Assay—[NOTE—Protect the *Standard preparation,* the *Resolution solution*, and the *Assay preparations* from light, and use within 2 hours.]

Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Cefotetan*.

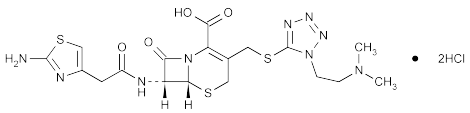
Assay preparation—Transfer about 40 mg of Cefotetan Disodium, accurately weighed, to a 200-mL volumetric flask, add 10 mL of methanol, swirl for several minutes, add 10 mL of acetonitrile, and swirl until dissolved. Dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Cefotetan*. Calculate the quantity, in µg, of cefotetan ($C_{17}H_{17}N_7O_8S_4$) per mg in the portion of Cefotetan Disodium taken by the formula:

$$200(CP / M)(r_U / r_S)$$

in which the terms are as defined therein.

Cefotiam Hydrochloride



$C_{18}H_{23}N_9O_4S_3 \cdot 2HCl$ 598.56

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7[[-(2-amino-4-thiazolyl)acetyl]-amino]-3-[[[1-[2-(dimethylamino)ethyl]-1*H*-tetrazol-5-yl]-thio]methyl]-8-oxo, hydrochloride, (6*R-trans*)-.

(6*R,7R*)-7-[2-(2-Amino-4-thiazolyl)acetamido]-3-[[[1-[2-(dimethylamino)ethyl]-1*H*-tetrazol-5-yl]thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid dihydrochloride.

7(*R*)-[2-(2-Amino-4-thiazolyl)acetamido]-3-[[[1-[2-dimethylamino)ethyl]-1*H*-tetrazol-5-yl]thio]methyl]-3-cephem-4-carboxylic acid dihydrochloride [66309-69-1].

» Cefotiam Hydrochloride contains the equivalent of not less than 790 µg and not more than 925 µg of cefotiam ($C_{18}H_{23}N_9O_4S_3$) per mg, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards ⟨11⟩**—**
USP Cefotiam Hydrochloride RS

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 20 µg per mL.

Medium: water.

B: The retention time of the cefotiam peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation* as obtained in the *Assay*.

Crystallinity ⟨695⟩: meets the requirements.

Pyrogen—Where the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements of the *Pyrogen Test* ⟨151⟩, the test dose being 1.0 mL per kg of a solution in pyrogen-free sodium carbonate solution (prepared by dissolving 25.6 g of sodium carbonate, previously heated at 170 ° for not less than 4 hours, in 1000 mL of Sterile W ater for Injection) containing 40 mg per mL.

Sterility ⟨71⟩**—**Where the label states that it is sterile, it meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

Water, *Method I* ⟨921⟩: not more than 7.0%, the *Test Preparation* being prepared as directed for a hygroscopic specimen, except to use a mixture of 20 mL of formamide (previously dried over anhydrous sodium sulfate for 24 hours) and methanol (2:1), instead of methanol, to dissolve the specimen, and to determine the water content of the formamide and methanol mixture.

Assay—

Mobile phase—Dissolve 13.1 g of ammonium sulfate in 850 mL of water, adjust with 2 N ammonium hydroxide to a pH of 6.5 ± 0.1, add 150 mL of acetonitrile, and mix. Filter through a suitable filter of 0.5 µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Cefotiam Hydrochloride RS , quantitatively in water to obtain a solution having a known concentration of about 1000 µg of cefotiam ($C_{18}H_{23}N_9O_4S_3$) per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains the equivalent of about 50 µg of cefotiam ($C_{18}H_{23}N_9O_4S_3$) per mL. Use this solution without delay.

Assay preparation—Transfer about 60 mg of Cefotiam Hydrochloride, accurately weighed, to a 50-mL volumetric flask, add water to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Use this solution without delay.

System suitability solution—Prepare a solution of USP Cefotiam Hydrochloride RS in water containing about 1 mg per mL. Heat this solution at 95 ° for 3 minutes, and cool. Transfer 1 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 25-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the column efficiency, determined from the cefotiam peak, is not less than 1985 theoretical plates when calculated by the formula:

$$5.545(t_r / W_{h/2})^2$$

the tailing factor for the cefotiam peak is not more than 1.8, and the relative standard deviation for replicate injections is not more than 1.0%. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for de-tetrazol-cefotiam and 1.0 for cefotiam; and the resolution, *R,* between the de-tetrazol-cefotiam peak and the cefotiam peak is not less than 4.0.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in µg, of cefotiam ($C_{18}H_{23}N_9O_4S_3$) in each mg of the Cefotiam Hydrochloride taken by the formula:

$$1000(C/W)(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of cefotiam ($C_{18}H_{23}N_9O_4S_3$) in the *Standard preparation*, based on the quantity of USP Cefotiam Hydrochloride RS taken to prepare the *Standard preparation*, the designated cefotiam ($C_{18}H_{23}N_9O_4S_3$) content, in µg per mg, of USP Cefotiam Hydrochloride RS , and the extent of dilution; *W* is the weight, in mg, of Cefotiam Hydrochloride taken to prepare the *Assay preparation*; and r_U and r_S are the cefotiam peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Cefotiam for Injection

» Cefotiam for Injection contains an amount of Cefotiam Hydrochloride equivalent to not less than 90.0 percent and not more than 120.0 percent of the labeled amount of cefotiam ($C_{18}H_{23}N_9O_4S_3$). It may contain Sodium Carbonate.

Packaging and storage—Preserve in *Containers for Sterile Solids* as described under *Injections* ⟨1⟩.

USP Reference standards ⟨11⟩**—**
USP Cefotiam Hydrochloride RS

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 20 µg per mL.

Medium: water.

B: The retention time of the cefotiam peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*; as obtained in the *Assay*.

Pyrogen—It meets the requirements of the *Pyrogen Test* ⟨151⟩, the test dose being 1.0 mL per kg of a solution prepared by diluting Cefotiam for Injection with Sterile W ater for Injection to a concentration of 40 mg of cefotiam per mL.

Sterility ⟨71⟩**—**It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

pH ⟨791⟩: between 5.7 and 7.2, in a solution containing the equivalent of 100 mg of cefotiam per mL.

Loss on drying ⟨731⟩**—**Dry about 100 mg, accurately weighed, in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 6.0% of its weight.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Assay—

Mobile phase, *Standard preparation, System suitability solution*, and *Chromatographic system*—Prepare as directed in the *Assay* under *Cefotiam Hydrochloride.*

Assay preparation 1 (where it is represented as being in a single-dose container)—Constitute a container of Cefotiam for Injection in a volume of water, accurately measured, corresponding to the volume of diluent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute quantitatively with water to obtain a solution containing the equivalent of about 1 mg of cefotiam ($C_{18}H_{23}N_9O_4S_3$) per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains the equivalent of about 50 µg of cefotiam per mL. Use this solution without delay.

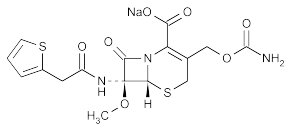
Assay preparation 2 (where the label states the quantity of cefotiam in a given volume of constituted solution)—Constitute a container of Cefotiam for Injection in a volume of water, accurately measured, equivalent to the volume of diluent specified in the labeling. Dilute an accurately measured volume of the constituted solution quantitatively with water to obtain a solution containing about 1 mg of cefotiam ($C_{18}H_{23}N_9O_4S_3$) per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains the equivalent of about 50 µg of cefotiam per mL. Use this solution without delay.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Cefotiam Hydrochloride.* Calculate the quantity, in mg, of cefotiam ($C_{18}H_{23}N_9O_4S_3$) withdrawn from the container, or in the portion of constituted solution taken by the formula:

$$C(L / D)(r_U / r_S)$$

in which C is the concentration, in µg per mL, of cefotiam ($C_{18}H_{23}N_9O_4S_3$) in the *Standard preparation,* based on the quantity of USP Cefotiam Hydrochloride RS taken to prepare the *Standard preparation,* the designated cefotiam ($C_{18}H_{23}N_9O_4S_3$) content, in µg per mg, of USP Cefotiam Hydrochloride RS , and the extent of dilution; L is the labeled quantity, in mg, of cefotiam ($C_{18}H_{23}N_9O_4S_3$) in the container, or in the volume of constituted solution taken; D is the concentration, in µg of cefotiam per mL, of *Assay preparation 1* or *Assay preparation 2*, based on the labeled quantity in the container or in the volume of constituted solution taken, respectively, and the extent of dilution; and r_U and r_S are the cefotiam peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Cefoxitin Sodium



$C_{16}H_{16}N_3NaO_7S_2$ 449.44

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(aminocarbonyl)oxy]methyl]-7-methoxy-8-oxo-7-[(2-thienylacetyl)-amino]-, sodium salt (6 *R-cis*)-.

Sodium (6 *R,7S*)-3-(hydroxymethyl)-7-methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate carbamate (ester) [33564-30-6; 35607-66-0].

» Cefoxitin Sodium contains the equivalent of not less than 927 µg and not more than 970 µg of cefoxitin ($C_{16}H_{17}N_3O_7S_2$) per mg, corresponding to not less than 97.5 per cent and not more than 102.0 percent of cefoxitin sodium ($C_{16}H_{16}N_3NaO_7S_2$), calculated on the anhydrous and acetone- and methanol-free basis.

Packaging and storage—Preserve in tight containers, and store in a cold place.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards ⟨11⟩**—**
USP Cefoxitin RS
USP Endotoxin RS

Identification—

A: The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits a major peak for cefoxitin, the retention time of which corresponds to that exhibited in the chromatogram of the *Standard preparation* obtained as directed in the *Assay*.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 20 µg per mL.

Medium: phosphate buffer (prepared by dissolving 1.0 g monobasic potassium phosphate and 1.8 g of anhydrous dibasic sodium phosphate in water to make 1000 mL).

C: A solution (1 in 20) responds to the tests for *Sodium* ⟨191⟩.

Specific rotation ⟨781S⟩: between +206° and +214°, calculated on the anhydrous and acetone- and methanol-free basis.