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.

  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 1H-dimer and 2H-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 to 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
  (See Chromatography (621), System Suitability.)
  Mode: LC
  Detector: UV 250 nm
  Column: 3.9-mm × 15-cm; 5-μm packing L7
  Flow rate: 1.0 mL/min
  Injection size: 10 μL
  System suitability
  Samples: System suitability solution and Standard solution
  Suitability requirements
  Tailing factor: NMT 2.0 for the losartan, 1H-dimer, and 2H-dimer peaks, System suitability solution
  Resolution: NLT 2.0 between the 1H-dimer and 2H-dimer, System suitability solution
  Column efficiency: NLT 3000 theoretical plates, Standard solution
  Mobile phase: Methanol, acetonitrile, and Buffer (20:20:60)

  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>

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:

\[ \text{Result} = \frac{(r_U/r_S) \times (C_S/C_U) \times 100}{100} \]

- \( r_U \): peak response of losartan from the Sample solution
- \( r_S \): peak response of losartan from the Standard solution
- \( C_S \): concentration of USP Losartan Potassium RS in the Standard solution (mg/mL)
- \( C_U \): 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 (88-1.4.6.2011)
  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 losartan potassium (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.

  \[ \text{Result} = \frac{(A_U/A_S) \times (C_U/L) \times V \times 100}{100} \]

- \( A_U \): absorbance of the Sample solution
- \( A_S \): absorbance of the Standard solution
- \( C_U \): 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
  Time: 30 min
  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)

  Calculate the percentage of losartan potassium (C22H22ClKN6O) dissolved:

  \[ \text{Result} = \frac{(A_U/A_S) \times (C_U/L) \times V \times 100}{100} \]

- \( A_U \): absorbance of the Sample solution
- \( A_S \): absorbance of the Standard solution
- \( C_U \): 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.

  Change to read:

  \( \text{Table 2} \)

<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:

\[ \text{Result} = \frac{(A_U/A_S) \times (C_U/L) \times V \times 100}{100} \]
### Analysis

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of losartan potassium \((C_22H_22ClKN_6O)\) in the portion of the Tablet taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100
\]

\(r_U\) = peak response of losartan from the Sample solution

\(r_S\) = peak response of losartan from the Standard solution

\(C_U\) = concentration of USP Losartan Potassium RS in the Standard solution (mg/mL)

\(C_S\) = concentration of losartan in the Sample solution (mg/mL)

**Acceptance criteria:** Meet the requirements

### IMPURITIES

- **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.

**Standard solution:** 2.5 \(\mu\)g/mL of USP Losartan Potassium RS in Solution A from the Standard stock solution

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

**System suitability**

**Samples:** System suitability solution, Standard solution, and Limit of quantitation solution

**Suitability requirements**

Signal-to-noise ratio: NLT 10 for the losartan peak from the first injection. If this is not met, then the Signal-to-noise ratio must be greater than 3 with a relative standard deviation of area counts less than 25% for three replicate injections, Limit of quantitation solution.

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

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

**Column efficiency:** NLT 3000 theoretical plates, Standard solution

**Tailing factor:** NMT 2.0, Standard solution

**Relative standard deviation:** NMT 5.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

[Note—Identify the peaks using the relative retention times provided in Table 3.]

Calculate the percentage of each impurity in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100
\]

\(r_U\) = peak response of each individual impurity from the Sample solution

\(r_S\) = peak response of losartan from the Standard solution

\(C_U\) = concentration of USP Losartan Potassium RS in the Standard solution (mg/mL)

\(C_S\) = nominal concentration of losartan potassium in the Sample solution (mg/mL)

**Acceptance criteria:** Meet the requirements

### UNIFORMITY OF DOSAGE UNITS (905)

**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.

**Sample solution:** 0.05 mg/mL of losartan potassium in Diluent from the Sample stock solution. Filter an aliquot of the solution, and use the filtrate.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 265 nm

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

**Flow rate:** 1.5 mL/min

**Injection size:** 20 µL

**System suitability**

**Samples:** Standard solution

**Suitability requirements**

**Column efficiency:** NLT 3000 theoretical plates

**Relative standard deviation:** NMT 2.0%
Losartan Potassium and Hydrochlorothiazide Tablets

Definition
Losartan Potassium and Hydrochlorothiazide Tablets contain NLT 95.0% and NMT 105.0% of the labeled amounts of losartan potassium (C22H22ClKN6O) and hydrochlorothiazide (C7H8ClN3O4S2) in the form of a combination tablet.

Identification
The retention times of the major peaks of the Sample solution correspond to those of the Standard solution, as obtained in the Assay.

Assay
Procedure
Buffer A: 2.76 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 2.5.
Buffer B: 1.25 g/L of monobasic potassium phosphate and 1.5 g/L of dibasic sodium phosphate in water. The pH of the resulting solution is about 7.0–7.5.
Diluent: Acetonitrile and Buffer A (3:2)
Solution A: Acetonitrile and Buffer B (7:93)
Solution B: Use acetonitrile.
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>100</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>92</td>
<td>8</td>
</tr>
<tr>
<td>28</td>
<td>38</td>
<td>62</td>
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<tr>
<td>30</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>35</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 280 nm
Column: 3.9-mm × 15-cm; 5-µm packing L7
Column temperature: 35°C
Flow rate: 1 mL/min
Injection size: 20 µL
System suitability
Sample: Standard solution
Suitability requirements
Tailing factor: Less than 2.5 for the losartan peak
Relative standard deviation: Less than 2.0% for both hydrochlorothiazide and losartan peaks

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of C22H22ClKN6O or C7H8ClN3O4S2 in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times (C_i/C_0) \times 100 \]

- \( r_U \) = peak response of losartan or hydrochlorothiazide from the Sample solution
- \( r_S \) = peak response of losartan or hydrochlorothiazide from the Standard solution