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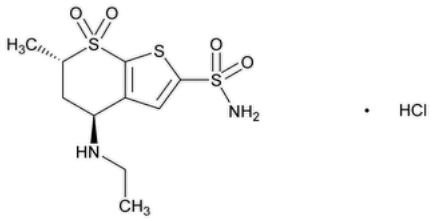
Dorzolamide Hydrochloride



$C_{10}H_{16}N_2O_4S_3 \cdot HCl$ 360.90

4*H*-Thieno[2,3-*b*]thiopyran-2-sulfonamide, 4-(ethylamino)-5,6-dihydro-6-methyl-, 7,7-dioxide, monohydrochloride, (4*S*-*trans*)-;

(4*S*,6*S*)-4-(Ethylamino)-5,6-dihydro-6-methyl-4*H*-thieno[2,3-*b*]thiopyran-2-sulfonamide 7,7-dioxide, monohydrochloride CAS RN®: 130693-82-2; UNII: QZO5366EW7.

DEFINITION

Dorzolamide Hydrochloride contains NLT 99.0% and NMT 101.0% of dorzolamide hydrochloride ($C_{10}H_{16}N_2O_4S_3 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** **Identification Tests—General, *Chloride* ⟨191⟩**

ASSAY

- **Procedure**

Buffer: 3.7 g/L of monobasic potassium phosphate in water

Solution A: Acetonitrile and *Buffer* (6.5:94)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
30	50	50
37	100	0
44	100	0

Standard solution: 0.6 mg/mL of USP Dorzolamide Hydrochloride RS in *Solution A*

Sample solution: 0.6 mg/mL of Dorzolamide Hydrochloride in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 6500 theoretical plates

Tailing factor: 0.6–1.2

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dorzolamide hydrochloride ($C_{10}H_{16}N_2O_4S_3 \cdot HCl$) in the portion of Dorzolamide Hydrochloride taken:

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

r_U = peak area of the *Sample solution*

r_S = peak area of the *Standard solution*

C_S = concentration of USP Dorzolamide Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 99.0%–101.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%, an ignition temperature of 600° being used
- **Organic Impurities**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Dorzolamide Hydrochloride taken:

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

r_U = peak area of each individual impurity from the *Sample solution*

r_T = sum of all the peak areas from the *Sample solution*

Acceptance criteria

Any individual impurity: NMT 0.1%

Total impurities: NMT 0.5%

- **Limit of Dorzolamide Hydrochloride Related Compound A**

Mobile phase: *tert*-Butyl methyl ether, chromatographic *n*-heptane, acetonitrile, and water (63:35:2:0.2)

System suitability solution: Transfer 18 mg of USP Dorzolamide Hydrochloride RS and 2 mg of USP Dorzolamide Hydrochloride Related Compound A RS, each, to a 15-mL centrifuge tube. Dissolve in 4 mL of 0.5 N ammonium hydroxide, and add 4 mL of ethyl acetate. Separate the ethyl acetate layer, and transfer to a 15-mL centrifuge tube. Add 4 mL of ethyl acetate to the aqueous layer, and mix. Separate the ethyl acetate layer, and combine it with the first extract. Evaporate the combined organic layers to dryness on a water bath maintained at 50° under a stream of nitrogen. Dissolve the residue in 3 mL of acetonitrile, add 3 drops of (*S*)-(−)-α-methylbenzyl isocyanate (discard the reagent if it is colored), and allow to react for 5 min on a water bath maintained at 50°. Evaporate the mixture to dryness on a water bath maintained at 50° under a stream of nitrogen. Dissolve the residue in 10 mL of a mixture of *tert*-butyl methyl ether, glacial acetic acid, and acetonitrile (87:10:3).

Sample solution: Transfer 20 mg of Dorzolamide Hydrochloride to a 15-mL centrifuge tube, dissolve in 4 mL of 0.5 N ammonium hydroxide, and add 4 mL of ethyl acetate. Separate the ethyl acetate layer, and transfer to a 15-mL centrifuge tube. Add 4 mL of ethyl acetate to the aqueous layer, and mix. Separate the ethyl acetate layer, and combine it with the first extract. Evaporate the combined organic layers to dryness on a water bath maintained at 50° under a stream of nitrogen. Dissolve the residue in 3 mL of acetonitrile, add 3 drops of (*S*)-(−)-α-methylbenzyl isocyanate (discard the reagent if it is colored), and allow to react for 5 min on a water bath maintained at 50°. Evaporate the mixture to dryness on a water bath maintained at 50° under a stream of nitrogen. Dissolve the residue in 10 mL of a mixture of *tert*-butyl methyl ether, glacial acetic acid, and acetonitrile (87:10:3).

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L3

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for dorzolamide and dorzolamide hydrochloride related compound A are about 1.0 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 4.0 between dorzolamide and dorzolamide hydrochloride related compound A

Column efficiency: NLT 4000 theoretical plates for the dorzolamide hydrochloride peak

Tailing factor: NMT 1.4

Analysis

Samples: *System suitability solution* and *Sample solution*

Calculate the percentage of dorzolamide hydrochloride related compound A in the portion of Dorzolamide Hydrochloride taken:

$$\text{Result} = [r_i/(r_i + r_S)] \times 100$$

r_i = peak area of dorzolamide hydrochloride related compound A from the *Sample solution*

r_S = peak area of dorzolamide hydrochloride from the *Sample solution*

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

• **WATER DETERMINATION,** *Method I* ⟨921⟩

Sample: 0.4 g

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers, protected from light, and store at 15°–30°.

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Dorzolamide Hydrochloride RS

USP Dorzolamide Hydrochloride Related Compound A RS

(4*R*,6*R*)-4-(Ethylamino)-5,6-dihydro-6-methyl-4*H*-thieno[2,3-*b*]thiopyran-2-sulfonamide-7,7- dioxide, monohydrochloride.

$C_{10}H_{16}N_2O_4S_3 \cdot HCl$ ▲360.89▲ (ERR 1-Aug-2021)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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