Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 15-cm; 3-µm packing L1
Column temperature: 35°
Flow rate: 1.2 mL/min
Injection size: 25 µL

System suitability
Sample: *Standard solution*
Suitability requirements
Resolution: NLT 2.0 between tranylcypromine and tranylcypromine related compound A
Tailing factor: NMT 2.0
Relative standard deviation: NMT 6.0%

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

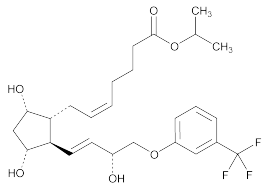
$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M \times M_{r1}/M_{r2}) \times 100$$

r_U = peak response of the impurity from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Tranylcypromine Sulfate RS in the *Standard solution* (mg/mL)
C_U = concentration of tranylcypromine in the *Sample solution* (mg/mL)
M = number of moles of tranylcypromine/mole of tranylcypromine sulfate, 2
M_{r1} = molecular weight of tranylcypromine, 133.19
M_{r2} = molecular weight of tranylcypromine sulfate, 364.46

Acceptance criteria
Individual impurities: NMT 0.2%
Total impurities: NMT 1.2%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Tranylcypromine Sulfate RS
  USP Tranylcypromine Related Compound A RS
  (±)-*cis*-2-Phenylcyclopropanamine hydrochloride; *cis*-tranylcypromine hydrochloride.
  $C_9H_{11}N \cdot HCl$ 169.65

Travoprost



$C_{26}H_{35}F_3O_6$ 500.55
[1*R*-[1α(*Z*),2β(1*E*,3*R**),3α,5α]]-7-[3,5-Dihydroxy-2-[3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl]cyclopentyl]-5-heptenoic acid, 1-methylethyl ester.
Isopropyl (*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(1*E*,3*R*)-3-hydroxy-4-[(α,α,α-trifluoro-*m*-tolyl)oxy]-1-butenyl]cyclopentyl]-5-heptenoate [157283-68-6].

» Travoprost contains not less than 96.0 percent and not more than 102.0 percent of $C_{26}H_{35}F_3O_6$, calculated on the anhydrous and solvent-free basis.

Caution—Great care should be taken to avoid contact with the body.

Packaging and storage—Preserve at –25° to –15° in tight, light-resistant containers under a nitrogen atmosphere.

USP Reference standards ⟨11⟩**—**
USP Travoprost RS

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—
Test solution—Use the *Assay preparation.*
Standard solution—Use USP Travoprost RS.
Developing solvent system: a mixture of ethyl acetate and ethanol (4:1).
Spray reagent: 20% solution of phosphomolybdic acid in ethanol.
Procedure—Separately apply 5 µL each of the *Test solution* and the *Standard solution* to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with silica gel that contains 20% silver nitrate. [NOTE—To keep the spot size small, it is usually necessary to apply approximately 1 to 2 µL at a time, allowing the spot to dry between each application.] Proceed as directed in the chapter. Spray the plate with *Spray reagent,* and heat it in an oven at 80° to 100°. The travoprost will appear as black spots.

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

Specific rotation ⟨781S⟩**:** from +52.0° to +58.0°, at 365 nm.
Test solution: 20 mg per mL, in dehydrated alcohol.

Water, *Method Ia* ⟨921⟩**:** not more than 1.0%, determined on a 0.2-g specimen. Use a solvent mixture of acetonitrile and methanol (1:1) and a titrant for which 1 mL is equivalent to 2 mg of water.

Limit of ethyl acetate—
Standard solution—Dilute an accurately measured quantity of ethyl acetate in *N,N*-dimethylacetamide to obtain a solution having a known concentration of about 50 µg per mL.
Test solution—Dissolve an accurately weighed quantity of Travoprost in *N,N*-dimethylacetamide to obtain a solution having a concentration of about 20 mg per mL.
Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and contains a 0.53-mm × 30-m column coated with a 1-µm film of liquid phase G16. The carrier gas is helium, flowing at a rate of 4 mL per minute. The chromatograph is programmed as follows. Initially the temperature of the column is maintained at 55° for 6 minutes, then the temperature is increased at a rate of 25° per minute to 240° and maintained at 240° for 20 minutes. The injection port temperature is maintained at 140°, and the detector temperature is maintained at 240°. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the retention time is about 2 to 5 minutes for ethyl acetate [NOTE—For the purpose of the peak identification, the approximate retention time range of ethyl acetate is given.]; the resolution, *R,* between ethyl acetate and any adjacent peak is not less than 1.5; and the relative standard deviation for replicate injections is not more than 15.0%.
Procedure—Separately inject equal volumes (about 1 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the concentration, in ppm, of ethyl acetate in the portion of Travoprost taken by the formula:

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

in which C_S is the concentration, in µg per mL, of ethyl acetate in the *Standard solution;* C_U is the concentration, in g per mL, of Travoprost in the *Test solution;* and r_U and r_S are the peak responses obtained from the *Test solution* and the *Standard solution,* respectively; not more than 5000 ppm of ethyl acetate is found.

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