Ceftriaxone Sodium

C18H18N8O7S3 · 3/2H2O 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, [6R-(6α,7βZ)]-
hydrate, (2:7); Samples:

ASSAY

Change to read:

• Procedure

Protect solutions containing ceftriaxone sodium from light. (IRA 1-Aug-2016)

Solution A: 9 g/L of monobasic potassium phosphate in water
Solution B: 24 g/L of dibasic sodium phosphate, dodecahydrate in water
Solution C: 20 g/L of citric acid in water. Adjust with 10 N sodium hydroxide to a pH of 5.0 prior to final dilution.
Buffer: Combine 389 mL of Solution A and 611 mL of Solution B. Adjust with 10 N sodium hydroxide to a pH of 7.0 or phosphoric acid to a pH of 7.0.
Mobile phase: Dissolve 2.0 g each of tetradeclammonium bromide and tetradeclammonium bromide in a mixture of 440 mL of water, 55 mL of Buffer, 5.0 mL of Solution C, and 500 mL of acetonitrile
System suitability solution: 50 µg/mL of USP Ceftriaxone Sodium RS and 50 µg/mL of USP Ceftriaxone Sodium E-Isomer RS in Mobile phase
Standard solution: 0.3 mg/mL of USP Ceftriaxone Sodium RS in Mobile phase
Sample solution: 0.3 mg/mL of Ceftriaxone Sodium in Mobile phase

Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 254 nm
Column: 4.6-mm x 25-cm; 5-µm packing L1
Flow rate: 1.5 mL/min
Injection volume: 20 µL

System suitability
Samples: System suitability solution and Standard solution

[Note—The relative retention times for ceftriaxone and ceftriaxone E-isomer are 1.0 and 1.4, respectively.]

Suitability requirements
Resolution: NLT 3.0 between the ceftriaxone and ceftriaxone E-isomer peaks, System suitability solution
Tailing factor: NMT 2, Standard solution
Relative standard deviation: NMT 0.7%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the quantity, in µg/mg, of ceftriaxone (C18H18N8O7S3) in the portion of Ceftriaxone Sodium taken:

Result = (rS/rU) × (C S /C U) × P

rU = peak response of ceftriaxone from the Sample solution
rS = peak response of ceftriaxone from the Standard solution
C S = concentration of USP Ceftriaxone Sodium RS in the Standard solution (mg/mL)
C U = concentration of Ceftriaxone Sodium in the Sample solution (mg/mL)
P = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)

Acceptance criteria: NLT 795 µg/mg on the anhydrous basis

IMPURITIES

Change to read:

• Organic Impurities

Protect solutions containing ceftriaxone sodium from light. (IRA 1-Aug-2016)


Standard solution: 3 µg/mL of USP Ceftriaxone Sodium RS in Mobile phase

System suitability
Samples: System suitability solution and Standard solution

[Note—The relative retention times for ceftriaxone and ceftriaxone E-isomer are listed in Table 1.]

Suitability requirements
Resolution: NLT 3.0 between the ceftriaxone E-isomer and ceftriaxone peaks, System suitability solution
Signal-to-noise ratio: NLT 10, Standard solution

Analysis
Samples: Sample solution and Standard solution
Calculate the percentage of each individual impurity in the portion of Ceftriaxone Sodium taken:

Result = (rS/rU) × (C S /C U) × P × F × 100

rU = peak response of each individual impurity from the Sample solution
rS = peak response of ceftriaxone from the Standard solution
C, = concentration of USP Ceftriaxone Sodium RS in the Standard solution (mg/mL)
C,U = concentration of Ceftriaxone Sodium in the Sample solution (mg/mL)
P = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)
F = conversion factor, 0.001 mg/µg

Acceptance criteria: See Table 1. Disregard any peak below 0.1%.

### Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deacetylcefotaxime lactone*</td>
<td>0.20</td>
<td>0.5</td>
</tr>
<tr>
<td>7-Aminocephalosporanic acid* (if present)</td>
<td>0.34</td>
<td>0.5</td>
</tr>
<tr>
<td>Ceftriaxone triazine analog†</td>
<td>0.62</td>
<td>1.0</td>
</tr>
<tr>
<td>Ceftriaxone benzothiazolylximate*</td>
<td>0.72</td>
<td>0.2</td>
</tr>
<tr>
<td>Decyl ceftriaxone†</td>
<td>0.78</td>
<td>0.5</td>
</tr>
<tr>
<td>Ceftriaxone 3-ene isomer†</td>
<td>1.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Ceftriaxone E-isomer‡</td>
<td>1.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* (Z)-2-(2-Aminothiazol-4-yl)-N-{[(5aR,6R)-1,7-dioxo-1,3,4,5,6,7-hexahydroazeto[2,1-b][3,4-d][1,3]thiazin-6-yl]-2-(methoxyimino)acetamide.
† 7-ACA; (6R,7R)-3-(Acetoxymethyl)-7-amino-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.
‡ To be reported if present in the impurity profile.
§ 3-Mercapto-2-methyl-1,2-dihydro-1,2,4-triazine-5,6-dione.

**SPECIFIC TESTS**

- **CRYSTALLINITY** (695): Meets the requirements
- **pH (791)**
  - Sample solution: 100 mg/mL
  - Acceptance criteria: 6.0–8.0
- **WATER DETERMINATION (921), Method I:** 8.0%–11.0%
- **STERILITY TESTS (71), Test for Sterility of the Product to Be Examined, Membrane Filtration:** Where the label states that it is sterile, it meets the requirements.
- **BACTERIAL ENDOTOXINS TEST (85):** Where the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.20 USP Endotoxin Units/mg of ceftriaxone.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light.
- **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or