Cefdinir for Oral Suspension

**DEFINITION**
Cefdinir for Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of cefdinir (C14H13N5O5S2). It may contain one or more suitable buffers, flavors, preservatives, stabilizing agents, sweeteners, and suspending agents.

**IDENTIFICATION**
- **A.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**
- **PROCEDURE**
  - **Buffer:** 10.7 mg/mL of anhydrous dibasic sodium phosphate and 3.4 mg/mL of monobasic potassium phosphate in water. Adjust with phosphoric acid or sodium hydroxide to a pH of 7.0 ± 0.05 before final dilution.
  - **Solution A:** 7 mg/mL of citric acid monohydrate. Adjust with phosphoric acid to a pH of 2.0 ± 0.05.
  - **Mobile phase:** Methanol, tetrahydrofuran, and Solution A (111:28:1000)
  - **System suitability solution:** 50 µg/mL of USP Cefdinir RS and 175 µg/mL of m-hydroxybenzoic acid in Buffer
  - **Standard solution:** 50 µg/mL of USP Cefdinir RS in Buffer
  - **Sample solution:** Equivalent to 50 µg/mL of cefdinir from constituted Cefdinir for Oral Suspension in Buffer

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

- **Mode:** LC
- **Detector:** UV 254 nm
- **Column:** 3.9-mm × 15-cm; 4-µm packing L1
- **Flow rate:** 1.4 mL/min
- **Injection volume:** 15 µL

**System suitability**
- **Samples:** System suitability solution and Standard solution
- **Suitability requirements**
  - **Resolution:** NLT 3.0 between cefdinir and m-hydroxybenzoic acid, System suitability solution
  - **Tailing factor:** NMT 2.0 for cefdinir, System suitability solution
  - **Relative standard deviation:** NMT 1.0% for cefdinir, Standard solution

**Analysis**
- **Samples:** Standard solution and Sample solution
- Calculate the percentage of the labeled amount of cefdinir (C14H13N5O5S2) in the portion of Cefdinir for Oral Suspension taken:
  
  \[ \text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_0} \right) \times 100 \]

  - \( r_0 \) = peak response of cefdinir from the Sample solution
  - \( r_s \) = peak response of cefdinir from the Standard solution
  - \( C_s \) = concentration of the Standard solution (µg/mL)
  - \( C_0 \) = nominal concentration of cefdinir in the Sample solution (µg/mL)

**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**
- **DISSOLUTION (711)**
  - **Medium:** 0.05 M phosphate buffer, pH 6.8; 900 mL
  - **Apparatus 2:** 50 rpm
  - **Time:** 30 min
  - **Detector:** UV 290 nm
  - **Standard solution:** 0.14 mg/mL of USP Cefdinir RS in Medium
  - **Sample solution:** Transfer 5 mL, by weight, of the reconstituted Cefdinir for Oral Suspension into the vessel. After the appropriate time, withdraw a portion of the solution under test, and pass through a suitable filter of 0.45-µm pore size. Dilute a portion of each filtered sample with Medium as necessary to obtain a solution having a concentration of about 0.14 mg/mL of cefdinir.

**Blank:** Medium

**Analysis**
- **Samples:** Standard solution and Sample solution
  - Determine the percentage of the labeled amount of cefdinir (C14H13N5O5S2) dissolved:
  
  \[ \text{Result} = \left( \frac{A_U}{A_S} \right) \times \frac{r_s}{r_0} \times d \times V \times D \times (1/L) \times 100 \]

  - \( A_U \) = absorbance of the Sample solution
  - \( A_S \) = absorbance of the Standard solution
  - \( C_s \) = concentration of the Standard solution (mg/mL)
  - \( d \) = density of Cefdinir for Oral Suspension (mg/mL)
  - \( V \) = volume of Medium, 900 mL
  - \( D \) = dilution factor of the Sample solution (mL/mL)
  - \( L \) = label claim (mg/mL)

**Tolerances:** NLT 80% (Q) of the labeled amount of cefdinir (C14H13N5O5S2) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS (905)**
  - For single-unit containers
    - **Acceptance criteria:** Meets the requirements

**Change to read:**

- **DELIBERABLE VOLUME (698)**
  - For multiple-unit containers
    - **Acceptance criteria:** Meets the requirements

**IMPURITIES**

**Change to read:**

- **ORGANIC IMPURITIES**
  - **Solution A:** 14.2 mg/mL of anhydrous dibasic sodium phosphate
  - **Solution B:** 13.6 mg/mL of monobasic potassium phosphate
  - **Buffer:** Combine appropriate amounts of Solution A and Solution B (about 2:1) to obtain a solution with a pH of 7.0 ± 0.1.
  - **Solution C:** Dilute tetramethylammonium hydroxide (10% aqueous) with water to obtain a 0.1% solution. Adjust with dilute phosphoric acid (1 in 10) to a pH of 5.5 ± 0.1.
  - **Solution D:** 37.2 mg/mL of edetate disodium
  - **Solution E:** To 1000 mL of Solution C add 0.4 mL of Solution D.
  - **Solution F:** Acetonitrile, methanol, Solution C, and Solution D (150: 100: 250: 0.2)
  - **Mobile phase:** See Table 1.
Cefdinir

System suitability stock solution 1: 40 µg/mL of USP Cefdinir Related Compound A RS in Solution C
System suitability stock solution 2: 40 µg/mL of USP Cefdinir Related Compound B RS in Buffer
System suitability solution: Transfer 37.5 mg of USP Cefdinir RS to a 25-mL volumetric flask, and add about 10 mL of Buffer. Add 5.0 mL each of System suitability stock solution 1 and System suitability stock solution 2, and dilute with Solution C to volume.
Standard stock solution: 750 µg/mL of USP Cefdinir RS in Buffer
Standard solution: 15 µg/mL of USP Cefdinir RS from the Standard stock solution in Solution C
Sample solution: Transfer a quantity equivalent to 150 mg of cefdinir from the constituted Cefdinir for Oral Suspension to a 100-mL volumetric flask. Dissolve in 30 mL of Buffer, and dilute with Solution C to volume.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 254 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Temperatures
 Autosampler: 4°C
Flow rate: 1 mL/min
Injection volume: 10 µL

System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 1.5 between cefdinir and the third peak of USP Cefdinir Related Compound A RS, System suitability solution
Tailing factor: NMT 1.5 for cefdinir related compound B, System suitability solution
Relative standard deviation: NMT 2.0% for the cefdinir peak, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of each impurity in the portion of Cefdinir for Oral Suspension taken:

\[
\text{Result} = \left( \frac{r_s}{r_0} \right) \times \left( \frac{C_s}{C_0} \right) \times (100/F)
\]

\( r_0 = \) peak response of each impurity from the Sample solution
\( r_s = \) peak response of cefdinir from the Standard solution
\( C_s = \) concentration of the Standard solution (mg/mL)
\( C_0 = \) nominal concentration of cefdinir in the Sample solution (mg/mL)
\( F = \) relative response factor (see Table 2)

Acceptance criteria: See Table 2. *The reporting threshold is 0.1%.

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiouzolacetyl glycine oxime</td>
<td>0.10</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Thiouzolacetyl glycine oxime acetyl</td>
<td>0.13</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Cefdinir sulfamide analog</td>
<td>0.46</td>
<td>0.68</td>
<td>0.2</td>
</tr>
<tr>
<td>3-Methyl cefdinir</td>
<td>0.75</td>
<td>1.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Cefdinir impurity 1</td>
<td>0.77</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Cefdinir related compound A (cefdinir open ring lactone a)</td>
<td>0.85</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Cefdinir related compound A (cefdinir open ring lactone b)</td>
<td>0.94</td>
<td>0.65</td>
<td>3.3</td>
</tr>
<tr>
<td>Cefdinir related compound A (cefdinir open ring lactone c)</td>
<td>1.11</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Cefdinir related compound A (cefdinir open ring lactone d)</td>
<td>1.14</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>7S-Cefdinir</td>
<td>1.18</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Cefdinir lactone</td>
<td>1.23</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Cefdinir related compound B</td>
<td>1.28</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Cefdinir isoxazole analog</td>
<td>1.37</td>
<td>0.72</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*N*[(2Z)-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

**Table 1**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution E (%)</th>
<th>Solution F (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>22</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>32</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>37</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>38</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>58</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 2**
Table 2 (Continued)

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefdinir impurity 2/</td>
<td>1.44</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Cefdinir glyoxylic analoga</td>
<td>1.49</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>E-Cefdinirb</td>
<td>1.51</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Cefdinir decarboxy open ring lactone a</td>
<td>1.62</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Cefdinir decarboxy open ring lactone b</td>
<td>1.64</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Cefdinir impurity 3/</td>
<td>1.82</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Individual unidentified impurities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total impurities</td>
<td></td>
<td></td>
<td>6.2</td>
</tr>
</tbody>
</table>

- **USP Reference Standards** (11)

USP Cefdinir RS
USP Cefdinir Related Compound A RS
(2R)-2-[(2S)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-2-[(2R,5S,RS)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1H-furo[3,4-d][1,3]thiazin-2-yl]acetic acid (three other stereoisomers are also present in this RS).
C_{16}H_{17}N_{3}O_{4}S_{2}  413.43

USP Cefdinir Related Compound B RS
C_{14}H_{13}N_{5}O_{4}S_{2}  365.41

- **SPECIFIC TESTS**

  - **pH** (791): 3.2–4.8

- **ADDITIONAL REQUIREMENTS**

  - **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

* Delete the following: The label specifies the directions for the constitution of the powder and states the equivalent amount of cefdinir (C_{14}H_{17}N_{3}O_{4}S_{2}) in a given volume of Cefdinir for Oral Suspension after constitution.*

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