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Lisinopril Tablets

DEFINITION
Lisinopril Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_5$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2022)

ASSAY

Change to read:

• **Procedure**

Buffer: Dissolve 4.1 g of monobasic potassium phosphate in about 900 mL of water in a 1000-mL flask, and adjust with phosphoric acid to a pH of 2.0. Dilute with water to volume, and mix.

Mobile phase: Dissolve 1.0 g of sodium 1-hexanesulfonate in 820 mL of *Buffer*. Add 180 mL of acetonitrile.

Diluent: Methanol and water (20:80)

Standard solution: 0.2 mg/mL of USP Lisinopril RS in *Diluent*

Sample solution: Nominally 0.2 mg/mL of lisinopril prepared as follows. Transfer 10 Tablets into a suitable volumetric flask. Add *Diluent*, and sonicate for 5 min. Shake the flask by mechanical means for 20 min. Dilute with *Diluent* to volume, mix, and filter.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 215 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Aug-2022)

Column: 4.6-mm × 20-cm; ▲10-µm▲ (USP 1-Aug-2022) packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2.4 times the retention time of lisinopril▲ (USP 1-Aug-2022)

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Aug-2022)

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_5$) in the portion of Tablets taken:

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

r_U = peak response of lisinopril from the *Sample solution*

r_S = peak response of lisinopril from the *Standard solution*

C_S = concentration of USP Lisinopril RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of lisinopril in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis 1

Procedure for pooled sample: Proceed as directed under *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms*. Combine equal volumes of the filtered solutions of the 6 or 12 individual specimens withdrawn, and use the pooled sample as the *Sample solution*. Inject a volume of the pooled sample into the chromatograph, record the chromatogram, and measure the response for the major peak.

Calculate the quantity of lisinopril ($C_{21}H_{31}N_3O_5$) dissolved in comparison with a *Standard solution* having a known concentration of USP Lisinopril RS in the same *Medium* and similarly chromatographed.

Tolerances 1: NLT 80% (*Q*) of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_5$) is dissolved: the requirements are met if the quantities of active ingredient dissolved from the pooled sample conform to the accompanying *Acceptance Table for a Pooled Sample*. Continue testing through the three stages unless the results conform at either S_1 or S_2. The quantity, *Q*, is the amount of dissolved active ingredient specified, expressed as a percentage of the labeled content.

Acceptance Table for a Pooled Sample

Stage	Number Tested	Acceptance Criteria
S_1	6	Average amount dissolved is NLT *Q* + 10%.
S_2	6	Average amount dissolved ($S_1 + S_2$) is equal to or greater than *Q* + 5%.
S_3	12	Average amount dissolved ($S_1 + S_2 + S_3$) is equal to or greater than *Q*.

Analysis 2

Procedure for unit sample: Proceed as directed under *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms*. Inject a volume of a filtered portion of the *Sample solution* into the chromatograph, record the chromatogram, and measure the response for the major peak.

Calculate the amount of lisinopril ($C_{21}H_{31}N_3O_5$) dissolved in comparison with the *Standard solution* having a known concentration of USP Lisinopril RS in the *Medium* and similarly chromatographed.

Tolerances 2: NLT 80% (*Q*) of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_5$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

▲▲ (USP 1-Aug-2022)

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Sensitivity solution:** 0.2 µg/mL of USP Lisinopril RS in *Diluent*▲ (USP 1-Aug-2022)

Standard solution: ▲0.2 mg/mL of USP Lisinopril RS and 0.002 mg/mL of USP Lisinopril Related Compound A RS▲ (USP 1-Aug-2022) in *Diluent*

System suitability

Samples: ▲*Sensitivity solution* and▲ (USP 1-Aug-2022) *Standard solution*

Suitability requirements

▲▲ (USP 1-Aug-2022)

Tailing factor: NMT 2.0 ▲for lisinopril and NMT 1.5 for lisinopril related compound A,▲ (USP 1-Aug-2022) *Standard solution*

Relative standard deviation: NMT 2% ▲for lisinopril and NMT 10% for lisinopril related compound A,▲ (USP 1-Aug-2022) *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Aug-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of lisinopril related compound A in the portion of Tablets taken:

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

r_U =peak response of lisinopril related compound A from the *Sample solution*

r_S = peak response of lisinopril related compound A from the *Standard solution*

C_S = concentration of USP Lisinopril Related Compound A RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of lisinopril in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2022)

Calculate the percentage of ▲any unspecified degradation product▲ (USP 1-Aug-2022) in the portion of Tablets taken:

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

r_U = ▲peak response of any unspecified degradation product▲ (USP 1-Aug-2022) from the *Sample solution*

r_S = peak response of lisinopril from the *Standard solution*

C_S = concentration of USP Lisinopril RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of lisinopril in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.1%.▲ (USP 1-Aug-2022)

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lisinopril	1.0	—
▲Lisinopril related compound A	2.1	1.5
Any unspecified degradation product	—	0.2▲ (USP 1-Aug-2022)
Total ▲degradation products▲ (USP 1-Aug-2022)	—	2.0

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** ▲Store at controlled room temperature. Protect from moisture, freezing, and excessive heat.▲ (USP 1-Aug-2022) Preserve in tight containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Lisinopril RS

▲ USP Lisinopril Related Compound A RS

(*S*)-2-{(3*S*,8a*S*)-3-(4-Aminobutyl)-1,4-dioxohexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl}-4-phenylbutanoic acid.

$C_{21}H_{29}N_3O_4$ 387.47▲ (USP 1-Aug-2022)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LISINOPRIL TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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