HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all of the information needed to use OMNISCAN safely and effectively. See full prescribing information for OMNISCAN.

OMNISCAN™ (gadodiamide) Injection for Intravenous Use
Initial U.S. Approval: 1993

WARNING: NOT FOR INTRATHECAL USE and NEPHROGENIC SYSTEMIC FIBROSIS (NSF)
See full prescribing information for complete boxed warning.

NOT FOR INTRATHECAL USE

- **Inadvertent intrathecal use of OMNISCAN has caused convulsions, coma, sensory and motor neurologic deficits (5.4).**

NSF

- **Gadolinium-based contrast agents (GBCAs) increase risk of NSF in patients with (5.2):**
  - **acute or chronic severe renal insufficiency (glomerular filtration rate < 30 mL/min/1.73m^2), or**
  - **acute renal insufficiency of any severity due to hepato-renal syndrome or in perioperative liver transplantation period.**
- **In these patients, avoid use of GBCAs unless diagnostic information is essential and not available with non-contrast enhanced MRI (5.2).**
- **NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs (5.2).**

----------RECENT MAJOR CHANGES----------

Boxed Warning: Nephrogenic Systemic Fibrosis (NSF)	9/2007
Warnings and Precautions: Hypersensitivity Reactions (5.1)	9/2007
Warnings and Precautions: NSF (5.2)	9/2007
Warnings and Precautions: Acute Renal Failure (5.3)	9/2007
Warnings and Precautions: Not for Intrathecal Use (5.4)	9/2007

----------INDICATIONS AND USAGE----------

OMNISCAN is a gadolinium-based contrast agent for diagnostic magnetic resonance imaging (MRI) indicated for intravenous use to:

- Visualize lesions with abnormal vascularity in the brain, spine, and associated tissues (1.1)
- Facilitate the visualization of lesions with abnormal vascularity within the thoracic, abdominal, pelvic cavities, and the retroperitoneal space (1.2)

----------DOSAGE AND ADMINISTRATION----------

- CNS – Adults and Pediatrics; 2-16 years of age: 0.2 mL/kg (0.1 mmol/kg) (2.1, 2.4)
- Body – Adults and Pediatrics; 2-16 years of age:
  Kidney: 0.1 mL/kg (0.05 mmol/kg)
  Intrathoracic, intra-abdominal, and pelvic cavities: 0.2 mL/kg (0.1 mmol/kg) (2.2, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------

Sterile aqueous solution for intravenous injection; 287 mg/mL (3)

----------CONTRAINDICATIONS----------

None (4)

----------WARNINGS AND PRECAUTIONS----------

- *Anaphylactoid and other serious hypersensitivity reactions* including fatal reactions have occurred particularly in patients with history of allergy or drug reactions. Monitor patients closely for need of emergency cardiorespiratory support (5.1).
- *Nephrogenic Systemic Fibrosis (NSF)* has occurred in patients with severe renal insufficiency. Higher than recommended dosing or repeat dosing appears to increase the risk (5.2).
- *Acute renal failure* has occurred in patients with preexisting renal insufficiency. Use the lowest necessary dose of OMNISCAN and evaluate renal function in these patients (5.3).

----------ADVERSE REACTIONS----------

- The most frequent adverse reactions (≤ 3%) observed during OMNISCAN adult clinical studies were nausea, headache, and dizziness (6.1)
- Serious or life-threatening reactions include: cardiac failure, arrhythmia and myocardial infarction (6.1, 6.3)

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: month/yr

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: NOT FOR INTRATHECAL USE and NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

NOT FOR INTRATHECAL USE

Inadvertent intrathecal use of OMNISCAN has caused convulsions, coma, sensory and motor neurologic deficits *[see Warnings and Precautions (5.4)]*.

NSF

Gadolinium-based contrast agents increase the risk for NSF in patients with:

- **acute or chronic severe renal insufficiency (glomerular filtration rate < 30 mL/min/1.73m^2), or**
- **acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period.**

In these patients, avoid use of gadolinium-based contrast agents unless the diagnostic information is essential and not available with non-contrast enhanced magnetic resonance imaging (MRI). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs. Screen all patients for renal dysfunction by obtaining a history and laboratory tests. When administering a gadolinium-based contrast agent, do not exceed the recommended dose and allow a sufficient period of time for elimination of the agent from the body prior to any readministration [*see Warnings and Precautions (5.2)*].

1 INDICATIONS AND USAGE

1.1 CNS (Central Nervous System)

OMNISCAN is a gadolinium-based contrast agent indicated for intravenous use in MRI to visualize lesions with abnormal vascularity (or those thought to cause abnormalities in the blood-brain barrier) in the brain (intracranial lesions), spine, and associated tissues [*see Clinical Studies (14.1)*].

1.2 Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal Regions)

OMNISCAN is a gadolinium-based contrast agent indicated for intravenous use in MRI to facilitate the visualization of lesions with abnormal vascularity within the thoracic (noncardiac), abdominal, pelvic cavities, and the retroperitoneal space [*see Clinical Studies (14.2)*].

2 DOSAGE AND ADMINISTRATION

2.1 CNS (Central Nervous System)

Adults: The recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. An additional 0.4 mL/kg (0.2 mmol/kg) can be given within 20 minutes of the first dose [*see Dosage and Administration (2.3)*].

Pediatric Patients (2-16 years): The recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection [*see Dosage and Administration (2.3)*].

2.2 Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal Regions)

Adult and Pediatric Patients (2-16 years of age): For imaging the kidney, the recommended dose of OMNISCAN is 0.1 mL/kg (0.05 mmol/kg). For imaging the intrathoracic (noncardiac), intra-abdominal, and pelvic cavities, the recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg) [*see Dosage and Administration (2.3)*].

2.3 Dosage Chart

BODY WEIGHT		PEDIATRIC		ADULTS		
Kg	lb	0.05 (mmol/kg) VOLUME (mL)	0.1 (mmol/kg) VOLUME (mL)	0.05 (mmol/kg) VOLUME (mL)	0.1 (mmol/kg) VOLUME (mL)	0.2 (mmol/kg) VOLUME (mL)
12	26	1.2	2.4	-	-	-
14	31	1.4	2.8	-	-	-
16	35	1.6	3.2	-	-	-
18	40	1.8	3.6	-	-	-
20	44	2	4	-	-	-
22	48	2.2	4.4	-	-	-
24	53	2.4	4.8	-	-	-
26	57	2.6	5.2	-	-	-
28	62	2.8	5.6	-	-	-
30	66	3	6	-	-	-
40	88	4	8	4	8	16
50	110	5	10	5	10	20
60	132	6	12	6	12	24
70	154	7	14	7	14	28
80	176	8	16	8	16	32
90	198	-	-	9	18	36
100	220	-	-	10	20	40
110	242	-	-	11	22	44
120	264	-	-	12	24	48
130*	286	-	-	13	26	52

*The heaviest patient in clinical studies weighed 136 kg.

2.4 Dosing Guidelines

Inspect OMNISCAN visually for particulate matter and discoloration before administration, whenever solution and container permit.

Do not use the solution if it is discolored or particulate matter is present.

Draw OMNISCAN into the syringe and use immediately. Discard any unused portion of OMNISCAN Injection.

To ensure complete delivery of the desired volume of contrast medium, follow the injection of OMNISCAN with a 5 mL flush of 0.9% sodium chloride, as provided in the Prefill Plus needle-free system. Complete the imaging procedure within 1 hour of administration of OMNISCAN.

2.5 Repeat Dosing

Sequential use during the same diagnostic session has been studied in adult CNS use only. If the physician determines repeat dosing is required in non-CNS imaging in adults or pediatric patients, renal function should be normal and the time interval between repeat doses should be at least 7 hours to allow for clearance of the drug from the body [*see Clinical Pharmacology (12.3)*].

3 DOSAGE FORMS AND STRENGTHS

Sterile aqueous solution for intravenous injection; 287 mg/mL.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Anaphylactoid and anaphylactic reactions, with cardiovascular, respiratory and/or cutaneous manifestations, resulting in death have occurred. If such a reaction occurs, stop OMNISCAN Injection and immediately begin appropriate therapy. Observe patients closely, particularly those with a history of drug reactions, asthma, allergy or other hypersensitivity disorders, during and up to several hours after OMNISCAN Injection.

5.2 Nephrogenic Systemic Fibrosis

[*see Boxed Warning*]

Gadolinium-based contrast agents increase the risk for nephrogenic systemic fibrosis (NSF) in patients with acute or chronic severe renal insufficiency (glomerular filtration rate < 30 mL/min/1.73m^2) and in patients with acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period. In these patients, avoid use of gadolinium-based contrast agents unless the diagnostic information is essential and not available with non-contrast enhanced MRI. For patients receiving hemodialysis, physicians may consider the prompt initiation of hemodialysis following the administration of a gadolinium-based contrast agent in order to enhance the contrast agent's elimination. The usefulness of hemodialysis in the prevention of NSF is unknown.

Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a gadolinium-based contrast agent and the degree of renal function impairment at the time of exposure.

Postmarketing reports have identified the development of NSF following single and multiple administrations of gadolinium-based contrast agents. These reports have not always identified a specific agent. Where a specific agent was identified, the most commonly reported agent was gadodiamide (Omniscan™), followed by gadopentetate dimeglumine (Magnevist®) and gadoversetamide (OptiMARK®). NSF has also developed following sequential administrations of gadodiamide with gadobenate dimeglumine (MultiHance®) or gadoteridol (ProHance®). The number of postmarketing reports is subject to change over time and may not reflect the true proportion of cases associated with any specific gadolinium-based contrast agent.

The extent of risk for NSF following exposure to any specific gadolinium-based contrast agent is unknown and may vary among the agents. Published reports are limited and predominantly estimate NSF risks with gadodiamide. In one retrospective study of 370 patients with severe renal insufficiency who received gadodiamide, the estimated risk for development of NSF was 4% (J Am Soc Nephrol 2006;17:2359). The risk, if any, for the development of NSF among patients with mild to moderate renal insufficiency or normal renal function is unknown.

Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. When administering a gadolinium-based contrast agent, do not exceed the recommended dose and allow a sufficient period of time for elimination of the agent prior to any readministration [*see Clinical Pharmacology (12.2) and Dosage and Administration (2)*].

5.3 Acute Renal Failure

In patients with renal insufficiency, acute renal failure requiring dialysis or worsening renal function have occurred, mostly within 48 hours of OMNISCAN Injection. The risk of renal failure may increase with increasing dose of gadolinium contrast. Use the lowest necessary dose of contrast and evaluate renal function in patients with renal insufficiency. Acute renal failure was observed in < 1% of patients in OMNISCAN clinical studies [*see Adverse Reactions (6)*].
OMNISCAN is cleared by glomerular filtration. Hemodialysis also enhances OMNISCAN clearance [*see Use in Specific Populations (8.5, 8.6)*].

5.4 Not for Intrathecal Use

Inadvertent intrathecal use of OMNISCAN has occurred and caused convulsions, coma, sensory and motor neurologic deficits.

5.5 Impaired Visualization of Lesions Detectable with Non-contrast MRI

Paramagnetic contrast agents such as OMNISCAN might impair the visualization of lesions which are seen on the non-contrast MRI. This may be due to effects of the paramagnetic contrast agent, or imaging parameters. Exercise caution when OMNISCAN MRI scans are interpreted in the absence of a companion non-contrast MRI.

5.6 Laboratory Test Findings

Asymptomatic, transitory changes in serum iron have been observed. The clinical significance is unknown.

OMNISCAN interferes with serum calcium measurements with some colorimetric (complexometric) methods commonly used in hospitals, resulting in serum calcium concentrations lower than the true values. In patients with normal renal function, this effect lasts for 12-24 hours. In patients with decreased renal function, the interference with calcium measurements is expected to last during the prolonged elimination of OMNISCAN. After patients receive OMNISCAN, careful attention should be used in selecting the type of method used to measure calcium.

6 ADVERSE REACTIONS

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

6.1 Clinical Studies Experience (Adults)

In clinical studies 1160 patients were exposed to OMNISCAN. The most frequent adverse reactions were nausea, headache, and dizziness that occurred in 3% or less of the patients. The majority of these reactions were of mild to moderate intensity.

The following adverse reactions occurred in 1% or less of patients:
Application Site Disorders: Injection site reaction.
Autonomic Nervous System Disorders: Vasodilation.
Body as a Whole-General Disorders: 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, parethesia, tremor, aggravated multiple sclerosis (characterized by sensory and motor disturbances), aggravated migraine.
Gastrointestinal System Disorders: Abdominal pain, diarrhea, eructation, dry mouth/vomiting, melena.
Hearing and Vestibular Disorders: Tinnitus.
Liver 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.
Special Senses, Other Disorders: Taste loss, taste perversion.
Urinary System Disorders: Acute reversible renal failure.
Vision Disorders: Abnormal vision.

6.2 Clinical Studies Experience (Pediatrics)

In the 97 pediatric patients in CNS studies with OMNISCAN [*see Clinical Studies (14.1)*] and the 144 pediatric patients in published literature, the adverse reactions were similar to those reported in adults.

6.3 Postmarketing Experience

Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
The following adverse reactions have been identified during the postmarketing use of OMNISCAN:
Nervous System Disorders: Inadvertent intrathecal use causes seizures, coma, paresthesia, paresis.
General Disorders: Nephrogenic Systemic Fibrosis (NSF) [*see Warnings and Precautions (5.2)*].

7 DRUG INTERACTIONS

Specific drug interaction studies have not been conducted.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: OMNISCAN has been shown to have an adverse effect on embryo-fetal development in rabbits at dosages as low as 0.5 mmol/kg/day for 13 days during gestation (approximately 0.6 times the human dose based on a body surface area comparison). These adverse effects are observed as an increased incidence of flexed appendages and skeletal malformations which may be due to maternal toxicity since the body weight of the dams was reduced in response to OMNISCAN administration during pregnancy. In rat studies, fetal abnormalities were not observed at doses up to 2.5 mmol/kg/day for 10 days during gestation (1.3 times the maximum human dose based on a body surface area comparison); however, maternal toxicity was not achieved in these studies and a definitive conclusion about teratogenicity in rats at doses above 2.5 mmol/kg/day cannot be made. Adequate and well controlled studies in pregnant women have not been conducted. OMNISCAN should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when administering OMNISCAN to a nursing woman.

8.4 Pediatric Use

The safety and efficacy of OMNISCAN at a single dose of 0.05 to 0.1 mmol/kg have been established in pediatric patients over 2 years of age based on adequate and well controlled studies of OMNISCAN in adults, a pediatric CNS imaging study, and safety data in the scientific literature. However, the safety and efficacy of doses greater than 0.1 mmol/kg and of repeated doses have not been studied in pediatric patients.
Pharmacokinetics of OMNISCAN have not been studied in pediatrics. The glomerular filtration rate of neonates and infants is much lower than that of adults. The pharmacokinetics volume of distribution is also different. Therefore, the optimal dosing regimen and imaging times in patients under 2 years of age have not been established.

8.5 Geriatric Use

In clinical studies of OMNISCAN, 243 patients were between 65 and 80 years of age while 15 were over 80. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity in the elderly cannot be ruled out. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.
OMNISCAN is excreted by the kidney, and the risk of toxic reactions to OMNISCAN may be greater in patients with impaired renal function [*see*

Warnings and Precautions (5.3)]. Because elderly patients are more likely to have decreased renal function, select dose carefully and consider assessment of renal function before OMNISCAN use.

8.6 Renal/Hepatic Impairment

Dose adjustments in renal or hepatic impairment have not been studied. Caution should be exercised in patients with impaired renal insufficiency [*see Warnings and Precautions (5.2, 5.3)*].

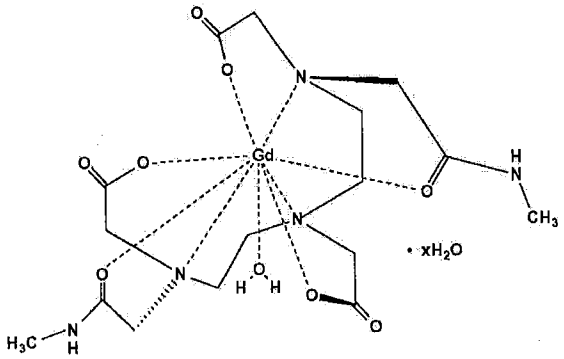
10 OVERDOSAGE

Clinical consequences of overdose with OMNISCAN have not been reported. The minimum lethal dose of intravenously administered OMNISCAN in rats and mice is greater than 20 mmol/kg (200 times the recommended human dose of 0.1 mmol/kg; 67 times the cumulative 0.3 mmol/kg dose). OMNISCAN is dialyzable.

11 DESCRIPTION

OMNISCAN (gadodiamide) Injection is the formulation of the gadolinium complex of diethylenetriamine pentaacetic acid bismethylamide, and is an injectable, nonionic extracellular enhancing agent for magnetic resonance imaging. OMNISCAN is administered by intravenous injection.

OMNISCAN is provided as a sterile, clear, colorless to slightly yellow, aqueous solution. Each 1 mL contains 287 mg gadodiamide and 12 mg caldiamide sodium in Water for Injection. The pH is adjusted between 5.5 and 7.0 with hydrochloric acid and/or sodium hydroxide. OMNISCAN contains no antimicrobial preservative. OMNISCAN is a 0.5 mol/L solution of aqua[5,8-bis(carboxymethyl)-11-[2-(methylamino)-2-oxoethyl]-3-oxo-2,5,8,11-tetraazatridecan-13-oato (3-)-N^5, N^8, N^{11}, O^3, O^5, O^8, O^{11}, O^{13}] gadolinium hydrate, with a molecular weight of 573.66 (anhydrous), an empirical formula of $C_{16}H_{28}GdN_5O_9 \cdot xH_2O$, and the following structural formula:



Pertinent physicochemical data for OMNISCAN are noted below:

PARAMETER		
Osmolality (mOsmol/kg water)	@ 37°C	789
Viscosity (cP)	@ 20°C	2
	@ 37°C	1.4
Density (g/mL)	@ 25°C	1.14
Specific gravity	@ 25°C	1.15

OMNISCAN has an osmolality approximately 2.8 times that of plasma at 37°C and is hypertonic under conditions of use.

12 CLINICAL PHARMACOLOGY

12.2 Pharmacodynamics

In magnetic resonance imaging, visualization of normal and pathologic tissue depends in part on variations in the radiofrequency signal intensity. These variations occur due to: changes in proton density; alteration of the spin-lattice or longitudinal relaxation time (T_1); and variation of the spin-spin or transverse relaxation time (T_2). OMNISCAN is a paramagnetic agent with unpaired electron spins which generate a local magnetic field. As water protons move through this local magnetic field, the changes in magnetic field experienced by the protons reorient them with the main magnetic field more quickly than in the absence of a paramagnetic agent.

By increasing the relaxation rate, OMNISCAN decreases both the T_1 and T_2 relaxation times in tissues where it is distributed. At clinical doses, the effect is primarily on the T_1 relaxation time, and produces an increase in signal intensity. OMNISCAN does not cross the intact blood-brain barrier and, therefore, does not accumulate in normal brain or in lesions that do not have an abnormal blood-brain barrier (e.g., cysts, mature postoperative scars). However, disruption of the blood-brain barrier or abnormal vascularity allows accumulation of OMNISCAN in lesions such as neoplasms, abscesses, and subacute infarcts. The pharmacokinetic parameters of OMNISCAN in various lesions are not known. There is no detectable biotransformation or decomposition of gadodiamide.

12.3 Pharmacokinetics

The pharmacokinetics of intravenously administered gadodiamide in normal subjects conforms to an open, two-compartment model with mean distribution and elimination half-lives (reported as mean ± SD) of 3.7 ± 2.7 minutes and 77.8 ± 16 minutes, respectively.

Gadodiamide is eliminated primarily in the urine with 95.4 ± 5.5% (mean ± SD) of the administered dose eliminated by 24 hours. The renal and plasma clearance rates of gadodiamide are nearly identical (1.7 and 1.8 mL/min/kg, respectively), and are similar to that of substances excreted primarily by glomerular filtration. The volume of distribution of gadodiamide (200 ± 61 mL/kg) is equivalent to that of extracellular water. Gadodiamide does not bind to human serum proteins *in vitro*. Pharmacokinetic and pharmacodynamic studies have not been systematically conducted to determine the optimal dose and imaging time in patients with abnormal renal function or renal failure, in the elderly, or in pediatric patients with immature renal function.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term animal studies have not been performed to evaluate the carcinogenic potential of gadodiamide. The results of the following genotoxicity assays were negative: *in vitro* bacterial reverse mutation assay, *in vitro* Chinese Hampster Ovary (CHO)/Hypoxanthine Guanine Phosphoribosyl Transferase (HGPT) forward mutation assay, *in vitro* CHO chromosome aberration assay, and the *in vivo* mouse micronucleus assay at intravenous doses of 27 mmol/kg (approximately 7 times the maximum human dose based on a body surface area comparison). Impairment of male or female fertility was not observed in rats after intravenous administration three times per week at the maximum dose tested of 1.0 mmol/kg (approximately 0.5 times the maximum human dose based on a body surface area comparison).

14 CLINICAL STUDIES

14.1 CNS (Central Nervous System)

OMNISCAN (0.1 mmol/kg) contrast enhancement in CNS MRI was evident in a study of 439 adults. In a study of sequential dosing, 57 adults received OMNISCAN 0.1 mmol/kg followed by 0.2 mmol/kg within 20 minutes (for cumulative dose of 0.3 mmol/kg). The MRIs were compared blindly. In 54/56 (96%) patients, OMNISCAN contrast enhancement was evident with both the 0.1 mmol/kg and cumulative 0.3 mmol/kg OMNISCAN doses relative to non-contrast MRI.

In comparison to the non-contrast MRI, increased numbers of brain and spine lesions were noted in 42% of patients who received OMNISCAN at any dose. In comparisons of 0.1 mmol/kg versus 0.3 mmol/kg, the results were comparable in 25/56 (45%); in 1/56 (2%) OMNISCAN 0.1 mmol/kg dose provided more diagnostic value and in 30/56 (54%) the cumulative OMNISCAN 0.3 mmol/kg dose provided more diagnostic value.

The usefulness of a single 0.3 mmol/kg bolus in comparison to the cumulative 0.3 mmol/kg (0.1 mmol/kg followed by 0.2 mmol/kg) has not been established.

OMNISCAN as a single 0.1 mmol/kg dose was evaluated in 97 pediatric patients with a mean age of 8.9 (2-18) years referred for CNS MRI. Postcontrast MRI provided added diagnostic information, diagnostic confidence, and new patient management information in 76%, 67%, and 52%, respectively, of pediatrics.

14.2 Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal Regions)

OMNISCAN was evaluated in a controlled trial of 276 patients referred for body MRI. These patients had a mean age of 57 (9-88) years. Patients received 0.1 mmol/kg OMNISCAN for imaging the thorax (noncardiac), abdomen, and pelvic organs, or a dose of 0.05 mmol/kg for imaging the kidney. Pre- and post-OMNISCAN images were evaluated blindly for the degree of diagnostic value rated on a scale of "remarkably improved, improved, no change, worse, and cannot be determined." The postcontrast results showed "remarkably improved" or "improved" diagnostic value in 90% of the thorax, liver, and pelvis patients, and in 95% of the kidney patients.

In a dose ranging study 258 patients referred for body MRI received OMNISCAN 0.025, 0.05, 0.1 mmol/kg. The lowest effective dose of OMNISCAN for the kidney was 0.05 mmol/kg.

16 HOW SUPPLIED/STORAGE AND HANDLING

OMNISCAN (gadodiamide) Injection is a sterile, clear, colorless to slightly yellow, aqueous solution containing 287 mg/mL of gadodiamide in rubber

stoppered vials and polypropylene syringes. OMNSICAN is supplied in the following sizes:

5 mL fill in 10 mL vial, box of 10 (NDC 0407-0690-05)
10 mL vial, box of 10 (NDC 0407-0690-10)
15 mL fill in 20 mL vial, box of 10 (NDC 0407-0690-15)
20 mL vial, box of 10 (NDC 0407-0690-20)
50 mL vial, box of 10 (NDC 0407-0690-55)
10 mL fill in 20 mL prefilled syringe, box of 10 (NDC 0407-0690-12)
15 mL fill in 20 mL prefilled syringe, box of 10 (NDC 0407-0690-17)
20 mL prefilled syringe, box of 10 (NDC 0407-0690-22)

Prefill Plus™ needle-free system
OMNISCAN 15 mL, box of 10 (NDC 0407-0691-62)
Contains: OMNISCAN 15 mL fill in 20 mL Single Dose Prefilled Syringe and 5 mL 0.9% Sodium Chloride Injection, USP I.V. Flush Syringe

Prefill Plus™ needle-free system
OMNISCAN 20 mL, box of 10 (NDC 0407-0691-63)
Contains: OMNISCAN 20 mL fill in 20 mL Single Dose Prefilled Syringe and 5 mL 0.9% Sodium Chloride Injection, USP I.V. Flush Syringe

Protect OMNISCAN from strong daylight and direct exposure to sunlight. **Do not freeze.** Freezing can cause small cracks in the vials, which would compromise the sterility of the product. Do not use if the product is inadvertently frozen.

Store OMNISCAN at controlled room temperature 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP].

17 PATIENT COUNSELING INFORMATION

Patients receiving OMNISCAN should be instructed to inform their physician if they:

- are pregnant or breast feeding, or
- have a history of renal disease, convulsions, asthma or allergic respiratory disorders, or recent administration of gadolinium-based contrast.

Gadolinium-based contrast agents increase the risk for NSF among patients with acute or chronic severe renal insufficiency or acute renal insufficiency due to the hepato-renal syndrome. This risk may increase with repetitive or higher than recommended doses of a gadolinium-based contrast agent. Instruct patients at increased risk for NSF to contact their physician if they develop burning, itching, swelling, scaling, hardening and tightening of the skin; red or dark patches on the skin; stiffness in joints with trouble moving, bending or straightening the arms, hands, legs or feet; pain deep in the hip bones or ribs; or muscle weakness.

Distributed by GE Healthcare Inc., Princeton, NJ

Manufactured by GE Healthcare AS, Oslo, Norway