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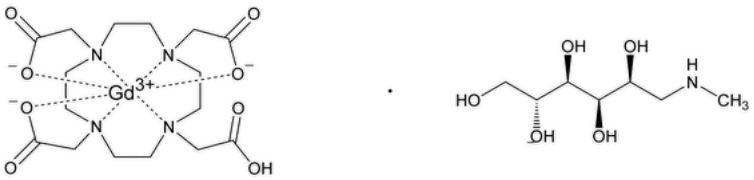
Gadoterate Meglumine Injection



$C_{16}H_{25}GdN_4O_8 \cdot C_7H_{17}NO_5$ 753.86

D-Glucitol, 1-deoxy-1-(methylamino)-, [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetato(4-)-κN^1,κN^4,κN^7,κN^{10},κO^1,κO^4,κO^7,κO^{10}]gadolinate(1-) (1:1);
1-Deoxy-1-(methylamino)-D-glucitol hydrogen [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetato(4-)-κN^1,κN^4,κN^7,κN^{10},κO^1,κO^4,κO^7,κO^{10}]gadolinate(1-) CAS RN®: 92943-93-6.

DEFINITION

Gadoterate Meglumine Injection is a sterile solution of Gadoterate Meglumine in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of gadoterate meglumine ($C_{16}H_{25}GdN_4O_8 \cdot C_7H_{17}NO_5$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**
  Analytical wavelength: 265–285 nm
  Sample solution: Dilute Injection with water (1:10).
  Acceptance criteria: The absorption spectrum exhibits maxima at 273 and 276 nm.
- **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**
  Buffer 1: 5.5 g/L of ammonium acetate. Adjust with acetic acid to a pH of 6.0.
  Buffer 2: 2.1 g/L of ammonium acetate. Adjust with acetic acid to a pH of 6.0.
  Mobile phase: Acetonitrile and *Buffer 1* (65:35)
  Diluent: Acetonitrile and *Buffer 2* (60:40)
  Standard solution: 3.6 mg/mL of USP Gadoterate Meglumine RS in *Diluent*. Vigorous shaking may be required for complete dissolution.
  Sample solution: Nominally 3.6 mg/mL of gadoterate meglumine from a suitable volume of Injection in *Diluent*. Vigorous shaking may be required for complete dissolution.
  Chromatographic system
  (See *Chromatography ⟨621⟩, System Suitability*.)
    Mode: LC
    Detector: Fluorescence
      Excitation wavelength: 274 nm
      Emission wavelength: 312 nm
    Column: 4.6-mm × 25.0-cm; 5-µm packing L114
    Column temperature: 50°
    Flow rate: 0.8 mL/min
    Injection volume: 5 µL
    Run time: NLT 2.5 times the retention time of gadoterate
  System suitability
    Sample: *Standard solution*
    Suitability requirements
      Tailing factor: NMT 2
      Relative standard deviation: NMT 1.0%
  Analysis
    Samples: *Standard solution* and *Sample solution*
      Calculate the percentage of the labeled amount of gadoterate meglumine ($C_{16}H_{25}GdN_4O_8 \cdot C_7H_{17}NO_5$) in the portion of Injection taken:

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

r_U = peak response of fluorescence emission for gadoterate from the *Sample solution*

r_S = peak response of fluorescence emission for gadoterate from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

Change to read:

• **Content of Meglumine**

Sample solution: Gadoterate Meglumine Injection

Blank: Water

Instrumental conditions

Mode: Polarimetry (see *Optical Rotation ⟨781S⟩, Procedures, Specific Rotation*), except for *Temperature*

Temperature: 20°

Lamp: Sodium

Analytical wavelength: 589 nm

Cell: 1 dm

Analysis:

Samples: *Sample solution* and *Blank*

Determine the angular rotation (see *Optical Rotation ⟨781⟩*).

Calculate the amount of meglumine as a percentage of the formulation content of meglumine ($C_7H_{17}NO_5$) in the portion of Injection taken:

$$\text{Result} = (a/\alpha) \blacktriangle\times 100\blacktriangle_{\text{(ERR 1-Jun-2021)}} \times (1/l) \times (1/L) \times 100$$

a = observed angular rotation of the *Sample solution* corrected for the *Blank* (°)

α = average specific rotation of meglumine, 24.0 deg · dm^{-1} · g^{-1} · dL

l = cell path length, dm

L = formulation content of meglumine in the Injection, 9.76 g/dL

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Limit of Free Gadolinium**

Buffer: 5.7 mL/L of glacial acetic acid and 8.2 g/L of sodium acetate (10:20). [Note—If necessary, adjust with 5.7 mL/L of glacial acetic acid or 8.2 g/L of sodium acetate to a pH between 4.8 and 5.2.]

Indicator solution: 0.1% xylenol orange in water

Sample solution: Transfer 20 mL of Injection into a suitable flask. Add 30 mL of water, 10 mL of *Buffer*, 1 drop of pyridine, and 5–10 drops of *Indicator solution*.

Blank: Water

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.01 M edetate disodium VS

Endpoint detection: Visual

Analysis

Sample: *Sample solution*

Titrate with *Titrant* to a yellow endpoint. Add an additional drop of pyridine. If a violet color appears, continue the analysis until it turns yellow.

Calculate the percentage of free gadolinium (% w/v) in the portion of Injection taken:

$$\text{Result} = [V_T \times M \times F \times (1/V_U)] \times (1/10)$$

V_T = volume of *Titrant* consumed (mL)

M = molarity of *Titrant* (mM/mL)

F = equivalency factor, 157.25 mg/mM

V_U = volume of Injection used to prepare the *Sample solution*, 20 mL

Acceptance criteria: NMT 0.001% (w/v)

• **Limit of Free Tetraxetan**

Buffer 1: 5.7 mL/L of glacial acetic acid and 8.2 g/L of sodium acetate (10:20). [Note—If necessary, adjust with 5.7 mL/L of glacial acetic acid or 8.2 g/L of sodium acetate to a pH between 4.8 and 5.2.]

Buffer 2: 0.5 g/L of copper sulfate in water

Sample solution: Transfer 5 mL of Injection into a suitable flask. Add 5 mL each of *Buffer 1* and *Buffer 2*.

Blank: Transfer 5 mL of water into a suitable flask. Add 5 mL each of *Buffer 1* and *Buffer 2*.

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.002 M edetate disodium VS

Endpoint detection: Potentiometric. [Note—An electrode system consisting of a copper indicator electrode and a calomel reference electrode is recommended.]

Analysis

Samples: *Sample solution* and *Blank*

Titrate potentiometrically with *Titrant*.

Calculate the percentage of free tetraxetan (% w/v) in the portion of Injection taken:

$$\text{Result} = [(V_B - V_T) \times M \times F] \times (1/V_U) \times (1/10)$$

V_B = volume of *Titrant* consumed by the *Blank* (mL)

V_T = volume of *Titrant* consumed by the *Sample solution* (mL)

M = actual molarity of *Titrant* (mM/mL)

F = equivalency factor, 404.42 mg/mM

V_U = volume of Injection used to prepare the *Sample solution*, 5 mL

Acceptance criteria: 0.005%–0.05% (w/v)

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 6.5–8.0

• **Particulate Matter in Injections** ⟨788⟩**:** It meets the requirements for small-volume injections.

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

• **Bacterial Endotoxins Test** ⟨85⟩**:** Meets the requirements

• **Container Content for Injections** ⟨697⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Gadoterate Meglumine RS

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

Topic/Question	Contact	Expert Committee
GADOTERATE MEGLUMINE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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