cent of $C_{17}H_{28}N_2O_3 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Benoxinate Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩: previously dried.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 15 µg per mL.

Medium: water.

C: A solution (1 in 100) responds to the tests for *Chloride* ⟨191⟩.

pH ⟨791⟩: between 5.0 and 6.0, in a solution (1 in 100).

Loss on drying ⟨731⟩—Dry it at 105 ° for 3 hours: it loses not more than 1.0% of its weight.

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

Ordinary impurities ⟨466⟩—

Test solution: methanol.

Standard solution: methanol.

Eluant: a mixture of chloroform, cyclohexane, and diethylamine (5:4:1).

Visualization: 12.

Assay—Dissolve about 250 mg of Benoxinate Hydrochloride, accurately weighed, in a mixture of 20 mL of glacial acetic acid and 20 mL of acetic anhydride, and titrate with 0.1 N per chloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessar y correction. Each mL of 0.1 N per chloric acid is equivalent to 34.49 mg of $C_{17}H_{28}N_2O_3 \cdot HCl$.

Benoxinate Hydrochloride Ophthalmic Solution

» Benoxinate Hydrochloride Ophthalmic Solution is a sterile solution of Benoxinate Hydrochloride in water. It contains not less than 95.0 per cent and not more than 105.0 per cent of the labeled amount of $C_{17}H_{28}N_2O_3 \cdot HCl$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Benoxinate Hydrochloride RS

Identification—Dilute a volume of Solution, equivalent to about 50 mg of benoxinate hydrochloride, with 0.01 N hydrochloric acid to 25 mL, and proceed as directed under *Identification—Organic Nitrogenous Bases* ⟨181⟩, beginning with "Transfer the liquid to a separator": the solution meets the requirements of the test.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 3.0 and 6.0.

Assay—

Standard preparation—Dissolve an accurately weighed quantity of USP Benoxinate Hydrochloride RS in 0.1 N hydrochloric acid to obtain a solution having a known concentration of about 400 µg per mL.

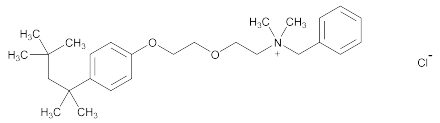
Assay preparation—Transfer a volume of Ophthalmic Solution, equivalent to about 20 mg of benoxinate hydrochloride, to a separator containing 15 mL of water, add 1 mL of ammonium hydroxide, and extract with five 20-mL portions of ether. Wash the combined ether extracts with 10 mL of water, extract the water washing with 10 mL of ether, and add this ether extract to the main extract. Extract the ether solution with three 5-mL portions of 0.1 N hydrochloric acid, collect the acid extracts in a 50-mL volumetric flask, dilute with 0.1 N hydrochloric acid to volume, and mix.

Procedure—Transfer 5.0 mL each of the *Standard preparation*, the *Assay preparation*, and 0.1 N hydrochloric acid to provide a blank, to separate 200-mL volumetric flasks. Dilute the contents of each flask with water to volume, and mix. Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 308 nm, with a suitable spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of $C_{17}H_{28}N_2O_3 \cdot HCl$ in each mL of the Ophthalmic Solution taken by the formula:

$$(0.05C / V)(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Benoxinate Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Ophthalmic Solution taken; and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Benzethonium Chloride



$C_{27}H_{42}ClNO_2$ 448.08

Benzenemethanaminium, *N*,*N*-dimethyl-*N*-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]-, chloride;
Benzyldimethyl[2-[2-[*p*-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]ammonium chloride [121-54-0].

DEFINITION

Benzethonium Chloride contains NLT 97.0% and NMT 103.0% of $C_{27}H_{42}ClNO_2$, calculated on the dried basis.

IDENTIFICATION

- **A. Procedure**
  Sample solution: 10 mg/mL
  Analysis: To 1 mL of the *Sample solution* add 2 mL of alcohol, 0.5 mL of 2 N nitric acid, and 1 mL of silver nitrate TS.
  Acceptance criteria: A white precipitate, which is insoluble in 2 N nitric acid but soluble in 6 N ammonium hydroxide, is formed.
- **B. Infrared Absorption** ⟨197K⟩

ASSAY

- **Procedure**
  Sample: 0.3 g of Benzethonium Chloride
  Analysis: Dissolve the *Sample* in 75 mL of water contained in a glass-stoppered, 250-mL flask. Add 0.4 mL of bromophenol blue solution (1 in 2000), 10 mL of chloroform, and 1 mL of 1 N sodium hydroxide. Titrate with 0.02 M sodium tetraphenylboron VS until the blue color disappears from the chloroform layer. Add the last portions of the sodium tetraphenylboron solution dropwise, agitating vigorously after each addition. Each mL of 0.02 M sodium tetraphenylboron is equivalent to 8.962 mg of $C_{27}H_{42}ClNO_2$.
  Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%

Organic Impurities

- **Procedure: Limit of Ammonium Compounds:** To 5 mL of a solution (1 in 50) add 3 mL of 1 N sodium hydroxide, and heat to boiling: the odor of ammonia is not perceptible.

SPECIFIC TESTS
- **MELTING RANGE OR TEMPERATURE ⟨741⟩:** 158°–163°, the specimen having been dried previously
- **LOSS ON DRYING ⟨731⟩:** Dry a sample at 105 ° for 4 h: it loses NMT 5.0% of its weight.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Benzethonium Chloride RS

Benzethonium Chloride Concentrate

» Benzethonium Chloride Concentrate contains not less than 94.0 per cent and not more than 106.0 percent of the labeled amount of benzethonium chloride ($C_{27}H_{42}ClNO_2$).

Packaging and storage—Preserve in tight, light-resistant containers. Store at room temperature.

Labeling— The label states that this article is not intended for direct administration to humans or animals.

Identification—Evaporate a volume of Concentrate, equivalent to about 200 mg of benzethonium chloride, on a steam bath: the residue so obtained meets the requirements of the tests for *Identification* under *Benzethonium Chloride*.

Oxidizing substances—To 5 mL of Concentrate add 0.5 mL of potassium iodide TS and a few drops of 3 N hydrochloric acid: the solution does not acquire a yellow color.

Limit of nitrites—To 1 drop of Concentrate on a spot plate add 1 drop each of glacial acetic acid, sulfanilic acid in acetic acid solution (1 in 100), and 1-naphthylamine–acetic acid solution (prepared by boiling 30 mg of 1-naphthylamine in 70 mL of water, decanting the colorless solution from the blue-violet residue, and mixing with 30 mL of glacial acetic acid): no red color develops in the resulting solution within 10 minutes.

Assay—Transfer a volume of Concentrate, equivalent to about 200 mg of benzethonium chloride, to a glass-stoppered flask, and proceed as directed in the *Assay* under *Benzethonium Chloride,* beginning with "Add 0.4 mL of bromophenol blue solution (1 in 2000)."

Benzethonium Chloride Topical Solution

» Benzethonium Chloride Topical Solution contains not less than 95.0 per cent and not more than 105.0 percent of the labeled amount of benzethonium chloride ($C_{27}H_{42}ClNO_2$).

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

Identification—The residue obtained by evaporating, on a steam bath, a volume of Topical Solution, equivalent to about 200 mg of benzethonium chloride, responds to the *Identification* tests under *Benzethonium Chloride.*

Oxidizing substances—To 5 mL add 0.5 mL of potassium iodide TS and a few drops of 3 N hydrochloric acid: the solution does not acquire a yellow color.

Limit of nitrites—To 1 drop of Topical Solution on a spot plate add 1 drop each of glacial acetic acid, sulfanilic acid in acetic acid (1 in 100), and 1-naphthylamine–acetic acid solution (prepared by boiling 30 mg of 1-naphthylamine in 70 mL of water, decanting the colorless solution from the blue-violet residue, and mixing with 30 mL of glacial acetic acid): no red color develops in the resulting solution within 10 minutes.

Assay—Transfer a volume of Topical Solution, equivalent to about 200 mg of benzethonium chloride, to a glass-stoppered flask, and proceed as directed in the *Assay* under *Benzethonium Chloride*, beginning with "Add 0.4 mL of bromophenol blue solution (1 in 2000)".

Benzethonium Chloride Tincture

» Benzethonium Chloride Tincture contains, in each 100 mL, not less than 190 mg and not more than 210 mg of $C_{27}H_{42}ClNO_2$.

Benzethonium Chloride	2 g
Alcohol	685 mL
Acetone	100 mL
Purified Water, a sufficient quantity to make	1000 mL

Dissolve the Benzethonium Chloride in a mixture of the Alcohol and the Acetone. Add sufficient Purified Water to make 1000 mL.

NOTE—Benzethonium Chloride Tincture may be colored by the addition of any suitable color or combination of colors certified by the FDA for use in drugs.

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

Identification—The residue obtained by evaporating 50 mL on a steam bath responds to *Identification* tests *A* and *B* under *Benzethonium Chloride.*

Specific gravity ⟨841⟩: between 0.868 and 0.876.

Alcohol and acetone content—To a 100-mL volumetric flask transfer 20.0 mL of Benzethonium Chloride Tincture and 5.0 mL of methanol as the internal standard, dilute with water to volume, and mix. Similarly prepare four 100-mL standard solutions in water, each containing 5.0 mL of methanol as the internal standard, and individually containing, respectively, 11.0 mL of dehydrated alcohol, 14.0 mL of dehydrated alcohol, 1.7 mL of acetone, and 2.2 mL of acetone. Inject 0.8 µL of the solution containing the substance under test into a suitable gas chromatograph equipped with a flame-ionization detector, and record the chromatogram. Similarly and successively record the chromatograms for 0.8-µL injected volumes of the four standard solutions. Under typical conditions, the instrument contains a 120-cm × 4-mm column packed with a suitable type of support, such as 80- to 100-mesh S3; the column is maintained at about 120°; the injection port and detector block temperatures are maintained at about 240 °; and dry helium is used as the carrier gas at a flow rate of about 90 mL per minute. From the respective chromatograms obtained as described previously, calculate the ratios of peak areas for alcohol to internal standard and for acetone to internal standard.

Calculate the percentage of alcohol and of acetone in the Tincture by the formula:

$$[A(Y - Z) + B(Z - X)] / (Y - X)$$

in which A and B are the percentage of alcohol, or of acetone, in the lower and higher standards, respectively; and X, Y, and Z are the ratios of the alcohol peak areas, or the acetone peak areas, to the internal standard peak areas for the lower standard, higher standard, and the material under test, respectively: the content of C_2H_5OH is between 62.0% and 68.0%, and the content of acetone (C_3H_6O) is between 9.0% and 11.0%.