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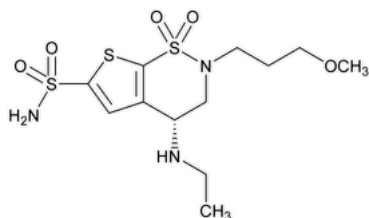
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Brinzolamide


 $C_{12}H_{21}N_3O_5S_3$ 383.51

2*H*-Thieno[3,2-*e*]-1,2-thiazine-6-sulfonamide, 4-(ethylamino)-3,4-dihydro-2-(3-methoxypropyl)-, 1,1-dioxide, (*R*)-;

(*R*)-4-(Ethylamino)-3,4-dihydro-2-(3-methoxypropyl)-2*H*-thieno[3,2-*e*]-1,2-thiazine-6-sulfonamide 1,1-dioxide CAS RN[®]: 138890-62-7; UNII: 9451Z89515.

DEFINITION

Brinzolamide contains NLT 98.0% and NMT 102.0% of brinzolamide ($C_{12}H_{21}N_3O_5S_3$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K**
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in *Limit of Brinzolamide Related Compound A*.

ASSAY

PROCEDURE

Buffer: Add 4.0 mL of triethylamine to 1000 mL of water, and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (25:75)

Standard solution: 0.1 mg/mL of [USP Brinzolamide RS](#) in *Mobile phase*

Sample solution: 0.1 mg/mL of Brinzolamide in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-μm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1200 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of brinzolamide ($C_{12}H_{21}N_3O_5S_3$) in the portion of Brinzolamide taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

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

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.1%

- **LIMIT OF BRINZOLAMIDE RELATED COMPOUND A**

Mobile phase: Dehydrated alcohol, chromatographic hexane, methanol, and diethylamine (55:40:5:0.2)

System suitability solution: 0.4 mg/mL of [USP Brinzolamide RS](#) and 0.02 mg/mL of [USP Brinzolamide Related Compound A RS](#) in dehydrated alcohol

Sample solution: 0.5 mg/mL of Brinzolamide in dehydrated alcohol

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L51

Flow rate: 0.75 mL/min

Injection volume: 5 µL

System suitability

Sample: System suitability solution

[NOTE—The relative retention times for brinzolamide and brinzolamide related compound A are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.8 between brinzolamide and brinzolamide related compound A peaks

Column efficiency: NLT 2000 theoretical plates for the brinzolamide peak

Tailing factor: NMT 1.8 for the brinzolamide peak

Analysis

Sample: Sample solution

Calculate the percentage of brinzolamide related compound A in the portion of Brinzolamide taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for brinzolamide related compound A

r_T = sum of the peak responses for brinzolamide and brinzolamide related compound A

Acceptance criteria: NMT 0.5%

- **ORGANIC IMPURITIES**

Buffer: Prepare as directed in the Assay.

Mobile phase A: Prepare as directed for *Mobile phase* in the Assay.

Mobile phase B: Acetonitrile and Buffer (35:65)

System suitability solution: 0.1 mg/mL each of [USP Brinzolamide RS](#) and [USP Brinzolamide Related Compound B RS](#) in *Mobile phase A*

Sample solution: 1 mg/mL of Brinzolamide in *Mobile phase A*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: System suitability solution

Use *Mobile phase A*.

[NOTE—The relative retention times for brinzolamide related compound B and brinzolamide are 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the brinzolamide and brinzolamide related compound B peaks

Column efficiency: NLT 1200 theoretical plates for the brinzolamide peak

Tailing factor: NMT 2.0 for the brinzolamide peak

Analysis 1

Use *Mobile phase A*.

Sample: Sample solution

Allow the elution to continue for 20 min, and measure the areas for all the peaks, excluding the peaks of *Mobile phase A*.

Calculate the percentage of each impurity in the portion of Brinzolamide taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria 1: NMT 0.3% for any individual impurity

Analysis 2

Use *Mobile phase B*.

Sample: *Sample solution*

Allow the elution to continue for 20 min, and measure the areas for brinzolamide and all the peaks having a relative retention greater than 6.

Calculate the percentage of each impurity in the portion of Brinzolamide taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

Acceptance criteria 2: NMT 0.3% for any individual impurity; NMT 1.0% for total impurities from *Analysis 1* and *Analysis 2*

SPECIFIC TESTS

• [Loss on Drying \(731\)](#)

Analysis: Dry under vacuum at 100°–105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.

Change to read:

• [USP Reference Standards \(11\)](#)

[USP Brinzolamide RS](#)

[USP Brinzolamide Related Compound A RS](#)

▲(S)-4-(Ethylamino)-2-(3-methoxypropyl)-3,4-dihydro-2H-thieno[3,2-e][1,2]thiazine-6-sulfonamide 1,1-dioxide.▲ (CN 1-Dec-2023)

$C_{12}H_{21}N_3O_5S_3$ ▲383.50▲ (CN 1-Dec-2023)

[USP Brinzolamide Related Compound B RS](#)

(R)-4-Amino-2-(3-methoxypropyl)-3,4-dihydro-2H-thieno[3,2-e][1,2]thiazine-6-sulfonamide 1,1-dioxide oxalate.

$C_{10}H_{17}N_3O_5S_3 \cdot C_2H_2O_4$ ▲445.48▲ (CN 1-Dec-2023)

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

Topic/Question	Contact	Expert Committee
BRINZOLAMIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. PF 40(1)

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