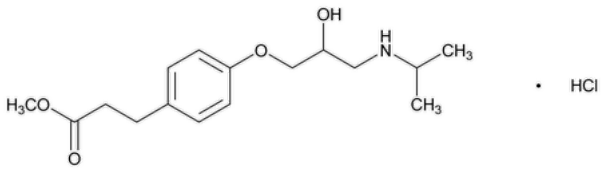
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-E7C8A5C0-201E-4213-BBD7-0F232E28ED6A_4_en-US
DOI: https://doi.org/10.31003/USPNF_M30580_04_01
DOI Ref: nq15q

Esmolol Hydrochloride



$C_{16}H_{25}NO_4 \cdot HCl$ 331.83

Benzenepropanoic acid, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]-, methyl ester, hydrochloride, (±)-;

(±)-Methyl *p*-[2-hydroxy-3-(isopropylamino)propoxy]hydrocinnamate hydrochloride CAS RN®: 81161-17-3; UNII: V05260LC8D.

DEFINITION

Esmolol Hydrochloride contains NLT 98.0% and NMT 102.0% of esmolol hydrochloride ($C_{16}H_{25}NO_4 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** 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: Dissolve 3.0 g of potassium dihydrogen phosphate in 650 mL of water.

Mobile phase: Acetonitrile, methanol, and *Buffer* (150:200:650)

System suitability stock solution: 1 mg/mL of USP Esmolol Hydrochloride RS prepared as follows. Transfer a suitable quantity of USP Esmolol Hydrochloride RS to an appropriate volumetric flask, and dissolve in and dilute with 1 N hydrochloric acid to volume. Allow the contents to stand for at least 30 min. [Note—This results in the partial degradation of the esmolol resulting in the production of esmolol free acid (see *System suitability* for the relative retention times).]

System suitability solution: 0.2 mg/mL of USP Esmolol Hydrochloride RS in water from the *System suitability stock solution*

Standard solution: 200 µg/mL of USP Esmolol Hydrochloride RS in water

Sample solution: 200 µg/mL of Esmolol Hydrochloride in water

Chromatographic system

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

Mode: LC

Detector: UV 222 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for esmolol free acid and esmolol are 0.41 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between esmolol free acid and esmolol, *System suitability solution*

Tailing factor: NMT 2.0 for the esmolol peak, *System suitability solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of esmolol hydrochloride ($C_{16}H_{25}NO_4 \cdot HCl$) in the portion of the Esmolol Hydrochloride taken:

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

r_U = peak response of esmolol from the *Sample solution*

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

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

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

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

IMPURITIES

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

Buffer and **System suitability solution:** Prepare as directed in the *Assay*.

Solution A: Methanol

Solution B: Prepare as directed for *Mobile phase* in the *Assay*.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	0	100
20	0	100
25	25	75
35	25	75
36	0	100
40	0	100

Sample solution: 1 mg/mL of Esmolol Hydrochloride in water

Chromatographic system: Proceed as directed in the *Assay*, except include a column temperature of 30°.

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 4.0 between esmolol free acid and esmolol

Tailing factor: NMT 2.0 for the esmolol peak

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Esmolol Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Esmolol free acid[a]	0.43	0.4
Esmolol *N*-isopropylamide analog[b] (if present)	0.65	0.25
N-Ethyl esmolol[c] (if present)	0.84	0.15

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Esmolol	1.0	—
Esmolol dimer[d]	6.5	0.5
Any other individual unspecified impurity	—	0.10
Total impurities	—	1.0

[a] 3-{4-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl}propionic acid.

[b] 3-{4-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl}-*N*-isopropylpropionamide.

[c] Methyl 3-{4-[3-(ethylamino)-2-hydroxypropoxy]phenyl}propionate.

[d] Methyl 3-{4-[2-hydroxy-3-(3-{4-[2-hydroxy-3-(isopropylamino)propoxy]phenyl}-*N*-isopropylpropionamido)propoxy]phenyl}propionate.

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 250 mg/mL of Esmolol Hydrochloride in water

  Acceptance criteria: 3.0–5.0

- **Water Determination** ⟨921⟩, *Method I*, *Method Ia*: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Protect from freezing, and store at room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Esmolol Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
ESMOLOL HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(3)

Current DocID: GUID-E7C8A5C0-201E-4213-BBD7-0F232E28ED6A_4_en-US

DOI: https://doi.org/10.31003/USPNF_M30580_04_01

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