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Triamterene Capsules

» Triamterene Capsules contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of triamterene ($C_{12}H_{11}N_7$).

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

USP Reference standards ⟨11⟩—

USP Triamterene RS

USP Triamterene Related Compound A RS

2,4,6-Triamino-5-nitrosopyrimidine.

$C_4H_6N_6O$ 154.13

USP Triamterene Related Compound B RS

2,7-Diamino-4-hydroxy-6-phenylpteridine.

$C_{12}H_{10}N_6O$ 254.25

USP Triamterene Related Compound C RS

2,4-Diamino-7-hydroxy-6-phenylpteridine.

$C_{12}H_{10}N_6O$ 254.25

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Ultraviolet-Visible Spectroscopy: 197U*▲ *(CN 1-May-2020)* —Transfer a portion of the contents of the Capsules, equivalent to about 0.1 g of triamterene, to a 250-mL volumetric flask. Add 100 mL of methoxyethanol, shake until dissolved, dilute with water to volume, and mix. Transfer 5 mL of this solution to a 200-mL volumetric flask, add 5 mL of formic acid, and dilute with water to volume. Prepare a solution of USP Triamterene RS in the manner described above to obtain a Standard solution with a final concentration of about 10 µg per mL. Determine the UV spectrum from 280 nm to 420 nm.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩—

TEST 1—

Medium: 1% w/v of polysorbate 20 in 0.1 N acetic acid; 900 mL.

Apparatus 2: 100 rpm.

Time: 120 minutes.

Procedure—Proceed as directed for *Test 2.*

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{12}H_{11}N_7$ is dissolved in 120 minutes.

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

Medium: 0.1 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{12}H_{11}N_7$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 357 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Triamterene RS in the same *Medium.*

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{12}H_{11}N_7$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Related compounds—

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

Standard solution—Transfer a known quantity of about 50 mg, accurately weighed, of each of USP Triamterene RS, USP Triamterene Related Compound A RS, USP Triamterene Related Compound B RS, and USP Triamterene Related Compound C RS into a 100-mL volumetric flask. Add approximately 4 mL of acetonitrile, and swirl the flask to wet the contents. Add 4 mL of water and swirl the flask to create a suspension. Add 2 drops (approximately 0.1 mL) of phosphoric acid directly into the suspension, followed by the addition of 50 mL of water. Shake for 15 minutes on a mechanical shaker. Warm the contents of the flask in a hot water bath (not higher than 60°) until the bulk of the material has dissolved (about 3 minutes or longer). Dissolve and dilute with water to volume, and mix well. Pass through a 0.45-µm suitable membrane filter. Dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.5 µg per mL of each of the reference standards.

Test solution—Use the *Assay preparation*.

Procedure—Inject equal quantities of about 10 µL of the *Standard solution* and the *Test solution* into the chromatograph, and measure the peak responses. Calculate the percentage of known triamterene related compounds A, B, and C in each Capsule taken by the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of the respective USP Triamterene Related Compound RS in the *Standard solution;* C_U is the concentration, in mg per mL, of triamterene in the *Test solution;* and r_U and r_S are the peak responses of each impurity obtained from the *Test solution* and the *Standard solution*, respectively. Calculate any other unknown impurity in the portion of the Capsule taken using the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of the USP Triamterene RS in the *Standard solution;* C_U is the concentration, in mg per mL, of triamterene in the *Test solution;* r_U is the peak response of any other unknown impurity obtained from the *Test solution*; and r_S is the peak response of the USP Triamterene RS in the *Standard solution:* not more than 0.2% of triamterene related compound A is found; not more than 0.2% of triamterene related compound B is found; not more than 0.2% of triamterene related compound C is found; not more than 0.2% of any other unknown individual impurity is found; and the sum of all impurities is not more than 1.0%.

Assay—

Buffer solution—Dissolve 6.8 g of sodium phosphate monobasic monohydrate (taken in a 1-L flask) in about 900 mL of water. To this solution, add 1.43 g of propylamine hydrochloride, and adjust the pH to 5.5 with 1 M sodium hydroxide. Dilute with water to volume, and mix well.

Mobile phase—Prepare a filtered and degassed mixture of the *Buffer solution* and acetonitrile (80:20). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Blank solution—Place 4 mL of acetonitrile and 4 mL of water in a 100-mL flask. Add 2 drops (approximately 0.l mL) of phosphoric acid. Dilute with water to volume, and mix well. Pass through a suitable 0.45-µg membrane filter.

System suitability solution—Accurately weigh about 5 mg of USP Triamterene Related Compound C RS and 50 mg of USP Triamterene RS into two separate 100-mL volumetric flasks. Add approximately 4 mL of acetonitrile into each flask to wet the material. Add approximately 4 mL of water into each flask to create a suspension. Add 2 drops (approximately 0.l mL) of phosphoric acid directly into the suspension in each flask. Add approximately 50 mL of water into each flask. Shake for 15 minutes on a mechanical shaker. Warm the contents of the flasks in a hot water bath (not higher than 60°), until the bulk of the material has dissolved (about 3 minutes or longer). Dissolve and dilute with water to volume, and mix well. Dilute with water appropriate portions of these solutions taken in a suitable volumetric flask, quantitatively and stepwise if necessary, to obtain a solution having a known concentration of 500 µg of USP Triamterene RS and 0.5 µg of USP Triamterene Related Compound C RS. Pass through a suitable 0.45-µm membrane filter.

Standard preparation—Accurately weigh about 50 mg of USP Triamterene RS into a 100-mL volumetric flask. Add approximately 4 mL of acetonitrile, and swirl to wet the material. Add 4 mL of water, and swirl to create a suspension. Add 2 drops of phosphoric acid into the suspension.

[**Caution—**Make sure that the phosphoric acid is not just adhering to the sides of the flask.]

Add approximately 50 mL of water into the flask, and shake for 15 minutes on a mechanical shaker. Warm the contents of the flasks in a hot water bath (not higher than 60°) until the bulk of the material has dissolved (about 3 minutes or longer). Dissolve and dilute with water to volume, and mix well. Pass through a suitable 0.45-µm membrane filter.

Assay preparation—Remove, as completely as possible, the contents of not fewer than 10 Capsules, and weigh. Transfer an accurately weighed portion of the powder, equivalent to about 500 mg of triamterene, to a 1000-mL volumetric flask. Wash the empty shells with 40 mL of acetonitrile, and add to the volumetric flask. Swirl the flask to wet the powder. Add 20 mL of water, and swirl the flask to create a suspension. Add 20 drops (approximately 1 mL) of phosphoric acid directly into the suspension. Add approximately 500 mL of water, and mix well. Shake well for 15 minutes on a mechanical shaker. Place in a hot water bath (not higher than 60°), until the bulk of the material has dissolved (about 3 minutes or longer). Cool to room temperature slowly (do not place in cold water bath). Dissolve and dilute with water to volume, and mix well. (The final solution could be slightly cloudy). Pass the solution through a suitable 0.45-µm membrane filter.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.0-mm × 300-mm column that contains 5-µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *System suitability solution* and the *Standard preparation,* and record the peak responses as directed for *Procedure:* the resolution between triamterene and triamterene related compound C is not less than 3; the tailing factor for triamterene is not more than 2.5; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure—Inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of $C_{12}H_{11}N_7$ in the portion of Tablets taken by the formula:

$$100(r_U/r_S)(C_S/C_U)$$

in which r_U is the peak response of triamterene obtained from the *Assay preparation;* r_S is the response of the corresponding peak in the *Standard preparation;* and C_S and C_U are the concentrations, in mg per mL, of triamterene in the *Standard preparation* and the *Assay preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
TRIAMTERENE 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

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