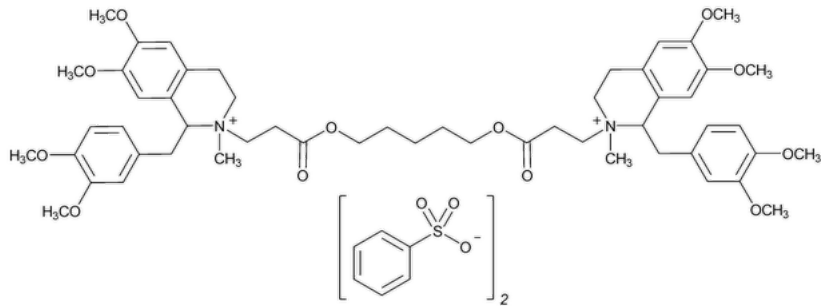


Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Jun-2022
Document Type: USP Monographs
DocId: GUID-D178E159-353B-441B-AD20-1502DFB672AA_5_en-US
DOI: https://doi.org/10.31003/USPNF_M6350_05_01
DOI Ref: if9p6

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Atracurium Besylate

Change to read:



$C_{65}H_{82}N_2O_{18}S_2$ 1243.48
Isoquinolinium, 2,2'-[1,5-pentanediy]bis[oxy(3-oxo-3,1-propanediyl)]bis[1-[(3,4-dimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-, dibenzenesulfonate;
▲2-(2-Carboxyethyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-1-veratrylisoquinolinium benzenesulfonate, pentamethylene ester ▲ (ERR 1-Jun-2022) CAS RN®: 64228-81-5; UNII: 40AX66P76P.

DEFINITION

Atracurium Besylate contains NLT 96.0% and NMT 102.0% of $C_{65}H_{82}N_2O_{18}S_2$, calculated on the anhydrous basis. It contains NLT 5.0% and NMT 6.5% of the *trans-trans* isomer, NLT 34.5% and NMT 38.5% of the *cis-trans* isomer, and NLT 55.0% and NMT 60.0% of the *cis-cis* isomer.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K**
- **B.** The retention times of the three main isomeric peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Buffer: 10.2 g of monobasic potassium phosphate in a 1000-mL volumetric flask. Dissolve in 950 mL of water. While stirring, adjust with phosphoric acid to a pH of 3.1, and dilute with water to volume.

Solution A: Acetonitrile, methanol, and *Buffer* (20:5:75)

Solution B: Acetonitrile, methanol, and *Buffer* (20:30:50)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
5	80	20
15	40	60
25	40	60
30	0	100
45	0	100
50	80	

Standard solution: 1 mg/mL of [USP Atracurium Besylate RS](#) in *Solution A*

Sample solution: 1 mg/mL of Atracurium Besylate in *Solution A*

Chromatographic system

(See [Chromatography, \(621\) System Suitability](#).)

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-μm base-deactivated packing L1

Flow rate: 1 mL/min

Injection size: 20 μL

System suitability

Sample: *Standard solution*

[NOTE—Refer to [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between the atracurium *trans-trans* isomer and the *cis-trans* isomer peaks; NLT 1.5 between the atracurium *cis-trans* isomer and the *cis-cis* isomer peaks

Relative standard deviation: NMT 2.0%, for the *cis-cis* isomer peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of atracurium besylate ($C_{65}H_{82}N_2O_{18}S_2$) in the portion of Atracurium Besylate taken:

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

r_U = sum of the peak responses for the *trans-trans* isomer, the *trans-cis* isomer, and the *cis-cis* isomer from the *Sample solution*

r_S = sum of the peak responses for the *trans-trans* isomer, the *trans-cis* isomer, and the *cis-cis* isomer from the *Standard solution*

C_S = concentration of [USP Atracurium Besylate RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Atracurium Besylate in the *Sample solution* (mg/mL)

Acceptance criteria: 96.0%–102.0%, calculated on the anhydrous basis. It contains NLT 5.0% and NMT 6.5% of the *trans-trans* isomer, NLT 34.5% and NMT 38.5% of the *cis-trans* isomer, and NLT 55.0% and NMT 60.0% of the *cis-cis* isomer.

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

• ORGANIC IMPURITIES

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

Standard solution: 0.01 mg/mL of [USP Atracurium Besylate RS](#) in *Solution A*

System suitability solution: 1 mg/mL of [USP Atracurium Besylate RS](#) in *Solution A*

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between the atracurium *trans-trans* isomer and the *cis-trans* isomer peaks; NLT 1.5 between the atracurium *cis-trans* isomer and the *cis-cis* isomer peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Record the chromatograms, and measure all of the peak responses, except the three main isomeric peaks.

Calculate the percentage of each impurity in the portion of Atracurium Besylate taken:

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

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

r_T = sum of peak responses due to the atracurium *cis-cis*, *trans-trans*, and *cis-trans* isomers from the *Standard solution*

C_S = concentration of [USP Atracurium Besylate RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Atracurium Besylate in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#). [NOTE—Disregard any peak less than 0.05%.]

Table 2