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Cisatracurium Besylate Injection

DEFINITION

Cisatracurium Besylate Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of cisatracurium ($C_{53}H_{72}N_2O_{12}$). Multiple-dose containers may contain benzyl alcohol.

IDENTIFICATION

Change to read:

- A. ▲ **SPECTROSCOPIC IDENTIFICATION TESTS (197)**, *Infrared Spectroscopy: 197F* ▲ (CN 1-MAY-2020)

Standard solution: 3 mg/mL of [USP Cisatracurium Besylate RS](#) in methylene chloride

Sample solution

[NOTE—If an emulsion forms during the extraction with methylene chloride, use a centrifuge to separate the layers.]

For Injections that do not contain benzyl alcohol: Nominally 2 mg/mL of cisatracurium from the Injection in methylene chloride prepared as follows. Transfer an amount of Injection equivalent to 10 mg of cisatracurium into a suitable separator, and extract with 5 mL of methylene chloride. Use the lower methylene chloride layer.

For Injections containing benzyl alcohol: Nominally 2 mg/mL of cisatracurium from the Injection in methylene chloride prepared as follows. Transfer an amount of Injection equivalent to 10 mg of cisatracurium into a suitable separator, and extract with 20.0 mL of ethyl acetate. Transfer the lower aqueous layer into another separator, and extract with 5 mL of methylene chloride. Use the lower methylene chloride layer.

Analysis

Samples: *Standard solution* and *Sample solution*

Add several drops of the *Standard solution* and *Sample solution* to separate potassium bromide plates. Allot the solvent to evaporate, and analyze the resulting residue.

Acceptance criteria: Meets the requirements

- 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

Solution A: Acetonitrile, methanol, water, and anhydrous formic acid (21:21:60:1)

Mobile phase: 19.4 g/L of ammonium formate in *Solution A*. Filter under vacuum using a suitable filter.

Diluent: Acetonitrile, methanol, and water (20:20:60). Add 0.4 mL of anhydrous formic acid per 1 L.

System suitability solution: 0.7 mg/mL of [USP Cisatracurium Besylate System Suitability Mixture RS](#) in *Diluent*

Standard solution: 0.7 mg/mL of [USP Cisatracurium Besylate RS](#) in *Diluent*

Sample solution: Nominally 0.7 mg/mL of cisatracurium besylate from the Injection in *Diluent*, equivalent to 0.5 mg/mL of cisatracurium, prepared as follows. Using a “to contain” pipet, transfer a suitable volume of Injection to an appropriate volumetric flask, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25.0-cm; 5-μm packing L1

Flow rate: 1.5 mL/min

Injection volume: 10 μL

System suitability

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

[NOTE—See [Table 1](#) for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between *R-cis-R'-trans*-atracurium and cisatracurium, *System suitability solution*

Tailing factor: NMT 1.7 for cisatracurium, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cisatracurium ($C_{53}H_{72}N_2O_{12}$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of cisatracurium, 929.14

M_{r2} = molecular weight of cisatracurium besylate, 1243.48

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• BENZYL ALCOHOL CONTENT (IF PRESENT)

Internal standard solution: 4.5 mg/mL of decanol in ethyl acetate

Standard stock solution: 9.0 mg/mL of [USP Benzyl Alcohol RS](#) in water

Standard solution: 0.45 mg/mL of benzyl alcohol from the *Standard stock solution* prepared as follows. Transfer 5.0 mL of *Standard stock solution* and 20.0 mL of ethyl acetate into a 50-mL centrifuge tube. Stopper, shake well for 30 s, and allow the phases to separate. Transfer 10.0 mL of the top (organic) layer and 5.0 mL of the *Internal standard solution* into a 50-mL volumetric flask. Dilute with ethyl acetate to volume.

Sample solution: Transfer 5.0 mL of the Injection and 20.0 mL of ethyl acetate into a 50-mL centrifuge tube. Stopper, shake well for 30 s, and allow the phases to separate. Transfer 10.0 mL of the top (organic) layer and 5.0 mL of the *Internal standard solution* into a 50-mL volumetric flask. Dilute with ethyl acetate to volume.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 15-m fused-silica capillary column coated with a 1.0-μm layer of liquid phase G16

Temperatures

Detector: 250°

Injection port: 220°

Column: 140°

Carrier gas: Helium

Flow rate: 5.0 mL/min

Injection volume: 1 μL

Injection type: Split ratio, 2.5:1

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for decanol and benzyl alcohol are 0.62 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between decanol and benzyl alcohol

Relative standard deviation: NMT 2.0% for peak area ratios of benzyl alcohol to decanol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzyl alcohol in the portion of Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/L) \times 100$$