

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 μ g 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 Water for Injection. It contains the equivalent of not less than 90.0 percent and not more than 115.0 percent 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 μ g 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. Withdraw 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 μ g 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 μ g of ceftriaxone per mL. Use this solution promptly after preparation.

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

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

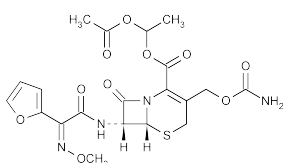
in which *C* is the concentration, in mg per mL, of USP Ceftriaxone Sodium RS in the *Standard preparation*; *P* is the designated potency, in μ g, of ceftriaxone per mg of USP Ceftriaxone Sodium RS; *W* is the quantity, in mg, of Ceftriaxone for Injection taken to prepare *Assay preparation 1*; and 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

container, or in the portion of constituted solution taken by the formula:

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

in which *L* is the labeled quantity, in mg, of ceftriaxone (C₁₈H₁₈N₈O₇S₃) in the container, or in the volume of constituted solution taken; *D* is the concentration, in μg per mL, of ceftriaxone in 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; *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; and *r_U* and *r_S* are the ceftriaxone peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Cefuroxime Axetil



C₂₀H₂₂N₄O₁₀S 510.48

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[(aminocarbonyloxy)methyl]-7-[[2-furanyl(methoxyimino)acetyl]amino]-8-oxo-, 1-(acetyloxy)ethyl ester, [6*R*-[6*α*,7*β*(*Z*)]]-.

(*RS*)-1-Hydroxyethyl (6*R*,7*R*)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7*Z*-(*Z*)-(O-methyloxime), 1-acetate 3-carbamate [64544-07-6].

» Cefuroxime Axetil is a mixture of the diastereoisomers of cefuroxime axetil (C₂₀H₂₂N₄O₁₀S). It contains the equivalent of not less than 745 μg and not more than 875 μg of cefuroxime (C₁₆H₁₆N₄O₈S) per mg, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

Labeling—Label it to indicate whether it is amorphous or crystalline.

USP Reference standards (11)—

USP Cefuroxime Axetil RS

USP Cefuroxime Axetil Delta-3 Isomers RS

Identification, Infrared Absorption (197K).

Crystallinity (695)—Particles that do not show birefringence or exhibit extinction positions are amorphous, and particles that show birefringence and exhibit extinction positions are crystalline.

Water, Method I (921): not more than 1.5%.

Diastereoisomer ratio—

0.2 *M* Monobasic ammonium phosphate, Mobile phase, Internal standard solution, Resolution solution, Standard preparation, Assay preparation, and Chromatographic system—Prepare as directed in the Assay.

Procedure—Proceed as directed for Procedure in the Assay. Calculate the ratio of cefuroxime axetil diastereoisomer A to the

sum of the cefuroxime axetil diastereoisomers A and B taken by the formula:

$$r_A/(r_A + r_B)$$

in which *r_A* and *r_B* are the peak responses of the cefuroxime axetil diastereoisomers A and B, respectively: between 0.48 and 0.55 is obtained.

Assay—

0.2 *M* Monobasic ammonium phosphate—Dissolve 23.0 g of monobasic ammonium phosphate in water to obtain 1000 mL of solution.

Mobile phase—Prepare a suitable filtered and degassed mixture of 0.2 *M* Monobasic ammonium phosphate and methanol (620: 380). Make adjustments if necessary (see System Suitability under Chromatography (621)).

Internal standard solution—Prepare a solution of acetanilide in methanol containing 5.4 mg per mL.

Resolution solution—In a 50-mL volumetric flask, mix 10.0 mL of a solution of USP Cefuroxime Axetil RS in methanol containing 1.2 mg per mL, 5.0 mL of Internal standard solution, and 3.8 mL of a solution of USP Cefuroxime Axetil Delta-3 Isomers RS in methanol containing 0.16 mg per mL. Dilute with 0.2 *M* Monobasic ammonium phosphate to volume, and mix.

Standard preparation—Transfer about 30 mg of USP Cefuroxime Axetil RS, accurately weighed, to a 25-mL volumetric flask, dissolve in methanol, dilute with methanol to volume, and mix. Promptly transfer 10.0 mL of this solution to a 50-mL volumetric flask, add 5.0 mL of Internal standard solution and 3.8 mL of methanol, dilute with 0.2 *M* Monobasic ammonium phosphate to volume, and mix. [NOTE—Use this Standard preparation promptly, or refrigerate and use on the day prepared.]

Assay preparation—Transfer about 30 mg of Cefuroxime Axetil to a 25-mL volumetric flask, dissolve in methanol, dilute with methanol to volume, and mix. Promptly transfer 10.0 mL of this solution to a 50-mL volumetric flask, add 5.0 mL of Internal standard solution and 3.8 mL of methanol, dilute with 0.2 *M* Monobasic ammonium phosphate to volume, and mix. [NOTE—Use this Assay preparation promptly, or refrigerate and use on the day prepared.]

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 278-nm detector and a 4.6-mm × 25-cm column containing 5-μm packing L13. The flow rate is about 1.5 mL per minute. Chromatograph the Resolution solution, and record the peak responses as directed for Procedure: the relative retention times are about 0.4 for acetanilide, 0.8 for cefuroxime axetil diastereoisomer B, 0.9 for cefuroxime axetil diastereoisomer A, and 1.0 for cefuroxime axetil delta-3 isomers; the resolution, *R*, between cefuroxime axetil diastereoisomer A and B is not less than 1.5; and the resolution, *R*, between cefuroxime axetil diastereoisomer A and cefuroxime axetil delta-3 isomers is not less than 1.5. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the column efficiency is not less than 3000 theoretical plates when measured using the cefuroxime axetil diastereoisomer A peak; and the relative standard deviation for replicate injections is not more than 2.0%.

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 cefuroxime (C₁₆H₁₆N₄O₈S) in each mg of Cefuroxime Axetil taken by the formula:

$$(W_S/W_U)(P_S/100)(100 - K)(R_U/R_S)$$

in which *W_S* is the weight, in mg, of USP Cefuroxime Axetil RS taken to prepare the Standard preparation; *W_U* is the weight, in mg, of Cefuroxime Axetil taken to prepare the Assay preparation; *P_S* is the designated cefuroxime (C₁₆H₁₆N₄O₈S) content, in μg per mg, of anhydrous USP Cefuroxime Axetil RS; *K* is the percentage water content of USP Cefuroxime Axetil RS; and *R_U* and *R_S* are the ratios of the sum of the peak responses of the