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.

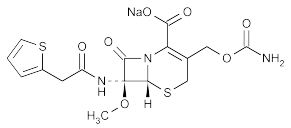
Assay preparation 2 (where the label states the quantity of cefotiam in a given volume of constituted solution)—Constitute a container of Cefotiam for Injection in a volume of water, accurately measured, equivalent to the volume of diluent specified in the labeling. Dilute an accurately measured volume 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.

Test solution: 10 mg per mL, in methanol.

Crystallinity ⟨695⟩: meets the requirements.

pH ⟨791⟩: between 4.2 and 7.0, in a solution containing 100 mg per mL.

Water, *Method I* ⟨921⟩: not more than 1.0%, a mixture of ethylene glycol and pyridine (3:1) being used in place of methanol in the titration vessel.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Limit of acetone and methanol—

Standard preparation—Transfer 5.0 mL of acetone to a 1000-mL volumetric flask, dilute with water to volume, and mix (*Solution A*). Transfer 5.0 mL of methanol to a 1000-mL volumetric flask, dilute with water to volume, and mix (*Solution B*). Transfer 50.0 mL of *Solution A* and 5.0 mL of *Solution B* to a 500-mL volumetric flask, dilute with water to volume, and mix to obtain a solution having concentrations of acetone and methanol of 0.050% and 0.005% (v/v), respectively.

Test preparation—Transfer 5.0 g of Cefoxitin Sodium to a 50-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Transfer 3.0 mL of the resulting solution to a 15-mL centrifuge tube, cool in an ice-water bath for 2 minutes, and add 3.0 mL of 0.24 N hydrochloric acid while swirling vigorously. Centrifuge to obtain a clear solution (*Test preparation*).

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector, and contains a 1.8-m × 6.3-mm glass column containing support S2, and a pre-column packed with 60- to 80-mesh silane-treated glass beads. The injection port is maintained at 100°, the columns are maintained at 110 °, the detector is maintained at 200 °, and nitrogen is used as the carrier gas at a flow rate of about 50 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure*: the column efficiency determined from the acetone and methanol peaks is not less than 160 and 200 theoretical plates, respectively; the tailing factors for the acetone and methanol peaks are not more than 1.3 and 2.3, respectively; and the relative standard deviation for replicate injections is not more than 5%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] Separately inject equal volumes (about 2 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph, record the chromatograms, and measure the acetone and methanol peak responses. Calculate the per centages of acetone and methanol in the Cefoxitin Sodium taken by the same formula:

$$DP/C(r_U / r_S)$$

in which *D* is the density of acetone and methanol at 20 ° in g per mL; *P* is the per centage (v/v) of acetone or methanol in the *Standard preparation*; *C* is the concentration, in g per mL, of Cefoxitin Sodium in the *Test preparation*; and r_U and r_S are the acetone or methanol peak responses of the *Test preparation* and the *Standard preparation*, respectively: not more than 0.7% of acetone and 0.1% of methanol are found.

Other requirements—Where the label states that Cefoxitin Sodium is sterile, it meets the requirements for *Sterility* and *Bacterial endotoxins* under *Cefoxitin for Injection*. Where the label states that Cefoxitin Sodium must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for *Bacterial endotoxins* under *Cefoxitin for Injection*.

Assay—

Mobile phase—Prepare a suitable mixture of water, acetonitrile, and glacial acetic acid (840:160:10), filter through a membrane filter (1 µm or finer porosity), and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Phosphate buffer—Dissolve 1.0 g of monobasic potassium phosphate and 1.8 g of dibasic sodium phosphate in 900 mL of water, adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 7.1 ± 0.1, dilute with water to make 1000 mL, and mix. Filter through a membrane filter of 1 µm or finer porosity.

Standard preparation—Dissolve an accurately weighed quantity of USP Cefoxitin RS in *Phosphate buffer* to obtain a solution having a known concentration of about 0.3 mg per mL. [NOTE—Sonicate, if necessary, to dissolve the specimen.] Use this solution within 5 hours.

Assay preparation—Transfer about 150 mg of Cefoxitin Sodium, accurately weighed, to a 500-mL volumetric flask, dissolve in and dilute with *Phosphate buffer* to volume, and mix. Use this solution within 5 hours.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains 5- to 10- µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure*: the column efficiency determined from the analyte peak is not less than 2800 theoretical plates, the tailing factor for the analyte peak is not more than 1.5, and the relative standard deviation for replicate injections is not more than 1.0%.

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 responses for the major peaks. Calculate the quantity, in µg, of cefoxitin ($C_{16}H_{17}N_3O_7S_2$) per mg of the Cefoxitin Sodium taken by the formula:

$$500(CP / W)(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Cefoxitin RS in the *Standard preparation*; *P* is the potency, in µg per mg, of USP Cefoxitin RS; *W* is the quantity, in mg, of Cefoxitin Sodium taken to prepare the *Assay preparation*; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Cefoxitin Injection

» Cefoxitin Injection is a sterile solution of Cefoxitin Sodium and one or more suitable buffer substances in Water for Injection. It contains Dextrose or Sodium Chloride as a tonicity-adjusting agent. It contains the equivalent of not less than 90.0 percent and not more than 120.0 per cent of the labeled amount of cefoxitin ($C_{16}H_{17}N_3O_7S_2$).

Packaging and storage—Preserve in *Containers for Injections* as described under *Injections* ⟨1⟩. Maintain in the frozen state.

Labeling—It meets the requirements for *Labeling* under *Injections* ⟨1⟩. The label states that it is to be thawed just prior to use, describes conditions for proper storage of the resultant solution, and directs that the solution is not to be refrozen.

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

Identification—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*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.13 USP Endotoxin Unit per mg of cefoxitin.

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