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Dorzolamide Hydrochloride Ophthalmic Solution

DEFINITION

Dorzolamide Hydrochloride Ophthalmic Solution is a sterile, isotonic, buffered, slightly viscous, aqueous solution of Dorzolamide Hydrochloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of dorzolamide ($C_{10}H_{16}N_2O_4S_3$). It may contain a suitable preservative.

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2021)

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

ASSAY

Change to read:

• **Procedure**

Buffer: Fill a 1-L volumetric flask approximately two-thirds full of water. Add 2.0 mL of phosphoric acid, and dilute with water to 900 mL. Adjust with triethylamine to a pH of 3.0, and dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (5:95)

Standard solution: 0.11 mg/mL of USP Dorzolamide Hydrochloride RS and 0.5 µg/mL each of USP Dorzolamide Related Compound B RS and USP Dorzolamide Related Compound D RS in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of dorzolamide in *Mobile phase*, from Ophthalmic Solution

Chromatographic system

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

Mode: LC

Detector: UV 253 nm.▲For *Identification A*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Dec-2021)

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between dorzolamide and dorzolamide related compound D; and NLT 3.0 between dorzolamide and dorzolamide related compound B

Tailing factor: NMT 1.8 for dorzolamide

Relative standard deviation: NMT 2.0% for dorzolamide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dorzolamide ($C_{10}H_{16}N_2O_4S_3$) in the portion of Ophthalmic Solution taken:

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

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

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

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

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

M_{r1} = molecular weight of dorzolamide, ▲324.43▲ (USP 1-Dec-2021)

M_{r2} = molecular weight of dorzolamide hydrochloride, ▲360.89▲ (USP 1-Dec-2021)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

• **Organic Impurities**

▲Buffer,▲ (USP 1-Dec-2021) Mobile phase, and **▲▲ (USP 1-Dec-2021) Sample solution▲▲ (USP 1-Dec-2021) :** Prepare as directed in the *Assay*.

▲Standard solution A: Use the *Standard solution* as prepared in the *Assay*.

Standard solution B: 0.5 µg/mL each of USP Dorzolamide Related Compound B RS and USP Dorzolamide Related Compound D RS in *Mobile phase*▲ (USP 1-Dec-2021)

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time*.

Run time: NLT 1.4 times the retention time of dorzolamide

▲System suitability

Sample: *Standard solution A*

Suitability requirements

Resolution: NLT 3.0 between dorzolamide and dorzolamide related compound D; NLT 3.0 between dorzolamide and dorzolamide related compound B

Tailing factor: NMT 1.8 for dorzolamide

Relative standard deviation: NMT 2.0% for dorzolamide▲ (USP 1-Dec-2021)

Analysis

Samples: *Standard solution* ▲*A*, *Standard solution B*,▲ (USP 1-Dec-2021) and *Sample solution*

Calculate the percentage of dorzolamide related compound D in the portion of Ophthalmic Solution taken:

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

r_U = peak area of dorzolamide related compound D from the *Sample solution*

r_S = peak area of dorzolamide related compound D from *Standard solution* ▲*B*▲ *(USP 1-Dec-2021)*

C_S = concentration of USP Dorzolamide Related Compound D RS in *Standard solution* ▲*B*▲ *(USP 1-Dec-2021)* (mg/mL)

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

M_{r1} = molecular weight of dorzolamide, ▲324.43▲ (USP 1-Dec-2021)

M_{r2} = molecular weight of dorzolamide related compound D, ▲332.83▲ (USP 1-Dec-2021)

Calculate the percentage of dorzolamide related compound B in the portion of Ophthalmic Solution taken:

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

r_U = peak area of dorzolamide related compound B from the *Sample solution*

r_S = peak area of dorzolamide related compound B from *Standard solution* ▲*B*▲ *(USP 1-Dec-2021)*

C_S = concentration of USP Dorzolamide Related Compound B RS in *Standard solution* ▲*B*▲ *(USP 1-Dec-2021)* (mg/mL)

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

M_{r1} = molecular weight of dorzolamide, ▲324.43▲ (USP 1-Dec-2021)

M_{r2} = molecular weight of dorzolamide related compound B, ▲360.89▲ (USP 1-Dec-2021)

Calculate the percentage of each individual unspecified impurity in the portion of Ophthalmic Solution taken:

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

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

r_S = peak area of dorzolamide from *Standard solution* ▲*A*▲ *(USP 1-Dec-2021)*

C_S = concentration of USP Dorzolamide Hydrochloride RS in *Standard solution* ▲*A*▲ *(USP 1-Dec-2021)* (mg/mL)

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

M_{r1} = molecular weight of dorzolamide, ▲324.43▲ (USP 1-Dec-2021)

M_{r2} = molecular weight of dorzolamide hydrochloride, ▲360.89▲ (USP 1-Dec-2021)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Dorzolamide related compound D▲▲ (USP 1-Dec-2021)	0.87	0.5
Dorzolamide	1.00	—
Dorzolamide related compound B▲▲ (USP 1-Dec-2021)	1.14	2.0
Total impurities[a]	—	3.0

[a] The sum of dorzolamide related compound D, dorzolamide related compound B, and all unspecified impurities.

SPECIFIC TESTS

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **pH ⟨791⟩:** 5.4–5.9

Add the following:

▲• **Other Requirements:** It meets the requirements in *Ophthalmic Products—Quality Tests ⟨771⟩*.▲ (USP 1-Dec-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers protected from light at controlled room temperature.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Dorzolamide Hydrochloride RS

USP Dorzolamide Related Compound B RS

(▲4*RS*,6*SR*▲ (USP 1-Dec-2021))-4-(Ethylamino)-6-methyl-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-2-sulfonamide 7,7-dioxide hydrochloride.

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

USP Dorzolamide Related Compound D RS

(4*S*,6*S*)-4-Amino-6-methyl-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-2-sulfonamide 7,7-dioxide hydrochloride.

$C_8H_{12}N_2O_4S_3 \cdot HCl$ ▲332.83▲ (USP 1-Dec-2021)

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

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

Chromatographic Database Information: Chromatographic Database

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