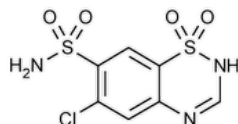


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Chlorothiazide



$C_7H_6ClN_3O_4S_2$ 295.72

2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-, 1,1-dioxide;

6-Chloro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide CAS RN®: 58-94-6; UNII: 77W477J15H.

DEFINITION

Chlorothiazide contains NLT 98.0% and NMT 102.0% of chlorothiazide ($C_7H_6ClN_3O_4S_2$), calculated on the dried basis.

IDENTIFICATION

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** 197M

Analysis: Previously dried at 105° for 1 h

Acceptance criteria: Meets the requirements

Delete the following:

- ▲ • **B. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy](#):** 197U

Medium: [sodium hydroxide](#) solution (1 in 250)

Standard solution: 10 µg/mL of [USP Chlorothiazide RS](#) in *Medium*

Sample solution: 10 µg/mL of Chlorothiazide in *Medium*

Acceptance criteria: Absorptivities at 292 nm, calculated on the dried basis, differ by NMT 3.0%.▲ (USP 1-Aug-2022)

Add the following:

- ▲ • **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.▲ (USP 1-Aug-2022)

ASSAY

Change to read:

- **PROCEDURE**

Mobile phase: [Acetonitrile](#) and 0.1 M monobasic sodium phosphate (10:90). Adjust with [phosphoric acid](#) to a pH of 3.0 ± 0.1.

System suitability solution: 0.15 mg/mL of [USP Chlorothiazide RS](#) and 1.5 µg/mL of [USP Benzothiadiazine Related Compound A RS](#) in *Mobile phase*

Standard solution: 0.15 mg/mL of [USP Chlorothiazide RS](#) in *Mobile phase*. [NOTE—A volume of [acetonitrile](#) not exceeding 10% of the total volume of the solution may be used to dissolve the Reference Standard. The *Standard solution* should be injected immediately upon preparation.]

Sample solution: 0.15 mg/mL of Chlorothiazide prepared as follows. Transfer about 30 mg of Chlorothiazide to a 200-mL volumetric flask, and dissolve in a small volume of [acetonitrile](#) not exceeding 10% of the total volume of the solution. Dilute with *Mobile phase* to volume. [NOTE—The *Sample solution* should be injected immediately upon preparation.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; ▲5-µm▲ (USP 1-Aug-2022) packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—The relative retention times are about 0.9 and 1.0 for benzothiadiazine related compound A and chlorothiazide, respectively.]

Suitability requirements

Resolution: NLT 3.5 between benzothiadiazine related compound A and chlorothiazide, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlorothiazide ($C_7H_6ClN_3O_4S_2$) in the portion of Chlorothiazide taken:

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

r_U = peak response of chlorothiazide from the *Sample solution*

r_S = peak response of chlorothiazide from the *Standard solution*

C_S = concentration of [USP Chlorothiazide RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **CHLORIDE**

Titrimetric system

Mode: Direct titration

Titrant: 0.050 N [silver nitrate](#)

Endpoint detection: Potentiometric

Analysis: Dissolve 1.00 g of Chlorothiazide in a mixture of 10 mL of [water](#) and 10 mL of [sodium hydroxide](#) solution (1 in 10). Cool in an ice bath, and add 20 mL of [water](#) and 5 mL of [nitric acid](#). A flocculent, white precipitate is formed. Titrate with *Titrant*, using a silver–silver chloride electrode system.

Acceptance criteria: NMT 0.28 mL of *Titrant* is required (0.05%).

Delete the following:

▲ [SELENIUM \(291\)](#): NMT 0.003%▲ (USP 1-Aug-2022)

• **ORGANIC IMPURITIES**

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

Standard solution A: 1.5 µg/mL of [USP Benzothiadiazine Related Compound A RS](#) in *Mobile phase*

System suitability

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

[NOTE—The relative retention times are about 0.9 and 1.0 for benzothiadiazine related compound A and chlorothiazide, respectively.]

Suitability requirements

Resolution: NLT 3.5 between benzothiadiazine related compound A and chlorothiazide, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution A* and *Sample solution*

Calculate the percentage of benzothiadiazine related compound A in the portion of Chlorothiazide 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 *Standard solution A*

C_S = concentration of [USP Benzothiadiazine Related Compound A RS](#) in *Standard solution A* (µg/mL)

C_U = concentration of Chlorothiazide in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 1.0%

SPECIFIC TESTS

- [Loss on Drying \(731\)](#)

Analysis: Dry at 105° for 1 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at 25°; excursions permitted between 15° and 30°.
- **USP REFERENCE STANDARDS (11).**

[USP Benzothiadiazine Related Compound A RS](#)

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



[USP Chlorothiazide RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
CHLOROTHIAZIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: [Chromatographic Database](#)

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