

Status: Currently Official on 15-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-DAD3A520-04BD-433D-B0D8-BF0F0E0F3DBB_1_en-US
DOI: https://doi.org/10.31003/USPNF_M45572_01_01
DOI Ref: 5y9jw

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Lisinopril and Hydrochlorothiazide Tablets

DEFINITION
Lisinopril and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_9$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION
• **A.** 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**
The Tablets must be assayed within 24 h of the time they are put in the solution.
Buffer: Dissolve 4.08 g of monobasic potassium phosphate in 800 mL of water. Adjust with phosphoric acid to a pH of 2.5, and dilute with water to 1 L.
Mobile phase: Acetonitrile, triethylamine, water, and phosphoric acid (280:3:1480:15)
Lisinopril standard stock solution: 0.5 mg/mL of [USP Lisinopril RS](#) in Buffer
Hydrochlorothiazide standard stock solution: 3.12 mg/mL of [USP Hydrochlorothiazide RS](#) in methanol
Lisinopril related compound A stock solution: 0.05 mg/mL of [USP Lisinopril Related Compound A RS](#) in methanol
Benzothiadiazine related compound A stock solution: 0.016 mg/mL of [USP Benzothiadiazine Related Compound A RS](#) in methanol
Standard solution: 0.1 mg/mL of [USP Lisinopril RS](#), 0.125 mg/mL of [USP Hydrochlorothiazide RS](#), 2 µg/mL of [USP Lisinopril Related Compound A RS](#), and 1.3 µg/mL of [USP Benzothiadiazine Related Compound A RS](#) in Buffer from *Lisinopril standard stock solution*, *Hydrochlorothiazide standard stock solution*, *Lisinopril related compound A stock solution*, and *Benzothiadiazine related compound A stock solution*. For Tablet strengths 20/12.5 of lisinopril/hydrochlorothiazide, the concentration of [USP Lisinopril RS](#) and [USP Lisinopril Related Compound A RS](#) in the *Standard solution* is 0.2 mg/mL and 4 µg/mL, respectively.
Sample stock solution: Transfer 10 Tablets to a suitable volumetric flask. Add Buffer (0.25 mL/mg of total lisinopril), sonicate for 5 min, and then add methanol (0.5 mL/mg of total lisinopril). Sonicate for an additional 10 min. Add more Buffer (0.75 mL/mg of total lisinopril), and mix by mechanical means for 20 min. Dilute with water to volume to prepare solutions as described in [Table 1](#).

Table 1

Tablet Strength of Lisinopril/ Hydrochlorothiazide (mg/Tablet)	Nominal Concentration of Lisinopril/ Hydrochlorothiazide (mg/mL)
10/12.5	0.4/0.5
20/12.5	0.4/0.25
20/25	0.4/0.5

Sample solution: Dilute the *Sample stock solution* with Buffer to prepare solutions as described in [Table 2](#). Pass a portion through a suitable filter of 0.45-µm pore size.

Table 2

Tablet Strength of Lisinopril/ Hydrochlorothiazide (mg/Tablet)	Nominal Concentration of Lisinopril/ Hydrochlorothiazide (mg/mL)
10/12.5	0.1/0.12
20/12.5	0.2/0.125
20/25	0.1/0.12

Chromatographic system(See [Chromatography \(621\), System Suitability](#).)**Mode:** LC**Detector:** UV 215 nm**Column:** 4.6-mm × 15-cm; 5-μm packing L7**Flow rate:** 1.5 mL/min**Injection volume:** 10 μL**Run time:** NLT 10 min**System suitability****Sample:** *Standard solution***Suitability requirements****Resolution:** NLT 3.0 between lisinopril and benzothiadiazine related compound A and NLT 4.0 between hydrochlorothiazide and benzothiadiazine related compound A**Tailing factor:** NMT 2 for both the lisinopril and hydrochlorothiazide peaks**Relative standard deviation:** NMT 2.0% for both the lisinopril and hydrochlorothiazide peaks**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lisinopril ($C_{21}H_{31}N_3O_5$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Tablets taken:

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

 r_U = peak response of lisinopril or hydrochlorothiazide from the *Sample solution*
 r_S = peak response of lisinopril or hydrochlorothiazide from the *Standard solution*
 C_S = concentration of [USP Lisinopril RS](#) or [USP Hydrochlorothiazide RS](#) in the *Standard solution* (mg/mL)

 C_U = nominal concentration of lisinopril or hydrochlorothiazide in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%**PERFORMANCE TESTS**• [DISSOLUTION \(711\)](#)**Test 1****Medium:** 0.1 N hydrochloric acid; 900 mL**Apparatus 2:** 50 rpm**Time:** 45 min for hydrochlorothiazide; 30 min for lisinopril**Buffer and Mobile phase:** Prepare as directed in the Assay.**Lisinopril standard stock solution:** 0.5 mg/mL of [USP Lisinopril RS](#) in *Buffer***Hydrochlorothiazide standard stock solution:** 0.44 mg/mL of [USP Hydrochlorothiazide RS](#) in methanol**Standard solution:** Prepare solutions in *Medium* as described in [Table 3](#) from the *Lisinopril standard stock solution* and *Hydrochlorothiazide standard stock solution*.**Table 3**