Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2019
Document Type: USP Monographs
DocId: GUID-9B6D2632-DF3B-4E43-A129-1246C8DAA3BA_2_en-US
DOI: https://doi.org/10.31003/USPNF_M84942_02_01
DOI Ref: qe5j9

Triamterene and Hydrochlorothiazide Capsules

DEFINITION

Triamterene and Hydrochlorothiazide Capsules contain NLT 90.0% and NMT 110.0% of the labeled amounts of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

[Note—The Capsule and Tablet dosage forms should not be considered bioequivalent. If patients are to be transferred from one dosage form to the other, retitration and appropriate changes in dosage may be necessary.]

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectra of the major peaks of the *Diluted sample solution* correspond to those of the *Diluted standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2019)

• **B.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

Buffer: Transfer 6.9 g of monobasic sodium phosphate and 1.43 g of propylamine hydrochloride to a 1-L volumetric flask. Dissolve in 900 mL of water, adjust with 1 N sodium hydroxide to a pH of 5.5, and dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (20:80)

▲**Diluent:** Acetonitrile, glacial acetic acid, and water (10:5:85)▲ (USP 1-Aug-2019)

Standard solution: ▲0.25 mg/mL of USP Hydrochlorothiazide RS and 0.25(*J*) mg/mL of USP Triamterene RS prepared as follows.▲ (USP 1-Aug-2019) Transfer 25 mg of USP Hydrochlorothiazide RS into a 100-mL volumetric flask. Add 25*J* mg of USP Triamterene RS, *J* being the ratio of the labeled amount, in milligrams, of triamterene to the labeled amount, in milligrams, of hydrochlorothiazide/Capsule. Add 10 mL of acetonitrile, 10 mL of water, and 5 mL of glacial acetic acid, sonicating for 2–3 min after each addition. Cool to room temperature, and dilute with water to volume.

▲**Diluted standard solution:** 0.125 mg/mL of USP Hydrochlorothiazide RS and 0.125(*J*) mg/mL of USP Triamterene RS from *Standard solution* in *Diluent*▲ (USP 1-Aug-2019)

Sample solution: ▲Nominally 0.25 mg/mL of hydrochlorothiazide prepared as follows.▲ (USP 1-Aug-2019) Transfer a portion nominally equivalent to 50 mg of hydrochlorothiazide from NLT 20 Capsules (remove, as completely as possible, the contents of Capsules) to a 200-mL volumetric flask. Add 20 mL of acetonitrile, and sonicate for 10 min. Add 20 mL of boiling water, sonicate for 5 min, and mix. Add 10 mL of acetic acid, sonicate for 10 min, and mix. Add 140 mL of water, mix, and allow to cool to room temperature. Dilute with water to volume, mix, and filter, discarding the first 3 mL of the filtrate.

▲**Diluted sample solution:** Nominally 0.125 mg/mL of hydrochlorothiazide from *Sample solution* in *Diluent*▲ (USP 1-Aug-2019)

Chromatographic system

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

Mode: LC

Detector: UV 280 nm. ▲For *Identification A*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Aug-2019)

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-Aug-2019) packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2 times the retention time of triamterene▲ (USP 1-Aug-2019)

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for hydrochlorothiazide and triamterene are 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between hydrochlorothiazide and triamterene

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution*, ▲*Diluted standard solution*, *Sample solution*, and *Diluted sample solution*. [NOTE—The *Diluted standard solution* and *Diluted sample solution* are used for *Identification A*.]▲ (USP 1-Aug-2019)

Calculate the percentage of the labeled amount of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Capsules taken:

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

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

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

C_S = concentration of ▲USP Triamterene RS or USP Hydrochlorothiazide RS▲ (USP 1-Aug-2019) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

Test 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.

Medium: 0.1 M acetic acid containing 1% polysorbate 20; 900 mL

Apparatus 2: 100 rpm

Time: 120 min

Standard solution: A known concentration of USP Triamterene RS and USP Hydrochlorothiazide RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with water as needed in comparison with the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelengths: 357 nm for triamterene; 271 nm for hydrochlorothiazide (corrected for interference from triamterene on the basis of the absorbances of triamterene at 271 and 357 nm)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) dissolved. ▲▲ (USP 1-Aug-2019)

Tolerances: NLT 80% (*Q*) ▲▲ (USP 1-Aug-2019) of the labeled amounts of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) are dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 4.0% tetrasodium ethylenediaminetetraacetate, 2.0% polysorbate 40, and 0.05% pancreatin prepared as follows. Add the polysorbate 40 and tetrasodium ethylenediaminetetraacetate to water, and mix thoroughly. Adjust with phosphoric acid to a pH of 8.0 ± 0.05. Heat to 37°, and add the pancreatin powder. Mix thoroughly, and transfer immediately to the dissolution vessel; 900 mL

Apparatus 1 (use 10-mesh baskets)**:** 100 rpm

Time: 8 h

Buffer: 0.08 M monobasic sodium phosphate

Mobile phase: Methanol and *Buffer* (25:75)

Standard stock solution: 0.22 mg/mL of USP Triamterene RS and 0.11 mg/mL of USP Hydrochlorothiazide RS prepared as follows. To the triamterene and hydrochlorothiazide in a suitable volumetric flask add methanol to fill about 1/5 of the flask volume, sonicate for 10 min, and heat in a steam bath until completely dissolved. Dilute with *Medium* to volume.

Standard solution: ▲0.055 mg/mL of USP Triamterene RS in *Medium* prepared as follows.▲ (USP 1-Aug-2019) Transfer 25 mL of *Standard stock solution* into a 100-mL volumetric flask, dilute with *Medium* to volume, and mix gently to minimize foaming.

Sample solution: Pass a portion of the solution under test through a suitable filter. [NOTE—Do not use nylon filters.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Columns

Guard: Packing L7

Analytical: 3.9-mm × 30-cm; packing L11

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

▲[NOTE—The relative retention times for hydrochlorothiazide and triamterene are about 1.0 and 3.6, respectively.]▲ (USP 1-AUG-2019)

Suitability requirements

Resolution: NLT 2.0 for the triamterene and hydrochlorothiazide peaks

Relative standard deviation: NMT 2.0% for the triamterene and hydrochlorothiazide peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of the labeled amount of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) dissolved:

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

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

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

C_S = concentration of ▲USP Triamterene RS or USP Hydrochlorothiazide RS▲ (USP 1-Aug-2019) in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 70% (*Q*) of the labeled amount of triamterene ($C_{12}H_{11}N_7$) and NLT 80% (*Q*) of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) are dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Analysis: Proceed as directed in *Test 1*.

Tolerances: NLT 75% (*Q*) of the labeled amounts of triamterene ($C_{12}H_{11}N_7$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) are dissolved.

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩, *Content Uniformity*:** Meet the requirements with respect to triamterene and hydrochlorothiazide

IMPURITIES

Change to read:

• **ORGANIC IMPURITIES**

Solution A: 6.8 g/L of sodium acetate trihydrate in water. Adjust with glacial acetic acid to a pH of 5.0.

Solution B: Acetonitrile and methanol (75:25)

Mobile phase: *Solution B* and *Solution A* (10:90)

Standard stock solution: 0.15 mg/mL of USP Benzothiadiazine Related Compound A RS in acetonitrile

Standard solution: ▲0.015 mg/mL of USP Benzothiadiazine Related Compound A RS prepared as follows.▲ (USP 1-Aug-2019) Transfer 10.0 mL of ▲*Standard stock solution*▲ (USP 1-Aug-2019) to a 100-mL volumetric flask, add 50 mL of acetonitrile, and 6 mL of glacial acetic acid, and dilute with water to volume.

Sample solution: ▲Nominally 1.5 mg/mL of hydrochlorothiazide prepared as follows.▲ (USP 1-Aug-2019) Transfer a portion nominally equivalent to 150 mg of hydrochlorothiazide from Capsules (remove, as completely as possible, the contents of NLT 20 Capsules) to a 100-mL volumetric flask. Add 60 mL of acetonitrile and 6 mL of glacial acetic acid, and sonicate for 10 min. Cool, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 273 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

▲[NOTE—The relative retention times for benzothiadiazine related compound A, hydrochlorothiazide, and triamterene are about 1.0, 1.5, and 10, respectively.]▲ (USP 1-AUG-2019)

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benzothiadiazine related compound A in the hydrochlorothiazide contained in the portion of Capsules 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% of benzothiadiazine related compound A

ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2019)
- **LABELING:** Label the Capsules to indicate the *Dissolution* test with which the product complies.
- **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 Hydrochlorothiazide RS

USP Triamterene RS

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

Topic/Question	Contact	Expert Committee
TRIAMTERENE AND HYDROCHLOROTHIAZIDE CAPSULES	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(2)
Current DocID: GUID-9B6D2632-DF3B-4E43-A129-1246C8DAA3BA_2_en-US
DOI: https://doi.org/10.31003/USPNF_M84942_02_01
DOI ref: qe5j9