SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Omniscan 0.5 mmol/ml Solution for injection, glass vials/bottles

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains: Gadodiamide 287 mg (0.5 mmol)
5 ml contains: Gadodiamide 1.44 g (2.5 mmol)
10 ml contains: Gadodiamide 2.87 g (5.0 mmol)
15 ml contains: Gadodiamide 4.31 g (7.5 mmol)
20 ml contains: Gadodiamide 5.74 g (10.0 mmol)
100 ml contains: Gadodiamide 28.70 g (50.0 mmol)

Excipient(s) with known effect:
Total sodium content: 0.62 mg/ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless to slightly yellow aqueous solution.
Osmolality at 37°C: 780 (mOsm/kg H_2O)
pH: 6.0 -7.0

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Omniscan is a contrast medium for cranial and spinal magnetic resonance imaging (MRI). Omniscan is also indicated for whole body MRI including head and neck region, thoracic space including the heart, extremities, abdomen and pelvis (prostate and bladder), female breast, abdomen (pancreas and liver), retroperitoneal space (kidney), musculoskeletal system and vessels (angiography) by intravenous administration.

Omniscan facilitates visualisation of abnormal structures or lesions and helps in the differentiation between healthy and pathological tissue.

4.2 Posology and method of administration

Posology

Omniscan should be drawn into the syringe immediately before use. All the recommended doses below can be administered as bolus intravenous injections. To ensure complete injection of Omniscan, the intravenous line may be flushed with 5 ml sodium chloride 9 mg/ml (0.9 %) solution for injection after injection.

CNS examinations
The recommended dosage to adults and children is 0.2 ml/kg body weight (b.w.) (0.1 mmol/kg b.w.) up to 100 kg. Above 100 kg body weight 20 ml is usually sufficient. When brain metastases are suspected, a dosage of 0.6 ml/kg b.w. (0.3 mmol/kg b.w.) can be administered to adults up to 100 kg. Above 100 kg bodyweight a total of 60 ml is usually sufficient. The dose of 0.6 ml/kg can be administered as a single injection. Alternatively a second bolus injection of 0.4 ml/kg b.w. (0.2 mmol/kg b.w.) may be administered within 20 minutes of the first injection of 0.2 ml/kg b.w. (0.1 mmol/kg b.w.).

Whole body examinations
The recommended dosage to adults and children above 6 months of age is 0.2 ml/kg b.w. (0.1 mmol/kg b.w.) up to 100 kg. Above 100 kg body weight 20 ml is usually sufficient. If needed 0.6 ml/kg b.w. (0.3 mmol/kg b.w.) can be administered to adults up to 100 kg body weight. Above 100 kg body weight a total of 60 ml is usually sufficient.
The MRI examination should start shortly after administration of Omniscan, 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. T_1-weighted scanning sequences are particularly suitable for contrast enhanced examinations with Omniscan.

If this medicinal product is intended to be used with an automatic application system, its suitability for the intended use has to be demonstrated by the manufacturer of the medical device. Instructions for use of the medical device must be followed absolutely.

Special Populations

Patients with renal impairment
Omniscan is contraindicated in patients with severe renal impairment (GFR < 30 ml/min/1.73m^2) and/or acute kidney injury and in patients in the perioperative liver transplantation period (see section 4.3). Omniscan should only be used after careful risk/benefit evaluation in patients with moderate renal impairment (GFR 30-59 ml/min/1.73m^2) at a dose not exceeding 0.1 mmol/kg body weight (see section 4.4). More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Omniscan injections should not be repeated unless the interval between injections is at least 7 days.

Neonates up to 4 weeks of age, infants up to 1 year of age and children
Omniscan is contraindicated in neonates up to 4 weeks of age (see section 4.3).
Due to immature renal function in infants up to 1 year of age, Omniscan should only be used in these patients after careful consideration at a dose not exceeding 0.1 mmol/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Omniscan injections should not be repeated unless the interval between injections is at least 7 days.

Use for whole body MRI is not recommended in children less than 6 months of age.

Elderly (aged 65 years and above)

No dosage adjustment is considered necessary. Caution should be exercised in elderly patients (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance gadodiamide or to any of the excipients listed in section 6.1.
Omniscan is contraindicated in patients with severe renal impairment (GFR <30 ml/min/1.73m^2) and/or acute kidney injury, in patients in the perioperative liver transplantation period and in neonates up to 4 weeks of age (see section 4.4).

4.4 Special warnings and precautions for use

The usual precaution measures for MRI examination should be taken, such as exclusion of pacemakers and ferro-magnetic implants.

Hypersensitivity

Allergoid and other idiosyncratic reactions may occur with all contrast media for intravenous application, also with Omniscan, which could become manifest in form of cardiovascular, respiratory and skin reactions up to shock (see section 4.8). Most of these reactions occur within half an hour after administering the contrast medium. As with all other contrast media of the same class, late reactions may occur (after hours or days) in rare cases.
If hypersensitivity reactions occur, the administration of the contrast medium must be discontinued immediately.
To enable immediate action in emergencies, the necessary medicinal products and equipment for intubation and adequate ventilation support must be immediately available.

The risk of hypersensitivity reactions is increased in the following cases:

- patients with allergic predisposition
- patients with bronchial asthma; in these patients especially the risk of bronchospasm is increased
- patients with a history of severe reactions on contrast agents

Patients with impaired renal function

Prior to administration of Omniscan, all patients should be screened for renal dysfunction by obtaining laboratory tests.

There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of Omniscan and some other gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 ml/min/1.73m^2) and/or acute kidney injury. Omniscan is contraindicated in these patients (see section 4.3).
Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. Therefore Omniscan must not be used in patients in the perioperative liver transplantation period and in neonates (see section 4.3).

The risk for development of NSF in patients with moderate renal impairment (GFR 30–59 ml/min/1.73 m^2) is unknown; therefore, Omniscan should be only used after careful risk-benefit evaluation in patients with moderate renal impairment.

Because of the lack of information on repeated administration, Omniscan injections should not be repeated unless the interval between injections is at least 7 days.

Haemodialysis shortly after Omniscan administration may be useful at removing Omniscan from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis.

Neonates and Infants:

Omniscan is contraindicated in neonates up to 4 weeks of age (see section 4.3). Due to immature renal function in infants up to 1 year of age, Omniscan should only be used in these patients after careful consideration.

Experience with Omniscan in children below 6 months with severe liver- or renal disease and in pre-term new-born infants below 4 weeks of age or with gestational age below 30 weeks is not available.

Patients taking beta-blocker

It should be noted that patients using beta-blockers do not necessarily respond to the beta-agonists usually used for the treatment of hypersensitivity reactions.

Patients with cardiovascular disease

In this group of patients hypersensitivity reactions may be more severe. Especially in patients with serious heart diseases (e.g. severe heart failure, coronary artery disease) cardiovascular reactions may deteriorate.

Patients with central nervous system disorders

In patients suffering from epilepsy or brain lesions the likelihood of convulsions during the examination may be increased, as it was rarely observed with other contrast media of the same class. Precautions are necessary when examining these patients (e.g. monitoring of the patient) and the equipment and medicinal products needed for rapid treatment of possible convulsions should be available.

Elderly

As the renal clearance of gadodiamide may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction.

This medicinal product contains sodium: 0.62 mg/ml. This needs to be taken into consideration for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Omniscan interferes with serum calcium measurements with some complexometric (colorimetric) methods commonly used. 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of gadodiamide in pregnant women. Animal studies have shown reproductive toxicity at repeated high doses (see section 5.3).Omniscan should not be used during pregnancy unless the clinical condition of the woman requires use of gadodiamide.

Lactation

It is unknown whether gadodiamide is excreted in human milk. Available data in animals have shown excretion of gadodiamide in milk (for details see section 5.3). A risk to the suckling child cannot be excluded. Breast-feeding should be discontinued for at least 24 hours after the administration of Omniscan.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Ambulant patients while driving vehicles or operating machinery should take account that nausea may incidentally occur.

4.8 Undesirable effects

Adverse reactions have been reported in approximately 6 % of the patients in clinical trials.

The most commonly reported spontaneous adverse effects after Omniscan are hypersensitivity reactions, nausea and vomiting. Cases of nephrogenic systemic fibrosis (NSF) have been reported with Omniscan (see section 4.4).

In clinical trials with Omniscan, adverse reactions have been reported with the following frequencies given in the table below (very common ≥1/10; common (≥1/100, <1/10); uncommon
(≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare <1/10,000). Not known (cannot be estimated from the available data)

Immune system disorders
Uncommon: Allergy-like skin and mucous membrane reactions, hypersensitivity
Not known: Anaphylactic/anaphylactoid reactions*

Psychiatric disorders
Rare: Anxiety

Nervous system disorders
Common: Headache
Uncommon: Dizziness, paraesthesia, transient perverted sensation of taste
Rare: Convulsions, tremor, somnolence, transient perverted sensation of smell

Eye disorders
Rare: Visual disturbance

Cardiac disorders
Not known: Tachycardia

Vascular disorders
Uncommon: Flushing

Respiratory, thoracic and mediastinal disorders
Rare: Dyspnoea, coughing
Not known: Bronchospasm, respiratory distress, throat irritation, sneezing

Gastrointestinal disorders
Common: Nausea
Uncommon: Vomiting, diarrhoea

Skin and subcutaneous tissue disorders
Uncommon: Pruritus
Rare: Oedema including face swelling and angioneurotic oedema, urticaria, rash
Not known: Nephrogenic systemic fibrosis (NSF), skin thickening**

Musculoskeletal and connective tissue disorders
Rare: Arthralgia

Renal and urinary system disorders
Rare: Acute renal failure

General disorders and administration site condition
Common: Transient sensation of warmth, coolness or local pressure in connection with injection.
Transient sensation of pain at the injection site.
Rare: Chest pain, fever, shivering

* Anaphylactic/anaphylactoid reactions which may occur, irrespective of the dose given and the method of administration may be the first signs of an incipient shock.

** Cases of gadolinium associated skin plaques with demonstrated sclerotic bodies on histology have been reported with gadodiamide in patients who do not otherwise have symptoms or sign of nephrogenic systemic fibrosis.

Late adverse reactions can occur hours to days after administration of Omniscan.

Transient changes in serum iron have been observed in some patients, but all these patients remained asymptomatic.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

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4.9 Overdose

In case of an excessive intravenous dose in a patient with renal insufficiency, Omniscan can be removed by haemodialysis. However there is no evidence that haemodialysis is suitable for prevention of nephrogenic systemic fibrosis (NSF).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Paramagnetic contrast media.
ATC code: V08C A03

Omniscan is a non-ionic paramagnetic contrast medium for use in magnetic resonance imaging (MRI). Omniscan contains gadodiamide that mainly affects the protons T_1-relaxation time. After intravenous injection this yields increased signal intensity and thereby contrast enhancement in MRI-investigations. 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.

The product provides contrast enhancement and facilitates visualisation of abnormal structures or lesions in various parts of the body including the CNS. In cases of blood-brain barrier dysfunction, administration of Omniscan may lead to improved visualisation of pathological changes, and lesions with abnormal vascularity (or those thought to cause abnormalities in the blood-brain barrier) in the brain (intracranial lesions), spine and associated tissues as well as lesions in the thorax, pelvic cavities and the retroperitoneal spaces. It also improves tumour delineation thus determining extent of invasiveness. Signal enhancement is not seen with all types of pathological processes, e.g. some types of low-grade malignancies or inactive MS-plaques fail to enhance. Omniscan can thus be used for differential diagnosis between healthy and pathological tissues**,** different pathological structures, and in differentiation between tumour and tumour recurrences and cicatricial tissue after treatment.

5.2 Pharmacokinetic properties

Distribution
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 the elimination half-life is prolonged inversely proportional to the impaired renal function. The contrast medium can be eliminated by haemodialysis.

Elimination
Gadodiamide is excreted through the kidneys by glomerular filtration. In patients with normal renal function approximately 85 % of the administered dose is recovered unchanged in the urine by 4 hours and 95-98 % by 24 hours after intravenous injection.

The kinetics is linear after doses of 0.l and 0.3 mmol/kg.
No metabolites have been detected. Gadodiamide is not bound to plasma proteins.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. After repeated administration of doses of 0.5 and 1.0 mmol/kg/day in pregnant rabbits there were skeletal anomalies indicative of developmental retardation. Carcinogenicity studies have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Caldiamide sodium
sodium hydroxide solution (for pH adjustment) 3.8 %
hydrochloric acid (for pH adjustment) 3.65 %
water for injections.

6.2 Incompatibilities

Omniscan must not be mixed with other medicinal products.

6.3 Shelf life

3 years.
Chemical and physical in-use stability has been demonstrated for 8 hours at 25 °C. From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store the vial/bottle in the outer carton in order to protect from light.
Do not freeze.

6.5 Nature and contents of container

5 ml, 10 ml, 15 ml and 20 ml glass vials (colourless glass Type I), closed with chlorobutyl rubber stoppers (latex free), sealed with caps of aluminium with coloured plastic tops.
Pack sizes of 10.

100 ml glass bottles (colourless glass Type I), closed with chlorobutyl rubber stoppers (latex free), sealed with caps of aluminium with coloured plastic tops.
Pack sizes of 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Each vial/bottle of contrast medium is intended for single use. Any unused portions must be discarded.
The peel-off tracking label on the vial/bottle should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record.

7 MARKETING AUTHORISATION HOLDER

GE Healthcare AS
P.O. Box 4220 Nydalen
NO-0401 OSLO
Norway

8 MARKETING AUTHORISATION NUMBER(S)

PA 0735/008/006

Date of First Authorisation/Renewal of the Authorisation

Date of first Authorisation: 29 June 2007
Date of last renewal: 30 June 2008

9 DATE OF REVISION OF THE TEXT

December 2019