Betaxolol Tablets

DEFINITION
Betaxolol Tablets contain an amount of Betaxolol Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$).

IDENTIFICATION
• **A.** 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: 0.025 M pH 6.0 ammonium phosphate buffer
Mobile phase: *Buffer*, acetonitrile, and methanol (35:35:30)
Diluent: Acetonitrile and water (1:1)
Standard solution: 2 mg/mL of USP Betaxolol Hydrochloride RS in *Diluent*
Sample solution: Nominally 2 mg/mL of betaxolol hydrochloride prepared as follows. Place NLT 20 Tablets in a suitable volumetric flask with an appropriate amount of *Diluent*. Sonicate until the Tablets are disintegrated. Cool to room temperature, dilute with *Diluent* to volume, and filter. Use the clear filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 273 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 3.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$) in the portion of Tablets 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 Betaxolol Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of betaxolol hydrochloride in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%

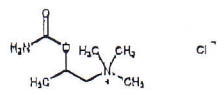
PERFORMANCE TESTS
• **DISSOLUTION** ⟨711⟩
Medium: 0.01 N hydrochloric acid; 500 mL
Apparatus 2: 50 rpm
Time: 30 min
Standard solution: USP Betaxolol Hydrochloride RS in *Medium*
Sample solutions: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Instrumental conditions
Mode: UV
Analytical wavelength: Maximum absorbance of about 274 nm
Cell path: A 5-cm path length cell may be used for lower dosage levels.
Tolerances: NLT 80% (Q) of the labeled amount of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$) is dissolved.
• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩
Procedure for content uniformity
Standard solution: 0.1 mg/mL of USP Betaxolol Hydrochloride RS in 0.1 N hydrochloric acid
Sample solution: Place 1 Tablet in a suitable volumetric flask to obtain a concentration of betaxolol hydrochloride, based on the labeled claim, of 0.1 mg/mL. Add an amount of 0.1 N hydrochloric acid equal to 70% of the volume of the flask. Shake by mechanical means until dissolved, dilute with 0.1 N hydrochloric acid to volume, and mix. Filter, and discard the first 20 mL of the filtrate.
Instrumental conditions
Mode: UV
Analytical wavelength: Maximum absorbance of about 274 nm
Cell path: 1 cm
Blank: 0.1 N hydrochloric acid
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$) in the Tablet taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Betaxolol Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of betaxolol hydrochloride in the *Sample solution* (mg/mL)
Acceptance criteria: Meet the requirements

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Preserve in tight containers.
• **LABELING:** Label the Tablets to state both the content of the betaxolol active moiety and the content of betaxolol hydrochloride used in formulating them.
• **USP REFERENCE STANDARDS** ⟨11⟩
USP Betaxolol Hydrochloride RS

Bethanechol Chloride



$C_7H_{17}ClN_2O_2$ 196.68
1-Propanaminium, 2-[(aminocarbonyl)oxy]-*N*,*N*,*N*-trimethyl-, chloride, (±)-;
(±)-(2-Hydroxypropyl)trimethylammonium chloride carbamate [590-63-6].

DEFINITION
Bethanechol Chloride contains NLT 98.0% and NMT 101.5% of bethanechol chloride ($C_7H_{17}ClN_2O_2$), calculated on the dried basis.

IDENTIFICATION

• **A. INFRARED ABSORPTION** ⟨197M⟩

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C. IDENTIFICATION TESTS—GENERAL,** *Chloride* ⟨191⟩: Meets the requirements

ASSAY

• **PROCEDURE**

Buffer: 29 mg/L of edetic acid in a solution prepared as follows. Transfer a portion of edetic acid to a suitable volumetric flask. Dissolve in water, using 50% of the final flask volume. Add 0.3 mL of nitric acid per L, and dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (5:95)

System suitability solution: 0.1 mg/mL of bethanechol chloride in a solution prepared as follows. Transfer a portion of bethanechol chloride to a suitable volumetric flask. Add 4% of the final flask volume of 0.1 N sodium hydroxide, and allow to stand for 15 min. Add 4% of the final flask volume of 0.1 N hydrochloric acid. Dissolve in and dilute with *Mobile phase* to volume.

Standard solution: 0.1 mg/mL of USP Bethanechol Chloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Bethanechol Chloride in *Mobile phase*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: Conductivity

Column: 3.9-mm × 15.0-cm; packing L55

Temperatures

Detector: 35°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 0.8 between desacetyl methacholine and bethanechol chloride, *System suitability solution*

Tailing factor: NMT 3.5, *Standard solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of bethanechol chloride ($C_7H_{17}ClN_2O_2$) in the portion of Bethanechol Chloride 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 Bethanechol Chloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Bethanechol Chloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.5% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION** ⟨281⟩: NMT 0.1%

• **HEAVY METALS,** *Method I* ⟨231⟩

Test preparation: Dissolve 667 mg of Bethacholine Chloride in 10 mL of water, add 2 mL of 1 N acetic acid, and dilute with water to 25 mL.

Acceptance criteria: NMT 30 ppm

• **ORGANIC IMPURITIES**

Buffer: 0.48 g/L of methanesulfonic acid in water

Mobile phase: Acetonitrile and *Buffer* (5:95)

System suitability solution: 0.1 mg/mL of bethanechol chloride in a solution prepared as follows. Transfer a portion of bethanechol chloride to a suitable volumetric flask. Add 4% of the final flask volume of 0.1 N sodium hydroxide, and allow to stand for 15 min. Add 4% of the final flask volume of 0.1 N hydrochloric acid. Dissolve in and dilute with *Mobile phase* to volume.

Standard solution: 1 µg/mL of USP Bethanechol Chloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Bethanechol Chloride in *Mobile phase*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: Conductivity

Column: 3.9-mm × 15.0-cm; packing L55

Temperatures

Detector: 35°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 0.8 between desacetyl methacholine and bethanechol chloride, *System suitability solution*

Relative standard deviation: NMT 10.0% for bethanechol chloride, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Bethanechol Chloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of any impurity from the *Sample solution*

r_S = peak response of bethanechol chloride from the *Standard solution*

C_S = concentration of USP Bethanechol Chloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Bethanechol Chloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desacetyl methacholine[a]	0.9	1.2	1.0
Bethanechol chloride	1.0	—	—
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	1.5

[a] 2-Hydroxypropyltrimethyl ammonium chloride.

SPECIFIC TESTS
- **pH** ⟨791⟩
  Sample solution: 10 mg/mL of Bethanechol Chloride in water
  Acceptance criteria: 5.5–6.5
- **Loss on Drying** ⟨731⟩
  Analysis: Dry at 105° for 2 h.
  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩
  USP Bethanechol Chloride RS

Bethanechol Chloride Injection

DEFINITION
Bethanechol Chloride Injection is a sterile solution of Bethanechol Chloride in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of bethanechol chloride ($C_7H_{17}ClN_2O_2$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B. Identification Tests—General,** *Chloride* ⟨191⟩: Meets the requirements

ASSAY
- **Procedure**
  Mobile phase: 20 mM methanesulfonic acid
  Diluent: 0.1 mg/mL of calcium chloride and 0.1 mg/mL of magnesium chloride in water
  System suitability solution: 1 mg/mL of USP Bethanechol Chloride RS in solution prepared as follows. Transfer a portion of USP Bethanechol Chloride RS to a suitable volumetric flask. Add 60% of the final volume of water, 8% of the final volume of *Diluent*, and 2% of the final volume of 0.1 N of sodium hydroxide. Dilute with water to volume.
  Standard solution: 1.0 mg/mL of USP Bethanechol Chloride RS in water
  Sample solution: Nominally 1.0 mg/mL of bethanechol chloride from a volume of Injection in water
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: Conductivity
  Column: 4-mm × 25-cm; packing L53
  Flow rate: 1 mL/min
  Injection volume: 50 µL
  System suitability
  Sample: *System suitability solution*
  [Note—See *Table 1* for the relative retention times.]
  Suitability requirements
  Resolution: NLT 2.0 between the calcium ion and desacetyl methacholine
  Tailing factor: NMT 4.5 for bethanechol chloride
  Relative standard deviation: NMT 2.0% for bethanechol chloride
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of bethanechol chloride ($C_7H_{17}ClN_2O_2$) in each mL of the Injection 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 Bethanechol Chloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

IMPURITIES
- **Organic Impurities**
  Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay*.
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of desacetyl methacholine in each mL of Injection taken:

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

r_U = peak response of desacetyl methacholine from the *Sample solution*
r_S = peak response of bethanechol chloride from the *Standard solution*
C_S = concentration of USP Bethanechol Chloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of bethanechol chloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sodium[a]	1.0	—
Magnesium[a]	1.4	—
Calcium[a]	1.6	—
Desacetyl methacholine[b]	2.0	4.0
Bethanechol chloride	2.8	—

[a] Included for identification purposes only.
[b] 2-Hydroxypropyltrimethyl ammonium chloride.

SPECIFIC TESTS
- **Bacterial Endotoxins Test** ⟨85⟩: NMT 25.0 USP Endotoxin Units/mg of bethanechol chloride
- **pH** ⟨791⟩: 5.5–7.5
- **Other Requirements:** It meets the requirements in *Injections* ⟨1⟩.

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass.
- **USP Reference Standards** ⟨11⟩
  USP Bethanechol Chloride RS
  USP Endotoxin RS

Bethanechol Chloride Oral Solution

DEFINITION
Bethanechol Chloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of bethanechol chloride ($C_7H_{17}ClN_2O_2$).
Prepare Bethanechol Chloride Oral Solution 5 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Bethanechol Chloride	500 mg
Vehicle for Oral Solution (regular or sugar-free), *NF*, a sufficient quantity to make	100 mL

USP Monographs