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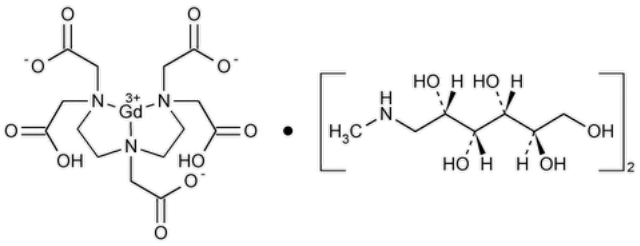
Gadopentetate Dimeglumine Injection



DEFINITION

Gadopentetate Dimeglumine Injection is a sterile solution of gadopentetate dimeglumine in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of gadopentetate dimeglumine ($C_{14}H_{20}GdN_3O_{10} \cdot 2C_7H_{17}NO_5$). It may contain small amounts of Meglumine and Pentetic Acid as stabilizers, and it may contain suitable buffers. Gadopentetate Dimeglumine Injection intended for intravascular use contains no antimicrobial agents.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

Standard solution: 74 mg/mL of USP Gadopentetate Monomeglumine RS

Sample solution: 94 mg/mL of gadopentetate dimeglumine

• **B.** The absorption of the gadolinium emission line at 368.4 nm by the *Sample solution* in the test for *Content of Gadolinium* confirms the presence of gadolinium.

• **C.** 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: Dissolve 1.37 g of tetrabutylammonium perchlorate in 1 L of a mixture of acetonitrile and water (12:88).

Standard solution: 1.85 mg/mL of USP Gadopentetate Monomeglumine RS prepared as follows. Transfer a suitable quantity to a suitable volumetric flask containing 50% of the flask volume of 0.1% meglumine solution. Dilute with water to volume.

Sample solution: Nominally 2.35 mg/mL of gadopentetate dimeglumine from Injection in water

Chromatographic system

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

Mode: LC

Detector: UV 195 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 800 theoretical plates

Tailing factor: NMT 3.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of gadopentetate dimeglumine ($C_{14}H_{20}GdN_3O_{10} \cdot 2C_7H_{17}NO_5$) 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 from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of gadopentetate dimeglumine, 938.02

M_{r2} = molecular weight of gadopentetate monomeglumine, 742.80

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Content of Meglumine**

Sample solution: Use the Injection.

Instrumental conditions

Mode: Polarimetry (see *Optical Rotation* ⟨781⟩)

Light source: Sodium lamp

Analytical wavelength: 589 nm

Cell: 10 cm

Analysis: Determine the angular rotation (see *Optical Rotation* ⟨781⟩) of the *Sample solution*.

Calculate the amount of meglumine as a percentage of the labeled amount of gadopentetate dimeglumine ($C_{14}H_{20}GdN_3O_{10} \cdot 2C_7H_{17}NO_5$) in the portion of the Injection taken:

$$\text{Result} = [(100a/\alpha) \times (1/L)] \times F \times 100$$

a = observed angular rotation corrected for the *Blank* (degrees)

α = average specific rotation of meglumine, 24.9 deg.dL/g

L = label claim of Injection (mg/mL)

F = unit conversion factor from g/dL to mg/mL, 10

Acceptance criteria: Meglumine content is 37.4%–45.8% of the labeled amount of gadopentetate dimeglumine.

• **Content of Gadolinium**

Cesium chloride solution: 100 mg/mL of cesium chloride in water

Blank solution: *Cesium chloride solution*, hydrochloric acid (spectrophotometric grade), and water (10:1:89)

Standard stock solution: Transfer 1.15 g of gadolinium (III) oxide to a 100-mL volumetric flask, add 2.0 mL of hydrochloric acid to dissolve, and dilute with water to volume.

Standard solution A: 600 µg/mL of gadolinium prepared as follows. Transfer 3.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, add 5.0 mL of *Cesium chloride solution* and 0.5 mL of hydrochloric acid (spectrophotometric grade), and dilute with water to volume.

Standard solution B: 800 µg/mL of gadolinium prepared as follows. Transfer 4.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, add 5.0 mL of *Cesium chloride solution* and 5.0 mL of hydrochloric acid (spectroscopic grade), and dilute with water to volume.

Standard solution C: 1000 µg/mL of gadolinium prepared as follows. Transfer 5.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, add 5.0 mL of *Cesium chloride solution* and 5.0 mL of hydrochloric acid (spectroscopic grade), and dilute with water to volume.

Sample solution: Treat a volume of Injection, equivalent to 469 mg of gadopentetate dimeglumine, with 0.2 mL of nitric acid in a porcelain crucible, concentrate on a hot plate, char with a burner, and ignite in a muffle furnace at 800° until all black particles disappear (approximately 1 h). Allow the residue to cool on a refractory surface for 5 min, then equilibrate to room temperature in a desiccator. Dissolve the white residue so obtained in a mixture of 1.0 mL of water and 1.0 mL of hydrochloric acid (spectrophotometric grade) with heating. Transfer this solution to a 100-mL volumetric flask, add 10.0 mL of *Cesium chloride solution*, and dilute with water to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption spectroscopy

Analytical wavelength: 368.4 nm at the gadolinium emission line

Lamp: Gadolinium hollow-cathode

Flame: Nitrous oxide–acetylene

Analysis

Samples: *Blank solution, Standard solutions*, and *Sample solution*

Blank the instrument with the *Blank solution*. Determine the absorbances of the *Standard solutions* and *Sample solution*. Plot the absorbances of the *Standard solutions* versus their concentrations, in µg/mL, of gadolinium, and draw the straight line best fitting the three plotted points. From the graph so obtained and the absorbance of the *Sample solution*, determine the concentration, in µg/mL, of gadolinium in the *Sample solution*.

Calculate the amount of gadolinium as a percentage of the labeled amount of gadopentetate dimeglumine ($C_{14}H_{20}GdN_3O_{10} \cdot 2C_7H_{17}NO_5$) in the portion of the Injection taken:

$$\text{Result} = [(C \times D)/(V \times L)] \times F \times 100$$

C = concentration of gadolinium in the *Sample solution* (µg/mL)

D = volume of the *Sample solution*, 100 mL

V = volume of Injection taken to prepare the *Sample solution* (mL)

L = label claim of Injection (mg/mL)

F = conversion factor from µg to mg, 0.001

Acceptance criteria: Gadolinium content is 15.1%–18.4% of the labeled amount of gadopentetate dimeglumine.

SPECIFIC TESTS

Change to read:

• **Limit of Pentetic Acid**

Buffer: 50 g of sodium acetate and 10 mL of glacial acetic acid in a 1000-mL volumetric flask. Dilute with degassed water to volume. Adjust with 0.1 N sodium hydroxide or glacial acetic acid to a pH of 5.

Indicator solution: 0.508 mg/mL of xylenol orange ▲tetrasodium salt▲ (IRA 1-Sep-2024) in degassed water

Diluent: *Buffer*, *Indicator solution*, and water ▲(30:30:140)▲ (IRA 1-Sep-2024)

Titrant: 0.001 M (1 µmol/mL) gadolinium sulfate prepared by dissolving a suitable quantity of gadolinium sulfate (purity ≥99.9%) in water

Sample solution: ▲Transfer 2.00 mL of Injection to a 50-mL glass container. Add 20.0 mL of water and 10.0 mL of *Diluent*. Adjust with 0.1 N sodium hydroxide or glacial acetic acid to a pH of 5.0.▲ (IRA 1-Sep-2024)

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Endpoint detection: Visual

Analysis: Titrate with *Titrant* until the color changes from yellow to reddish violet.

Calculate the amount of pentetic acid as ▲µg/mL▲ (IRA 1-Sep-2024) in the portion of the Injection taken:

$$\text{Result} = [(V_T \times M \times F) \times (1/V_U)] \times {}^{\blacktriangle}F_C{}^{\blacktriangle} \text{ (IRA 1-Sep-2024)}$$

V_T = volume of *Titrant* consumed

M = molarity of *Titrant* (µmol/mL)

F = equivalent weight of pentetic acid, 0.7867 mg/µmol

V_U = injection volume used to prepare the *Sample solution*

▲F_C = conversion factor from mg to µg, 1000▲ (IRA 1-Sep-2024)

Acceptance criteria: ▲275–400 µg/mL▲ (IRA 1-Sep-2024)

• **pH** ⟨791⟩**:** 6.5–8.0

• **Bacterial Endotoxins Test** ⟨85⟩**:** It contains NMT 25 USP Endotoxin Units/mL of Injection.

• **Sterility Tests** ⟨71⟩**:** Meets requirements

• **Particulate Matter in Injections** ⟨788⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose containers, preferably of Type I glass, protected from light. Store at controlled room temperature. Do not freeze.

• **Labeling:** Label containers of Injection intended for intravascular injection to direct the user to discard any unused portion remaining in the container. The labeling also states that it is not to be used if it contains solids.

• **USP Reference Standards** ⟨11⟩

USP Gadopentetate Monomeglumine RS

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

Topic/Question	Contact	Expert Committee
GADOPENTETATE DIMEGLUMINE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 50(2)
Current DocID: GUID-CBF753A8-3B10-4CD4-B531-1C1901872235_5_en-US
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