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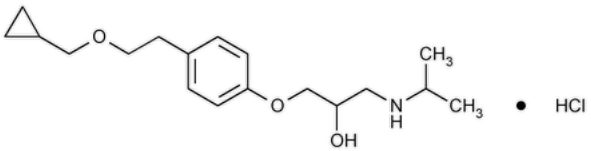
Betaxolol Hydrochloride



$C_{18}H_{29}NO_3 \cdot HCl$ 343.89

2-Propanol, 1-[4-[2-(cyclopropylmethoxy)ethyl]phenoxy]-3-[(1-methylethyl)amino]-, hydrochloride, (±)-;

(±)-1-[*p*-[2-(Cyclopropylmethoxy)ethyl]phenoxy]-3-(isopropylamino)-2-propanol hydrochloride CAS RN®: 63659-19-8; UNII: 6X97D2XT0O.

DEFINITION

Betaxolol Hydrochloride contains NLT 98.0% and NMT 102.0% of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

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

Change to read:

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Analysis: Proceed as directed for ▲amine hydrochlorides.▲ (USP 1-May-2021)

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Buffer: 3.4 g/L of monobasic potassium phosphate in water, adjusted with phosphoric acid to a pH of 3.0

Mobile phase: Acetonitrile, methanol, and *Buffer* (175:175:650)

Standard solution: 1 mg/mL of USP Betaxolol Hydrochloride RS in *Mobile phase*. Sonicate if necessary.

Sample solution: 1 mg/mL of Betaxolol Hydrochloride in *Mobile phase*. Sonicate if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

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 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of betaxolol hydrochloride ($C_{18}H_{29}NO_3 \cdot HCl$) in the portion of Betaxolol Hydrochloride 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 = concentration of Betaxolol Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

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

Buffer, Mobile phase, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 1 mg/mL of USP Betaxolol Hydrochloride RS and 30 µg/mL of USP Betaxolol Related Compound A RS in *Mobile phase*

Standard solution: 0.003 mg/mL of USP Betaxolol Hydrochloride RS in *Mobile phase*

System suitability

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

[Note—The relative retention times for betaxolol related compound A and betaxolol are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the betaxolol related compound A and betaxolol peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the impurities in the *Sample solution* on the basis of the relative retention times in *Table 1*.

Calculate the percentage of each impurity in the portion of Betaxolol Hydrochloride taken:

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

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

r_S = peak response of betaxolol from the *Standard solution*

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

C_U = concentration of Betaxolol Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor for each individual impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Betaxolol hydroxyethyl analog[a]	0.3	1.3	0.5
Betaxolol related compound A[b]	0.9	1.2	0.5
Betaxolol	1.0	1.0	—
Betaxolol phenol analog[c]	1.6	1.3	0.5
Betaxolol open chain analog[d]	1.7	0.95	0.5
Betaxolol oxirane analog[e]	3.7	1.3	0.5
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 1-[4-(2-Hydroxyethyl)phenoxy]-3-(isopropylamino)propan-2-ol.

[b] 1-(4-Ethylphenoxy)-3-(isopropylamino)propan-2-ol.

[c] 4-[2-(Cyclopropylmethoxy)ethyl]phenol.

[d] 1-[4-(2-Butoxyethyl)phenoxy]-3-(isopropylamino)propan-2-ol.

[e] 2-({[4-(2-Cyclopropylmethoxy)ethyl]phenoxy}methyl)oxirane.

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 20 mg/mL

  Acceptance criteria: 4.5–6.5

- **Loss on Drying** ⟨731⟩

  Analysis: Dry under vacuum at 65° for 2 h.

  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Betaxolol Hydrochloride RS

  USP Betaxolol Related Compound A RS

  1-(4-Ethylphenoxy)-3-(isopropylamino)propan-2-ol.

  $C_{14}H_{23}NO_2$ 237.34

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
BETAXOLOL HYDROCHLORIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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