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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 25J 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.