Assay preparation 1 (where it is represented as being in a single-dose container)—Constitute Ceftizoxime for Injection in a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute quantitatively with *pH 7.0 Buffer* to obtain a solution containing about 1 mg of ceftizoxime per mL. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, add 5.0 mL of *Internal standard solution*, dilute with *pH 7.0 Buffer* to volume, and mix.

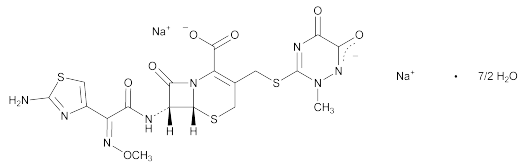
Assay preparation 2 (where the label states the quantity of ceftizoxime in a given volume of constituted solution)—Constitute Ceftizoxime for Injection in a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. Dilute an accurately measured volume of the constituted solution quantitatively with *pH 7.0 Buffer* to obtain a solution containing about 1 mg of ceftizoxime per mL. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, add 5.0 mL of *Internal standard solution*, dilute with *pH 7.0 Buffer* to volume, and mix.

Procedure—Proceed with Ceftizoxime for Injection as directed for *Procedure* in the *Assay* under *Ceftizoxime Sodium*. Calculate the quantity, in mg, of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$) withdrawn from the container, or in the portion of constituted solution taken by the formula:

$$(L / D)(C)(R_U / R_S)$$

in which L is the labeled quantity, in mg of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$), in the container, or in the volume of constituted solution taken, and D is the concentration, in mg of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$) per mL, of *Assay preparation 1* or *Assay preparation 2*, based on the labeled quantity in the container or in the portion of constituted solution taken, respectively; and the extent of dilution, C is the concentration, in mg of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$) per mL, of the *Standard preparation*; and R_U and R_S are the peak response ratios of the ceftizoxime peak to the internal standard peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Ceftriaxone Sodium



$C_{18}H_{16}N_8Na_2O_7S_3 \cdot 3^1/_2H_2O$ 661.60

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-8-oxo-3-[[(1,2,5,6-tetrahydro-2-methyl-5-, 6-dioxo-1,2,4-triazin-3-yl)thio]methyl]-, disodium salt, [6*R*-[6α,7β(*Z*)]]-, hydrate, (2:7).

(6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-[[(1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-*as*-triazin-3-yl)thio]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7²-(*Z*)-(O-methyloxime), disodium salt, sesquaterhydrate [104376-79-6].

Anhydrous 598.56

» Ceftriaxone Sodium contains the equivalent of not less than 795 µg of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) 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 Ceftriaxone Sodium RS
USP Ceftriaxone Sodium *E*-Isomer RS
USP Endotoxin RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

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

C: It responds to the tests for *Sodium* ⟨191⟩.

Crystallinity ⟨695⟩: meets the requirements.

pH ⟨791⟩: between 6.0 and 8.0 in a solution (1 in 10).

Water, *Method I* ⟨921⟩: between 8.0% and 11.0%.

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

Assay—

pH 7.0 Buffer—Dissolve 13.6 g of dibasic potassium phosphate and 4.0 g of monobasic potassium phosphate in water to obtain 1000 mL of solution. Adjust this solution with phosphoric acid or 10 N potassium hydroxide to a pH of 7.0 ± 0.1.

pH 5.0 Buffer—Dissolve 25.8 g of sodium citrate in 500 mL of water, adjust with citric acid solution (1 in 5) to a pH of 5.0 ± 0.1, and dilute with water to a volume of 1000 mL.

Mobile phase—Dissolve 3.2 g of tetraheptylammonium bromide in 400 mL of acetonitrile, add 44 mL of *pH 7.0 Buffer* and 4 mL of *pH 5.0 Buffer*, and add water to make 1000 mL. Filter through a membrane 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 Ceftriaxone Sodium RS in *Mobile phase*, to obtain a solution having a known concentration of about 0.2 mg per mL. Use this solution promptly after preparation.

Resolution solution—Dissolve a suitable quantity of USP Ceftriaxone Sodium E-Isomer RS in *Standard preparation*, and dilute with *Mobile phase* to obtain a solution containing about 160 µg of USP Ceftriaxone Sodium E-Isomer RS per mL and 160 µg of USP Ceftriaxone Sodium RS per mL. Use this solution promptly after preparation.

Assay preparation—Transfer about 40 mg of Ceftriaxone Sodium, accurately weighed, to a 200-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Use this solution promptly after preparation.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 270-nm detector and a 4.0-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Resolution solution*, and record the peak responses as directed under *Procedure:* the resolution, *R,* between the ceftriaxone E-isomer and ceftriaxone peaks is not less than 3. 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 1500 theoretical plates; the tailing factor for the analyte peak is not more than 2; and the relative standard deviation for replicate injections is not more than 2%.

Procedure—Separately inject equal volumes (about 20 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

ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) per mg of the Ceftriaxone Sodium taken by the formula:

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

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

Ceftriaxone Injection

» Ceftriaxone Injection is a sterile solution of Ceftriaxone Sodium in a diluent containing one or more tonicity-adjusting agents in W ater for Injection. It contains the equivalent of not less than 90.0 percent and not more than 115.0 per cent of the labeled amount of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$).

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 Ceftriaxone Sodium RS
USP Ceftriaxone Sodium *E*-Isomer RS
USP Endotoxin RS

Identification—The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits a major peak for ceftriaxone, 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 0.20 USP Endotoxin Unit per mg of ceftriaxone.

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 6.0 and 8.0.

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

Assay—

pH 7.0 Buffer, pH 5.0 Buffer, Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Prepare as directed in the *Assay* under *Ceftriaxone Sodium.*

Assay preparation—Allow 1 container of Injection to thaw, and mix. Transfer an accurately measured volume of the Injection, equivalent to about 40 mg of ceftriaxone, to a 200-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Use this solution promptly after preparation.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Ceftriaxone Sodium.* Calculate the quantity, in mg, of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) in each mL of the Injection taken by the formula:

$$200(C / V)(r_U / r_S)$$

in which *V* is the volume, in mL, of Injection taken; and the other terms are as defined therein.

Ceftriaxone for Injection

» Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to not less than 776 µg of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) per mg, calculated on the anhydrous basis, and the equivalent of not less than 90.0 per cent and not more than 115.0 per cent of the labeled amount of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$).

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

USP Reference standards ⟨11⟩**—**
USP Ceftriaxone Sodium RS
USP Ceftriaxone Sodium *E*-Isomer RS
USP Endotoxin RS

Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* ⟨1⟩.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.20 USP Endotoxin Unit per mg of ceftriaxone.

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

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

Other requirements—It responds to the *Identification* tests and meets the requirements for *Crystallinity*, *pH*, and *Water* under *Ceftriaxone Sodium.* It meets also the requirements for *Uniformity of Dosage Units* ⟨905⟩ and for *Labeling* under *Injections* ⟨1⟩.

Assay—

pH 7.0 Buffer, pH 5.0 Buffer, Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Prepare as directed in the *Assay* under *Ceftriaxone Sodium.*

Assay preparation 1—Transfer about 40 mg of Ceftriaxone for Injection, accurately weighed, to a 200-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Use this solution promptly after preparation.

Assay preparation 2 (where it is represented as being in a single-dose container)—Constitute Ceftriaxone for Injection in a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. W ithdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute quantitatively with *Mobile phase* to obtain a solution containing about 180 µg of ceftriaxone per mL. Use this solution promptly after preparation.

Assay preparation 3 (where the label states the quantity of ceftriaxone in a given volume of constituted solution)—Constitute Ceftriaxone for Injection in a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. Dilute an accurately measured volume of the constituted solution quantitatively with *Mobile phase* to obtain a solution containing about 180 µg of ceftriaxone per mL. Use this solution promptly after preparation.

Procedure—Proceed as directed in the *Assay* under *Ceftriaxone Sodium.* Calculate the quantity, in µg, of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) per mg of the Ceftriaxone for Injection taken by the formula:

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

in which *C* is the concentration, in mg per mL, of USP Ceftriaxone Sodium RS in the *Standard preparation; P* is the designated potency, in µg, of ceftriaxone per mg of USP Ceftriaxone Sodium RS; *W* is the quantity, in mg, of Ceftriaxone for Injection taken to prepare *Assay preparation 1;* and r_U and r_S are the ceftriaxone peak responses obtained from *Assay preparation 1* and the *Standard preparation,* respectively. Calculate the quantity, in mg, of ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) withdrawn from the