§ 442.222 Cefmenoxime hydrochloride for injection.

(a) Requirements for certification—(1) Standards of identity, strength, quality, and purity. Cefmenoxime hydrochloride for injection is a dry mixture of cefmenoxime hydrochloride and sodium carbonate. Each milligram of cefmenoxime hydrochloride for injection contains not less than 869 and not more than 1,015 micrograms of cefmenoxime on an anhydrous and sodium carbonate-free basis. Its cefmenoxime content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of cefmenoxime that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 1.5 percent. Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 6.4 and not more than 7.9. The cefmenoxime hydrochloride used in making the batch forms a dry mixture of the cefmenoxime working standard, accurately weighed, in 10 milligrams of the cefmenoxime working standard, accurately weighed, in 10 milligrams.

(b) The batch for cefmenoxime content, moisture, identity, and crystallinity.

(i) Reagents—(A) 0.1M Phosphate buffer solution, pH 6.8. Dissolve 6.4 grams of monobasic potassium phosphate and 18.9 grams of dibasic sodium phosphate in 750 milliliters of water. Adjust the pH to 6.8 with 1N sodium hydroxide and dilute to 1,000 milliliters.

(B) Internal standard solution. Dissolve and dilute 0.15 gram of phthalimide in methanol to 100 milliliters.

(C) Mobile phase. Mix water:acetonitrile:glacial acetic acid (50:10:1). Filter through a suitable filter capable of removing particulate matter to 0.5 micron in diameter. Degas the mobile phase just prior to its introduction into the chromatograph.


(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 cefmenoxime hydrochloride used in making the batch for cefmenoxime content, moisture, identity, and crystallinity.

(B) The batch for cefmenoxime content, sterility, pyrogens, loss on drying, pH, and sodium carbonate content.

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

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

(B) The batch:

(1) For all tests except sterility: A minimum of 10 immediate containers.

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

§ 442.220 Sterile cefonicid sodium.

The requirements for certification and the tests and methods of assay for sterile cefonicid sodium packaged for dispensing are described in §442.20a.

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milliliters of 0.1M phosphate buffer solution, pH 6.8 and dilute to 50 milliliters with mobile phase. Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter.

(B) Sample solutions. Determine both micrograms of cefmenoxime per milligram of the sample and milligrams of cefmenoxime per container. Use separate containers for preparation of each sample solution as described in paragraphs (b)(1)(ii)(B) (1) and (2) of this section.

(1) Micrograms of cefmenoxime per milligram. Dissolve the accurately weighed dry contents of a sample with sufficient distilled water to obtain a solution containing 1 milligram of cefmenoxime per milliliter (estimated). Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter (estimated).

(2) Milligrams of cefmenoxime per container. Reconstitute the sample as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the solution thus obtained with sufficient distilled water to obtain a solution containing 1 milligram of cefmenoxime per milliliter (estimated). Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter (estimated).

(iii) System suitability requirements—
(A) Tailing factor. The tailing factor (T) for the cefmenoxime peak is satisfactory if it is not more than 1.6 at 5 percent of peak height.

(B) Efficiency of the column. The efficiency of the column (n) is satisfactory if it is greater than 1,200 theoretical plates for the cefmenoxime peak.

(C) Resolution. The resolution (R) between the peak for cefmenoxime and phthalimide is satisfactory if it is not less than 2.3.

(D) Coefficient of variation. The coefficient of variation (S in percent) of 5 replicate injections is satisfactory if it is not more than 2.0 percent. If the system suitability requirements have been met, then proceed as described in §436.363(b) of this chapter.

(iv) Calculations—(A) Micrograms per milligram. Calculate the micrograms of cefmenoxime per milligram as follows:

\[
\text{Micrograms of cefmenoxime per milligram} = \frac{T \times R_u \times P_s \times 100 \times d}{R_s \times C_u \times (100 - L - S)}
\]

where:
- \(R_u\) = Area of the cefmenoxime peak in the chromatogram of the sample/Area of internal standard peak;
- \(R_s\) = Area of the cefmenoxime peak in the chromatogram of the cefmenoxime working standard/Area of internal standard peak;
- \(P_s\) = Cefmenoxime activity in the cefmenoxime working standard solution in micrograms per milliliter;
- \(C_u\) = Milligrams of sample per milliliter of sample solution;
- \(d\) = Dilution factor of the sample;
- \(L\) = Percent loss on drying (determined as directed in paragraph (b)(4) of this section); and
- \(S\) = Percent sodium carbonate (determined as directed in paragraph (b)(6) of this section).

(B) Milligrams of cefmenoxime per vial. Calculate the cefmenoxime content of the vial as follows:

\[
\text{Milligrams of cefmenoxime per vial} = \frac{R_v \times P_v \times d}{R_s \times 1,000}
\]

where:
- \(R_v\) = Area of the cefmenoxime peak in the chromatogram of the sample/Area of internal standard peak;
- \(R_s\) = Area of the cefmenoxime peak in the chromatogram of the cefmenoxime working standard/Area of internal standard peak;
- \(P_v\) = Cefmenoxime activity in the cefmenoxime working standard solution in micrograms per milliliter; and
- \(d\) = Dilution factor of the sample.
§ 442.225b Sterile cephalothin sodium injection.

(a) Requirements for certification—(1) Standards of identity, strength, quality, and purity. Cephalothin sodium injection is a frozen aqueous solution of cephalothin sodium with one or more suitable and harmless buffer substances. It may contain sodium chloride or dextrose. Each milliliter contains cephalothin sodium equivalent to 20 milligrams, 40 milligrams, or 100 milligrams of cephalothin. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cephalothin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 6.0 and not more than 8.5. The cephalothin sodium used conforms to the standards prescribed by § 442.25(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 cephalothin sodium used in making the batch for potency, loss on drying, pH, specific rotation, identity, and crystallinity.

(b) The batch for potency, sterility, pyrogens, and pH.

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of 10 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 ampoule contents as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) Potency. Use either of the following methods; however, the results obtained from the microbiological agar diffusion 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: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion from each container and dilute with sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 microgram of cephalothin per milliliter (estimated).

(ii) Hydroxylamine colorimetric assay. Proceed as directed in § 436.205 of this chapter, preparing the sample as follows: Using a suitable hypodermic needle and syringe, remove an accurately measured representative portion from each container and dilute with distilled...