Assay preparation and the *Standard preparation,* respectively. Where the test for *Uniformity of dosage units* has been performed using the *Procedure for content uniformity,* use the average of these determinations as the *Assay* value.

Oxacillin Sodium for Oral Solution

» Oxacillin Sodium for Oral Solution contains the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of oxacillin ($C_{19}H_{19}N_3O_5S$). It contains one or more suitable buffers, colors, flavors, preservatives, and stabilizers.

Packaging and storage—Preserve in tight containers at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Oxacillin Sodium RS

Identification—The chromatogram of the *Assay preparation* obtained as directed in the *Assay* exhibits a major peak for oxacillin, the retention time of which corresponds to that exhibited in the chromatogram of the *Standard preparation* obtained as directed in the *Assay*.

Uniformity of dosage units ⟨905⟩**—**

FOR SOLID PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

Deliverable volume ⟨698⟩: meets the requirements.

pH ⟨791⟩: between 5.0 and 7.5, in the solution constituted as directed in the labeling.

Water, *Method I* ⟨921⟩: not more than 1.0%.

Assay—

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay* under *Oxacillin Sodium.*

Diluent—Prepare a mixture of water and acetonitrile (700:300).

Standard preparation—Prepare a solution of USP Oxacillin Sodium RS in *Diluent* having a known concentration of about 0.11 mg per mL. [NOTE—Use this solution on the day prepared.]

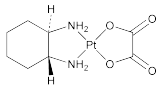
Assay preparation—Transfer an accurately measured volume of Oxacillin Sodium for Oral Solution, constituted as directed in the labeling, equivalent to about 250 mg of oxacillin ($C_{19}H_{19}N_3O_5S$), to a 250-mL volumetric flask, dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix. Filter about 5 mL of this solution through a 0.5-µm or finer porosity filter, discarding the first 2 mL of the filtrate. Use the clear filtrate as the *Assay preparation.* [NOTE—Use this *Assay preparation* on the day prepared.]

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Oxacillin Sodium.* Calculate the quantity, in mg, of oxacillin ($C_{19}H_{19}N_3O_5S$) in each mL of the constituted Oxacillin Sodium for Oral Solution taken by the formula:

$$2.5(CE / V)(r_U / r_S)$$

in which V is the volume, in mL, of the constituted Oxacillin Sodium for Oral Solution taken, and the other terms are as defined therein.

Oxaliplatin



$C_8H_{14}N_2O_4Pt$ 397.29

[*SP*-4-2-(1*R*-*trans*)]-(1,2-Cyclohexanediamine-*N,N'*)[ethanedioato(2-)-*O,O'*]platinum;
cis-[(1*R,*2*R*)-1,2-Cyclohexanediamine-*N,N'*][oxalato(2-)-*O,O'*]platinum [61825-94-3].

DEFINITION

Oxaliplatin contains NLT 98.0% and NMT 102.0% of $C_8H_{14}N_2O_4Pt$, calculated on the dried basis.

[**CAUTION—**Great care should be taken in handling Oxaliplatin, because it is a potentially cytotoxic agent.]

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨197K⟩
- **B.** The retention time of the major peak in the *Sample solution* corresponds to that in the *Standard solution,* as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

[NOTE—Use vigorous shaking and very brief sonication to dissolve the substance to be examined. Inject the *Sample solution* within 20 min of preparation. Polypropylene HPLC autosampler vials should be used.]

Buffer: Weigh 2.72 g of monobasic potassium phosphate (anhydrous) and 1.80 g of 1-pentanesulfonic acid sodium salt into a suitable container. Add 2000 mL of water, and mix well to completely dissolve all solids. Transfer 0.5 mL of triethylamine to the buffer solution, and mix thoroughly. Adjust the solution by dropwise addition of phosphoric acid to a pH of 4.30 ± 0.05.

Mobile phase: Methanol and *Buffer* (3:17)

Oxaliplatin standard stock solution: 0.5 mg/mL of USP Oxaliplatin RS in water

Oxaliplatin related compound B standard stock solution: Transfer USP Oxaliplatin Related Compound B RS to a suitable volumetric flask, add 25% of the final volume of methanol, and sonicate for approximately 2 min to disperse the solids. Add approximately 65% of the final volume of 0.001 M nitric acid, and sonicate for an additional 30 min to dissolve the solids. Allow to cool if necessary. Dilute with 0.001 M nitric acid to volume, and mix to obtain a solution having a known concentration of 0.125 mg/mL. [NOTE—USP Oxaliplatin Related Compound B RS is converted to (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N,N'*]platinum in solution preparation.]

Oxaliplatin related compound C standard stock solution: 0.1 mg/mL of USP Oxaliplatin Related Compound C RS in water

System suitability solution: 2 mg/mL of Oxaliplatin in 0.005 M sodium hydroxide. Allow this solution to stand at room temperature for at least 5 days. Transfer 10 mL of this solution, 10 mL of *Oxaliplatin related compound B standard stock solution,* and 5 mL of *Oxaliplatin related compound C standard stock solution* into a 100-mL volumetric flask, and dilute with water to volume. [NOTE—The preparation of the *System suitability solution* forms diaquodiaminocyclohexaneplatinum dimer.]

Standard solution: 0.1 mg/mL of USP Oxaliplatin RS in water, from *Oxaliplatin standard stock solution*

Sample solution: 0.1 mg/mL of Oxaliplatin in water

Chromatographic system

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

Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection size: 50 µL

System suitability

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

[NOTE—The relative retention times, measured with respect to oxaliplatin, of oxaliplatin related compounds C and B and diaquodiaminocyclohexaneplatinum dimer are 0.8, 2.7, and 6, respectively.]

Suitability requirements

Resolution: NLT 2.0 between oxaliplatin and oxaliplatin related compound C, *System suitability solution*

Tailing factor: Between 0.8 and 2.0 for the oxaliplatin peak, *System suitability solution*

Relative standard deviation: NMT 2.0% for the oxaliplatin peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_8H_{14}N_2O_4Pt$ in the portion of Oxaliplatin 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 Oxaliplatin RS in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities

- **LIMIT OF SILVER**

Sample stock solution: Dissolve 100 mg of Oxaliplatin, weighed, in 50 mL of water to obtain a solution having a concentration of 2 mg/mL.

Sample solution: 1 mg/mL of Oxaliplatin in 0.5 M nitric acid from *Sample stock solution*

Standard stock solution: Dilute a commercially available silver nitrate atomic absorption standard solution containing 1000 ppm of silver in 0.5 M nitric acid quantitatively, and stepwise if necessary, with 0.5 M nitric acid to obtain a 10-ppb solution.

Standard solution 1: Mix 20 µL of the *Sample stock solution* and 8 µL of the *Standard stock solution*, and dilute with 0.5 M nitric acid to 40 µL.

Standard solution 2: Mix 20 µL of the *Sample stock solution* and 16 µL of the *Standard stock solution,* and dilute with 0.5 M nitric acid to 40 µL.

Spectrometric conditions

(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

Mode: Atomic absorption spectrophotometer equipped with a silver hollow-cathode lamp and graphite furnace

Analytical wavelength: Silver emission line of 328.1 nm

Blank: 0.5 M nitric acid

Analysis

Samples: *Sample solution*, *Standard solution 1*, and *Standard solution 2*

Plot the absorbances of the *Sample solution, Standard solution 1*, and *Standard solution 2* versus their concentrations, in ppb, of silver, and draw the straight line best fitting the three plotted points. The intercept on the x-axis of the extended regression line indicates the silver concentration in the *Sample solution*.

Calculate the silver, in ppm, in the portion of Oxaliplatin taken:

$$\text{Result} = (C/W) \times 100$$

C = absolute value of the intercept, in ppb of silver, on the x-axis
W = weight of Oxaliplatin taken for the preparation of the *Sample stock solution* (mg)

Acceptance criteria: NMT 5 ppm

- **HEAVY METALS**

Standard stock solution: Transfer 1 mL each of 1000-ppm standard solutions of cadmium, chromium, copper, iron, nickel, and lead (commercially available) to a 100-mL volumetric flask. Add 5 mL of nitric acid, and dilute with water to volume.

Internal standard solution: Transfer 1 mL of a 10,000-ppm standard solution of yttrium (commercially available) to a 100-mL volumetric flask, and dilute with 5% nitric acid to volume.

Standard solutions: Transfer 0.2, 2.0, and 20.0 mL of *Standard stock solution* to separate 100-mL volumetric flasks. Add 1.0 mL of *Internal standard solution* and 5.0 mL of nitric acid to each flask, and dilute with water to volume. The concentrations of these solutions are 0.02, 0.20, and 2.00 ppm, respectively.

Blank solution: Transfer 1.0 mL of *Internal standard solution* and 5.0 mL of nitric acid to a 100-mL volumetric flask, and dilute with water to volume.

Sample solution: Weigh 1 g of Oxaliplatin into a 100-mL volumetric flask, and add 80 mL of water. Stir vigorously for several min with a magnetic stirrer until no more sample seems to be dissolving. Add 5 mL of nitric acid, and mix again until the sample is completely dissolved. Remove the stirrer bar from the flask, rinsing it before removal. Add 1.0 mL of the *Internal standard solution,* and dilute with water to volume.

Spectrometric conditions

(See *Plasma Spectrochemistry* ⟨730⟩.)

Measure the responses of the elements cadmium, chromium, copper, iron, nickel, lead, and yttrium (internal standard), using an inductively coupled plasma–atomic optical emission spectrometer (ICP–OES), by measuring the emissions at 226.502, 283.563, 327.395, 259.940, 221.648, 220.353, and 371.029 nm, respectively. Optimize the instrument settings as directed by the manufacturer.

System suitability

Before samples are analyzed, the instrument must pass a suitable performance check. Generate the calibration curve, using the *Blank solution* and the *Standard solutions,* and run these solutions in the following order: the *Blank solution,* then the 0.02-, 0.20-, and 2.00-ppm solutions. The linear regression coefficient is NLT 0.99; the response of the *Blank solution* is between –5.0 and 5.0 ppb for each element; and the responses of yttrium obtained from the *Standard solutions* are drifted by NMT 5.0% of the response obtained from the *Blank solution.* Run the *Standard solution* of 0.20 ppm, and record the responses of each element: the relative standard deviations for replicate runs are NMT 5.0%; and the recovery against the calibration curve is between 95% and 105%. After samples are analyzed, the instrument must pass the same suitable performance check to ensure that the calibration is still valid.

Analysis

Sample: *Sample solution*

Record the responses of each element, and determine the concentration of each element, using the calibration graph. Calculate the content of total elements, in ppm, in the portion of Oxaliplatin taken:

$$\text{Result} = [(\Sigma C_i)/W] \times 100$$

C_i = concentration of each element in the *Sample solution* (ppm)
W = weight of Oxaliplatin taken to prepare the *Sample solution* (g)

Acceptance criteria: NMT 20 ppm

- **CONTENT OF PLATINUM**

Sample: Ignite an empty porcelain crucible fitted with a lid in a furnace at 800° for 30 min. Cool in a desiccator, and

weigh. Add 200 mg of the Oxaliplatin, weighed, to the crucible, and ignite in a furnace by stepwise increments as follows: introduce into the furnace; and increase the temperature to 200° within 15 min, then to 400° within 15 min, then to 600° within 15 min, then finally to 800° within 15 min. Allow to remain in the furnace at 800° for 30 min. Remove, cool in a desiccator, and reweigh. Calculate the percentage of platinum in the portion of Oxaliplatin taken:

$$\text{Result} = (W_2/W_1) \times 100$$

W_2 = weight of residue after ignition (mg)
W_1 = weight of oxaliplatin before ignition (mg)

Acceptance criteria: 48.1%–50.1% of the oxaliplatin taken, on the dried basis

Organic Impurities

- **Procedure 1: Limit of Oxalic Acid**

[NOTE—Use vigorous shaking and very brief sonication to dissolve the substance to be examined. Inject the *Sample solution* within 20 min of preparation. Polypropylene HPLC autosampler vials should be used.]

Buffer: Add 1.36 g of potassium dihydrogen phosphate to 10 mL of 10% tetrabutylammonium hydroxide in water, and dilute with water to 1000 mL. Adjust with phosphoric acid to a pH of 6.0.

Mobile phase: Acetonitrile and *Buffer* (1:4)

Standard stock solution: 0.06 mg/mL of USP Oxaliplatin Related Compound A RS in water

Standard solution: 15 µg/mL of USP Oxaliplatin Related Compound A RS in water, from the *Standard stock solution*

System suitability solution: 0.05 mg/mL of sodium nitrate in water. Transfer 2 mL of this solution and 25 mL of the *Standard stock solution* to a 100-mL volumetric flask, and dilute with water to volume.

Sensitivity solution: 1.5 µg/mL of USP Oxaliplatin Related Compound A RS in water, from the *Standard solution*

Sample solution: 2 mg/mL of Oxaliplatin in water

Chromatographic system

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

Mode: LC
Detector: UV 205 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 2 mL/min
Injection size: 20 µL

System suitability

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

[NOTE—The elution order is sodium nitrate, followed by oxalic acid.]

Suitability requirements

Resolution: NLT 2.0 between oxalic acid and sodium nitrate, *System suitability solution*

Relative standard deviation: NMT 3.0% for the oxalic acid peak, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of oxalic acid in the portion of Oxaliplatin taken:

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

r_U = peak response of oxalic acid from the *Sample solution*
r_S = peak response of oxalic acid from the *Standard solution*
C_S = concentration of USP Oxaliplatin Related Compound A RS in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of anhydrous oxalic acid, 90.03
M_{r2} = molecular weight of USP Oxaliplatin Related Compound A RS, 126.07

Acceptance criteria: NMT 0.1%

- **Procedure 2: Limit of (*SP*-4-2-)-Diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum, Oxaliplatin Related Compound C, and Unspecified Impurities**

[NOTE—Use vigorous shaking and very brief sonication to dissolve the substance to be examined. Inject the *Sample solution* within 20 min of preparation. Polypropylene HPLC autosampler vials should be used.]

Mobile phase, Oxaliplatin standard stock solution, Oxaliplatin related compound B standard stock solution, Oxaliplatin related compound C standard stock solution, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.01 mg/mL of oxaliplatin, 0.01 mg/mL of oxaliplatin related compound B, and 0.004 mg/mL of oxaliplatin related compound C in water, from *Oxaliplatin standard stock solution, Oxaliplatin related compound B standard stock solution,* and *Oxaliplatin related compound C standard stock solution*, respectively

Sample solution: 2 mg/mL of Oxaliplatin in water

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between oxaliplatin and oxaliplatin related compound C, *System suitability solution*

Tailing factor: Between 0.8 and 2.0 for the oxaliplatin peak, *System suitability solution*

Relative standard deviation: NMT 3.0% for the oxaliplatin, oxaliplatin related compound B, and oxaliplatin related compound C peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum in the portion of Oxaliplatin taken:

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

r_U = peak response of (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum from the *Sample solution*
r_S = peak response of (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum from the *Standard solution*
C_S = concentration of USP Oxaliplatin Related Compound B RS in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum, 345.30
M_{r2} = molecular weight of USP Oxaliplatin Related Compound B RS, 433.28

[NOTE—USP Oxaliplatin Related Compound B RS is converted to (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum in solution preparation.]

Calculate the percentage of oxaliplatin related compound C in the portion of Oxaliplatin taken:

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

r_U = peak response of oxaliplatin related compound C from the *Sample solution*
r_S = peak response of oxaliplatin related compound C from the *Standard solution*
C_S = concentration of USP Oxaliplatin Related Compound C RS in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)

Calculate the percentage of diaquodiaminocyclohexaneplatinum dimer in the portion of Oxaliplatin taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of diaquodiaminocyclohexaneplatinum dimer from the *Sample solution*
r_S = peak response of oxaliplatin related compound B from the *Standard solution*
C_S = concentration of USP Oxaliplatin Related Compound B RS in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of (*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum, 345.30
M_{r2} = molecular weight of USP Oxaliplatin Related Compound B RS, 433.28
F = relative response factor for diaquodiaminocyclohexaneplatinum dimer, measured with respect to USP Oxaliplatin Related Compound B RS, 2.5

Calculate the percentage of any other unspecified impurity in the portion of Oxaliplatin taken:

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

r_U = peak response of any other unspecified impurity from the *Sample solution*
r_S = peak response of oxaliplatin from the *Standard solution*
C_S = concentration of oxaliplatin in the *Standard solution* (mg/mL)
C_U = concentration of Oxaliplatin in the *Sample solution* (mg/mL)

Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 0.30%. [NOTE—Total impurities include oxalic acid (from *Procedure 1*) and all impurities from *Procedure 2* listed in *Impurity Table 1*.]

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxaliplatin related compound C	0.8	—	0.1
Oxaliplatin	1.0	—	—
(*SP*-4-2)-diaqua[(1*R*,2*R*)-cyclohexane-1,2-diamine-*N*,*N*′]platinum	2.7	—	0.1
Diaquodiamino-cyclohexane-platinum dimer	6	2.5	0.1
Any individual unspecified impurity	—	—	0.10

- **PROCEDURE 3: LIMIT OF OXALIPLATIN RELATED COMPOUND D**

[NOTE—Use vigorous shaking and very brief sonication to dissolve the substance to be examined. Inject the *Sample solution* within 20 min of preparation. Polypropylene HPLC autosampler vials should be used.]
Mobile phase: Methanol and ethanol (7:3)
Oxaliplatin related compound D standard stock solution: 0.05 mg/mL of USP Oxaliplatin Related Compound D RS in methanol
Oxaliplatin related compound D standard solution: 15 µg/mL of USP Oxaliplatin Related Compound D RS in methanol, from *Oxaliplatin related compound D standard stock solution*
Oxaliplatin standard stock solution: 0.75 mg/mL of USP Oxaliplatin RS in methanol
Oxaliplatin standard solution: 37.5 µg/mL of USP Oxaliplatin RS in methanol, from the *Oxaliplatin standard stock solution*
Standard solutions: Transfer 40 mL of *Oxaliplatin standard stock solution* to separate 50-mL volumetric flasks. Add 1.0, 3.0, and 5.0 mL of *Oxaliplatin related compound D standard solution* to each flask, and dilute with methanol to volume. The concentration of oxaliplatin in these solutions is 0.6 mg/mL. The concentrations of oxaliplatin related compound D in these solutions are 0.3, 0.9, and 1.5 µg/mL, respectively.
System suitability solution: Transfer 5.0 mL of *Oxaliplatin standard solution* and 4.0 mL of *Oxaliplatin related compound D standard stock solution* to a 50-mL volumetric flask, and dilute with methanol to volume.
Sample solution: Transfer 30 mg of Oxaliplatin into a 50-mL volumetric flask, and dilute with methanol to volume.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 4.6-mm × 25-cm; 5-µm packing L70
Column temperature: 40°
Flow rate: 0.3 mL/min
Injection size: 20 µL
Run time: 30 min
System suitability
Samples: 0.9-µg/mL *Standard solution* and *System suitability solution*
Suitability requirements
Resolution: NLT 1.5 between oxaliplatin and oxaliplatin related compound D, *System suitability solution*
Relative standard deviation: NMT 3.0% for the peak height ratio of oxaliplatin related compound D to the sum of oxaliplatin and oxaliplatin related compound D; 0.9-µg/mL *Standard solution*
Analysis
Samples: *Standard solutions* and *Sample solution*
Plot a calibration curve for the *Standard solutions* with the peak response ratios of oxaliplatin related compound D to the sum of oxaliplatin and oxaliplatin related compound D on the y-axis and the concentrations of oxaliplatin related compound D, in µg/mL, on the x-axis. Read the concentration of oxaliplatin related compound D, in µg/mL, in the *Sample solution* from the calibration curve obtained.
Calculate the percentage of oxaliplatin related compound D in the portion of Oxaliplatin taken:

$$\text{Result} = (C/W) \times 5$$

C = concentration of oxaliplatin related compound D in the *Sample solution* (µg/mL)
W = weight of Oxaliplatin taken to prepare the *Sample solution* (mg)

Acceptance criteria: NMT 0.1%

SPECIFIC TESTS

- **ACIDITY**

Sample solution: Dissolve 100 mg in 50 mL of carbon dioxide-free water, and add 0.5 mL of phenolphthalein TS.
Acceptance criteria: The solution is colorless, and NMT 0.6 mL of 0.01 M sodium hydroxide is required to change the color to pink.

- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** NMT 1.0 USP Endotoxin Unit/mg of oxaliplatin
- **LOSS ON DRYING ⟨731⟩:** Dry 1 g at 100° to 105° for 2 h: it loses NMT 0.5% of its weight.
- **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** The total aerobic microbial count

does not exceed 20 cfu/g, and the total combined molds and yeast count does not exceed 5 cfu/g.

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩**:** Between +74.5° and +78.0°, measured at 20°
  Sample solution: 5 mg/mL, in water

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Endotoxin RS
  USP Oxaliplatin RS
  USP Oxaliplatin Related Compound A RS
  Oxalic acid dihydrate.
  $C_2H_2O_4 \cdot 2H_2O$ 126.07
  USP Oxaliplatin Related Compound B RS
  [*SP*-4-2-(1*R-trans*)]-(1,2-Cyclohexanediamine-*N,N'*) dinitratoplatinum(II).
  $C_6H_{14}N_4O_6Pt$ 433.28
  USP Oxaliplatin Related Compound C RS
  [1*R-trans*-(1,2-Cyclohexanediamine-*N,N'*)]-*trans*-dihydroxido-[oxalato(2-)-*O,O'*]platinum(IV).
  $C_8H_{16}N_2O_6Pt$ 431.30
  USP Oxaliplatin Related Compound D RS
  cis-[(1*S,2S*)-1,2-Cyclohexanediamine-*N,N'*][oxalato(2-)-*O,O'*] platinum.
  $C_8H_{14}N_2O_4Pt$ 397.29

Oxaliplatin Injection

DEFINITION

Oxaliplatin Injection is a sterile solution of Oxaliplatin in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of oxaliplatin ($C_8H_{14}N_2O_4Pt$).

IDENTIFICATION

- **A. ULTRAVIOLET ABSORPTION** ⟨**197U**⟩
  Sample solution: 100 µg/mL
  Medium: Water
- **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

[NOTE—All HPLC autosampler vials should be made of polypropylene.]

- **PROCEDURE**
  Acidified water: Adjust with phosphoric acid to a pH of 3.0.
  Mobile phase: Acetonitrile and *Acidified water* (1:99)
  System suitability solution: 0.1 mg/mL of USP Oxaliplatin RS and 0.1 mg/mL of USP Oxaliplatin System Suitability RS in water. [NOTE—USP Oxaliplatin System Suitability RS is [*SP*-4-2-(1*R-trans*)]-(1,2-cyclohexanediamine-*N,N'*) dichloridoplatinum(II).]
  Standard solution: 0.1 mg/mL of USP Oxaliplatin RS in water
  Sample solution: 0.1 mg/mL of oxaliplatin in water, from the combined contents of NLT three vials of Injection
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 210 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L1
  Column temperature: 40°
  Flow rate: 1.2 mL/min
  Injection size: 20 µL
  System suitability
  Sample: *System suitability solution*
  [NOTE—The relative retention times for USP Oxaliplatin System Suitability RS and oxaliplatin are 0.9 and 1.0, respectively.]
  Suitability requirements
  Resolution: NLT 2.0 between USP Oxaliplatin System Suitability RS and oxaliplatin
  Tailing factor: NMT 2.0, oxaliplatin peak
  Relative standard deviation: NMT 1.0%, oxaliplatin peak
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of $C_8H_{14}N_2O_4Pt$ in the portion of 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 Oxaliplatin RS in the *Standard solution* (mg/mL)
  C_U = nominal concentration of oxaliplatin in the *Sample solution* (mg/mL)
  Acceptance criteria: 90.0%–110.0%

IMPURITIES

Organic Impurities

- **PROCEDURE 1: LIMIT OF OXALIC ACID** [NOTE—All HPLC autosampler vials should be made of polypropylene.]
  Solution A: Dissolve 1.36 g of monobasic potassium phosphate in 10 mL of 10% tetrabutylammonium hydroxide, dilute with water to 1 L, and adjust with phosphoric acid to a pH of 6.0.
  Mobile phase: Acetonitrile and *Solution A* (1:4)
  Standard solution: 35 µg/mL of USP Oxaliplatin Related Compound A RS in water. [NOTE—USP Oxaliplatin Related Compound A RS is available as dihydrate oxalic acid.]
  System suitability solution: 0.1 mg/mL of succinic acid in *Standard solution*
  Sensitivity solution: 3.5 µg/mL of USP Oxaliplatin Related Compound A RS in water, from the *Standard solution*
  Sample solution: Combined contents of NLT three vials of Injection
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 210 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L1
  Column temperature: 40°
  Flow rate: 2 mL/min
  Injection size: 10 µL
  System suitability
  Samples: *Standard solution*, *System suitability solution*, and *Sensitivity solution*
  [NOTE—The relative retention times for succinic acid and oxalic acid are 0.8 and 1.0, respectively.]
  Suitability requirements
  Resolution: NLT 2.0 between succinic acid and oxalic acid, *System suitability solution*
  Tailing factor: Between 0.5 and 2.0, oxalic acid peak, *System suitability solution*
  Signal-to-noise ratio: NLT 10, *Sensitivity solution*
  Relative standard deviation: NMT 3.0%, *Standard solution*
  Analysis
  Sample: *Standard solution* and *Sample solution*
  Calculate the percentage of each impurity 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 oxalic acid from the *Sample solution*
  r_S = peak response of oxalic acid from the *Standard solution*
  C_S = concentration of USP Oxaliplatin Related Compound A RS in the *Standard solution* (mg/mL)