Benzethonium Chloride

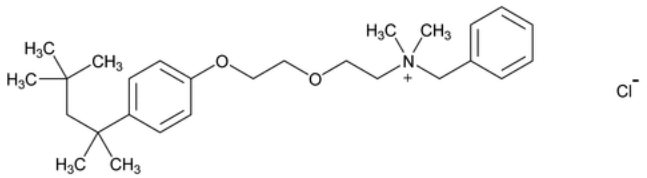
Type of Posting	Revision Bulletin
Posting Date	25–Jan–2019
Official Date	01–Feb–2019
Expert Committee	Chemical Medicines Monographs 6
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 6 Expert Committee has revised the Benzethonium Chloride monograph. The purpose for the revision is to delete the acceptance criterion of NMT 0.10% for any individual unspecified impurity under *Organic Impurities* to accommodate several products in the market. USP will propose a separate revision to include the specified and unspecified impurity limits upon further evaluation and supporting data.

The Benzethonium Chloride Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Sujatha Ramakrishna, Principal Scientific Liaison (301-816-8349 or sxr@usp.org).

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 benzethonium chloride ($C_{27}H_{42}ClNO_2$), calculated on the dried basis.

IDENTIFICATION

• **A.**
Sample solution: 10 mg/mL
Analysis: Add 2 mL of alcohol, 0.5 mL of 2 N nitric acid, and 1 mL of silver nitrate TS to 1 mL of the *Sample solution*.
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** ⟨197⟩**:** [Note—Methods described in ⟨197K⟩ or ⟨197A⟩ may be used.]

• **C.** 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: Dilute 20 mL of triethylamine with water to 1000 mL, and adjust with phosphoric acid to a pH of 3.0.
Mobile phase: Acetonitrile and *Buffer* (42:58)
Diluent: Acetonitrile and water (42:58)
System suitability solution: 0.15 mg/mL each of USP Benzethonium Chloride RS and USP Methylbenzethonium Chloride RS in *Diluent*
Standard solution: 0.15 mg/mL of USP Benzethonium Chloride RS in *Diluent*
Sample solution: 0.15 mg/mL of Benzethonium Chloride in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 225 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 40°
Flow rate: 1 mL/min
Injection volume: 10 µL
Run time: 1.5 times the retention time of the methylbenzethonium peak
System suitability
Sample: *System suitability solution*
[Note—The relative retention times for benzethonium and methylbenzethonium are 0.7 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 7.0 between the benzethonium and methylbenzethonium peaks
Tailing factor: NMT 2.0 for the benzethonium peak
Relative standard deviation: NMT 1.0% for the benzethonium peak
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of benzethonium chloride ($C_{27}H_{42}ClNO_2$) in the portion of Benzethonium Chloride taken:

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

r_U = peak response of benzethonium from the *Sample solution*
r_S = peak response of benzethonium from the *Standard solution*
C_S = concentration of USP Benzethonium Chloride RS in the *Standard solution* (mg/mL)
C_U = concentration of Benzethonium Chloride in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

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

Change to read:

• **Organic Impurities**
Buffer, Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 1 µg/mL of USP Benzethonium Chloride RS in *Diluent*
Sample solution: 1 mg/mL of Benzethonium Chloride in *Diluent*
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements: Proceed as directed in the *Assay*, except for *Relative standard deviation*.
Relative standard deviation: NMT 5.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of any individual ▲▲ (RB 1-Feb-2019) impurity in the portion of Benzethonium Chloride taken:

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

r_U = peak response of any individual ▲▲ (RB 1-Feb-2019) impurity from the *Sample solution*
r_S = peak response of benzethonium from the *Standard solution*
C_S = concentration of USP Benzethonium Chloride RS in the *Standard solution* (mg/mL)
C_U = concentration of Benzethonium Chloride in the *Sample solution* (mg/mL)

Acceptance criteria
▲▲ (RB 1-Feb-2019)
Total impurities: ▲NMT▲ (ERR 1-Feb-2019) 1.0%

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩
Analysis: Dry at 105° for 4 h.
Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Benzethonium Chloride RS
USP Methylbenzethonium Chloride RS