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

Assay—

pH 7 Buffer—Dissolve 42.59 g of anhydrous dibasic sodium phosphate and 27.22 g of monobasic potassium phosphate in water to make 1000 mL of solution.

Mobile phase—Mix 40 mL of acetonitrile and 200 mL of *pH 7 Buffer*, and dilute with water to obtain 2000 mL of solution. Filter, using a filter having a porosity of 1 µm or finer, and degas. Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 29 mg of USP Ceftazidime Pentahydrate RS, accurately weighed, to a 25-mL volumetric flask containing 2.5 mL of *pH 7 Buffer,* and shake until dissolved. Dilute with water to volume, and mix. [NOTE—Protect this solution from light.] Immediately prior to chromatography, transfer 5.0 mL of this stock solution to a 50-mL volumetric flask, dilute with water to volume, and mix. This solution contains about 100 µg of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) per mL.

Assay preparation—Transfer about 115 mg of Ceftazidime, accurately weighed, to a 100-mL volumetric flask containing 10.0 mL of *pH 7 Buffer,* and shake until dissolved. Dilute with water to volume, and mix. [NOTE—Protect this solution from light.] Immediately prior to chromatography, transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix.

Resolution solution—Prepare a solution of USP Ceftazidime, Delta-3-Isomer RS in *pH 7 Buffer* containing about 0.1 mg per mL. Immediately prior to chromatography, mix 1 mL of this solution with 8 mL of water and 1 mL of the stock solution used to prepare the *Standard preparation.*

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-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 for *Procedure:* the resolution, *R,* between ceftazidime and ceftazidime, delta-3-isomer is not less than 2.0. Chromatograph the *Standard preparation,* and record the responses as directed for *Procedure:* the tailing factor for the analyte peak is not less than 0.75 and 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 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 mg, of $C_{22}H_{22}N_6O_7S_2$ in the portion of Ceftazidime taken by the formula:

$$C(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Ceftazidime Injection

» Ceftazidime Injection is a sterile isoosmotic solution of Ceftazidime in W ater for Injection. It contains one or more suitable buffers and a tonicity-adjusting agent. It contains not less than 90.0 percent and not more than 120.0 per cent of the labeled amount of $C_{22}H_{22}N_6O_7S_2$.

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 Ceftazidime Delta-3-Isomer RS
USP Ceftazidime Pentahydrate RS
USP Endotoxin RS

Identification—The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits a major peak for ceftazidime, 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 0.1 USP Endotoxin Unit per mg of ceftazidime.

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 5.0 and 7.5.

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

Assay—

pH 7 Buffer, Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Ceftazidime.*

Assay preparation—Allow a container of the Injection to thaw, and mix the solution. T ransfer an accurately measured volume of the Injection, equivalent to about 50 mg of ceftazidime, to a 50-mL volumetric flask, dilute with *pH 7 buffer* to volume, and mix. Transfer 5.0 mL of this solution to a second 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Ceftazidime.* Calculate the quantity, in mg, of $C_{22}H_{22}N_6O_7S_2$ in each mL of the Injection taken by the formula:

$$0.5(C / V)(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) in the *Standard preparation; V* is the volume, in mL, of Injection taken; and r_U and r_S are the ceftazidime peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Ceftazidime for Injection

» Ceftazidime for Injection is a sterile mixture of Sterile Ceftazidime and Sodium Carbonate or Arginine. It contains not less than 90.0 per cent and not more than 105.0 per cent of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) on the dried and sodium carbonate- or arginine-free basis, and not less than 90.0 percent and not more than 120.0 per cent of the labeled amount of ceftazidime ($C_{22}H_{22}N_6O_7S_2$).

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

USP Reference standards ⟨11⟩**—**
USP L-Arginine RS
USP Ceftazidime Delta-3-Isomer RS
USP Ceftazidime Pentahydrate RS
USP Endotoxin RS

Identification—

A: The chromatograms of the *Assay preparations* exhibit a major peak for ceftazidime, the retention time of which corre-

sponds to that in the chromatogram of the *Standard preparation.*

B: It dissolves in 1 N hydrochloric acid with effervescence, evolving a colorless gas, which when passed into *calcium hydroxide TS* produces a white precipitate immediately.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.1 USP Endotoxin Unit per mg of ceftazidime.

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 5.0 and 7.5, in a solution constituted in the sealed container, taking care to relieve the pressure inside the container during constitution, containing 100 mg of ceftazidime per mL.

Loss on drying ⟨731⟩**—**Dry about 300 mg, accurately weighed, in vacuum at a pressure not exceeding 5 mm of mercury at 25° for 4 hours: where it contains arginine, it loses not more than 12.5% of its weight. Where it contains sodium carbonate, it loses not more than 13.5% of its weight. Where it contains arginine, use the percentage loss obtained, *m*, to calculate, on the dried and arginine-free basis, the result from *Assay preparation 1* obtained as directed in the *Assay.* Where it contains sodium carbonate, heat the residue in vacuum at a pressure not exceeding 5 mm of mercury at 100° an additional 3 hours, and calculate the total percentage of weight loss. Use this percentage, *m*, to calculate, on the dried and sodium carbonate-free basis, the result from *Assay preparation 1* obtained as directed in the *Assay.*

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

Sodium carbonate *(where present)—*

Potassium chloride solution—Dissolve 19.07 g of potassium chloride in water to make 1000 mL of solution.

Standard preparation—Dissolve a suitable quantity of sodium chloride, previously dried at 105° for 2 hours and accurately weighed, in water to obtain a solution having a known concentration of about 14 µg per mL. Transfer 10 mL of this solution to a 100-mL volumetric flask, add 10.0 mL of *Potassium chloride solution,* dilute with water to volume, and mix.

Test preparation—Use the stock solution used to prepare *Assay preparation 1* in the *Assay,* diluting it quantitatively, and stepwise if necessary, with water to obtain a solution containing about 12.5 µg of sodium carbonate per mL. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, add 10.0 mL of *Potassium chloride solution,* dilute with water to volume, and mix.

Blank solution—Transfer 10.0 mL of *Potassium chloride solution* to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Concomitantly determine the absorbances of the *Standard preparation* and the *Test preparation* at the sodium emission line of 589.0 nm, with a suitable atomic absorption spectrophotometer (see *Spectrophotometry and Light-Scattering* ⟨851⟩) equipped with a sodium hollow-cathode lamp and an air–acetylene flame, using the *Blank solution* as the blank. Calculate the percentage of sodium carbonate (Na_2CO_3) in the portion of Ceftazidime for Injection taken by the formula:

$$(105.99/116.88)(0.1C/M)(A_U / A_S)$$

in which 105.99 is the molecular weight of sodium carbonate; 116.88 is twice the molecular weight of sodium chloride; *C* is the concentration, in µg per mL, of sodium chloride in the *Standard preparation; M* is the quantity, in mg, of Ceftazidime for Injection in each mL of the *Test preparation,* based on the quantity taken to prepare the stock solution and the extent of dilution; and A_U and A_S are the absorbances of the *Test preparation* and the *Standard preparation,* respectively. Use this percentage to calculate, on the dried and sodium carbonate-free basis, the result from *Assay preparation 1* obtained as directed in the *Assay.*

Limit of pyridine—

Mobile phase—Mix 300 mL of acetonitrile and 100 mL of 0.25 M monobasic ammonium phosphate, dilute with water to obtain 1000 mL of solution, and adjust with ammonium hydroxide to a pH of 7.0 ± 0.1. Pass this solution through a filter having a 1-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

pH 7 Buffer—Dissolve 5.68 g of anhydrous dibasic sodium phosphate and 3.63 g of monobasic potassium phosphate in water to make 1000 mL of solution.

Standard solution—Transfer about 250 mg of pyridine, accurately weighed, to a 100-mL volumetric flask, dilute with water to volume, and mix. Immediately prior to chromatography, transfer 2.0 mL of this solution to a 200-mL volumetric flask, dilute with *pH 7 Buffer* to volume, and mix. This solution contains about 25 µg of pyridine per mL.

Test solution—Transfer about 660 mg of Ceftazidime for Injection, just removed from its container and accurately weighed, to a 100-mL volumetric flask, promptly add *pH 7 buffer* to volume, and mix. Store this solution in a cool place, and use it within 1 hour.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.6 mL per minute. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the tailing factor for the analyte peak is not more than 2.5; and the relative standard deviation for replicate injections is not more than 3%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas of the responses for the pyridine peaks. Calculate the percentage of pyridine in the portion of Ceftazidime for Injection taken by the formula:

$$10(C/W)(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of pyridine in the *Standard solution; W* is the weight, in mg, of Ceftazidime for Injection taken; and r_U and r_S are the pyridine peak responses obtained from the *Test solution* and the *Standard solution,* respectively: not more than 0.4% of pyridine is found where it contains sodium carbonate; and not more than 0.3% where it contains arginine.

Content of arginine *(where present)—*

Mobile phase—Dissolve 1.15 g of monobasic ammonium phosphate in about 800 mL of water. Adjust with phosphoric acid to a pH of 2.0 ± 0.1, dilute with water to 1000 mL, and mix. Prepare a filtered and degassed mixture of acetonitrile and this solution (750:250). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve accurately weighed quantities of USP Ceftazidime Pentahydrate RS and USP L-Arginine RS in water to obtain a solution containing known concentrations of about 0.2 mg of each per mL.

Test preparation—Quantitatively dissolve an accurately weighed portion of Ceftazidime for Injection in water to obtain a solution having a concentration of about 0.2 mg of ceftazidime per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 206-nm detector, a 4.6-mm × 50-cm saturator pre-column containing packing L27, and a 4-mm × 25-cm analytical column containing packing L20. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the responses as directed for *Procedure:* the resolution, *R,* between the ceftazidime and the arginine peaks is not less than 6.0; and the tailing factor for the arginine peak is not more than 4.0.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph, record the chromatograms, and measure the re-

sponses for the major peaks. Calculate the per centage of arginine ($C_6H_{14}N_4O_2$) in the Ceftazidime for Injection taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of USP L-Arginine RS in the *Standard preparation;* C_U is the concentration, in mg per mL, of Ceftazidime for Injection in the *Test preparation,* based on the weight, in mg, of Ceftazidime for Injection taken and the extent of dilution; and r_U and r_S are the arginine peak responses obtained from the *Test preparation* and the *Standard preparation,* respectively. Use this per centage to calculate, on the anhydrous and arginine-free basis, the assay result from *Assay preparation 1* obtained as directed in the *Assay.*

Other requirements—It meets the requirements for *Uniformity of Dosage Units* ⟨905⟩ and for *Labeling* under *Injections* ⟨1⟩.

Assay—

pH 7 buffer, Mobile phase, Standard preparation, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Ceftazidime*.

Assay preparation 1—Transfer an accurately weighed quantity of Ceftazidime for Injection, equivalent to about 250 mg of ceftazidime ($C_{22}H_{22}N_6O_7S_2$), to a 250-mL volumetric flask, dilute with water to volume, and mix to obtain a stock solution. [NOTE—Protect this solution from light.] Immediately prior to chromatography, transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix.

Assay preparation 2 (where it is represented as being in a single-dose container)—Constitute a container of Ceftazidime 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 water to obtain a solution containing about 1 mg of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) per mL. [NOTE—Protect this solution from light.] Immediately prior to chromatography, transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix.

Assay preparation 3 (where the label states the quantity of ceftazidime in a given volume of constituted solution)—Constitute a container of Ceftazidime 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 water to obtain a solution containing about 1 mg of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) per mL. [NOTE—Protect this solution from light.] Immediately prior to chromatography, transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Ceftazidime.* Calculate the per centage of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) on the dried and sodium carbonate-free or arginine-free basis in the portion of Ceftazidime for Injection taken by the formula:

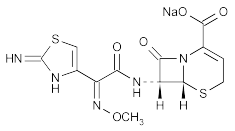
$$250{,}000[C/W\ (100 - m - s)](r_U / r_S)$$

in which C is the concentration, in µg per mL, of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) in the *Standard preparation; W* is the quantity, in mg, of Ceftazidime for Injection taken to prepare *Assay preparation 1; m* is the total per centage of loss on dr ying; *s* is the percentage of sodium carbonate or arginine in the Ceftazidime for Injection taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively. Calculate the quantity, in mg, of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) 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 ceftazidime ($C_{22}H_{22}N_6O_7S_2$) in the container, or in the volume of constituted solution taken; and D is the concentration, in µg, of ceftazidime ($C_{22}H_{22}N_6O_7S_2$) per mL, of *Assay preparation 2* or *Assay preparation 3,* based on the labeled quantity in the container or in the portion of constituted solution taken, respectively, and the extent of dilution.

Ceftizoxime Sodium



$C_{13}H_{12}N_5NaO_5S_2$ 405.39

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2,3-dihydro-2-imino-4-thiazoly)(methoxyimino)acetyl] amino]-8-oxomonosodium salt, [6*R*-[6α,7β(*Z*)]]-.

Sodium (6*R*,7*R*)-7-[2-(2-imino-4-thiazolin-4-yl)glyoxylamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate 7 [2]-(*Z*)-(*O*-methyloxime) [68401-82-1].

» Ceftizoxime Sodium contains the equivalent of not less than 850 µg and not more than 995 µg of ceftizoxime ($C_{13}H_{13}N_5O_5S_2$) 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 Ceftizoxime RS
USP Endotoxin RS

Identification—

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

B: 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⟩: not more than 8.5%.

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

Assay—

pH 3.6 Buffer—Dissolve 1.42 g of citric acid monohydrate and 1.73 g of dibasic sodium phosphate in water to obtain 1000 mL of solution.

pH 7.0 Buffer—Dissolve 3.63 g of monobasic potassium phosphate and 10.73 g of dibasic sodium phosphate in water to obtain 1000 mL of solution.

Mobile phase—Prepare a mixture of *pH 3.6 Buffer* and acetonitrile (about 9:1). Filter through a filter (1 µm or finer porosity), and degas. Adjust the composition, if necessar y, to meet the performance requirements under *Chromatographic system.*

Internal standard solution—Dissolve 1.2 g of salicylic acid in 10 mL of methanol, and dilute with *pH 7.0 Buffer* to obtain 200 mL of solution.