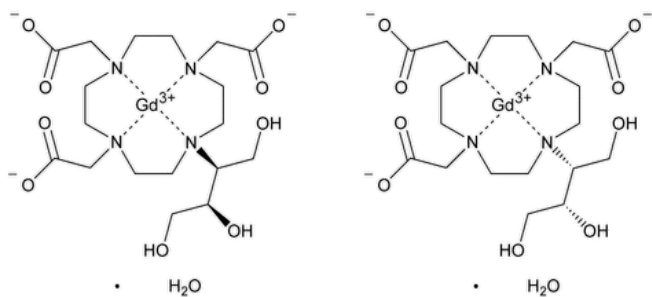


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Add the following:

▲Gadobutrol



$C_{18}H_{31}GdN_4O_9 \cdot H_2O$ 622.73
 $C_{18}H_{31}GdN_4O_9$ 604.72
Gadolinium, [10-[2-(hydroxy-κO)-3-hydroxy-1-(hydroxymethyl)propyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN¹, κN⁴, κN⁷, κN¹⁰, κO¹, κO⁴, κO⁷]-, monohydrate, [SA-8-1425362'5'-(R*,S*)];
Gadolinium(III) [10-[(2*RS*,3*SR*)-1,3,4-trihydroxybutan-2-yl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetate] monohydrate CAS RN[®]: 198637-52-4.
Anhydrous CAS RN[®]: 770691-21-9.

DEFINITION
Gadobutrol contains NLT 98.0% and NMT 102.0% of gadobutrol ($C_{18}H_{31}GdN_4O_9$) on the anhydrous basis.

IDENTIFICATION

- A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K. If the spectra obtained show differences, dissolve Gadobutrol and [USP Gadobutrol RS](#) separately in 0.5 mL of [water](#). Add 5 mL of [absolute alcohol](#). Evaporate to dryness and record the spectra of residues.
- 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**

[NOTE—Plastic labware and plastic vials may be suitable for the preparation of solutions.]

Diluted formic acid: [Anhydrous formic acid](#) and [water](#) (50:50)

Solution A: Adjust 995 mL of [water](#) with *Diluted formic acid* to a pH of 3.6. Add 5 mL of [acetonitrile](#).

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
30	75	25
30.1	100	0

Time (min)	Solution A (%)	Solution B (%)
40	100	0

Standard solution: 1.0 mg/mL of [USP Gadobutrol RS](#) in *Solution A*

Sample solution: 1.0 mg/mL of Gadobutrol in *Solution A*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 195 nm

Column: 4.6-mm × 25-cm; 3-μm packing [L11](#)

Temperatures

Autosampler: 10°

Column: 50°

Flow rate: 1 mL/min

Injection volume: 40 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5 for gadobutrol

Relative standard deviation: NMT 0.73% for gadobutrol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gadobutrol ($C_{18}H_{31}GdN_4O_9$) on the anhydrous basis in the portion of Gadobutrol taken:

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

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

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

C_S = concentration of [USP Gadobutrol RS](#) in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• LIMIT OF FREE GADOLINIUM

Buffer: Dissolve 50.0 g of [sodium acetate](#) in 10.0 mL of [glacial acetic acid](#) and add [water](#). Adjust with a suitable concentration of [sodium hydroxide](#) or [glacial acetic acid](#) to a pH of 5.0, and dilute with [water](#) to 1000.0 mL.

Xylenol orange solution: 0.5 mg/mL of [xylenol orange](#) in [water](#)

Indicator solution: Transfer 30.0 mL of *Buffer* to a suitable flask. Add 1.5 mL of *Xylenol orange solution*. Dilute with [water](#) to 200 mL.

0.25 mM sodium edetate solution: Transfer 5.0 mL of [0.05 M edetate sodium VS](#) to a 1-L volumetric flask. Dilute with [water](#) to volume.

Standard solution: 93.4 mg/L of [gadolinium sulfate](#) octahydrate in [water](#)

Titrimetric system

Mode: Direct titration

Titrant: 0.25 mM *sodium edetate solution*

Endpoint detection: Photometric at 570–574 nm

Analysis

Sample titration: Dissolve 250 mg of Gadobutrol in 5.0 mL of the *Standard solution* and 30 mL of [water](#) with sonication. Add 10.0 mL of the *Indicator solution* and adjust with 0.1 N [hydrochloric acid](#) or 1 N [sodium hydroxide](#) to a pH of 5.0. Titrate with *Titrant*, determining the endpoint photometrically using a suitable autotitrator (V_U).

Blank titration: Transfer 5.0 mL of the *Standard solution* and 30 mL of [water](#) to the titration vessel. Add 10.0 mL of the *Indicator solution* and adjust with 0.1 N [hydrochloric acid](#) or 1 N [sodium hydroxide](#) to a pH of 5.0. Titrate with *Titrant*, determining the endpoint photometrically using a suitable autotitrator (V_B).