Losartan Potassium Tablets

DEFINITION

Losartan Potassium Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$).

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* (15:85)

Solution B: Use acetonitrile.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
10	40	60
11	80	20
15	80	20

System suitability stock 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° 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 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 volume: 10 µL

System suitability
Samples: *System suitability solution* and *Standard solution*

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 ($C_{22}H_{22}ClKN_6O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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**• (RB 1-Jul-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 ($C_{22}H_{22}ClKN_6O$) 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 2

Tablet Strength (mg/Tablet)	Cell Size (cm)
25	1.0
50	0.5
100	0.2

Calculate the percentage of losartan potassium ($C_{22}H_{22}ClKN_6O$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = 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 ($C_{22}H_{22}ClKN_6O$) 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)
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 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°
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability
Sample: *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 the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = 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 85% (*Q*) of the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved. ● (RB 1-Jul-2011)

• **Test 3:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.
Medium: Water; 900 mL, deaerated
Apparatus 2: 50 rpm
Time: 30 min for 25-mg and 50-mg Tablet strengths, and 45 min for 100-mg Tablet strength.
Buffer: 0.025 M phosphoric acid. Adjust with 1 N sodium hydroxide to a pH of 2.15.
Mobile phase: Acetonitrile and *Buffer* (400:600)
Standard stock solution: 0.27 mg/mL of USP Losartan Potassium RS prepared as follows. Add methanol to USP Losartan Potassium RS to fill about 10% of the volume of the flask, and add *Medium* to fill about 50% of the volume of the flask. Sonicate for NLT 15 min. Cool to room temperature, and dilute with *Medium* to volume.
Standard solution: Prepare as directed in *Table 3* from the *Standard stock solution*.

Table 3

Tablet Strength (mg/Tablet)	Concentration (mg/mL)
25	0.027
50	0.054
100	0.108

Sample solution: Pass a portion of the solution under test through a suitable polyethylene filter of 10-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 10-cm; 3.5-µm packing L7
Column temperature: 40°
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability
Sample: *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 the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

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)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL
Tolerances: NLT 75% (*Q*) of the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved for 25-mg and 50-mg Tablet strengths.
NLT 80% (*Q*) of the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved for 100-mg Tablet strength. ● (RB 1-May-2012)

• **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. Further dilute with water (1 in 10), and mix well.
Mobile phase: Acetonitrile and *Buffer* (60:40)
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 230 nm
Column: 4.6-mm × 25-cm; 10-µm packing L7
Flow rate: 1.4 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 3000 theoretical plates
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of losartan potassium ($C_{22}H_{22}ClKN_6O$) in the portion of the Tablet taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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: Meet the requirements

IMPURITIES

Change to read:

- **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 µg/mL of USP Losartan Potassium RS in *Solution A* from the *Standard stock solution*
Sensitivity solution: Dilute 1 mL of the *Standard solution* to 10 mL in *Solution A*.
System suitability
Samples: *System suitability solution*, *Standard solution*, and *Sensitivity 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, *Sensitivity solution*.
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 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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*
r_S = peak response of losartan from the *Standard solution*
C_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: See *Table 4*.

Table 4

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Losartan	1.0	—
1*H*-Dimer[a]	2.4	0.5
2*H*-Dimer[b]	2.9	0.5
Total impurities[c]	—	1.0

[a] 5-[4′-({2-Butyl-5-[(5-{4′-[(2-butyl-4-chloro-5-hydroxymethyl-1*H*-imidazol-1-yl)methyl]biphenyl-2-yl}-1*H*-tetrazol-1-yl)methyl]-4-chloro-1*H*-imidazol-1-yl}methyl)biphenyl-2-yl]tetrazol, potassium salt.
[b] 5-[4′-({2-Butyl-5-[(5-{4′-[(2-butyl-4-chloro-5-hydroxymethyl-1*H*-imidazol-1-yl)methyl]biphenyl-2-yl}-2*H*-tetrazol-2-yl)methyl]-4-chloro-1*H*-imidazol-1-yl}methyl)biphenyl-2-yl]tetrazol, potassium salt.
[c] The total impurities include the sum of all the specified impurities and the sum of all the unspecified impurities. Disregard peaks equal to or ●less● (RB 1-May-2012) than 0.1%.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Store in tightly closed containers, protected from light, at controlled room temperature.

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.● (RB 1-Jul-2011)
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Losartan Potassium RS