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Carboplatin for Injection

DEFINITION

Carboplatin for Injection is a sterile, lyophilized mixture of Carboplatin and Mannitol. It contains NLT 90.0% and NMT 110.0% of the labeled amount of carboplatin ($C_6H_{12}N_2O_4Pt$).

[Caution—Great care should be taken in handling Carboplatin because it is a suspected carcinogen.]

IDENTIFICATION

• **A. Thin-Layer Chromatography**

Standard solution: 10 mg/mL of USP Carboplatin RS in water

Sample solution: Nominally equivalent to 10 mg/mL of carboplatin in water from the contents of one container

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 10 µL

Developing solvent system: Acetone and water (80:20)

Spray reagent: Add 5.6 g of stannous chloride to 10 mL of hydrochloric acid, and stir for 5 min. [Note—It is not necessary that all of the solids dissolve.] Add 90 mL of water and 1 g of potassium iodide, and stir. Prepare this solution fresh daily.

Analysis

Samples: *Standard solution* and *Sample solution*

Place the plate in a chromatographic chamber lined with filter paper and equilibrated for 2 h in *Developing solvent system*. Develop the chromatogram until the solvent front has moved 10 cm from the origin. Remove the plate from the chamber, and air-dry at room temperature for 2 h. Spray with the *Spray reagent*, and heat at 110° for 10 min.

Acceptance criteria: The principal spot of the *Sample solution* corresponds in appearance and R_F value to that of the *Standard solution*.

• **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**

Mobile phase: Acetonitrile and water (87:13)

Standard solution: 1 mg/mL of USP Carboplatin RS. Use this solution within 2 h.

Sample solution: Nominally equivalent to 1 mg/mL of carboplatin from the contents of one container diluted with water. Complete chromatographic analysis of this solution within 2 h.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L8

Flow rate: 2.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 1.2%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carboplatin ($C_6H_{12}N_2O_4Pt$) in the portion of Carboplatin for Injection 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 Carboplatin RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

Change to read:

• **Limit of 1,1-Cyclobutanedicarboxylic Acid**

Solution A: Dissolve 8.5 g of tetrabutylammonium hydrogen sulfate in 80 mL of water. Add 3.4 mL of phosphoric acid, and adjust with 10 N sodium hydroxide to a pH of 7.55.

Mobile phase: Acetonitrile, *Solution A*, and water (100:20:880)

Standard solution A: 0.01 mg/mL of 1,1-cyclobutanedicarboxylic acid in *Mobile phase*

Standard solution B: 5 µg/mL of 1,1-cyclobutanedicarboxylic acid in *Mobile phase*

System suitability solution: 2.5 µg/mL of 1,1-cyclobutanedicarboxylic acid and 0.5 mg/mL of carboplatin prepared as follows. Mix 1.0 mL of *Standard solution B* with 1.0 mL of *Standard solution* in the *Assay*.

Sample solution: Nominally equivalent to 1 mg/mL of carboplatin from the contents of one container diluted with *Mobile phase*. Complete the chromatographic analysis of the solution within 2 h.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: ▲3.9-mm▲ (ERR 1-Jan-2022) × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 100 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for carboplatin and 1,1-cyclobutanedicarboxylic acid are 0.65 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between the carboplatin and 1,1-cyclobutanedicarboxylic acid peaks

Relative standard deviation: NMT 10%

Analysis

Samples: *Standard solution A* and *Sample solution*

Calculate the percentage of 1,1-cyclobutanedicarboxylic acid in the portion of Carboplatin for Injection taken:

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

r_U = peak response of 1,1-cyclobutanedicarboxylic acid from the *Sample solution*

r_S = peak response of 1,1-cyclobutanedicarboxylic acid from *Standard solution A*

C_S = concentration of 1,1-cyclobutanedicarboxylic acid in *Standard solution A* (mg/mL)

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

Acceptance criteria: NMT 1.0%

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.54 USP Endotoxin Units/mg of carboplatin

• **Sterility Tests ⟨71⟩, *Test for Sterility of the Product to Be Examined, Membrane Filtration*:** Meets the requirements

• **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

• **pH ⟨791⟩**

Sample solution: Use Sterile Water for Injection, and constitute as directed in the labeling.

Acceptance criteria: 5.0–7.0

• **Water Determination ⟨921⟩, *Method I***

Analysis: Use anhydrous formamide as the extraction solvent. Introduce 50 mL of anhydrous formamide into the titration vessel, and titrate with the *Reagent* to the electrometric endpoint. Use the formamide thus dried to rinse a suitable glass syringe equipped with an 8-cm long, 22-gauge needle. Add the rinse back to the titration vessel, and titrate the vessel contents again, if necessary. Via the syringe, withdraw 5 mL of the formamide thus titrated and, through the closure of the container, expel the contents into the container. Shake the container to

obtain a solution. With the same syringe, withdraw all of the contents of the container, and transfer to the titration vessel. Titrate to the endpoint, adjusting the feeding speed control to the lowest setting to avoid overtitration.

Acceptance criteria: NMT 3.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** *Packaging and Storage Requirements* ⟨659⟩, *Injection Packaging*, *Packaging for constitution*, and protect from light.
- **USP Reference Standards** ⟨11⟩

USP Carboplatin RS

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

Topic/Question	Contact	Expert Committee
CARBOPLATIN FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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