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Add the following:

▲Cisplatin Injection

DEFINITION

Cisplatin Injection is a sterile solution of Cisplatin in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of cisplatin ($Cl_2H_6N_2Pt$).

[**Caution—**Cisplatin is potentially cytotoxic. Great care should be taken in handling the powder and preparing solutions.]

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **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**

[**Caution—**Protect the platinum containing solutions from light. Do not heat the platinum containing solutions, and use them within 4 h.]

Mobile phase: Dissolve 1.08 g of octanesulfonic acid sodium salt, 1.70 g of tetrabutylammonium hydrogen sulfate, and 2.72 g potassium phosphate monobasic in 950 mL of water. Adjust with 1 N sodium hydroxide to a pH of 5.9 and transfer to a 1000-mL volumetric flask. Dilute with water to volume.

Diluent: 9.0 g/L of sodium chloride in water

Standard solution: 1.0 mg/mL of USP Cisplatin RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of cisplatin from Injection in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.0-mm × 250-mm; 4-µm packing L7

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cisplatin ($Cl_2H_6N_2Pt$) in the portion of the Injection taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

[**Caution—**Protect the platinum containing solutions from light. Do not heat the platinum containing solutions, and use them within 4 h.]

Mobile phase, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*, except for the *Injection volume* and *Run time*.

Injection volume: 20 µL

Run time: NLT 8 times the retention time of cisplatin

System suitability solution: 1.0 mg/mL of USP Cisplatin RS, 0.01 mg/mL of USP Transplatin RS, and 0.02 mg/mL of USP Potassium Trichloroammineplatinate RS in *Diluent*

Sensitivity solution: 0.5 µg/mL of USP Cisplatin RS in *Diluent*

Standard solution: 0.002 mg/mL of USP Cisplatin RS, 0.01 mg/mL of USP Transplatin RS, and 0.02 mg/mL of USP Potassium Trichloroammineplatinate RS in *Diluent*

System suitability

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

[Note—The cisplatin aquo complex peak is observed in the *System suitability solution* and *Sample solution*. The relative retention times for cisplatin and cisplatin aquo complex peaks are 1.00 and 1.13, respectively.]

Suitability requirements

Resolution: NLT 2.5 between transplatin and aminotrichloroplatinum; NLT 2.5 between aminotrichloroplatinum and cisplatin, *System suitability solution*

Relative standard deviation: NMT 10.0% for cisplatin; NMT 5.0% for transplatin and aminotrichloroplatinum, *Standard solution*

Signal-to-noise: NLT 10 for cisplatin, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of transplatin in the portion of Injection taken:

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

r_U = peak area of transplatin from the *Sample solution*

r_S = peak area of transplatin from the *Standard solution*

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

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

Calculate the percentage of aminotrichloroplatinum 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 area of aminotrichloroplatinum from the *Sample solution*

r_S = peak area of aminotrichloroplatinum from the *Standard solution*

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

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

M_{r1} = molecular weight of aminotrichloroplatinum, 318.47

M_{r2} = molecular weight of potassium trichloroammineplatinate, 357.56

Calculate the percentage of any unspecified degradation product in the portion of Injection taken:

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

r_U = peak area of any unspecified degradation product from the *Sample solution*

r_S = peak area of cisplatin from the *Standard solution*

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%. Disregard any peak due to cisplatin aquo complex.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Transplatin	0.62	2.0
Aminotrichloroplatinum	0.77	2.5
Cisplatin	1.00	—
Any unspecified degradation product	—	0.2

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **pH ⟨791⟩:** 3.2–6.0
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in multiple-dose containers. Protect from light. Store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Cisplatin RS

USP Potassium Trichloroammineplatinate RS

Potassium amminetrichloroplatinate(1-).

Cl_3H_3KNPt 357.56

USP Transplatin RS

trans-Diamminedichloroplatinum.

$Cl_2H_6N_2Pt$ 300.05▲ (USP 1-Dec-2023)

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

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

Chromatographic Database Information: Chromatographic Database

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