areas. Calculate the percentage of benzothiadiazine related compound A in the portion of Tablets taken by the formula:

$$50(C/L)(r_U / r_S)$$

in which *C* is the concentration in µg per mL, of USP Benzothiadiazine Related Compound A RS in the *Standard solution; L* is the amount, in mg, of hydrochlorothiazide in the portion of Tablets taken, based on the labeled amount; and r_U and r_S are the peak areas of benzothiadiazine related compound A obtained from the *Test solution* and *Standard solution*, respectively: not more than 1.0% is found.

Assay—

Tetrabutylammonium hydroxide solution—Use a suitable aqueous or methanolic solution having a known concentration of tetrabutylammonium hydroxide.

Buffer—Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water in a 2000-mL volumetric flask. Add 3.4 mL of phosphoric acid and a volume of *Tetrabutylammonium hydroxide solution* equivalent to about 2.6 g of tetrabutylammonium hydroxide, dilute with water to volume, and mix. Adjust, if necessary, with phosphoric acid or 10 N potassium hydroxide to a pH of 2.5 ± 0.1, and pass through a filter having a 0.5-µm or finer porosity.

Mobile phase—Prepare a suitable mixture of *Buffer* and methanol (850:150). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩) so that the retention time of propranolol is between 12 and 25 minutes.

Standard hydrochlorothiazide stock solution—Transfer about 25 mg of USP Hydrochlorothiazide RS, accurately weighed, to a 100-mL volumetric flask, add 15 mL of methanol, and mix to dissolve. Dilute with *Buffer* to volume, and mix.

Standard propranolol hydrochloride stock solution—Dissolve an accurately weighed quantity of USP Propranolol Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 0.25*J* mg per mL, *J* being the ratio of the labeled quantity, in mg, of propranolol hydrochloride to the labeled quantity, in mg, of hydrochlorothiazide per Tablet.

Standard preparation—Transfer 5.0 mL of *Standard hydrochlorothiazide stock solution* and 5.0 mL of *Standard propranolol hydrochloride stock solution* to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. This solution contains about 50 µg of hydrochlorothiazide and 50*J* µg of propranolol hydrochloride per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 25 mg of hydrochlorothiazide, to a 500-mL volumetric flask. Add 5 mL of water, mix, and allow to stand for 5 minutes, with occasional swirling. Add 75 mL of methanol, mix, and sonicate for 10 minutes, with occasional swirling, adding ice to the bath, if necessary, to maintain the temperature at not more than 20°. Add about 350 mL of *Buffer* to the flask, and sonicate for 10 minutes, with occasional swirling, maintaining the temperature of the bath at not more than 20°. Dilute with *Buffer* to volume, and mix. Centrifuge a portion of this solution, if necessary, to obtain a clear solution (*Assay preparation*).

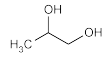
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 270-nm detector and a 4-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the column efficiency determined from the propranolol peak is not less than 2500 theoretical plates; the tailing factor for the propranolol and hydrochlorothiazide peaks is not more than 1.5; and the relative standard deviation for replicate injections is not more than 2.0%. [NOTE—The relative retention times are about 0.25 for benzothiadiazine related compound A, 0.4 for hydrochlorothiazide, and 1.0 for propranolol.]

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantities, in mg, of propranolol hydrochloride ($C_{16}H_{21}NO_2 \cdot HCl$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Tablets taken by the same formula:

$$0.5C(r_U / r_S)$$

in which *C* is the concentration, in µg per mL, of the appropriate Reference Standard in the *Standard preparation;* and r_U and r_S are the peak responses of the corresponding analyte obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Propylene Glycol



$C_3H_8O_2$ 76.09

1,2-Propanediol;
Propane-1,2-diol [57-55-6].

DEFINITION

Propylene Glycol contains NLT 99.5% of $C_3H_8O_2$.

IDENTIFICATION

[NOTE—Compliance is determined by meeting the requirements of *Identification* tests *A*, *B*, and *C*.]

- **A. INFRARED ABSORPTION** ⟨197F⟩
  [NOTE—Undried specimen.]
- **B. LIMIT OF DIETHYLENE GLYCOL AND ETHYLENE GLYCOL**
  Diluent: Methanol
  Standard solution: 2.0 mg/mL of USP Propylene Glycol RS, 0.050 mg/mL of USP Ethylene Glycol RS, 0.050 mg/mL of USP Diethylene Glycol RS, and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol
  Sample solution: 50 mg/mL of Propylene Glycol and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: GC
  Detector: Flame ionization
  Column: 0.53-mm × 30-m fused-silica coated with 3.0-µm G43 stationary phase, and a deactivated split liner with glass wool
  Temperature
  Injector: 220°
  Detector: 250°
  Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	—	100	4
100	50	120	10
120	50	220	6

Carrier gas: Helium
Injection size: 1.0 µL
Flow rate: 4.5 mL/min
Injection type: The split flow ratio is about 10:1.
System suitability
Sample: *Standard solution*
[NOTE—For informational purposes only. See *Impurity Table 1* for relative retention times for ethylene glycol, internal standard, and diethylene glycol. The retention time for propylene glycol is 4 min.]

Impurity Table 1

Component	Relative Retention Time
Ethylene glycol	0.8
Propylene glycol	1.0
Internal standard	1.7
Diethylene glycol	2.4

Suitability requirements
Resolution: NLT 5 between ethylene glycol and propylene glycol
Analysis
Sample: *Sample solution*
Acceptance criteria
Diethylene glycol: If a peak at the retention time for diethylene glycol is present in the *Sample solution*, the peak response ratio relative to 2,2,2-trichloroethanol is NMT the peak response ratio for diethylene glycol relative to 2,2,2-trichloroethanol in the *Standard solution*: NMT 0.10% for diethylene glycol.
Ethylene glycol: If a peak at the retention times for ethylene glycol is present in the *Sample solution*, the peak response ratio relative to 2,2,2-trichloroethanol is not more than the peak response ratio for ethylene glycol relative to 2,2,2-trichloroethanol in the *Standard solution*: NMT 0.10% for ethylene glycol is found.

• **C.** Examine the chromatograms obtained in *Identification* test *B*. The retention time of the propylene glycol peak of the *Sample solution* corresponds to that of the *Standard solution*.

ASSAY

• **PROCEDURE**
Sample: Propylene Glycol
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: GC
Detector: Thermal conductivity
Column: 1-m × 4-mm; 5% phase G16; support S5
Temperature
Injector: 240°
Detector: 250°
Column: Increase from 120° to 200° at a rate of 5°/min.
Carrier gas: Helium
Injection size: 10 µL
[NOTE—The approximate retention time for propylene glycol is 5.7 min, and the approximate retention times for the three isomers of dipropylene glycol, when present, are 8.2, 9.0, and 10.2 min, respectively.]
Analysis: Calculate the percentage of $C_3H_8O_2$ in the *Sample* by dividing the area under the propylene glycol peak by the sum of the areas under all of the peaks, excluding those due to air and water, and multiplying by 100:

$$\text{Result} = [r_U/(r_U + \Sigma r_U)] \times 100$$

r_U = peak response for Propylene Glycol from the *Sample*
Σr_U = sum of individual impurity peak responses, excluding those due to air and water, from the *Sample*
Acceptance criteria: NLT 99.5%

IMPURITIES

Inorganic Impurities

• **RESIDUE ON IGNITION** ⟨**281**⟩
Sample: 50 g
Analysis: Heat the *Sample* in a tared 100-mL shallow dish until it ignites, and allow it to burn without further application of heat in a place free from drafts. Cool, moisten the residue with 0.5 mL of sulfuric acid, and ignite to constant weight.
Acceptance criteria: The weight of the residue is NMT 3.5 mg.
• **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩**:** A 1-mL portion shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (70 ppm).
• **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩**:** A 5.0-mL portion shows no more sulfate than corresponds to 0.30 mL of 0.020 N sulfuric acid (60 ppm).

Delete the following:

•• **HEAVY METALS** ⟨**231**⟩
Analysis: Mix 4.0 mL with water to make 25 mL.
Acceptance criteria: NMT 5 ppm •• (Official 1-Jan-2018)

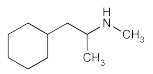
SPECIFIC TESTS

• **SPECIFIC GRAVITY** ⟨**841**⟩**:** 1.035–1.037
• **ACIDITY**
Sample: 10 mL of Propylene Glycol
Analysis: Add 1 mL of phenolphthalein TS to 50 mL of water, then add 0.1 N sodium hydroxide until the solution remains pink for 30 s. Add the *Sample*, and titrate with 0.10 N sodium hydroxide until the original pink color returns and remains for 30 s.
Acceptance criteria: NMT 0.20 mL of 0.10 N sodium hydroxide
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.2%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Diethylene Glycol RS
USP Ethylene Glycol RS
USP Propylene Glycol RS

Propylhexedrine



$C_{10}H_{21}N$ 155.28
Cyclohexaneethanamine, *N*,α-dimethyl-, (±)-.
(±)-*N*,α-Dimethylcyclohexaneethylamine [101-40-6].

» Propylhexedrine contains not less than 98.0 percent and not more than 101.0 percent of $C_{10}H_{21}N$.

Packaging and storage—Preserve in tight containers.
Identification—

A: To 3 mL of water contained in a small flask add about 0.1 mL of it and 0.5 mL of 1 N hydrochloric acid, and agitate the mixture until clear. Add 20 mL of trinitrophenol TS, insert the stopper in the flask, shake vigorously for a few minutes, and allow to stand for 2 hours. Filter, wash the