NAME OF THE PROPRIETARY MEDICINAL PRODUCT

OMNISCAN injection 0.5 mmol/ml

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient	Content pr ml	Function
GADODIAMIDE (Gd-DTPA-BMA) equiv. 0.5 mmol	287 mg	MRI-contrast agent

OMNISCAN injection is a non-ionic paramagnetic contrast medium with the following physicochemical properties:

Osmolality (mOsm/kg H2O) 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	
r1 (mM-1 • s-1) at 20 MHz and 37°C	3.9
r1 (mM-1 • s-1) at 10 MHz and 37°C	4.6
r2(mM-1 • s-1) at 10 MHz and 37°C	5.1

pH 6.0-7.0

Gadodiamide is freely soluble in water.

PHARMACEUTICAL FORM

Injection, for intravenous use.

The product is a clear, colourless to slightly yellow aqueous solution.

CLINICAL PARTICULARS

Indications

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 visualization of abnormal structures or lessions in various parts of the body including CNS.

Posology and method of administration

No special preparation of the patient is required. OMNISCAN should be drawn into the syringe immediately Before use. Each vial or polypropylene bottle is intended for one patient only. Contrast medium not used in one examination must be discarded.

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

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 to provide diagnostically adequate contrast.

Adults only

When brain metastases are suspected, a dosage of 0.3 mmol/kg BW (equiv. to 0.6 ml/kg BW) can be administered up to 100 kg. Above 100 kg BW a total of 60 ml is usually sufficient. The dose of 0.3 mmol/kg BW can be administered as a bolus intravenous injection. In patients with equivocal scans after administration of the 0.1 mmol/kg BW injection, a second bolus injection of 0.2 mmol/kg BW

(equiv. to 0.4 ml/kg BW) 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 BW (equiv. to 0.2 ml/kg BW) or occasionally 0.3 mmol/kg BW (equiv to 0.6 ml/kg BW) up to 100 kg. Above 100 kg BW 20 ml or 60 ml is usually sufficient to provide diagnostically adequate contrast.

Dosage for children from 6 months of age
The recommended dosage is 0.1 mmol/kg BW (equiv. to 0.2 ml/kg BW).

CNS and whole body
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
OMNISCAN should not be used in patients known to have hypersensitivity to OMNISCAN or its constituents.

Special warnings and special precautions for use
The possibility of a reaction, including serious, lifethreatening, fatal, anaphylactoid or cardiovascular Reactions or other idiosyncratic reactions should always be considered, especially in those patients with a known clinical hypersensitivity or a history of asthma or other allergic respiratory disorders. A course of action should therefore be planned in advance, with necessary drugs and equipment available for immediate treatment should a serious reaction occur.
There have been reports of nephrogenic systemic fibrosis (NSF)/ nephrogenic fibrosing dermopathy (NFD) associated with the use of OMNISCAN (gadodiamide) and some gadolinium-containing contrast agents in patients with severe renal impairment (GFR < 30ml/ min/1.73m2) or acute renal insufficiency of any severity due to the hepato-renal syndrome or in post operative liver transplantation period. Therefore, OMNISCAN should not be used in these patients. Cases of NSF/NFD have also been reported in patients with moderate renal impairment (GFR 30-59 ml/min/1.73m2) with gadodiamide. Hence, OMNISCAN should be used with caution in these patients.
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.
Central nervous system disorders: In patients suffering from epilepsy or brain lesions the likehood of convulsions during the examination may be increased. Precautions are necessary when examining these patients (e.g. monitoring of the patient) and the equipment and medicinal products needed for the rapid treatment of possible convulsions should be available
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.

Interaction with other medicaments and other forms of interaction
None known.

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, and 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 recommenced until at least 24 hours after the administration of OMNISCAN.

Effects on ability to drive and use machines
None known.

Undesirable Effects
The following undesirable effects are recognized for Omniscan :

- General Disorders body as a Whole : Hypersensitivity, Anaphylactoid reactions (characterized by cardiovascular, respiratory, and cutaneous symptoms), fever, hot flushes, rigors, fatigue, malaise, pain, syncope.
- Cardiovascular Disorders : Cardiac failure, rare arrhythmia and myocardial infarction resulting in death in patients with ischemic heart disease, flushing, chest pain, deep thrombophlebitis
- Central and Peripheral Nervous System Disorders : Convulsions including grand mal, ataxia, abnormal coordination, paresthesia, tremor, aggravated multiple sclerosis (characterized by sensory and motor disturbances), aggravated migraine, dizziness, headache
- Gastrointestinal System Disorders : Abdominal pain, diarrhea, eructation, dry mouth/ vomiting, melena, nausea
- Hearing and Vestibular Disorders : Tinnitus
- Livers and Biliary System Disorders : Abnormal hepatic function
- Musculoskeletal System Disorders : Arthralgia, myalgia
- Respiratory System Disorders : Rhinitis, dyspnea
- Skin and Appendage Disorders : Pruritus, rash, erythematous rash, sweating increased, urticaria, nephrogenic systemic fibrosis in patients with severe renal impairment
- Urinary System Disorders : Acute reversible renal failure
- Vision disorders : Abnormal vision
- Application Site Disorders : Injection site reaction
- Autonomic Nervous System Disorders : Vasodilation
- Special senses, Other, Disorders : Taste loss, taste perversion

Overdose
Clinical consequences of overdose 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 can be eliminated by haemodialysis.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
The paramagnetic properties of OMNISCAN provides contrast enhancement during MRI.
There were no clinically significant 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.
OMNISCAN 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.

Pharmacokinetic properties
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.
In patients with impaired renal function (GFR < 30 ml/min) the elimination half-life will be prolonged to an extent inversely proportional to GFR.
Gadodiamide is excreted through the kidneys by glomerular filtration. In patients with normal renal function, 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 protein binding has been observed.

Preclinical safety data
The efficacy of OMNISCAN as a contrast enhancing agent during MRI has been demonstrated in a series of animal studies.
Safety pharmacology studies in dogs and rats have demonstrated that OMNISCAN has no significant effects on the cardiovascular system. *In vitro* studies have demonstrated no or insignificant effects on mast cell histamine release, human serum complement activation factors, human erythrocyte cholinesterase activity, lysozyme activity, human erythrocyte fragility and morphology, and on tension in isolated bovine blood vessels. No evidence of antigenicity was seen in a dermal test in Guinea pigs.
Pharmacokinetic studies in several animal species have demonstrated OMNISCAN to be rapidly distributed in the extracellular volume, and quantitatively excreted via the kidneys by glomerular filtration. The elimination half-lives in man and monkey are similar. The calculated distribution volume is approximately 25% of body size.
Toxicological studies have demonstrated a high acute tolerance of OMNISCAN, the approximate LD50 in mice was > 30 mmol/kg. The common finding after high single doses or repeated dosing was proximal tubular vacuolation, which was reversible, and was not associated with altered renal function.

OMNISCAN was found to be non-irritating after intravenous, intraarterial, paravenous, intramuscular and subcutaneous administration, or when applied to the skin or the eye.
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.

PHARMACEUTICAL PARTICULARS

List of excipients

The following excipients are included:
Caldiamide sodium, sodium hydroxide 1 M and/or hydrochloric acid 1 M, water for injections.

Incompatibilities

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

Shelf life

See expiry date printed on the label.

Special precautions for storage

OMNISCAN should be kept at room temperature, below 30°C and store protected from light.

Nature and content of containers

The product is filled in injection vials/bottles with a fill volume of 5 ml, 10 ml, 15 and 20 ml. The vials are made of colourless highly resistant borosilicate glass (Ph.Eur. Type I) and are closed with latex free rubber stoppers (Ph.Eur. Type I) size 20 mm, sealed with complete tear off caps of aluminium with coloured plastic “flip-off” tops.

Presentations

The product is supplied as:
10 vials of 10 ml
In certain countries certain pack sizes may not be available.

Manufactured by:

GE Healthcare Ireland Limited
IDA Business Park
Carrigtohill Co.Cork, Ireland

Imported and distributed by:

PT Menarini Indria Laboratories
Bekasi, Indonesia

Instructions for use/handling:

Vials and polypropylene bottles are intended for one patient only. Any unused portions may be discarded.

DATE OF REVISION OF TEXT

August 2023
HARUS DENGAN RESEP DOKTER.
No. Reg. DKIXXXXXXXXXXXX