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* (3:17)

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 size: 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 size: 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)

• **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 230 nm

Column: 4.6-mm × 25-cm; 10-µm packing L7

Flow rate: 1.4 mL/min

Injection size: 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 = 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 µg/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, 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 3*.

Table 3

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 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.

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

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 ($C_{22}H_{22}ClKN_6O$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

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.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
12	92	8
28	38	62
30	100	0
35	100	0

Standard solution: Transfer USP Losartan Potassium RS and USP Hydrochlorothiazide RS into a suitable volumetric flask, and dissolve in *Diluent* (50% of the volume of the flask). Dilute with *Buffer A* to volume to obtain a solution having concentrations as directed in the table below. Pass a portion of the solution through a PTFE or equivalent filter of 0.45-µm pore size.

Tablet Strength Losartan Potassium/Hydrochlorothiazide (mg)	Concentration of USP Losartan Potassium RS (mg/mL)	Concentration of USP Hydrochlorothiazide RS (mg/mL)
50/12.5	0.4	0.1
100/12.5	0.4	0.05
100/25	0.4	0.1

Sample stock solution: Transfer 10 Tablets into a suitable volumetric flask and add *Diluent* as directed in the table below. Mix well and mechanically shake or stir until the solid is dispersed. Dilute with *Buffer A* to volume, and sonicate.

Tablet Strength Losartan Potassium/Hydrochlorothiazide (mg)	Flask Size (mL)	Volume of Diluent (mL)
50/12.5	250	210
100/12.5	500	420
100/25	500	420

Sample solution: Dilute a portion of the *Sample stock solution* first with acetonitrile (20% of the volume of the flask) and then with *Buffer A*, to obtain a solution having nominal concentrations as directed in the table below. Pass a portion of this solution through a PTFE or equivalent filter of 0.45-µm pore size, and use the filtrate.

Tablet Strength Losartan Potassium/Hydrochlorothiazide (mg)	Concentration of USP Losartan Potassium RS (mg/mL)	Concentration of USP Hydrochlorothiazide RS (mg/mL)
50/12.5	0.4	0.1
100/12.5	0.4	0.05
100/25	0.4	0.1

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°
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 $C_{22}H_{22}ClKN_6O$ or $C_7H_8ClN_3O_4S_2$ 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 or hydrochlorothiazide from the *Sample solution*
r_S = peak response of losartan or hydrochlorothiazide from the *Standard solution*