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Triamterene and Hydrochlorothiazide Tablets

DEFINITION

Triamterene and Hydrochlorothiazide Tablets 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 Capsules and Tablets 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 retention ▲times of the major peaks▲ (USP 1-Dec-2019) of the *Sample solution*▲correspond to those of▲ (USP 1-Dec-2019) the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **B.** ▲The UV spectra of the major 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**

Buffer:▲ Dissolve 0.82 g of sodium acetate anhydrous in 1000 mL of water, and adjust with glacial acetic acid to a pH of 4.5.▲ (USP 1-Dec-2019)

Mobile phase: Acetonitrile and *Buffer*▲(35:65)▲ (USP 1-Dec-2019)

Diluent: Acetonitrile, glacial acetic acid, and water▲(350:35:650)

System suitability stock solution: 1.5 µg/mL of USP Benzothiadiazine Related Compound A RS in *Diluent*. Sonicate the solution to aid the dissolution.

Standard stock solution: 0.75 mg/mL of USP Triamterene RS and 0.50 mg/mL of USP Hydrochlorothiazide RS in *Diluent*. Sonicate the solution to aid the dissolution.

System suitability solution: 22.5 µg/mL of USP Triamterene RS, 15 µg/mL of USP Hydrochlorothiazide RS, and 0.075 µg/mL of USP Benzothiadiazine Related Compound A RS from the *Standard stock solution* and *System suitability stock solution*, diluted with *Mobile phase*

Standard solution: 0.023 mg/mL of USP Triamterene RS and 0.015 mg/mL of USP Hydrochlorothiazide RS in *Mobile phase* from *Standard stock solution*

Sample stock solution: Nominally 0.5 mg/mL of hydrochlorothiazide in *Diluent* prepared as follows. Transfer a suitable number of Tablets (NLT 10) to a suitable volumetric flask. Add *Diluent* to 80% of the flask volume and sonicate for 30 min. Dilute with *Diluent* to volume. Centrifuge and use the supernatant.▲ (USP 1-Dec-2019)

Sample solution: ▲Nominally 0.015 mg/mL of hydrochlorothiazide from the *Sample stock solution*, diluted with *Mobile phase*▲ (USP 1-Dec-2019)

Chromatographic system

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

Mode: LC

Detector: ▲UV 272 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Dec-2019)

Column: ▲4.6-mm × 25-cm; 5-µm packing L1▲ (USP 1-Dec-2019)

Flow rate: ▲1 mL/min▲ (USP 1-Dec-2019)

Injection volume: ▲20 µL

Run time: NLT 2 times the retention time of hydrochlorothiazide▲ (USP 1-Dec-2019)

System suitability

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

[NOTE—The relative retention times for benzothiadiazine related compound A and hydrochlorothiazide are 0.93 and 1.0, respectively.]▲ (USP 1-DEC-2019)

Suitability requirements

Resolution:▲ NLT 1.5 between hydrochlorothiazide and benzothiadiazine related compound A, *System suitability solution*▲ (USP 1-Dec-2019)

Relative standard deviation: NMT 2.0%, ▲*Standard solution*▲ (USP 1-Dec-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of triamterene ($C_{12}H_{11}N_7$) 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 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-Dec-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⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

▲**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)▲ (USP 1-Dec-2019)

Standard solution: USP Triamterene RS and USP Hydrochlorothiazide RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

▲**Chromatographic system**

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

Mode: LC

Detector: UV 280 nm

Column: 4.0-mm × 25-cm; packing L1

Flow rate: 1.2 mL/min

Injection volume: 10 µL

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%▲ (USP 1-Dec-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts 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*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL▲ (USP 1-Dec-2019)

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

Change to read:

• **Uniformity of Dosage Units ⟨905⟩, *Content Uniformity*:** Meet the requirements ▲▲ (USP 1-Dec-2019)

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: 6.8 mg/mL 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: ▲▲ (USP 1-Dec-2019) 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-Dec-2019) Transfer 10.0 mL of the *Standard stock solution* 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-Dec-2019) Transfer an equivalent to 150 mg of hydrochlorothiazide from powdered Tablets (NLT 20) 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-Dec-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 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*▲ (USP 1-Dec-2019) (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-Dec-2019)

• **USP Reference Standards ⟨11⟩**

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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 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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