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

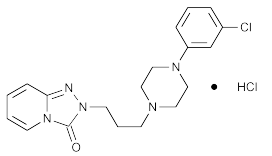
SPECIFIC TESTS

- **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.

Residue on ignition ⟨281⟩: not more than 0.2%.

Chromatographic purity—

Mobile phase—Prepare a filtered and degassed mixture of 0.5% trifluoroacetic acid, tetrahydrofuran, acetonitrile, and methanol (13.5:3:3:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Dissolve an accurately weighed quantity of USP Trazodone Hydrochloride RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 2 µg per mL.

System suitability solution—Dissolve suitable quantities of 3-chloroaniline and USP Trazodone Hydrochloride RS in *Mobile phase* to obtain a solution containing about 0.1 mg per mL of 3-chloroaniline and 0.01 mg per mL of trazodone hydrochloride, respectively.

Test solution—Transfer about 50 mg of trazodone hydrochloride, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 248-nm detector and a 4.6-mm × 15-cm column that contains 3-µm packing L7. The flow rate is about 1.0 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for 3-chloroaniline and 1 for trazodone hydrochloride, and the resolution, *R,* between 3-chloroaniline and trazodone hydrochloride, is not less than 12. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the tailing factor for the analyte peak is not more than 2.0, and the relative standard deviation for replicate injections is not more than 5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for all of the peaks. Calculate the percentage of each peak, other than the trazodone hydrochloride peak, in the Trazodone Hydrochloride taken by the formula:

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

in which C_S is the concentration, in mg per mL, of USP Trazodone Hydrochloride RS in the *Standard solution*, C_T is the concentration, in mg per mL, of trazodone hydrochloride in the *Test solution*, r_U is the response of each peak, other than the trazodone hydrochloride peak, obtained from the *Test solution*, and r_S is the peak response for trazodone hydrochloride obtained from the *Standard solution:* not more than 0.4% for any single impurity and not more than 1.0% of total impurities are found.

Ordinary impurities ⟨466⟩**—**

Test solution: methanol.

Standard solution: methanol.

Eluant: a mixture of cyclohexane, acetone, and ammonium hydroxide (8:4.5:0.5).

Visualization: 1.

Assay—

0.01 M Ammonium phosphate buffer—Transfer 1.15 g of monobasic ammonium phosphate to a 1000-mL volumetric flask, and dissolve in water. Add 1.0 mL of 1 N sodium hydroxide, dilute with water to volume, and mix. Adjust this solution, if necessary, with either 10% phosphoric acid or 1 N sodium hydroxide to a pH of 6.0 ± 0.1, and filter.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *0.01 M Ammonium phosphate buffer* (60:40). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Dissolve a suitable quantity of butylparaben in methanol to obtain a solution containing about 2 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Trazodone Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 2.5 mg per mL. Transfer 4.0 mL of this solution to a 100-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix to obtain a solution having a known concentration of about 0.1 mg of USP Trazodone Hydrochloride RS per mL.

Assay preparation—Transfer an accurately weighed quantity of about 125 mg of Trazodone Hydrochloride to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Transfer 4.0 mL of this solution to a 100-mL volumetric flask, add 2.0 mL of the *Internal standard solution*, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between the trazodone and butylparaben peaks is not less than 3.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.6 for butylparaben and 1.0 for trazodone. Calculate the quantity, in mg, of $C_{19}H_{22}ClN_5O \cdot HCl$ in the portion of Trazodone Hydrochloride taken by the formula:

$$1250C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Trazodone Hydrochloride RS in the *Standard preparation*, and R_U and R_S are the ratios of the peak responses of the trazodone to the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Trazodone Hydrochloride Tablets

» Trazodone Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of trazodone hydrochloride ($C_{19}H_{22}ClN_5O \cdot HCl$).

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

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

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Test solution—Place a number of Tablets, equivalent to about 150 mg of trazodone hydrochloride, in a clean scintillation vial, add about 7.5 mL of methanol, and sonicate until the Tablets have disintegrated. Shake the vials, by hand, for a few seconds to mix, and filter to obtain the test solution.

Standard solution: 20 mg per mL, in methanol.

Application volume: 1 µL.

Developing solvent system: a mixture of cyclohexane, alcohol, toluene, and diethylamine (80:30:20:20).

Procedure: Proceed as directed in the chapter except locate the spots on the plate by examination under long-wavelength UV light.

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*.