Table 1

Name	Relative Retention Time	Relative Response Factor (*F*)	Limit (%)
USP Travoprost Related Compound A RS	about 0.11	1.0	0.2
Epoxide derivative[1]	about 0.55	1.0	0.4
15-*epi* Diastereomer[2]	about 0.90	1.1	0
5,6-*trans* Isomer[3]	about 1.16	1.0	3
15-Keto derivative[4]	about 1.45	1.6	0.3

[1](5*Z*)-(9*S*,11*R*,15*S*)-9,11,15-Trihydroxy-13,14-epoxy-16-(*m*-trifluoromethylphenoxy)-17,18,19,20-tetranor-5-prostadienoic acid, isopropyl ester.
[2](5*Z*,13*E*)-(9*S*,11*R*,15*S*)-9,11,15-Trihydroxy-16-(*m*-trifluoromethylphenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.
[3](5*E*,13*E*)-(9*S*,11*R*,15*R*)-9,11,15-Trihydroxy-16-(*m*-trifluoromethylphenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.
[4](5*Z*,13*E*)-(9*S*,11*R*)-9,11,-Dihydroxy-15-oxo-16-(*m*-trifluoromethylphenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.

Related compounds—

Buffer, Mobile phase, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay*.

Test solution—Use the *Assay preparation*.

Procedure—Inject a volume (about 100 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity in the portion of Travoprost taken by the formula:

$$100(1/F)(r_i / r_s)$$

in which F is the relative response factor for each impurity; r_i is the individual peak response of each individual impurity; and r_s is the sum of the responses of all the peaks. In addition to not exceeding the limits for each impurity in *Table 1,* not more than 0.1% of any other individual impurity is found, and not more than 4.0% of total impurities is found.

Assay—

Buffer—Add 2.0 mL of phosphoric acid to 1 L of water. Adjust with sodium hydroxide to a pH of 3.0.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer* and acetonitrile (7:3). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Use USP Travopost RS without dilution (0.5 mg per mL).

Assay preparation—Transfer about 25 mg of Travoprost, accurately weighed, to a 50-mL volumetric flask, and dissolve in 15 mL of acetonitrile. Add 25 mL of water, mix, and wait until the solution reaches room temperature. Dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm × 5-cm column that contains packing L1. The flow rate is about 3.0 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 1.0 for travoprost and 1.1 for 5,6-*trans* isomer; the resolution, *R,* between travoprost and the 5,6-*trans* isomer is not less than 1.5; the column efficiency is not less than 1500 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%. [NOTE—USP Travoprost RS contains a small percentage of 5,6-*trans* isomer.]

Procedure—Separately inject equal volumes (about 100 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_{26}H_{35}F_3O_6$ in the portion of Travoprost taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per mL, of travoprost in the *Standard preparation*; C_U is the concentration of Travoprost in the *Assay preparation*; and r_U and r_S are the peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

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

ASSAY

- **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 the Ophthalmic Solution without dilution.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 2.0 mL/min
Injection size: 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

Column efficiency: NLT 2000 theoretical plates
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{26}H_{35}F_3O_6$ in the portion of Ophthalmic Solution taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of travoprost 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

Organic Impurities

- **PROCEDURE 1: 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 the Ophthalmic Solution without dilution.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 5-cm; packing L1
Flow rate: 3.0 mL/min
Injection size: 100 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 2000 theoretical plates
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 from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Travoprost Related Compound A RS in the *Standard solution* (mg/mL)
C_U = concentration of travoprost in the *Sample solution* (mg/mL)
Acceptance criteria
Travoprost related compound A: NMT 0.2%

- **PROCEDURE 2: LIMIT OF DEGRADATION PRODUCTS**

Buffer, Mobile phase, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Prepare 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 *Impurity Table 1*)
Acceptance criteria
Degradation products: See *Impurity Table 1*.
Total impurities: NMT 5.5%. [NOTE—Sum of all degradation products, including travoprost related compound A, obtained in *Procedure 1*.]

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
5,6-*trans* Isomer	1.1	1.0	5.0
15-keto Derivative	1.4	1.7	0.3

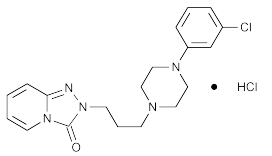
SPECIFIC TESTS

- **STERILITY TESTS ⟨71⟩:** Meets the requirements when tested as directed under *Test for Sterility of the Product to Be Examined, Membrane Filtration*
- **PH ⟨791⟩:** 5.5–6.5

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store between 2° and 25°.
- **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.
$C_{23}H_{29}F_3O_6$ 458.52

Trazodone Hydrochloride



$C_{19}H_{22}ClN_5O \cdot HCl$ 408.32
1,2,4-Triazolo[4,3-*a*]pyridin-3(2*H*)-one,2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-, monohydrochloride.
2-[3-[4-(*m*-Chlorophenyl)-1-piperazinyl]propyl]*s*-triazolo[4,3-*a*]-pyridin-3(2*H*)-one monohydrochloride [25332-39-2].

» Trazodone Hydrochloride contains not less than 97.0 percent and not more than 102.0 percent of $C_{19}H_{22}ClN_5O \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Trazodone Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation*, both relative to the internal standard, as obtained in the *Assay*.

Loss on drying ⟨731⟩**—**Dry it at a pressure of about 50 mm of mercury at 105° for 3 hours: it loses not more than 0.5% of its weight.