Cetirizine Hydrochloride Oral Solution

DEFINITION
Cetirizine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of C21H25ClN2O3 ¦ 2HCl.

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.

B. Identification Tests—General, Chloride (191): Meets the requirements

ASSAY

PROCEDURE

Solution A: Acetonitrile

Solution B: 1.36 g/L of monobasic potassium phosphate in water. Adjust with a 2% solution of phosphoric acid in water to a pH of 3.5 ± 0.05.

Diluent: Acetonitrile and water (3:7)

Mobile phase: See the gradient table below.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>15</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>22</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>35</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>40</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>50</td>
<td>5</td>
<td>95</td>
</tr>
</tbody>
</table>

Standard stock solution: 5 mg/mL of USP Cetirizine Hydrochloride RS in water

Standard solution: 0.1 mg/mL of USP Cetirizine Hydrochloride RS in Diluent, from the Standard stock solution

Sample solution: Transfer an amount of Oral Solution to a suitable volumetric flask to obtain a nominal concentration of 0.1 mg/mL of cetirizine hydrochloride. Dissolve in 60% of the flask volume of Diluent by swirling. Sonicate 3 min, and dilute with Diluent to volume. Pass through a suitable filter.

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 233 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Column temperature: 50°C

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: Standard solution

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of C21H25ClN2O3 · 2HCl in the portion of Oral Solution taken:

Result = \( \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times 100 \)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• Deliverable Volume (698): Meets the requirements

IMPURITIES

Organic Impurities

PROCEDURE

Solution A: Transfer 50 mL of water to a 100-mL volumetric flask, add 5.5 mL of sulfuric acid, and dilute with water to volume.

Mobile phase: Acetonitrile, water, and Solution A (965:33:1)

Solution A:

Acetonitrile

Diluent: Acetonitrile and water (7:13)

Solution B: 1.36 g/L of monobasic potassium phosphate in water. Adjust with a 2% solution of phosphoric acid in water to a pH of 3.5 ± 0.05.

Standard solution: 6 µg/mL of USP Cetirizine Hydrochloride RS in Diluent

Sample solution: 0.6 mg/mL of cetirizine hydrochloride in Diluent. Transfer an amount of Oral Solution to a suitable volumetric flask, dissolve in Diluent, sonicate for 10 min, and dilute with Diluent to volume. Pass through a suitable filter.

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 233 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Column temperature: 30°C

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Sample: Standard solution

Suitability requirements

Column efficiency: NLT 10,000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 5.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of each impurity in the portion of Oral Solution taken:

Result = \( \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times 100 \)

Acceptance criteria: See Impurity Table 1.

Total impurities: NMT 0.8%
### Impurity Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetirizine acetic acid&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.69</td>
<td>Pb</td>
</tr>
<tr>
<td>2-Chlorocetirizine&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.83</td>
<td>P</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>1.00</td>
<td>—</td>
</tr>
<tr>
<td>Cetirizineethanol&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.30</td>
<td>P</td>
</tr>
<tr>
<td>Ethoxycetirizine&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.38</td>
<td>P</td>
</tr>
<tr>
<td>CBHP&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.52</td>
<td>P</td>
</tr>
<tr>
<td>Propylene glycol ester of cetirizine (diastereomer 1)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1.53</td>
<td>0.2</td>
</tr>
<tr>
<td>Propylene glycol ester of cetirizine (diastereomer 2)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1.61</td>
<td>0.2</td>
</tr>
<tr>
<td>Deschlorocetirizine&lt;sup&gt;h&lt;/sup&gt;</td>
<td>1.65</td>
<td>P</td>
</tr>
<tr>
<td>Glyceryl ester of cetirizine&lt;sup&gt;i&lt;/sup&gt;</td>
<td>2.20</td>
<td>0.5</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>0.2</td>
</tr>
</tbody>
</table>

<sup>a</sup> 2-[4-[[4-Chlorophenyl]phenylmethyl]piperazin-1-yl]acetic acid.
<sup>b</sup> P = Process impurity. Provided for information only; the content is not calculated and not reported. The content is controlled in the drug substance monograph.
<sup>c</sup> 2-[2-[[4-Chlorophenyl]phenylmethyl]piperazin-1-yl]ethoxy]acetic acid.
<sup>d</sup> 2-[4-[[4-Chlorophenyl]phenylmethyl]piperazin-1-yl]ethanol.
<sup>e</sup> 2-[2-[[4-Chlorophenyl]phenylmethyl]piperazin-1-yl]ethoxy]acetic acid (ethoxycetirizine).
<sup>f</sup> 1-[[4-Chlorophenyl]phenylmethyl]piperazine.
<sup>g</sup> 2-Hydroxypropyl 2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetate.
<sup>h</sup> 2-[[4-(Diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid.
<sup>i</sup> 2,3-Dihydroxypropyl 2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetate.

### ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and protect from light. Store at controlled room temperature or in a cold place.

- **USP Reference Standards (11)**
  - **USP Cetirizine Hydrochloride RS<sup>o</sup> (RB 1-May-2010)**

### SPECIFIC TESTS

**Change to read:**

- **PH (791):** 4.0–5.1<sup>o</sup> (RB 1-Sep-2010)
- **Microbial Enumeration Tests (61) and Tests for Specified Microorganisms (62):** The total aerobic microbial count does not exceed 100 cfu/mL, and the total combined molds and yeasts count does not exceed 10 cfu/mL. It meets the requirements of the tests for absence of *Escherichia coli.*