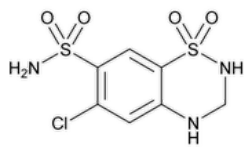


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Hydrochlorothiazide



$C_7H_8ClN_3O_4S_2$ 297.74
2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-, 1,1-dioxide;
6-Chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide CAS RN®: 58-93-5; UNII: 0J48LPH2TH.

DEFINITION
Hydrochlorothiazide contains NLT 98.0% and NMT 102.0% of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$), calculated on the dried basis.

IDENTIFICATION

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** 197K
Sample: Potassium bromide–hydrochlorothiazide mixture, previously heated at 105° for 2 h
Acceptance criteria: Meets the requirements
Delete the following:
- ▲ **B. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy](#):** 197U
Sample solution: 10 µg/mL in [methanol](#)
Acceptance criteria: Meets the requirements▲ (USP 1-May-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-May-2022)

ASSAY
Change to read:

- **PROCEDURE**
Buffer: 2.76 g of [sodium phosphate, monobasic](#) in a 1000-mL volumetric flask. Add 990 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 2.7 ± 0.1, and dilute with [water](#) to volume.
Diluent: [Acetonitrile](#) and *Buffer* (30:70)
Solution A: [Acetonitrile](#) and [methanol](#) (75:25)
Solution B: 0.5% [formic acid, anhydrous](#) solution in [water](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	3	97
5	3	97
14	36	64

Time (min)	Solution A (%)	Solution B (%)
18	3	97
20	3	97

System suitability solution: 0.32 mg/mL of [USP Hydrochlorothiazide RS](#), 0.0032 mg/mL of [USP Chlorothiazide RS](#), and 0.0032 mg/mL of [USP Benzothiadiazine Related Compound A RS](#) in *Diluent*. Sonicate if necessary to dissolve. Pass a portion through a filter of 0.45-μm or finer pore size.

Standard solution: 0.32 mg/mL of [USP Hydrochlorothiazide RS](#) in *Diluent*. Sonicate if necessary to dissolve. Pass a portion through a filter of 0.45-μm or finer pore size.

Sample solution: 0.32 mg/mL of Hydrochlorothiazide in *Diluent*, prepared as follows. Transfer 32 mg of Hydrochlorothiazide into a 100-mL volumetric flask. Add 70 mL of *Diluent*, sonicate for 10 min if necessary to dissolve, and allow to cool to ambient temperature. Dilute with *Diluent* to volume. Pass a portion through a filter of 0.45-μm or finer pore size.

Chromatographic system

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

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 5-cm; 3.5-μm packing [L1](#)

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

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

[NOTE—See [Table 2](#) for the relative retention times.]

▲ (USP 1-May-2022)

Suitability requirements

Resolution: NLT 2.0 between benzothiadiazine related compound A and chlorothiazide and NLT 1.5 between chlorothiazide and hydrochlorothiazide, *System suitability solution*

Tailing factor: ▲NMT 1.5, *Standard solution* ▲ (USP 1-May-2022)

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Hydrochlorothiazide taken:

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

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

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

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

C_U = concentration of Hydrochlorothiazide 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 AND SULFATE \(221\)](#), [Chloride](#)

Sample solution: Shake 0.50 g with 40 mL of [water](#) for 5 min, and filter.

Acceptance criteria: 0.035%; the filtrate shows no more chloride than corresponds to 0.25 mL of 0.020 N [hydrochloric acid](#).

Delete the following:

▲ [SELENIUM \(291\)](#)

Sample: 200 mg