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Brinzolamide Ophthalmic Suspension

DEFINITION

Brinzolamide Ophthalmic Suspension is a sterile, aqueous suspension of Brinzolamide containing a suitable antimicrobial preservative. It contains NLT 90.0% and NMT 110.0% of the labeled amount of brinzolamide ($C_{12}H_{21}N_3O_5S_3$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of *Standard solution A*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 11.75 g/L of ammonium acetate in water. Adjust with acetic acid to a pH of 5.2.

Mobile phase: Methanol and *Buffer* (35:65)

Standard solution A: 0.2 mg/mL of USP Brinzolamide RS in *Mobile phase*

System suitability solution: 0.06 mg/mL of USP Brinzolamide Related Compound B RS in *Standard solution A*

Sample solution: Nominally 0.2 mg/mL of brinzolamide in *Mobile phase* prepared as follows. Transfer a volume of Ophthalmic Suspension, equivalent to 10 mg of brinzolamide, into a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for brinzolamide related compound B are between 0.48 and 0.61, and the relative retention time for brinzolamide is 1.0.]

Suitability requirements

Resolution: NLT 4.5 between the brinzolamide and brinzolamide related compound B peaks, *System suitability solution*

Tailing factor: NMT 2.0, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution A*

Analysis

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

Calculate the percentage of the labeled amount of brinzolamide ($C_{12}H_{21}N_3O_5S_3$) in the portion of Ophthalmic Suspension 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 *Standard solution A*

C_S = concentration of USP Brinzolamide RS in *Standard solution A* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **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: Transfer a volume of Ophthalmic Suspension, equivalent to 10 mg of brinzolamide, to a 25-mL volumetric flask. Dilute with alcohol to volume.

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 the 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 Ophthalmic Suspension 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 1.5%

• **ORGANIC IMPURITIES**

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

Standard solution B: 2.5 µg/mL of USP Brinzolamide Related Compound B RS in *Mobile phase*

Analysis

Samples: *Sample solution* and *Standard solution B*

Calculate the percentage of each impurity in the portion of Ophthalmic Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response for brinzolamide related compound B from *Standard solution B*

C_S = concentration of USP Brinzolamide Related Compound B RS in *Standard solution B* (mg/mL)

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

M_{r1} = molecular weight of des-ethyl brinzolamide, 356.46

M_{r2} = molecular weight of des-ethyl brinzolamide oxalate, 445.49

Acceptance criteria

Any individual impurity: NMT 0.5%

Total impurities: NMT 2.0%

SPECIFIC TESTS

• **STERILITY TESTS ⟨71⟩:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **pH ⟨791⟩:** 6.5–8.5

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers. Store at a temperature between 4° and 30°.

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-2*H*-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-2*H*-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 OPHTHALMIC SUSPENSION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

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