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Atracurium Besylate Injection

DEFINITION

Atracurium Besylate Injection is a sterile solution containing NLT 90.0% and NMT 115.0% of the labeled amount of atracurium besylate ($C_{65}H_{82}N_2O_{18}S_2$). It contains an amount of the *trans-trans* isomer equivalent to NLT 5.0% and NMT 6.5% of the labeled amount of atracurium besylate, an amount of the *cis-trans* isomer equivalent to NLT 34.5% and NMT 38.5% of the labeled amount of atracurium besylate, and an amount of the *cis-cis* isomer equivalent to NLT 55.0% and NMT 60.0% of the labeled amount of atracurium besylate.

[Note—The Injection is unstable at room temperature. Store all samples in the refrigerator. Analyze all preparations as soon as possible, or use a refrigerated injector.]

IDENTIFICATION

• **A.** The retention times of the peaks of the three atracurium besylate isomers from the *Sample solution* correspond to those from 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	20

Standard solution: 1 mg/mL of USP Atracurium Besylate RS in *Solution A*

Sample solution: Nominally equivalent to 1 mg/mL of atracurium besylate from Injection 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* under *Organic Impurities* 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*

Measure the responses for the three atracurium besylate isomer peaks.

Calculate the percentage of the labeled amount of atracurium besylate ($C_{65}H_{82}N_2O_{18}S_2$) in each mL of the Injection 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 = nominal concentration of atracurium besylate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–115.0% of the labeled amount of atracurium besylate ($C_{65}H_{82}N_2O_{18}S_2$). 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

• **Organic Impurities**

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

Standard stock solution: 1 mg/mL of USP Atracurium Besylate RS in *Solution A*

Standard solution: 0.02 mg/mL of USP Atracurium Besylate RS in *Solution A*, from *Standard stock solution*

System suitability

Sample: *Standard 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*

Calculate the percentage of each impurity in the portion of *Sample solution* 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 all the peak responses from the *Standard solution*

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

C_U = nominal concentration of atracurium besylate in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Benzenesulfonic acid[a]	0.08	—	—
Acidic compound	0.22	1.0	6.0
Impurity G (laudanosine)	0.29	2.0	3.0
cis- and *trans*-isomers of the hydroxy compound	0.44[b] and 0.50[c]	1.0	6.0[f]

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Atracurium *trans-trans* isomer	0.8	—	—
Atracurium *cis-trans* isomer	0.9	—	—
Atracurium *cis-cis* isomer	1.0	—	—
cis- and *trans*-isomers of the monoacrylate	1.28[d] and 1.33[e]	1.0	3.0[f]
Any individual unspecified degradation product	—	1.0	0.1
Total impurities	—	—	15.0

[a] For identification purposes only.

[b] *trans* isomer of the hydroxy compound.

[c] *cis* isomer of the hydroxy compound.

[d] *trans* isomer of the monoacrylate.

[e] *cis* isomer of the monoacrylate.

[f] Impurity consists of two isomers that are separated under these conditions; integrate both peaks for the impurity calculations.

SPECIFIC TESTS

• **pH ⟨791⟩:** 3.00–3.65

• **Sterility Tests ⟨71⟩:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 5.56 USP Endotoxin Units/mg of atracurium besylate.

• **Injections and Implanted Drug Products ⟨1⟩:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass, in a refrigerator, and protect from freezing. Protect from light.

• **USP Reference Standards ⟨11⟩**

USP Atracurium Besylate RS

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

Topic/Question	Contact	Expert Committee
ATRACURIUM BESYLATE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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