

## USP Aztreonam RS

Propanoic acid, 2-[[[1-(2-amino-4-thiazolyl)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidiny]amino]-2-oxoethylidene]amino]oxy]-2-methyl-, [2S-[2 $\alpha$ ,3 $\beta$ (Z)]]-  
 $C_{13}H_{17}N_5O_8S_2$  435.43

## USP Aztreonam E-Isomer RS

(E)-2-[[[2-Amino-4-thiazolyl]{{(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidiny]carbonyl}methylene]amino]oxy)-2-methylpropionic acid.  
 $C_{13}H_{17}N_5O_8S_2$  435.43

## USP Endotoxin RS

$r_s$  = peak response of aztreonam from the *Standard solution*

$C_s$  = concentration of USP Aztreonam RS in the *Standard solution* (mg/mL)

$C_u$  = nominal concentration of aztreonam in the *Sample solution* (mg/mL)

$P$  = potency of aztreonam in USP Aztreonam RS ( $\mu$ g/mg)

$F$  = conversion factor (0.001 mg/ $\mu$ g)

**Acceptance criteria:** 90.0%–120.0%

## Aztreonam Injection

### DEFINITION

Aztreonam Injection is a sterile solution of Aztreonam and Arginine and a suitable osmolality adjusting substance in Water for Injection. It contains NLT 90.0% and NMT 120.0% of the labeled amount of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ).

### IDENTIFICATION

- A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

### ASSAY

#### PROCEDURE

**Buffer:** 1.15 g/L of monobasic ammonium phosphate in water. Before final dilution, adjust with phosphoric acid to a pH of  $2.0 \pm 0.1$ .

**Mobile phase:** Acetonitrile and *Buffer* (75:25).

**System suitability solution:** 0.2 mg/mL of each of USP Aztreonam RS and USP Open Ring Aztreonam RS in *Mobile phase*

**Standard solution:** 0.2 mg/mL each of USP Aztreonam RS and USP L-Arginine RS in *Mobile phase*

**Sample solution:** Equivalent to 0.2 mg/mL of aztreonam from Injection in *Mobile phase*

#### Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

**Mode:** LC

**Detector:** UV 206 nm

**Pre-column:** 4.6-mm  $\times$  5- to 10-cm saturator precolumn containing packing L27

**Column:** 4-mm  $\times$  25-cm analytical column containing packing L20

**Flow rate:** 1 mL/min

**Injection size:** 20  $\mu$ L

#### System suitability

**Sample:** *System suitability solution*

[NOTE—The relative retention times for aztreonam and open ring aztreonam are 0.8 and 1.0, respectively. The relative retention times for aztreonam and arginine are 0.3 and 1.0, respectively.]

#### Suitability requirements

**Resolution:** NLT 2.0 between aztreonam and open ring aztreonam

**Column efficiency:** NLT 1000 theoretical plates determined from the aztreonam peak

**Tailing factor:** NMT 2.0 for the aztreonam peak

**Relative standard deviation:** NMT 2.0% for the aztreonam peak

#### Analysis

**Samples:** *Standard solution* and *Sample solution*  
 Calculate the percentage of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ) in the portion of Injection taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times P \times F \times 100$$

$r_u$  = peak response of aztreonam from the *Sample solution*

### SPECIFIC TESTS

- PYROGEN TEST** <151>: It meets the requirements, the test dose being a measured volume of Injection sufficient to provide 50 mg/kg of aztreonam.
- STERILITY TESTS** <71>: It meets the requirements when tested as directed for *Test for Sterility of the Product to be Examined, Membrane Filtration*.
- PH** <791>: 4.5–7.5
- PARTICULATE MATTER IN INJECTIONS** <788>: It meets the requirements for small-volume injections.

### ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE:** Preserve as described under *Injections* <1>, *Containers for Sterile Solids*. Maintain in the frozen state.
- LABELING:** It meets the requirements for *Injections* <1>, *Labels and Labeling*. 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 L-Arginine RS
  - USP Aztreonam RS
  - USP Open Ring Aztreonam RS
  - $C_{13}H_{19}N_5O_9S_2$  453.45

## Aztreonam for Injection

### DEFINITION

Aztreonam for Injection is a dry mixture of sterile Aztreonam and Arginine. It contains NLT 90.0% and NMT 105.0% of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ), calculated on the anhydrous and arginine-free basis. Each container contains NLT 90.0% and NMT 120.0% of the labeled amount of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ).

### IDENTIFICATION

- A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

### ASSAY

#### PROCEDURE

**Buffer:** 1.15 g/L of monobasic ammonium phosphate in water. Before final dilution, adjust with phosphoric acid to a pH of  $2.0 \pm 0.1$ .

**Mobile phase:** Acetonitrile and *Buffer* (75:25)

**System suitability solution:** 0.2 mg/mL each of USP Aztreonam RS and USP Open Ring Aztreonam RS in *Mobile phase*

**Standard solution:** 0.2 mg/mL each of USP Aztreonam RS and USP L-Arginine RS in *Mobile phase*

**Sample solution 1:** Equivalent to 0.2 mg/mL of aztreonam in *Mobile phase* from Aztreonam for Injection. Weigh 1 container of Aztreonam for Injection, transfer the contents to a suitable container and dilute with *Mobile phase* to the appropriate volume. Weigh the empty container and calculate the weight, in mg, of Aztreonam for Injection used.

**Sample solution 2:** Equivalent to 0.2 mg/mL of aztreonam from Aztreonam for Injection constituted as directed below and diluted with *Mobile phase*. Where the vial has a capacity of less than 100 mL, constitute with water using the volume of solvent specified in the labeling.

Where the vial capacity is equal to or greater than 100 mL, constitute with 10 mL of water and dilute the entire withdrawable contents of the container with *Mobile phase* to obtain the final concentration.

#### Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

**Mode:** LC

**Detector:** UV 206 nm

**Pre-column:** 4.6-mm × 5- to 10-cm saturator precolumn containing packing L27

**Column:** 4-mm × 25-cm analytical column containing packing L20

**Flow rate:** 1 mL/min

**Injection size:** 20 µL

#### System suitability

**Sample:** *System suitability solution*

[NOTE—The relative retention times for aztreonam and open ring aztreonam are about 0.8 and 1.0, respectively. The relative retention times for aztreonam and arginine are 0.3 and 1.0, respectively.]

#### Suitability requirements

**Resolution:** NLT 2.0 between aztreonam and open ring aztreonam

**Column efficiency:** NLT 1000 theoretical plates determined from the aztreonam peak

**Tailing factor:** NMT 2.0 for the aztreonam peak

**Relative standard deviation:** NMT 2.0% for the aztreonam peak

#### Analysis

**Samples:** *Standard solution*, *Sample solution 1*, and *Sample solution 2*

Calculate the percentage of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ) in the portion of Aztreonam for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F \times 100$$

$r_U$  = peak response for aztreonam from *Sample solution 1*

$r_S$  = peak response for aztreonam from the *Standard solution*

$C_S$  = concentration of USP Aztreonam RS in the *Standard solution* (mg/mL)

$C_U$  = concentration of Aztreonam for Injection in *Sample solution 1* (mg/mL), corrected for water and arginine content (see *Content of Arginine*)

$P$  = potency of aztreonam in USP Aztreonam RS (µg/mg)

$F$  = conversion factor (0.001 mg/µg)

**Acceptance criteria:** 90.0%–105.0% on the anhydrous and arginine-free basis

Calculate the percentage of aztreonam ( $C_{13}H_{17}N_5O_8S_2$ ) in each container of Aztreonam for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F \times 100$$

$r_U$  = peak response for aztreonam from *Sample solution 2*

$r_S$  = peak response for aztreonam from the *Standard solution*

$C_S$  = concentration of USP Aztreonam RS in the *Standard solution* (mg/mL).

$C_U$  = nominal concentration of aztreonam in *Sample solution 2* (mg/mL)

$P$  = potency of aztreonam in USP Aztreonam RS (µg/mg)

$F$  = conversion factor (0.001 mg/µg)

**Acceptance criteria:** 90.0%–120.0% of the labeled content of aztreonam

#### OTHER COMPONENTS

• **CONTENT OF ARGININE:** Use the result of this test to calculate, on the anhydrous and arginine-free basis, the *Assay* result from *Sample solution 1*, obtained as directed in the *Assay*.

**Buffer, Mobile phase, System suitability solution, Standard solution, Sample solution 1, Chromatographic system, and System suitability:** Proceed as directed in the *Assay*.

#### Analysis

**Sample:** *Sample solution 1*

Calculate the percentage of arginine ( $C_6H_{14}N_4O_2$ ) in the portion of Aztreonam for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$  = peak response for arginine from *Sample solution 1*

$r_S$  = peak response for arginine from the *Standard solution*

$C_S$  = concentration of USP L-Arginine RS in the *Standard solution* (mg/mL)

$C_U$  = concentration of Aztreonam for Injection in *Sample solution 1*

#### PERFORMANCE TESTS

• **UNIFORMITY OF DOSAGE UNITS (905):** Meets the requirements

#### SPECIFIC TESTS

- **CONSTITUTED SOLUTION:** At the time of use, it meets the requirements for *Injections* <1>, *Constituted Solutions*.
- **BACTERIAL ENDOTOXINS TEST (85):** It contains NMT 0.17 USP Endotoxin Unit/mg of aztreonam.
- **STERILITY TESTS (71):** It meets the requirements when tested as directed for *Test for Sterility of the Product to be Examined, Membrane Filtration*.
- **PH (791)**  
**Sample solution:** 100 mg/mL of aztreonam  
**Acceptance criteria:** 4.5–7.5
- **WATER DETERMINATION, Method I (921):** NMT 2.0%
- **PARTICULATE MATTER IN INJECTIONS (788):** Meets the requirements for small-volume injections
- **OTHER REQUIREMENTS:** It meets the requirements for *Injections* <1>, *Labeling*.

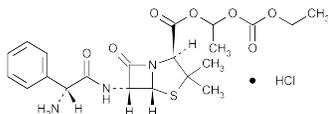
#### ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve as described in *Injections* <1>, *Containers for Sterile Solids*.

• **USP REFERENCE STANDARDS (11)**

USP L-Arginine RS  
USP Aztreonam RS  
USP Endotoxin RS  
USP Open Ring Aztreonam RS  
 $C_{13}H_{19}N_5O_9S_2$  453.45

## Bacampicillin Hydrochloride



$C_{21}H_{27}N_3O_7S \cdot HCl$  501.98

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-,1-[(ethoxycarbonyl)oxyethyl ester, monohydrochloride, [2S-[2 $\alpha$ ,5 $\alpha$ ,6 $\beta$ (S\*)]]]-, (2S,5R,6R)-6-[(R)-(2-Amino-2-phenylacetamido)]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid ester with ethyl 1-hydroxyethyl carbonate, monohydrochloride [37661-08-8].

» Bacampicillin Hydrochloride has a potency of not less than 623  $\mu$ g and not more than 727  $\mu$ g of ampicillin ( $C_{16}H_{19}N_3O_4S$ ) per mg.

**Packaging and storage**—Preserve in tight containers.

**USP Reference standards** (11)—

USP Bacampicillin Hydrochloride RS

**Identification**—Prepare a test solution of it in alcohol containing 2 mg per mL. Prepare a Standard solution of USP Bacampicillin Hydrochloride RS in alcohol containing 2 mg per mL. Apply two 5- $\mu$ L portions of the test solution 4.0 cm apart to a thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel mixture (see *Chromatography* (621)). After the spots dry, apply two 5- $\mu$ L portions of the Standard solution, one midway between the test solution spots and the other to one of the test solution spots. Allow the spots to dry, place the plate in a suitable chromatographic chamber, and develop the chromatogram in a solvent system consisting of a mixture of methylene chloride, chloroform, and alcohol (10:1:1). When the solvent front has moved about three-fourths of the length of the plate, remove the plate from the chamber, and allow to dry. Spray the plate with a spray reagent containing 1 g of ninhydrin and 1 mL of pyridine in each 100 mL of solution in butyl alcohol, and heat at 100° for 10 minutes: bacampicillin appears as a purple spot, and the  $R_f$  values of the spots from the test solution and from the combined test solution and Standard solution, respectively, correspond to the  $R_f$  value of the spot obtained from the Standard solution.

**pH** (791): between 3.0 and 4.5, in a solution containing 20 mg per mL.

**Water**, *Method I* (921): not more than 1.0%.

**Dimethylaniline** (223): meets the requirement, the *Test Preparation* being prepared using 2 N sodium hydroxide instead of 1 N sodium hydroxide.

**Assay**—

*Mobile phase*—To 500 mL of 0.02 M dibasic sodium phosphate add portions of 0.02 M monobasic sodium phosphate until a pH of 6.8  $\pm$  0.05 is reached. Prepare a suitable filtered mixture of this pH 6.8 buffer and acetonitrile (500:500). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

*Standard preparation*—Prepare a solution of USP Bacampicillin Hydrochloride RS, accurately weighed, in water having a known concentration of about 0.8 mg per mL, sonicating for about 20 minutes to achieve complete dissolution. Pass through a filter of 0.5- $\mu$ m or finer porosity.

*Assay preparation*—Transfer about 80 mg of Bacampicillin Hydrochloride, accurately weighed, to a 100-mL volumetric flask, add 90 mL of water, and sonicate for about 20 minutes. Dilute with water to volume, mix, and pass through a filter of 0.5- $\mu$ m or finer porosity.

*Chromatographic system* (see *Chromatography* (621))—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm  $\times$  15-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure*: the column efficiency determined from the analyte peak is not less than 3000 theoretical plates, and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*—Separately inject equal volumes (about 20  $\mu$ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in  $\mu$ g, of ampicillin ( $C_{16}H_{19}N_3O_4S$ ) equivalent in each mg of the Bacampicillin Hydrochloride taken by the formula:

$$(349.41/501.99)(100,000C/W)(r_U/r_S)$$

in which 349.41 and 501.99 are the molecular weights of anhydrous ampicillin and bacampicillin hydrochloride, respectively, C is the concentration, in mg per mL, of USP Bacampicillin Hydrochloride RS in the *Standard preparation*, W is the weight, in mg, of the portion of Bacampicillin Hydrochloride taken, and  $r_U$  and  $r_S$  are the bacampicillin peak area responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

## Bacampicillin Hydrochloride for Oral Suspension

» Bacampicillin Hydrochloride for Oral Suspension contains an amount of Bacampicillin Hydrochloride equivalent to not less than 90.0 percent and not more than 125.0 percent of the labeled amount of ampicillin ( $C_{16}H_{19}N_3O_4S$ ) when constituted as directed. It contains one or more suitable buffers, colors, flavors, suspending agents, and sweetening ingredients.

**Packaging and storage**—Preserve in tight containers.

**USP Reference standards** (11)—

USP Ampicillin RS

USP Bacampicillin Hydrochloride RS

**Identification**—Constitute Bacampicillin Hydrochloride for Oral Suspension as directed in the labeling. Transfer a portion of the resulting suspension, equivalent to about 140 mg of ampicillin, to a 100-mL volumetric flask, add 70 mL of alcohol, shake by mechanical means for 30 minutes, dilute with alcohol to volume, and mix: the solution so obtained responds to the *Identification* test under *Bacampicillin Hydrochloride*.

**Uniformity of dosage units** (905)—

FOR SOLID PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

**Deliverable volume** (698): meets the requirements.

**pH** (791): between 6.5 and 8.0, in the suspension constituted as directed in the labeling.

**Loss on drying** (731)—Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at 60° for 3 hours: it loses not more than 2.0% of its weight.

**Assay**—

*Standard preparation*—Using USP Ampicillin RS, prepare as directed for *Standard preparation* under *Iodometric Assay—Antibiotics* (425).

*Assay preparation*—Transfer an accurately measured volume of Bacampicillin Hydrochloride for Oral Suspension,