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Dorzolamide Hydrochloride and Timolol Maleate Ophthalmic Solution

DEFINITION

Dorzolamide Hydrochloride and Timolol Maleate Ophthalmic Solution is a sterile, isotonic, buffered, slightly viscous, aqueous solution of Dorzolamide Hydrochloride and Timolol Maleate. It contains NLT 90.0% and NMT 110.0% of the labeled amount of dorzolamide ($C_{10}H_{16}N_2O_4S_3$) and NLT 90.0% and NMT 110.0% of the labeled amount of timolol ($C_{13}H_{24}N_4O_3S$). 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*, *Procedure for Dorzolamide*.▲ (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*, *Procedure for Dorzolamide*.

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

Add the following:

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

ASSAY

Change to read:

• **Procedure for Dorzolamide**

Solution A: Acetonitrile

Solution B: 0.2% (v/v) phosphoric acid in water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	5	95
15.0	5	95
15.1	95	5
20.0	95	5
20.1	5	95
30.0	5	95

Diluent: Acetonitrile and *Solution B* (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 *Diluent*

Sample solution: Nominally 0.1 mg/mL of dorzolamide in *Diluent*, 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: 1.2 mL/min

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Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

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

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%

Change to read:

• **PROCEDURE FOR TIMOLOL**

Buffer: Transfer 22 g of sodium phosphate, monobasic into a 2000-mL volumetric flask. Dissolve in 1995 mL of water, and adjust with phosphoric acid to a pH of 2.8. Dilute with water to volume.

Mobile phase: Methanol and *Buffer* (40:60)

System suitability solution: Transfer 88 mg of USP Timolol Maleate RS into a 50-mL volumetric flask. Transfer 8 mL of 0.1 M sodium hydroxide into the flask, mix, and heat at 70° for 15 h. Dilute with *Mobile phase* to volume, and mix well. Transfer 5 mL of this solution into a 25-mL volumetric flask, and add 28 mg of USP Dorzolamide Hydrochloride RS into the same flask. Dilute with *Mobile phase* to volume. [NOTE—The preparation generates timolol impurity G and timolol related compound B.]

Standard solution: 0.35 mg/mL of USP Timolol Maleate RS in *Mobile phase*

Sample solution: Nominally 0.25 mg/mL of timolol in *Mobile phase*, from Ophthalmic Solution

Chromatographic system

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

Mode: LC

Detector: UV 295 nm. ▲For *Identification D*, 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 L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between timolol impurity G and timolol related compound B

Relative standard deviation: NMT 2.5% for timolol for 5 replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of timolol ($C_{13}H_{24}N_4O_3S$) 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 timolol from the *Sample solution*

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

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

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