Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2019
Document Type: USP Monographs
DocId: GUID-4A6E0401-8389-4BE1-8657-2A863C3F4D92_2_en-US
DOI: https://doi.org/10.31003/USPNF_M12398_02_01
DOI Ref: umb2x

Captopril and Hydrochlorothiazide Tablets

DEFINITION

Captopril and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount each of captopril ($C_9H_{15}NO_3S$) 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*.

Add the following:

▲• **B.** The UV spectra of the hydrochlorothiazide and captopril peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2019)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Methanol, phosphoric acid, and water (250:0.5:750)

System suitability solution: 0.3 mg/mL each of USP Captopril RS, USP Hydrochlorothiazide RS, and USP Benzothiadiazine Related Compound A RS in *Mobile phase*

Standard solution: 0.3 mg/mL of USP Hydrochlorothiazide RS and about 0.3*J* mg/mL of USP Captopril RS in *Mobile phase*, *J* being the ratio of the labeled amount of captopril (mg) to the labeled amount of hydrochlorothiazide (mg) per Tablet

Sample solution: Nominally equivalent to 0.3 mg/mL of hydrochlorothiazide prepared as follows. Transfer 15 mg of hydrochlorothiazide from NLT 20 finely powdered Tablets into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume. Sonicate for 15 min with occasional shaking, and centrifuge.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Dec-2019)

Column: 4.6-mm × 30-cm; ▲10-µm▲ (USP 1-Dec-2019) packing L11

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for benzothiadiazine related compound A, hydrochlorothiazide, and captopril are 0.4, 0.5, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.7 between the void volume and benzothiadiazine related compound A; NLT 1.8 between benzothiadiazine related compound A and hydrochlorothiazide; and NLT 2.0 between captopril and hydrochlorothiazide, *System suitability solution*

Relative standard deviation: NMT 3.0% ▲for both the hydrochlorothiazide and captopril peaks,▲ (USP 1-Dec-2019) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of captopril ($C_9H_{15}NO_3S$) 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 captopril or hydrochlorothiazide from the *Sample solution*

r_S = peak response of captopril or hydrochlorothiazide from the *Standard solution*

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

C_U = nominal concentration of captopril or hydrochlorothiazide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 50 rpm

Times

Captopril: 20 min

Hydrochlorothiazide: 30 min

Standard solution: Known concentrations of USP Captopril RS and USP Hydrochlorothiazide RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to a concentration similar to that of the *Standard solution*.

Chromatographic system and **System suitability**▲ (USP 1-Dec-2019) **:** Proceed as directed in the *Assay*.

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of captopril ($C_9H_{15}NO_3S$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) dissolved:

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

r_U = peak response of captopril or hydrochlorothiazide from the *Sample solution*

r_S = peak response of captopril or hydrochlorothiazide from the *Standard solution*

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

L = label claim of captopril or hydrochlorothiazide (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*

▲ (USP 1-Dec-2019)

Tolerances: NLT 80% (Q) of the labeled amount of captopril ($C_9H_{15}NO_3S$) and NLT 60% (Q) of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) are dissolved.

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

IMPURITIES

Change to read:

• **Limit of Captopril Disulfide**

Mobile phase: Methanol, phosphoric acid, and water (450:0.5:550)

System suitability solution: 0.0075 mg/mL each of USP Captopril RS and USP Hydrochlorothiazide RS, and 0.015 mg/mL of USP Captopril Disulfide RS in *Mobile phase*

Standard solution: 0.015 mg/mL of USP Captopril Disulfide RS in *Mobile phase*

Sample solution: Nominally equivalent to 0.5 mg/mL of captopril prepared as follows. Transfer 25 mg of captopril from NLT 20 finely powdered Tablets into a 50-mL volumetric flask, add about 20 mL of *Mobile phase*, and sonicate for 15 min with occasional shaking. Dilute with *Mobile phase* to volume, and centrifuge. Use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: ▲4.6-mm × 30-cm; 10-µm▲ (USP 1-Dec-2019) packing L11

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for ▲hydrochlorothiazide,▲ (USP 1-Dec-2019) captopril, and captopril disulfide are ▲0.2,▲ (USP 1-Dec-2019) 0.3, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between captopril and captopril disulfide. Both peaks are resolved from hydrochlorothiazide, *System suitability solution*.

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of captopril disulfide in the portion of Tablets taken:

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

r_U = peak response of captopril disulfide from the *Sample solution*

r_S = peak response of captopril disulfide from the *Standard solution*

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

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

Acceptance criteria: NMT 3.0%

• **Limit of Benzothiadiazine Related Compound A**

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

Standard solution: 0.01 mg/mL of USP Benzothiadiazine Related Compound A RS in *Mobile phase*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benzothiadiazine 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 benzothiadiazine related compound A from the *Sample solution*

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

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

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

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at controlled room temperature.▲ (USP 1-Dec-2019)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Benzothiadiazine Related Compound A RS

4-Amino-6-chloro-1,3-benzenedisulfonamide.

$C_6H_8ClN_3O_4S_2$ 285.73

USP Captopril RS

USP Captopril Disulfide RS

▲(2′*S*)-[(2*S*,2′*S*)-3,3′-Disulfanediylbis(2-methylpropanoyl)]di-L-proline.▲ (USP 1-Dec-2019)

$C_{18}H_{28}N_2O_6S_2$ 432.55

USP Hydrochlorothiazide RS

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

Topic/Question	Contact	Expert Committee
CAPTOPRIL AND HYDROCHLOROTHIAZIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(4)

Current DocID: GUID-4A6E0401-8389-4BE1-8657-2A863C3F4D92_2_en-US

DOI: https://doi.org/10.31003/USPNF_M12398_02_01

DOI ref: umb2x