Interim Revision Announcement
Official: September 1, 2020

Travoprost Ophthalmic Solution

DEFINITION
Travoprost Ophthalmic Solution is a sterile buffered aqueous solution of Travoprost. It contains NLT 90.0% and NMT 110.0% of the labeled amount of travoprost ($C_{26}H_{35}F_3O_6$). It may contain suitable stabilizers, buffers, and antimicrobial agents.

[**Caution—**Great care should be taken when handling the active ingredient to avoid contact with the body.]

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum 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: 2.18 mg/mL of sodium 1-octanesulfonate in water. Adjust with phosphoric acid to a pH of 3.5.
Mobile phase: Acetonitrile and *Buffer* (17:33)
Standard solution: 0.04 mg/mL of travoprost from USP Travoprost RS in a mixture of acetonitrile and water (3:7)
Sample solution: Use Ophthalmic Solution without dilution.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 220 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.
Column: 4.6-mm × 15-cm; 5-µm packing L1
Flow rate: 2.0 mL/min
Injection volume: 100 µL
System suitability
Sample: *Standard solution*
[Note—USP Travoprost RS contains a small percentage of the 5,6-*trans* isomer. The relative retention times for travoprost and the 5,6-*trans* isomer are 1.0 and 1.1, respectively.]
Suitability requirements
Resolution: NLT 1.5 between travoprost and the 5,6-*trans* isomer
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of travoprost ($C_{26}H_{35}F_3O_6$) in the portion of Ophthalmic Solution taken:

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

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

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

C_S = concentration of ▲USP Travoprost RS▲ (IRA 1-Sep-2020) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

- **Limit of Travoprost Related Compound A**

Buffer: Add 1.0 mL of phosphoric acid to 1.0 L of water, and adjust with sodium hydroxide to a pH of 3.0.
Mobile phase: Acetonitrile and *Buffer* (6:19)
Standard solution: 0.3 µg/mL of USP Travoprost Related Compound A RS in a mixture of acetonitrile and water (1:4)
Sample solution: Use Ophthalmic Solution without dilution.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 5-cm; 3-µm packing L1
Flow rate: 3.0 mL/min
Injection volume: 100 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 10.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of travoprost related compound A in the portion of Ophthalmic Solution taken:

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

r_U = peak response of travoprost related compound A from the *Sample solution*

r_S = peak response of travoprost related compound A from the *Standard solution*

C_S = concentration of USP Travoprost Related Compound A RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 1.0%

Change to read:

• **Limit of Degradation Products**

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Ophthalmic Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each degradation product from the *Sample solution*

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Travoprost	1.0	—	—
5,6-*trans*-travoprost ▲(IRA 1-Sep-2020)▲ [a]	1.1	1.0	5.0
15-Keto-travoprost ▲(IRA 1-Sep-2020)▲ [b]	1.4	1.7	1.0
Total impurities[c]	—	—	5.5

[a] ▲Isopropyl (*E*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(*R*,*E*)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]but-1-enyl]cyclopentyl]hept-5-enoate.▲ (IRA 1-Sep-2020)

[b] ▲Isopropyl (*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(*E*)-3-oxo-4-[3-(trifluoromethyl)phenoxy]but-1-enyl]cyclopentyl]hept-5-enoate.▲ (IRA 1-Sep-2020)

[c] It is the sum of all degradation products, including travoprost related compound A, obtained in the test for *Limit of Travoprost Related Compound A*.

SPECIFIC TESTS

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

Change to read:

• **pH** ⟨791⟩

Acceptance criteria: 5.5–6.5

▲**If labeled to contain polyquarternium-1 as a preservative:** 6.4–7.0

If labeled to contain zinc chloride as an ingredient: 5.5–5.9▲ (IRA 1-Sep-2020)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store between 2° and 25°.

Add the following:

▲• **Labeling:** If the Ophthalmic Solution is formulated with polyquarternium-1 as a preservative, it is so labeled. If the Ophthalmic Solution is formulated with zinc chloride as an ingredient, it is so labeled.▲ (IRA 1-Sep-2020)

• **USP Reference Standards** ⟨11⟩

USP Travoprost RS

USP Travoprost Related Compound A RS

(5*Z*,13*E*)-(9*S*,11*R*,15*R*)-9,11,15-Trihydroxy-16-(*m*-trifluoromethylphenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid;
Also known as (*Z*)-7-((1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-{(*R*,*E*)-3-hydroxy-4-[3-(trifluoromethyl)phenoxy]but-1-enyl}cyclopentyl)hept-5-enoic acid.

$C_{23}H_{29}F_3O_6$ 458.47

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