Ceftriaxone for Injection

DEFINITION
Ceftriaxone for Injection contains an amount of Ceftriaxone Sodium equivalent to NLT 776 µg/mg of ceftriaxone (C18H18N8O7S3), calculated on the anhydrous basis, and the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of ceftriaxone (C18H18N8O7S3).

IDENTIFICATION
A. INFRARED ABSORPTION (197K)
B. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY

Change to read:

• PROCEDURE

<table>
<thead>
<tr>
<th>Protect solutions containing ceftriaxone sodium from light. (IRA 1-Aug-2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution A: 9 g/L of monobasic potassium phosphate in water</td>
</tr>
<tr>
<td>Solution B: 24 g/L of dibasic sodium phosphate, dodecahydrate in water</td>
</tr>
<tr>
<td>Solution C: 20 g/L of citric acid in water. Adjust with 10 N sodium hydroxide TS to a pH of 5.0 prior to dilution.</td>
</tr>
<tr>
<td>Buffer: Combine 389 mL of Solution A and 611 mL of Solution B. Adjust with 10 N sodium hydroxide TS or phosphoric acid to a pH of 7.0.</td>
</tr>
<tr>
<td>Mobile phase: Dissolve 2.0 g each of tetracyclammonium bromide and tetraheptylammonium bromide in a mixture of 440 mL of water, 55 mL of Buffer, 5.0 mL of Solution C, and 500 mL of acetonitrile.</td>
</tr>
<tr>
<td>System suitability solution: 50 µg/mL each of USP Ceftriaxone Sodium RS and USP Ceftriaxone Sodium E-isomer RS in Mobile phase</td>
</tr>
<tr>
<td>Standard solution: 0.3 mg/mL of USP Ceftriaxone Sodium RS in Mobile phase</td>
</tr>
<tr>
<td>Sample solution 1: Nominally 0.3 mg/mL of ceftriaxone from Ceftriaxone for Injection in Mobile phase</td>
</tr>
<tr>
<td>Sample solution 2 (where it is represented as being in a single-dose container): Nominally 0.3 mg/mL of ceftriaxone in Mobile phase prepared as follows. Constitute Ceftriaxone for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Withdraw all of the withdrawable contents using a suitable hypodermic needle and syringe, and transfer to a suitable volumetric flask. Dilute with Mobile phase to volume.</td>
</tr>
<tr>
<td>Sample solution 3 (where the label states the quantity of ceftriaxone in a given volume of constituted solution): Nominally 0.3 mg/mL of ceftriaxone in Mobile phase prepared as follows. Constitute Ceftriaxone for Injection in a volume of water corresponding to the volume of solvent specified in the labeling, and dilute with Mobile phase to final volume.</td>
</tr>
<tr>
<td>Chromatographic system</td>
</tr>
<tr>
<td>(See Chromatography (621), System Suitability.)</td>
</tr>
<tr>
<td>Mode: LC</td>
</tr>
<tr>
<td>Detector: UV 254 nm</td>
</tr>
<tr>
<td>Column: 4.6-mm × 25-cm; S-µm packing L1</td>
</tr>
<tr>
<td>Flow rate: 1.5 mL/min</td>
</tr>
<tr>
<td>Injection volume: 20 µL</td>
</tr>
<tr>
<td>System suitability</td>
</tr>
<tr>
<td>Samples: System suitability solution and Standard solution</td>
</tr>
</tbody>
</table>

(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, Sample solution 1, and Sample solution 2 or Sample solution 3 (IRA 1-Aug-2016)
Calculate the quantity, in µg/mg of ceftriaxone (C18H18N8O7S3) in the portion of Ceftriaxone for Injection taken:

Result = (rS/rU) × (C2/C1) × P

rS = peak response of ceftriaxone from Sample solution 1
rU = peak response of ceftriaxone from the Standard solution
C2 = concentration of USP Ceftriaxone Sodium RS in the Standard solution (mg/mL)
C1 = nominal concentration of ceftriaxone in Sample solution 1 (mg/mL)
P = potency of ceftriaxone in USP Ceftriaxone Sodium RS (µg/mg)

Acceptance criteria: NLT 776 µg/mg on the anhydrous basis.
Calculate the percentage of the labeled amount of ceftriaxone (C18H18N8O7S3) in the portion of Ceftriaxone for Injection withdrawn from the container or in the portion of the constituted solution:

Result = (rS/rU) × (C2/C1) × P × F × 100

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–115.0% of the labeled amount of ceftriaxone

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

IMPURITIES
Change to read:

• ORGANIC IMPURITIES

| Protect solutions containing ceftriaxone sodium from light. (IRA 1-Aug-2016) |
| Solution A, Solution B, Solution C, Buffer, Mobile phase, System suitability solution, Chromatographic system: Proceed as directed in the Assay |
| Standard solution: 3 µg/mL of USP Ceftriaxone Sodium RS in Mobile phase |
| Sample solution: Nominally 0.3 mg/mL of ceftriaxone from Ceftriaxone for Injection in Mobile phase |

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2 Ceftriaxone

System suitability
Sample: System suitability 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 and
ceftriaxone E-isomer

Analysis
Samples: Standard solution and Sample solution

Calculate the percentage of each individual impurity in the portion of Ceftriaxone for Injection taken:

\[
\text{Result} = \frac{r_0}{r_s} \times \frac{C_t}{C_u} \times P \times F \times 100
\]

- \(r_0\) = peak response of each individual impurity from the Sample solution
- \(r_s\) = peak response of ceftriaxone from the Standard solution
- \(C_t\) = concentration of USP Ceftriaxone Sodium RS in the Standard solution (mg/mL)
- \(C_u\) = nominal concentration of ceftriaxone 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-Aminopenicillamycin triazine analog†</td>
<td>0.34</td>
<td>0.2</td>
</tr>
<tr>
<td>Ceftriaxone triazine analog†</td>
<td>0.62</td>
<td>1.0</td>
</tr>
<tr>
<td>Ceftriaxone benzothiazolyl oxime†</td>
<td>0.72</td>
<td>0.2</td>
</tr>
<tr>
<td>Deacyl ceftriaxone†</td>
<td>0.78</td>
<td>1.0</td>
</tr>
</tbody>
</table>

- \(†\) Process impurities that are controlled in the drug substance are not to be reported, are not included in total impurities, and are listed here for information only.
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SPECIFIC TESTS

Change to read:

- **Constituted solution**: At the time of use, it meets the requirements for Injections and Implanted Drug Products (1).

- **Bacterial endotoxins test (85)**: NMT 0.20 USP Endotoxin Units/mg of ceftriaxone.

- **Sterility Test (71)**: Test for Sterility of the Product to Be Examined; Membrane Filtration: It meets the requirements.

- **Particulate Matter in Injections (788)**: Meets the requirements for small-volume injections.

- **Crystallinity (695)**: Meets the requirements.

- **pH (791)**: Sample solution: 100 mg/mL

- **Water Determination (921), Method I**: 8.0%–11.0%

**Change to read:**

- **Other requirements**: It meets the requirements for Labeling (7), Labels and Labeling for Injectable Products.
ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** *Preserve as described in Packaging and Storage Requirements (659), Injection Packaging, Sterile solids packaging, and protected from light.* (CN 1-May-2016)
- **USP REFERENCE STANDARDS** (11)
  USP Ceftriaxone Sodium RS
  USP Ceftriaxone Sodium E-Isomer RS
  \(6R,7R\)-7-{[(E)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-3-\{(6-hydroxy-2-methyl-5-oxo-2,5-dihydro-1,2,4-triazin-3-yl)thio[methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, disodium salt, \(C_{16}H_{16}N_8Na_2O_7S_3\) 598.53
  USP Endotoxin RS