gadolinium-containing contrast media should be restricted in patients with severe renal impairment (GFR less than 30 mL/minute per 1.73 m^2). The MHRA contra-indicates the use of gadodiamide or gadopentetate in such patients (other gadolinium-containing contrast media are under review), whereas the FDA advises that all gadolinium-containing contrast media should be avoided unless the diagnostic information is essential and cannot be obtained another way. The FDA gives a similar warning for use in patients with acute renal failure associated with hepato-renal syndrome or around the time of liver transplantation. The value of haemodialysis to remove gadolinium-containing contrast media after use is unknown.

1. Perazella MA, Rodby RA. Gadolinium-induced nephrogenic systemic fibrosis in patients with kidney disease. *Am J Med* 2007; **120:** 561–2.
2. Health Canada. Gadolinium-containing contrast agents and nephrogenic systemic fibrosis: update. *Can Adverse React News* 2007; **17** (4): 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v17n4-eng.php#1 (accessed 14/07/08)
3. Moreno-Romero JA, *et al.* Nephrogenic systemic fibrosis: a case series suggesting gadolinium as a possible aetiological factor. *Br J Dermatol* 2007; **157:** 783–7.
4. Penfield JG, Reilly RF. Nephrogenic systemic fibrosis risk: is there a difference between gadolinium-based contrast agents? *Semin Dial* 2008; **21:** 129–34.
5. FDA. Gadolinium-containing contrast agents for magnetic resonance imaging (MRI): Omniscan, OptiMARK, Magnevist, ProHance, and MultiHance (issued 08/06/06, updated 22/12/06 and 23/05/07). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705.htm (accessed 14/07/08)
6. MHRA/CHM. Gadolinium-containing MRI contrast agents: nephrogenic systemic fibrosis. *Drug Safety Update* 2007; **1** (1): 2–3. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2031801&RevisionSelectionMethod=LatestReleased (accessed 14/07/08)

Pharmacokinetics

Gadopentetate is rapidly distributed into the extracellular space after intravenous injection. An elimination half-life of 1.6 hours has been reported. It is not metabolised and about 90% of a dose is excreted in the urine within 24 hours. It does not appear to bind to plasma proteins. A small amount is distributed into breast milk. Gadopentetate is removed by haemodialysis.

Uses and Administration

Gadopentetic acid is an ionic gadolinium chelate used as a contrast medium in magnetic resonance imaging (p.1474). Gadolinium has paramagnetic properties that affect the relaxivity of hydrogen ions, increasing the signal intensity and therefore enhancing the contrast between tissues. Chelation of gadolinium reduces its toxicity while retaining its paramagnetic properties; it also affects distribution within the body. Most gadolinium chelates distribute freely into extracellular fluid but do not cross the blood-brain barrier, and they are particularly useful for imaging the brain and associated structures.

Gadopentetic acid is given intravenously as meglumine gadopentetate for contrast enhancement in magnetic resonance imaging of cranial and spinal structures, and of the whole body, and may also be used for evaluation of renal function. It is given by intra-articular injection for arthrography, and has been used orally and rectally in imaging of the gastrointestinal tract.

For cranial, spinal, and whole body imaging, a solution containing meglumine gadopentetate 469.01 mg/mL (0.5 mmol/mL) is used. The usual dose in adults, children, and neonates is 0.2 mL/kg (0.1 mmol/kg) intravenously. For cranial and spinal imaging, a further dose of 0.2 mL/kg (0.1 mmol/kg) may be given within 30 minutes if necessary; in adults this second dose may be 0.4 mL/kg (0.2 mmol/kg). For whole body imaging in adults and children over 2 years, a dose of 0.4 mL/kg (0.2 mmol/kg) may be needed in some cases to produce adequate contrast and in special circumstances a dose of 0.6 mL/kg (0.3 mmol/kg) may be used in adults.

For arthrography a solution containing meglumine gadopentetate 1.876 mg/mL (0.002 mmol/mL) is given by intra-articular injection. The dose depends on the joint being imaged; the usual range is from 1 to 20 mL.

For imaging of the gastrointestinal tract a solution containing meglumine gadopentetate 9.38 mg/mL has been used, diluted further before use.

Preparations

USP 31: Gadopentetate Dimeglumine Injection.

Proprietary Preparations (details are given in Part 3)

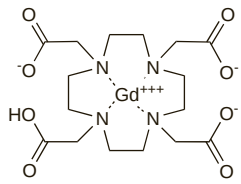
Arg.: Magnevist; Opacite; Viewgam; ***Austral.:*** Magnevist; ***Austria:*** Magnevist; ***Belg.:*** Magnevist; ***Braz.:*** Magnevistan; ***Canad.:*** Magnevist; ***Chile:*** Magnevistan; ***Cz.:*** Magnegita; Magnevist; ***Denm.:*** Magnevist; ***Fin.:*** Magnevist; ***Fr.:*** Magnevist; ***Ger.:*** Magnevist; ***Gr.:*** Magnevist; ***Hung.:*** Magnevist; ***Ital.:*** Magnevist; ***Mex.:*** Viewgam; ***Neth.:*** Magnevist; ***Norw.:*** Magnevist; ***NZ:*** Magnevist; ***Port.:*** Magnevist; ***Rus.:*** Magnevist (Магневист); ***S.Afr.:*** Magnevist; ***Spain:*** Magnevist; Magnograf; ***Swed.:*** Magnevist; ***Switz.:*** Magnevist; ***UK:*** Magnevist; ***USA:*** Magnevist; ***Venez.:*** Magnevistan.

Gadoteric Acid *(BAN, rINN)*

Acide Gadotérique; Ácido gadotérico; Acidum Gadotericum; Gadoteerihappo; Gadotersyra; Gd-DOTA; ZK-112004. Hydrogen [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraaceto(4–)]-gadolinate(1–); Hydrogen [1,4,7,10-tetrakis(carboxylatomethyl)-1,4,7,10-tetra-azacyclododecane-κ^4N]gadolinate(1–).

Гадотеровая Кислота

$C_{16}H_{25}GdN_4O_8$ = 558.6.
CAS — 72573-82-1.
ATC — V08CA02.
ATC Vet — QV08CA02.



Meglumine Gadoterate *(BANM, rINNM)*

Gadotérate de Méglumine; Gadoterate Meglumine; Gadoterato de meglumina; Meglumini Gadoteras.

Меглумина Гадотерат

ATC — V08CA02.
ATC Vet — QV08CA02.

Adverse Effects and Precautions

As for Gadopentetic Acid, p.1479.

Hypersensitivity. For reports of anaphylactoid reactions with gadoterate, see under Adverse Effects of Gadopentetic Acid, p.1479.

Pharmacokinetics

Gadoterate is distributed into the extracellular space after intravenous injection. It is not bound to plasma proteins. A plasma half-life of about 1.5 hours has been reported. It is not metabolised and about 90% of a dose is excreted in the urine within 24 hours.

Uses and Administration

Gadoteric acid is an ionic gadolinium chelate with actions and uses similar to those of gadopentetic acid (above). It has paramagnetic properties and is used as a magnetic resonance contrast medium (p.1474). It distributes mainly into extracellular fluid, but does not cross the blood-brain barrier, and is used in imaging of cranial and spinal structures and of the whole body, and in magnetic resonance angiography.

Gadoteric acid is given intravenously as the meglumine salt. It is available as a solution containing meglumine gadoterate 376.9 mg/mL (0.5 mmol/mL). The usual dose in adults and children is 0.2 mL/kg (0.1 mmol/kg) by intravenous injection. A second dose of up to 0.4 mL/kg (0.2 mmol/kg) may be given if necessary. For angiography, a dose of 0.1 to 0.2 mL/kg (0.05 to 0.1 mmol/kg) may be given, repeated if required.

Preparations

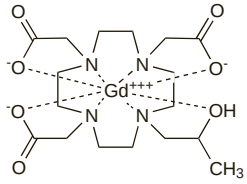
Proprietary Preparations (details are given in Part 3)
Arg.: Dotarem; ***Austral.:*** Dotarem; ***Austria:*** Dotarem; ***Belg.:*** Artirem; Dotarem; ***Braz.:*** Dotarem†; ***Chile:*** Dotarem; ***Cz.:*** Dotarem; ***Denm.:*** Dotarem; ***Fin.:*** Dotarem; ***Fr.:*** Artirem; Dotarem; ***Ger.:*** Artirem; Dotarem; ***Gr.:*** Dotarem; ***Hung.:*** Dotarem; ***Israel:*** Dotarem; ***Ital.:*** Dotarem; ***Neth.:*** Artirem; Dotarem; ***Norw.:*** Dotarem; ***Port.:*** Dotarem; ***Spain:*** Dotarem; ***Swed.:*** Dotarem; ***Switz.:*** Artirem; Dotarem; ***Venez.:*** Dotarem.

Gadoteridol *(BAN, USAN, rINN)*

Gadotéridol; Gadoteridoli; Gadoteridolum; Gd-HP-DO3A; SQ-32692. (±)-[10-(2-Hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3–)]gadolinium.

Гадотеридол

$C_{17}H_{29}GdN_4O_7$ = 558.7.
CAS — 120066-54-8.
ATC — V08CA04.
ATC Vet — QV08CA04.



Pharmacopoeias. In *US.*
USP 31 (Gadoteridol). A white to off-white, odourless, crystalline powder. Freely soluble in water and in methyl alcohol; soluble in isopropyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Gadopentetic Acid, above.

◊ Reviews.

1. Runge VM, Parker JR. Worldwide clinical safety assessment of gadoteridol injection: an update. *Eur Radiol* 1997; **7** (suppl 5): 243–5.

Hypersensitivity. For a report of an anaphylactoid reaction with gadoteridol, see under Adverse Effects of Gadopentetic Acid, p.1479.

Pharmacokinetics

Gadoteridol is distributed into extracellular fluid after intravenous injection. About 94% of a dose is excreted unchanged in the urine within 24 hours. An elimination half-life of about 1.57 hours has been reported.

Uses and Administration

Gadoteridol is a nonionic gadolinium chelate with actions and uses similar to those of gadopentetic acid (p.1480). It has paramagnetic properties and is used as a magnetic resonance contrast medium (p.1474). It distributes mainly into extracellular fluid, but does not cross the blood-brain barrier, and is used in imaging of cranial and spinal structures and of the whole body.

Gadoteridol is available as a solution containing 279.3 mg/mL (0.5 mmol/mL). The usual adult dose is 0.2 mL/kg (0.1 mmol/kg) intravenously; for CNS imaging, an additional dose of up to 0.4 mL/kg (0.2 mmol/kg) may be given up to 30 minutes after the first if necessary. A single dose of 0.2 mL/kg (0.1 mmol/kg) is used in children from 6 months of age.

Preparations

USP 31: Gadoteridol Injection.

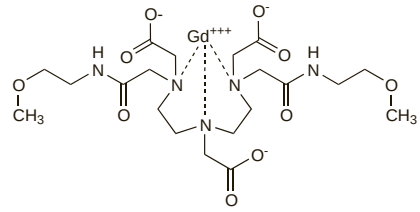
Proprietary Preparations (details are given in Part 3)
Austral.: Prohance; ***Austria:*** Prohance; ***Belg.:*** Prohance; ***Cz.:*** Prohance; ***Denm.:*** Prohance; ***Fin.:*** Prohance; ***Fr.:*** Prohance; ***Ger.:*** Prohance; ***Irl.:*** Prohance†; ***Ital.:*** Prohance; ***Jpn:*** Prohance; ***Neth.:*** Prohance; ***Norw.:*** Prohance; ***Spain:*** Prohance; ***Swed.:*** Prohance; ***Switz.:*** Prohance; ***UK:*** Prohance; ***USA:*** Prohance.

Gadoversetamide *(BAN, USAN, rINN)*

Gadoversetamida; Gadoversétamide; Gadoversetamidum; MP-1177. {*N*,*N*-Bis[2-({(carboxymethyl)[(2-methoxyethyl)carbamoyl]methyl}amino)ethyl]glycinato(3–)}gadolinium.

Гадоверсетамид

$C_{20}H_{34}GdN_5O_{10}$ = 661.8.
CAS — 131069-91-5.
ATC — V08CA06.
ATC Vet — QV08CA06.



Pharmacopoeias. In *US.*
USP 31 (Gadoversetamide). A white odourless powder. Freely soluble in water. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Gadopentetic Acid, p.1479.

Interference with diagnostic tests. Like gadodiamide (see p.1479), gadoversetamide may interfere with colorimetric methods for measuring serum-calcium concentrations.

Gadoversetamide may also interfere with measurement of serum-copper, iron, and zinc concentrations.

Renal impairment. For the view that gadoversetamide may carry an increased risk of the development of nephrogenic systemic sclerosis in patients with renal impairment, see p.1479.

Pharmacokinetics

Gadoversetamide is distributed into the extracellular space after intravenous injection. It is not bound to plasma proteins. An elimination half-life of about 1.7 hours has been reported. It is not metabolised and about 95.5% of a dose is excreted in the urine within 24 hours. Gadoversetamide is removed by haemodialysis.

Uses and Administration

Gadoversetamide is a nonionic gadolinium chelate with actions and uses similar to those of gadopentetic acid (p.1480). It has paramagnetic properties and is used as a magnetic resonance contrast medium (p.1474). It distributes mainly into extracellular fluid, but does not cross the blood-brain barrier, and is used in imaging of cranial and spinal structures and of the whole body.

Gadoversetamide is available as a solution containing 330.9 mg/mL (0.5 mmol/mL). The usual dose is 0.2 mL/kg (0.1 mmol/kg) intravenously.