Losartan Potassium Tablets

DEFINITION
Losartan Potassium Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of losartan potassium (C22H22ClKN6O).

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: 1.25 mg/mL of monobasic potassium phosphate and 1.5 mg/mL of dibasic sodium phosphate in water. The resulting pH is approximately 7.0. Pass the solution through a PTFE or equivalent filter of 0.45-µm pore size, and degas before use.

Solution A: Acetonitrile and Buffer (3:17)
Solution B: Use acetonitrile.

Mobile phase: See Table 1.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>11</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>15</td>
<td>80</td>
<td>20</td>
</tr>
</tbody>
</table>

Chromatographic system

Chromatographic system

System suitability solution: Dissolve 12 mg of USP Losartan Potassium RS in a 50-mL volumetric flask, first using 5 mL of water, followed by 5 mL of 0.1 N hydrochloric acid. Place the flask in a 105° C oven for 1–2 h, and allow to cool to room temperature. Pipet 5 mL of 0.1 N sodium hydroxide into the flask, and dilute with water to volume. Adjust with either 0.1 N hydrochloric acid or 0.1 N sodium hydroxide to a pH of 6.0. [NOTE—The resulting solution contains the 1-H-dimer and 2-H-dimer, and the resulting solution may be cloudy.] System suitability solution: Add 3 mL of acetonitrile to 7 mL of System suitability stock solution to clear the cloudy solution, and mix well.

Standard solution: 0.25 mg/mL of USP Losartan Potassium RS in Solution A. Pass through a PTFE or equivalent filter of 0.45-µm pore size.

Sample stock solution: Transfer 10 Tablets to a 500-mL volumetric flask, add Solution A to fill the flask about 50% of the final volume, and sonicate with intermittent shaking for 15 min. Sonicate for an additional 10 min. Dilute with Solution A to volume, and mix well.

Sample solution: 0.25 mg/mL of losartan potassium in Solution A from the Sample stock solution. Mix well. Pass an aliquot of the solution through a PTFE filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system

Chromatographic system

Suitability requirements

Tailing factor: NMT 2.0 for the losartan, 1-H-dimer, and 2-H-dimer peaks; System suitability solution

Resolution: NLT 2.0 between the 1-H-dimer and 2-H-dimer, System suitability solution

Column efficiency: NLT 3000 theoretical plates, Standard solution

Tailing factor: NMT 2.0, Standard solution

Relative standard deviation: NMT 2.0%, Standard solution

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of losartan potassium (C22H22ClKN6O) in the portion of Tablets taken:

Result = (r0/rS) × (CS/CI) × 100

r0 = peak response of losartan from the Sample solution
rS = peak response of losartan from the Standard solution
CS = concentration of USP Losartan Potassium RS in the Standard solution (mg/mL)
CI = nominal concentration of losartan potassium in the Sample solution (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• DISSOLUTION (711)

Test 1: (0811-134-2013)

Medium: Water; 900 mL, deaerated
Apparatus 2: 50 rpm
Time: 30 min

Standard solution: (L/1000) mg/mL of USP Losartan Potassium RS in Medium, where L is the Tablet label claim, in mg

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Analysis: Determine the amount of C22H22ClKN6O dissolved by using UV absorption at the wavelength of maximum absorbance at about 256 nm on portions of the Sample solution in comparison with the Standard solution, using Medium as blank. Use the appropriate cell size as listed in Table 2 or make the appropriate dilution of the solutions with Medium to be within the linearity range of the spectrophotometer.

Table 1

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<td>15</td>
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<td>20</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Tablet Strength (mg/Tablet)</th>
<th>Cell Size (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>1.0</td>
</tr>
<tr>
<td>50</td>
<td>0.5</td>
</tr>
<tr>
<td>100</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Calculate the percentage of losartan potassium (C22H22ClKN6O) dissolved:

Result = (AQ/AI) × (CS/L) × V × 100

AQ = absorbance of the Sample solution
AI = absorbance of the Standard solution
CS = concentration of USP Losartan Potassium RS in the Standard solution (mg/mL)
L = label claim (mg/Tablet)
V = volume of Medium, 900 mL
Tolerances: NLT 75% (Q) of the labeled amount of losartan potassium (C22H22ClKN6O) is dissolved.

**Test 2**: If the product complies with this test, the labeling indicates that the product meets USP Dissolution Test 2.

**Medium**: Water; 900 mL

**Apparatus 2**: 75 rpm

**Buffer**: 1.4 g/L of anhydrous monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.3 ± 0.1

**Mobile phase**: Methanol, acetonitrile, and Buffer (20:20:60)

**Standard solution**: 0.028 mg/mL of USP Losartan Potassium RS in Medium

Sample solution

For Tablets labeled to contain 25 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

For Tablets labeled to contain 50 mg and 100 mg: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Further dilute the filtrate with Medium to prepare a 0.028-mg/mL solution.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode**: LC

**Detector**: UV 265 nm

**Column**: 4.6-mm × 15-cm; 5-µm packing L10

**Column temperature**: 45°C

**Flow rate**: 1.5 mL/min

**Injection size**: 10 µL

**System suitability**

**Samples**: Standard solution

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

**Analysis**

**Samples**: Standard solution and Sample solution

Calculate the percentage of losartan potassium (C22H22ClKN6O) in the portion of Tablet taken:

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

**Organic Impurities**

Solution A, Solution B, Mobile phase, System suitability solution, Sample solution, and Chromatographic system: Prepare as directed in the Assay.

**Standard stock solution**: Use the Standard solution, prepared as directed in the Assay.

**Limit of quantitation solution**: Dilute Standard solution in Solution A (1 in 10).

**Acceptance criteria**: Meet the requirements

**Uniformity of Dosage Units (905)**: Meet the requirements

**Procedure for content uniformity**

**Buffer**: Dissolve 1.36 mg/mL of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.5.

**Diluent**: Dissolve 17.42 g of dibasic potassium phosphate in 900 mL of water. Adjust with phosphoric acid to a pH of 8.0. Dilute with water to a volume of 1000 mL, and mix well. Prepare a dilution in water (1 in 10), and mix well.

**Mobile phase**: Acetonitrile and Buffer (3:2)

**Standard solution**: 0.05 mg/mL of USP Losartan Potassium RS in Diluent

**Sample stock solution**: Transfer 1 Tablet to a 100-mL volumetric flask, add about 65 mL of Diluent, and shake mechanically for 30 min. Dilute with Diluent to volume, and mix well.
Add the following:

**Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if Test 1 is not used.

**USP Reference Standards (11)**

USP Losartan Potassium RS

### Table 3

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>1-H-Dimer&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.4</td>
<td>0.5</td>
</tr>
<tr>
<td>2-H-Dimer&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Total impurities&lt;sup&gt;c&lt;/sup&gt;</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> S-[4′-{2-Butyl-S-(S-[4′-([2-butyl-4-chloro-5-hydroxymethyl-1H-imidazol-1-yl]methyl)biphenyl-2-yl]-1H-tetrazol-1-yl)ethyl]-4-chloro-1H-imidazol-1-yl]methyl)biphenyl-2-yl]tetrazol, potassium salt.

<sup>b</sup> S-[4′-{2-Butyl-S-(S-[4′-([2-butyl-4-chloro-5-hydroxymethyl-1H-imidazol-1-yl]methyl)biphenyl-2-yl]-2H-tetrazol-2-yl)ethyl]-4-chloro-1H-imidazol-1-yl]methyl)biphenyl-2-yl]tetrazol, potassium salt.

<sup>c</sup> The total impurities include the sum of all the specified impurities and the sum of all the unspecified impurities that are equal to or greater than 0.1%.

### Additional Requirements

**Packaging and Storage:** Store in tightly closed containers, protected from light, at controlled room temperature.