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 \((\text{C}_{20}\text{H}_{35}\text{F}_{3}\text{O})\). 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
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 \((\text{C}_{20}\text{H}_{35}\text{F}_{3}\text{O})\) in the portion of Ophthalmic Solution taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

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:

\[
\text{Result} = \left( \frac{r_d}{r_S} \right) \times \left( \frac{C_d}{C_U} \right) \times 100
\]
\[ r_U \] = 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:**

<table>
<thead>
<tr>
<th><strong>LIMIT OF DEGRADATION PRODUCTS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer, Mobile phase, Standard solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay. Analysis</td>
</tr>
</tbody>
</table>

Samples: Standard solution and Sample solution

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

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{1}{F} \right) \times 100
\]

\[ r_U \] = 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

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travoprost</td>
<td>1.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5,6-trans(^a)-travoprost(^b) (IRA 1-Sep-2020)</td>
<td>1.1</td>
<td>1.0</td>
<td>5.0</td>
</tr>
<tr>
<td>15-Keto(^a)-travoprost(^b) (IRA 1-Sep-2020)</td>
<td>1.4</td>
<td>1.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Total impurities(^c)</td>
<td>-</td>
<td>-</td>
<td>5.5</td>
</tr>
</tbody>
</table>


^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


  \[ C_{23}H_{25}F_3O_6 \] 458.47