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GE Healthcare

OMNISCAN™

GADODIAMIDE

PRESENTATION

Vials containing a clear, colourless to slightly yellow sterile aqueous solution. Each 1 ml injection contains as active ingredient 287 mg gadodiamide (GdDTPA-BMA) equivalent to 0.5 mmol/ml. Other ingredients are: caldiamide sodium, sodium hydroxide 1M or hydrochloric acid 1M and water for injections.

USES

Indications
Non-ionic paramagnetic contrast medium for cranial and spinal magnetic resonance imaging (MRI) and for general MRI of the body after intravenous administration.

The product provides contrast enhancement and facilitates visualisation of abnormal structures or lesions in various parts of the body including the CNS.

Clinical pharmacology
Gadodiamide does not cross the intact blood-brain barrier. Administration of Omniscan causes signal enhancement from areas where blood-brain barrier dysfunction has been induced by pathological processes, and may provide greater diagnostic yield than unenhanced MRI. Lack of enhancement need not indicate absence of pathology since some types of low grade malignancies or inactive MS-plaques fail to enhance; it can be used for differential diagnosis between different pathologies.

Gadodiamide is rapidly distributed in the extracellular fluid. The volume of distribution is equivalent to that of extracellular water. The distribution half-life is approximately 4 minutes and the elimination half-life is approximately 70 minutes.
Gadodiamide is excreted through the kidneys by glomerular filtration. Approximately 85 % of the administered dose is recovered in the urine by 4 hours and 95-98 % by 24 hours after intravenous injection. The renal and total clearance rates of gadodiamide are nearly identical, and are similar to that of substances excreted primarily by glomerular filtration.
No dose dependent kinetics have been observed after injection of 0.1 and 0.3 mmol/kg.
No metabolites have been detected. No proteinbinding has been observed.

There were no clinically signifcant deviations from preinjection values in haemodynamic and blood and urine laboratory parameters following intravenous injection of gadodiamide in healthy volunteers. However, a minor transient change in serum iron levels 8 to 48 hours after gadodiamide injection was observed.

DOSAGE AND ADMINISTRATION

No special preparation of the patient is required. OMNISCAN should be drawn into the syringe immediately before use.

For intravenous use. For both adults and children the required dose should be administered as a single intravenous injection. To ensure complete injection of the contrast medium, the intravenous line may be flushed with sodium chloride injection 0.9%.

CNS
Dosage for adults and children from 2 years of age
The recommended dosage is 0.1 mmol/kg body weight (equivalent to 0.2 ml/kg b.w.) up to 100 kg. Above 100 kg body weight 20 ml is usually sufficient.

Adults only
When brain metastases are suspected, a dosage of 0.3 mmol/kg b.w. (equiv. to 0.6 ml/kg b.w.) can be administered up to 100 kg. Above 100 kg b.w. a total of 60 ml is usually sufficient. The dose of 0.3 mmol/kg b.w. can be administered as a bolus intravenous injection. In patients with equivocal scans after administration of the 0.1 mmol/kg b.w. injection, a second bolus injection of 0.2 mmol/kg b.w. (equiv. to 0.4 ml/kg b.w.) may be of additional diagnostic value when administered within 20 minutes of the first injection.

Whole body
Dosage for adults
The recommended dosage is usually 0.1 mmol/kg b.w. (equiv. to 0.2 ml/kg b.w.) or occasionally 0.3 mmol/kg b.w. (equiv to 0.6 ml/kg b.w.) up to 100 kg. Above 100 kg b.w. 20 ml resp. 60 ml is usually sufficient to provide diagnostically adequate contrast.

Dosage for children from 2 years of age
The recommended dosage is 0.1 mmol/kg b.w. (equiv. to 0.2 ml/kg b.w.)

Contrast-enhanced MRI should start shortly after administration of the contrast medium, depending on the pulse sequences used and the protocol for the examination. Optimal enhancement is observed within the first minutes after injection (time depending on type of lesion/tissue). Enhancement is generally lasting up to 45 minutes after contrast medium injection. T1-weighted scanning sequences are particularly suitable for contrast-enhanced examinations with Omniscan. In the investigated range of field strengths, from 0.15 Tesla up to 1.5 Tesla, the relative image contrast was found to be independent of the applied field strength.

CONTRA-INDICATIONS, WARNINGS ETC.

Contra-indications
Omniscan should not be used in patients known to have hypersensitivity to Omniscan or its constituents.

Omniscan should not be used in patients with impaired renal function (GFR<10ml/min).

Precautions
Rarely hypersensitivity reactions (urticaria and other possible allergic phenomenal may occur. Anaphylactic shock has been observed with related products. Familiarity with the practice and technique of resuscitation and treatment of anaphylaxis is essential. Appropriate drugs and instruments should be readily available.

Warnings
There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of Omniscan (gadodiamide) and other gadolinium-containing contrast agents in patients with severe renal impairment. Therefore do not use Omniscan in these patients. Caution should be exercised in use and dose selection of Omniscan in patients with hepatorenal syndrome. The risk, if any, for the development of NSF among patients with moderate renal insufficiency is unknown.
Transitory changes in serum iron (within the normal range in the majority of cases) have been observed in some patients after administration of Omniscan. The clinical significance of this, if any, is not known, but all patients in whom this effect was observed remained asymptomatic.
Omniscan interferes with serum calcium measurements with some colorimetric (complexometric) methods commonly used in hospitals. It may also interfere with determinations of other electrolytes (e.g. iron). Thus it is recommended not to use such methods for 12-24 hours after administration of Omniscan. If such measurements are necessary, the use of other methods is recommended.

Use during pregnancy and lactation
Use during pregnancy
There is no experience of the use of Omniscan during human pregnancy. The product should not be used during pregnancy, unless an enhanced MR investigation is essential, an no suitable alternative is available.
Omniscan had no effects on fertility or reproductive performance in rats or in teratology studies in rats and rabbits at doses that did not cause maternal toxicity.

Use during lactation
The degree of excretion into human milk is not known, although expected to be low. Breast feeding should be discontinued prior to administration and should not be re-commenced until at least 24 hours after the administration of Omniscan.

Overdosage
Clinical consequences of overdosage have not been reported and acute symptoms of toxicity are unlikely in patients with a normal renal function. Treatment is symptomatic. There is no antidote for this contrast medium. In patients with delayed elimination due to renal insufficiency and in patients who have received excessive doses, the contrast medium may theoretically be eliminated by haemodialysis.

Effects on ability to drive and use machines
None known.

Interactions
None known.

Undesirable effects
Most events have been transient and the majority of mild intensity. The following has been reported during clinical trials: Discomfort with general sensation of warmth, coolness or a sensation of local pressure or pain at the injection site are occasionally seen. Less frequently reported are dizziness, nausea, headache and a perverted sensation of taste or smell. Rare reactions are allergy-like symptoms such as urticaria, itching or an irritation in the throat. Others are vomiting or somnolence.

In patients with pre-existing severe renal insufficiency: rare acute kidney injury and increase in blood creatinine (frequency: not known) have been reported.

Cases of nephrogenic systemic fibrosis (NSF) have been reported with Omniscan in patients with severe renal impairment.
Transient renal failure was observed in one patient included in the clinical trials. The patient had received an X-ray contrast medium for myelography 22 hours prior to the injection of Omniscan. The causality for the reaction has not been established.

Anaphylactic shock has been observed with related products.

PHARMACEUTICAL PRECAUTIONS

Omniscan should be stored at room temperature protected from light.

INCOMPATIBILITIES

Omniscan should not be directly mixed with other drugs. A separate syringe and needle should be used.

SHELF LIFE

The expiry date is stated on the label.

NATURE AND CONTENT OF THE CONTAINERS

The product is supplied as:
10 vials of 5 ml
10 vials of 10 ml — 10 prefilled syringes of 10 ml
10 vials of 15 ml — 10 prefilled syringes of 15 ml
10 vials of 20 ml — 10 prefilled syringes of 20 ml
10 polypropylene bottles of 10 ml
10 polypropylene bottles of 15 ml
10 polypropylene bottles of 20 ml
10 polypropylene bottles of 40 ml
10 polypropylene bottles of 50 ml

INSTRUCTIONS FOR USE/HANDLING

Vials, polypropylene bottles and prefilled syringes are intended for one patient only. Any unused portions must be discarded.

FURTHER INFORMATION

Osmolality (mOsm/kg H_2O) at 37°C	780
Viscosity (mPa•s) at 20°C	2.8
Viscosity (mPa•s) at 37°C	1.9
Density at 20°C (kg/l)	1.15
Molar Relaxivity	
r_1 ($mM^{-1}•s^{-1}$) at 10 MHz and 37°C	4.6
r_2 ($mM^{-1}•s^{-1}$) at 10 MHz and 37°C	5.1

pH 6.0 - 7.0

DATE OF REVISION OF THE TEXT

Feb 2013

WARNING
To be sold by retail on prescription of a Registered Medical Practitioner only.

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