

Gadodiamide (BAN, USAN, rINN)

Gadodiamid; Gadodiamida; Gadodiamidi; Gadodiamidum; Gd-DTPA-BMA; S-041. [N,N-Bis(2-((carboxymethyl)[(methylcarbamoyl)methyl]amino)ethyl)glycinato(3-))gadolinium; a complex of gadolinium with diethylenetriamine penta-acetic acid bis-methylamide.

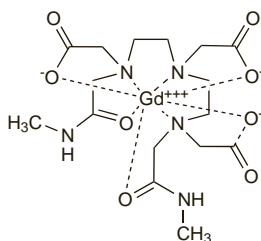
Гадодамида

$C_{16}H_{26}GdN_5O_8 = 573.7$.

CAS — 131410-48-5 (anhydrous gadodiamide); 122795-43-1 (gadodiamide hydrate).

ATC — V08CA03.

ATC Vet — QV08CA03.

**Pharmacopoeias.** In US.

USP 31 (Gadodiamide). A white, odourless, powder. Freely soluble in water and in methyl alcohol; soluble in alcohol; slightly soluble in acetone and in chloroform. Store in airtight containers.

Adverse Effects and Precautions

As for Gadopentetic Acid, below.

Effects on the pancreas. Acute pancreatitis developed in a patient shortly after injection of gadodiamide for hepatic imaging.¹ Another patient² developed both acute pancreatitis and acute renal failure after use of gadodiamide for angiography.

- Terzi C, Sökmen S. Acute pancreatitis induced by magnetic-resonance-imaging contrast agent. *Lancet* 1999; **354**: 1789–90. Correction. *ibid.* 2000; **355**: 660.
- Schenker MP, et al. Gadolinium arteriography complicated by acute pancreatitis and acute renal failure. *J Vasc Interv Radiol* 2001; **12**: 393.

Interference with diagnostic tests. Gadodiamide may interfere with colorimetric methods for measuring serum calcium concentrations, resulting in falsely low measurements. Severe pseudohypocalcaemia has been reported^{1–3} after the use of gadodiamide, particularly in patients with renal impairment.² There is also *in vitro* evidence that a similar interference may occur with gadoversetamide.²

- Doornbos CJ, et al. Severe pseudohypocalcaemia after gadolinium-enhanced magnetic resonance angiography. *N Engl J Med* 2003; **349**: 817–18.
- Prince MR, et al. Gadodiamide administration causes spurious hypocalcaemia. *Radiology* 2003; **227**: 639–46.
- Williams SF, et al. Spurious hypocalcaemia after gadodiamide administration. *Mayo Clin Proc* 2005; **80**: 1655–7.

Renal impairment. For the view that gadodiamide may carry a particular risk of the development of nephrogenic systemic sclerosis in patients with renal impairment, see p.1479.

Pharmacokinetics

Gadodiamide is rapidly distributed into extracellular fluid. About 96% of a dose is excreted unchanged in the urine within 24 hours. An elimination half-life of about 70 minutes has been reported. Gadodiamide is not bound to plasma proteins. It is removed by haemodialysis.

Uses and Administration

Gadodiamide 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, imaging of the whole body, angiography, and mammography.

Gadodiamide is available as a solution containing 287 mg/mL (0.5 mmol/mL). Usual doses are:

- cranial and spinal imaging: for adults and children, 0.2 mL/kg (0.1 mmol/kg). Adults may be given a second dose of 0.4 mL/kg (0.2 mmol/kg) within 20 minutes if required.
- whole body imaging: for adults and children, 0.2 mL/kg (0.1 mmol/kg)
- kidneys: 0.1 mL/kg (0.05 mmol/kg) may be adequate
- angiography: for adults, 0.2 mL/kg (0.1 mmol/kg)
- mammography: 0.2 to 0.4 mL/kg (0.1 to 0.2 mmol/kg).

Preparations

USP 31: Gadodiamide Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Omniscant; **Austral.:** Omniscant; **Austria:** Omniscant; **Belg.:** Omniscant; **Braz.:** Omniscant; **Canad.:** Omniscant; **Chile:** Omniscant; **Cz.:** Omniscant; **Denm.:** Omniscant; **Fin.:** Omniscant; **Fr.:** Omniscant; **Ger.:** Omniscant; **Gr.:** Omniscant; **Hung.:** Omniscant; **Israel:** Omniscant; **Ital.:** Omniscant;

The symbol † denotes a preparation no longer actively marketed

Jpn.: Omniscant; **Neth.:** Omniscant; **Norw.:** Omniscant; **NZ:** Omniscant; **Port.:** Omniscant; **Rus.:** Omniscant (Омнискан); **Spain:** Omniscant; **Swed.:** Omniscant; **Switz.:** Omniscant; **UK:** Omniscant; **USA:** Omniscant; **Venez.:** Omniscant†.

Gadofosveset Trisodium (USAN, rINN)

Gadofosveset trisódico; Gadofosvésset Trisodique; Gadofosvesetum Trinitricum; MS-32520; MS-325 (gadofosveset). Trisodium (N-[2-[bis(carboxymethyl)amino]ethyl]-N-((R)-2-[bis(carboxymethyl)amino]-3-hydroxypropyl)glycine 4,4-diphenylcyclohexyl hydrogen phosphato(6-))gadoliniate(3-).

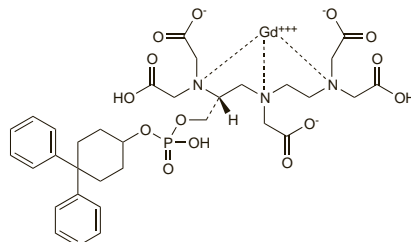
Тринатрий Гадофосвесет

$C_{33}H_{38}GdN_3Na_3O_{14}P = 957.9$.

CAS — 201688-00-8 (gadofosveset); 193901-90-5 (gadofosveset trisodium).

ATC — V08CA11.

ATC Vet — QV08CA11.



(gadofosveset)

Profile

Gadofosveset is a gadolinium chelate used as a paramagnetic contrast medium (p.1474) in magnetic resonance angiography. It binds to plasma proteins, particularly albumin, and therefore acts as a blood pool agent, allowing visualisation of the vasculature. Gadofosveset is given intravenously as the trisodium salt. It is available as a solution containing gadofosveset trisodium 244 mg/mL (0.25 mmol/mL). The usual dose is 0.12 mL/kg (0.03 mmol/kg) by intravenous injection.

References.

- Henness S, Keating GM. Gadofosveset. *Drugs* 2006; **66**: 851–7.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: Vasovist; **Gr.:** Vasovist; **Hung.:** Vasovist; **Neth.:** Vasovist; **Port.:** Vasovist; **UK:** Vasovist.

Gadopentetic Acid (BAN, rINN)

Acide Gadopentétique; Acido gadopentético; Acidum Gadopenteticum; Gadolinium-DTPA. Dihydrogen (N,N-bis(2-[bis(carboxymethyl)amino]ethyl)glycinato(5-))gadoliniate(2-); a complex of gadolinium with diethylenetriamine penta-acetic acid.

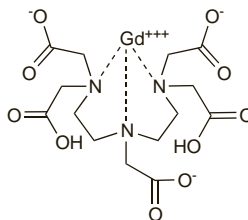
Гадопентетовая Кислота

$C_{14}H_{20}GdN_5O_{10} = 547.6$.

CAS — 80529-93-7.

ATC — V08CA01.

ATC Vet — QV08CA01.

**Meglumine Gadopentetate** (BANM, rINN)

Dimeglumine Gadopentetate; Gadopentétate de Méglumine; Gadopentetate Dimeglumine (USAN); Gadopentetate Meglumine; Gadopentétate méglumine; Gadopentetato de meglumina; Meglumini gadopentetas; SH-L-451-A.

Меглумина Гадопентетат

$C_{14}H_{20}GdN_5O_{10}(C_7H_{17}NO_5)_2 = 938.0$.

CAS — 86050-77-3.

ATC — V08CA01.

ATC Vet — QV08CA01.

Pharmacopoeias. *Chin.* and *US* include only as an injection.

Adverse Effects

There may be headache, nausea, vomiting, and transient sensations of heat or cold or taste disturbances on injection of gado-

pentetate or other gadolinium chelates. Rarely, convulsions, hypotension, allergic or anaphylactoid reactions, and shock may occur. Paraesthesia, dizziness, and localised pain have also been reported. Transient elevations of serum iron and bilirubin values have been observed. Nephrogenic systemic fibrosis may occur rarely in patients with renal impairment (see under Precautions, below).

General references.

- Nelson KL, et al. Clinical safety of gadopentetate dimeglumine. *Radiology* 1995; **196**: 439–43.

Effects on the nervous system. Subacute encephalopathy has been reported¹ in a woman who was given repeated doses of a gadolinium chelate for magnetic resonance imaging. It was suggested that renal impairment may have contributed to retention of gadolinium, with subsequent diffusion into the CSF.

- Maramattom BV, et al. Gadolinium encephalopathy in a patient with renal failure. *Neurology* 2005; **64**: 1276–8.

Hypersensitivity. Although rare, anaphylactoid reactions have occurred with a number of gadolinium chelates.¹ Severe reactions have been reported with gadopentetate,² gadoterate,^{3,4} and gadoteridol,⁵ including a fatal reaction with gadopentetate.⁶ There has also been a report⁷ of a severe reaction with gadoteridol in a patient who had previously tolerated gadopentetate. Reactions may occur despite premedication with antihistamines and corticosteroids.⁸

- Runge VM. Safety of approved MR contrast media for intravenous injection. *J Magn Reson Imaging* 2000; **12**: 205–13.

- Tardy B, et al. Anaphylactic shock induced by intravenous gadopentetate dimeglumine. *Lancet* 1992; **339**: 494.

- Meuli RA, Maeder P. Life-threatening anaphylactoid reaction after IV injection of gadoterate meglumine. *Am J Roentgenol* 1996; **166**: 729.

- Beaudouin E, et al. Anaphylactic shock induced by gadoterate meglumine (DOTAREM). *Allerg Immunol (Paris)* 2003; **35**: 382–5.

- Shellock FG, et al. Adverse reaction to intravenous gadoteridol. *Radiology* 1993; **189**: 151–2.

- Jordan RM, Mintz RD. Fatal reaction to gadopentetate dimeglumine. *Am J Roentgenol* 1995; **164**: 743–4.

- Witte RJ, Anzai LL. Life-threatening anaphylactoid reaction after intravenous gadoteridol administration in a patient who had previously received gadopentetate dimeglumine. *Am J Neuroradiol* 1994; **15**: 523–4.

- Dillman JR, et al. Allergic-like breakthrough reactions to gadolinium contrast agents after corticosteroid and antihistamine premedication. *Am J Roentgenol* 2008; **190**: 187–90.

Precautions

Gadopentetate should not be used in patients with severe renal impairment (GFR less than 30 mL/minute per 1.73 m²) or with acute renal impairment associated with hepato-renal syndrome or liver transplantation (see Renal Impairment, below). It should be given with care to patients with moderate renal impairment, epilepsy, hypotension, or a history of hypersensitivity, asthma, or other allergic respiratory disorders. Care should be taken to avoid extravasation. Gadopentetate may interfere with tests of serum iron or bilirubin concentrations.

Breast feeding. Studies^{1–3} have shown that gadopentetate is distributed into breast milk in very small amounts; the total amount excreted in the milk within 24 hours was less than 0.04% of the intravenous dose in all cases. No adverse effects have been seen in breast-feeding infants whose mothers were receiving gadopentetic acid and the American Academy of Pediatrics considers⁴ that it is therefore usually compatible with breast feeding.

- Schmiedl U, et al. Excretion of gadopentetate dimeglumine in human breast milk. *Am J Roentgenol* 1990; **154**: 1305–6.
- Rofsky NM, et al. Quantitative analysis of gadopentetate dimeglumine excreted in breast milk. *J Magn Reson Imaging* 1993; **3**: 131–2.
- Kubik-Huch RA, et al. Gadopentetate dimeglumine excretion into human breast milk during lactation. *Radiology* 2000; **216**: 555–8.
- American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108**: 776–89. Correction. *ibid.*: 1029. Also available at: <http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776> (accessed 27/03/06)

Myasthenia gravis. Acute deterioration of myasthenia gravis has been reported¹ in a patient after imaging of the brain using gadopentetate.

- Nordenbo AM, Somnier FE. Acute deterioration of myasthenia gravis after intravenous administration of gadolinium-DTPA. *Lancet* 1992; **340**: 1168.

Renal impairment. Nephrogenic systemic fibrosis (nephrogenic fibrosing dermopathy) is a rare condition that has been reported in patients with renal impairment. Use of gadolinium-containing contrast media appears to be a risk factor;^{1–3} most cases have occurred with gadodiamide given in high doses for magnetic resonance angiography, but there have also been reports with other gadolinium-containing contrast media and with lower doses. It has been suggested that the mechanism involves release of free gadolinium ions into the tissues, and that the potential for this varies between the different gadolinium-based contrast media available, with gadodiamide and gadoversetamide more likely to do so.⁴ The macrocyclic structure of gadoteridol and gadoterate was thought to be less prone to this effect, but further research is needed. The FDA⁵ and the MHRA⁶ advise that use of