a 25-centimeter by 4.6-millimeter (inside diameter) column packed with microparticulate (5 micrometers in diameter) reversed phase packing material such as octadecyl silane bonded to silicas, a flow rate of 1.5 milliliters per minute, and a known injection volume between 10 and 20 microliters. The retention time for loracarbef is between 10 and 13 minutes. Mobile phase, working standard, sample and resolution test solutions, system suitability requirements, and calculations are as follows:

(i) *Mobile phase*. Dissolve 2.0 grams of pentanesulfonic acid sodium salt monohydrate in 1,560 milliliters of water. Add 20 milliliters of triethylamine. Adjust the pH to 2.5 with phosphoric acid. Add 440 milliliters of methanol and mix. Filter the mobile phase through a suitable filter capable of removing particulate matter 0.5 micron in diameter and degas it just prior to its introduction into the chromatograph.