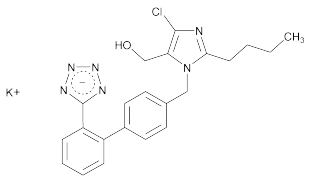
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 230-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.0; and the relative standard deviation is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of lorazepam ($C_{15}H_{10}Cl_2N_2O_2$) in each Tablet taken by the formula:

$$100(C / 20)(V_U / V)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Lorazepam RS in the *Standard preparation;* V_U is the final volume, in mL, of the *Assay preparation;* V is the volume, in mL, of the clear supernatant taken to prepare the *Assay preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Losartan Potassium



$C_{22}H_{22}ClKN_6O$ 461.00

1*H*-Imidazole-5-methanol, 2-butyl-4-chloro-1-[[2′-(1*H*-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl]-, monopotassium salt.

2-Butyl-4-chloro-1-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl] imidazole-5-methanol, monopotassium salt [124750-99-8].

» Losartan Potassium contains not less than 98.5 percent and not more than 101.0 percent of $C_{22}H_{22}ClKN_6O$ calculated on the anhydrous, solvent-free basis.

Packaging and storage—Preserve in well-closed containers. Store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Losartan Potassium RS

Identification—

A: *Infrared Absorption* ⟨197M⟩—

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg per mL.

Medium: methanol.

C: It meets the requirements of the test for *Potassium* ⟨191⟩.

Water, *Method I* ⟨921 ⟩**:** not more than 0.5%.

Heavy metals, *Method II* ⟨231⟩**:** 0.001%.

Chromatographic purity—

Solution A—Prepare a 0.1% solution of phosphoric acid in water.

Solution B—Use acetonitrile.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩.

System suitability solution—Dissolve an accurately weighed quantity of USP Losartan Potassium RS and triphenylmethanol in methanol, and dilute quantitatively, and stepwise if necessary, to obtain a solution having known concentrations of about 0.3 mg per mL and 0.002 mg per mL, respectively.

Test solution—Transfer about 30 mg of Losartan Potassium, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.0-mm × 25-cm column containing packing L1. The flow rate is about l mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	75	25	equilibration
0–25	75→10	25→90	linear gradient
25–35	10	90	isocratic
35–45	10→75	90→25	linear gradient
45–50	75	25	re-equilibration

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for losartan and 1.9 for triphenylmethanol; and the tailing factor for losartan is not more than 1.6. [NOTE—The typical retention time for triphenylmethanol is about 20 minutes.]

Procedure—Inject a volume (about 10 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Losartan Potassium taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity; and r_s is the sum of the responses for all the peaks: not more than 0.2% of any individual impurity is found; and not more than 0.5% of total impurities is found.

Assay—

Solution A and *Solution B*—Proceed as directed in the test for *Chromatographic purity.*

Mobile phase—Prepare a filtered and degassed mixture of *Solution A* and *Solution B* (3:2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Losartan Potassium RS in methanol, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.25 mg per mL.

Assay preparation—Transfer about 25 mg of Losartan Potassium, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.0-mm × 25-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. The column temperature is maintained at about 35°. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 5600 theoretical plates; the tailing factor is not more than 1.4; and the relative standard deviation for replicate injections is not more than 0.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{22}H_{22}ClKN_6O$ in the portion of Losartan Potassium taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Losartan Potassium RS in the *Standard preparation;* and r_U and r_S are the peak areas for the losartan peak obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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)