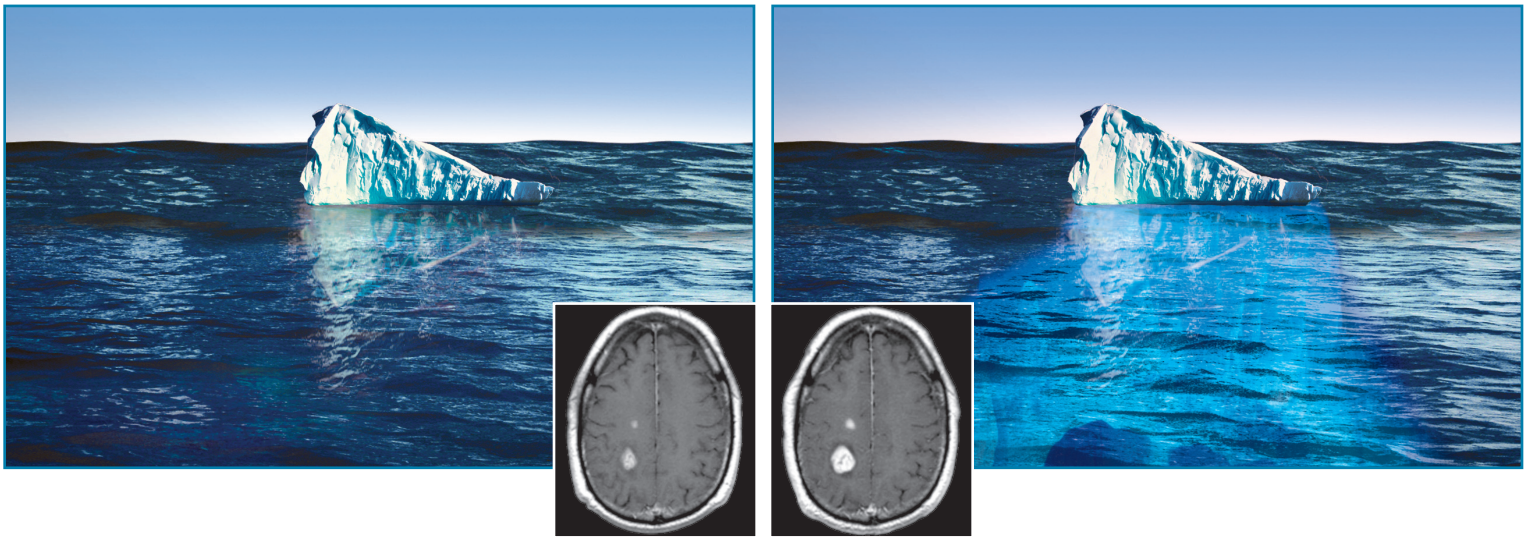
multihance® (gadobenate dimeglumine) injection, 529 mg/mL

MultiHance®

Much More Than Meets The Eye



See what you have to gain

As with all paramagnetic contrast agents, caution should be exercised in patients with deoxygenated sickle erythrocytes. The possibility of a reaction, including serious, life-threatening, or fatal anaphylactic or cardiovascular reactions, or other idiosyncratic reactions, should always be considered, especially in those patients with history of a known clinical hypersensitivity or a history of asthma or other allergic respiratory disorders.

Contact Us:

For more information about MultiHance®, please contact Bracco Professional Services at 1.800.257.5181 or email Bracco Customer Service at bracco.otc@diag.bracco.com.

Available in 5, 10, 15, and 20 mL single-dose vials, and 50 and 100 mL Multipack®* (Pharmacy Bulk Packages)

Size	NDC Number
5 mL vials	0270-5164-12
10 mL vials	0270-5164-13
15 mL vials	0270-5164-14
20 mL vials	0270-5164-15
50 mL Multipack	0270-5264-16
100 mL Multipack	0270-5264-17

* Not for Direct Infusion.

MultiHance has a significantly greater relaxivity, and provides statistically significant ($p<0.0001$) better contrast enhancement and diagnostic information in MRI of CNS lesions compared to Magnevist at an equivalent dose.[1],[2]

MultiHance (gadobenate dimeglumine) injection, 529 mg/mL is the first extracellular fluid (ECF) contrast agent (CA) to possess a weak and transient interaction with plasma proteins, a characteristic that endows **MultiHance** with up to twice the in vivo relaxivity of all other ECF contrast agents.[3] de Haen, 1999. This improved relaxation effect could potentially contribute to improved lesion visualization.

The **MultiHance** molecule, gadobenate, has a structure very similar to that of gadopentetate, except that **MultiHance** has a benzyloxymethyl group protruding from the molecule.[4] This lipophilic structure provides **MultiHance** with the ability to weakly and reversibly interact with plasma proteins and also to be taken up by functioning hepatocytes. MultiHance (gadobenate dimeglumine injection, 529 mg/mL) provides statistically significant ($p<0.0001$) better contrast enhancement and diagnostic information in MRI of CNS lesions compared with Magnevist (gadopentetate dimeglumine) at an equivalent dose.[5]

For more information on MultiHance, visit www.multihanceUSA.com.
For more medical information, call Bracco Professional Services at 1-800-257-5181.
For more information about Bracco products, visit www.bracco.com or call Bracco Customer Service at 1-877-Bracco-9 (1-877-272-2269).

BRACCO
LIFE FROM INSIDE

(1) Knopp MV, Runge VM, Essig M, et al. Primary and secondary brain tumors at MR imaging: bicentric intraindividual crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine. Radiology 2004; 230:55-64.
(2) Maravilla KR, Maldjian JA, Schmalfuss IM, et al. Contrast Enhancement of Central Nervous System Lesions: Multicenter Intraindividual Crossover Comparative Study of Two MR Contrast Agents. Radiology 2006; 240: 389-400.
(3) deHaen C, Cabrini M, Akhnana L, et al. Gadobenate Dimeglumine 0.5 M Solution for Injection (MultiHance ®): Pharmaceutical Formulation and Physiochemical Properties of a New Magnetic Resonance Imaging Contrast Medium. J Comput Assist Tomogr; Vol. 23 (Suppl. 1), 1999.
(4) deHaen C, Cabrini M, Akhnana L, et al. Gadobenate Dimeglumine 0.5 M Solution for Injection (MultiHance ®): Pharmaceutical Formulation and Physiochemical Properties of a New Magnetic Resonance Imaging Contrast Medium. J Comput Assist Tomogr; Vol. 23 (Suppl. 1), 1999.
(5) Maravilla KR, Maldjian JA, Schmalfuss IM, et al. Contrast Enhancement of Central Nervous System Lesions: Multicenter Intraindividual Crossover Comparative Study of Two MR Contrast Agents. Radiology 2006; 240: 389-400.

BRACCO DIAGNOSTICS

Rx only

Please see full prescribing information. A brief summary follows

multihance®
(gadobenate dimeglumine) injection, 529 mg/mL

DESCRIPTION

MULTIHANCE injection is supplied as a sterile, non-pyrogenic, clear, colorless aqueous solution intended for intravenous use only. Each mL of solution contains 529 mg gadobenate dimeglumine. MULTIHANCE contains no preservatives.

CLINICAL PHARMACOLOGY

Gadobenate dimeglumine is a paramagnetic agent and, as such, develops a magnetic moment when placed in a magnetic field. The large magnetic moment produced by the paramagnetic agent results in a large local magnetic field, which can enhance the relaxation rates of water protons in its vicinity leading to an increase of signal intensity (brln magnetic resonance imaging (MRI), visualization of normal and pathological tissue depends in part on variations in the radiofrequency signal intensity that occur with 1) differences in proton density; 2) differences of the spin-lattice or longitudinal relaxation times (Tl); and 3) differences in the spin-spin or transverse relaxation time (T2). When placed in a magnetic field, gadobenate dimeglumine decreases the T1 and T2 relaxation time in target tissues. At recommended doses, the effect is observed with greatest sensitivity in the Tl-weighted sequences.

Pharmacokinetics

Three single-dose intravenous studies were conducted in 32 healthy male subjects to assess the pharmacokinetics of gadobenate dimeglumine. The doses administered in these studies ranged from 0.005 to 0.4 mmol/kg. Upon injection, the meglumine salt is completely dissociated from the gadobenate dimeglumine complex. Thus, the pharmacokinetics is based on the assay of gadobenate ion, the MRI contrast effective ion in gadobenate dimeglumine. Data for plasma concentration and area under the curve demonstrated linear dependence on the administered dose. The pharmacokinetics of gadobenate ion following intravenous administration can be best described using a two-compartment model.

Distribution: Gadobenate ion has a rapid distribution half-life (reported as mean ± SD) of 0.084 ± 0.012 to 0.605 ± 0.072 hours. Volume of distribution of the central compartment ranged from 0.074 ± 0.017 to 0.158 ± 0.038 L/kg, and estimates of volume of distribution by area ranged from 0.170 ± 0.016 to 0.282 ± 0.079 L/kg. These latter estimates are approximately equivalent to the average volume of extracellular body water in man. In vitro studies showed no appreciable binding of gadobenate ion to human serum proteins.

Metabolism: There was no detectable biotransformation of gadobenate ion. Dissociation of gadobenate ion in vivo has been shown to be minimal, with less than 1% of the free chelating agent being recovered alone in feces.

Elimination: Gadobenate ion is eliminated predominately via the kidneys, with 78% to 96% of an administered dose recovered in the urine. Total plasma clearance and renal clearance estimates of gadobenate ion were similar, ranging from 0.093 ± 0.010 to 0.133 ± 0.270 L/hr/kg and 0.082 ± 0.007 to 0.104 ± 0.039 L/hr/kg, respectively. The clearance is similar to that of substances that are subject to glomerular filtration. The mean elimination half-life ranged from 1.17 ± 0.26 to 2.02 ± 0.60 hours. A small percentage of the administered dose (0.6% to 4%) is eliminated via the biliary route and recovered in feces.

Pharmacokinetics in Special Populations

Renal Impairment: A single intravenous dose of 0.2 mmol/kg of MULTIHANCE was administered to 20 subjects with impaired renal function (6 men and 3 women with moderate renal impairment [urine creatinine clearance >30 to <60 mL/min] and 5 men and 6 women with severe renal impairment [urine creatinine clearance >10 to <30 mL/min]). Mean estimates of the elimination half-life were 6.1 ± 3.0 and 9.5 ± 3.1 hours for the moderate and severe renal impairment groups, respectively as compared with 1.0 to 2.0 hours in healthy volunteers. However, the overall extent of elimination of gadobenate was not influenced by impaired renal function. Also, no differences were noted in renally impaired patients in the rate and type of adverse events reported compared with healthy volunteers, and no deterioration in renal function was observed in this population following the administration of MULTIHANCE. Therefore, dosage adjustment is not recommended **(See PRECAUTIONS).**

Hemodialysis: A single intravenous dose of 0.2 mmol/kg of MULTIHANCE was administered to 11 subjects (5 males and 6 females) with end-stage renal disease requiring hemodialysis to determine the pharmacokinetics and dialyzability of gadobenate. Approximately 72% of the dose was recovered by hemodialysis over a 4-hour period. The mean elimination half-life on dialysis was 1.21 ± 0.29 hours as compared with 42.4 ± 24.4 hours when off dialysis.

Hepatic Impairment: A single intravenous dose of 0.1 mmol/kg of MULTIHANCE was administered to 11 subjects (8 males and 3 females) with impaired liver function (Class B or C modified Child-Pugh Classification). Hepatic impairment had little effect on the pharmacokinetics of MULTIHANCE with the parameters being similar to those calculated for healthy subjects. **(See PRECAUTIONS)**

Gender: A multiple regression analysis performed using pooled data from several pharmacokinetic studies found no significant effect of sex upon the pharmacokinetics of gadobenate.

Age: Clearance appeared to decrease slightly with increasing age. Since variations due to age appeared marginal, dosage adjustment for geriatric population is not recommended.

Race: Pharmacokinetic differences due to race have not been systematically studied.

Drug-Drug Interactions: Pharmacokinetic drug interaction studies have not been performed.

Pharmacodynamics

Unlike other paramagnetic contrast agents, MULTIHANCE demonstrates weak and transient interactions with serum proteins that causes slowing in the molecular tumbling dynamics, resulting in strong increases in relaxivity in solutions containing serum proteins. (See Table 1). The improved relaxation effect could potentially contribute to improved visualization.

TABLE 1: RELAXIVITY ($mM^{-1}s^{-1}$) OF GADOLINIUM CHELATES

	Human plasma	
	r_1	r_2
Gadobenate	9.7[1]	12.5[1]
Gadopentetate	4.9[1]	6.3[1]
Gadodiamide	5.4[2]	---
Gadoteridol	5.4[2]	---

r_1 and r_2 relaxivities indicate the efficiency in shortening T1 and T2 relaxation times, respectively.
[1] In heparinized human plasma, at 39°C.
[2] In citrated human plasma, at 37°C.
--- Not available

MULTIHANCE (gadobenate dimeglumine) does not cross the intact blood-brain barrier and, therefore, does not enhance normal brain or lesions that have a normal blood-brain barrier, e.g., cysts, mature post-operative scars, etc. However, disruption of the blood-brain barrier or abnormal vascularity allows enhancement of gadobenate dimeglumine in lesions such as neoplasms, abscesses, and infarcts. Uptake into hepatocytes has been demonstrated for gadobenate. The pharmacokinetics of MULTIHANCE in various lesions is not known.

Effects on Electrocardiography

ECG parameters were investigated in a double-blind, placebo-controlled, 24-hour post dose continuous monitoring, crossover study conducted in 47 subjects (24 healthy volunteers and 23 patients with coronary artery disease [CAD] designed to evaluate the effect of 0.2 mmol/kg MULTIHANCE on ECG intervals, including QTc. Results of the analyses indicate that average changes in QTc values compared with placebo were minimal (< 5 msec). For most individual subjects changes in QTc values were less than 20 msec and evenly distributed between increases and decreases of the same magnitude. QTc prolongation between 30 and 60 msec were noted in 20 subjects (9 healthy volunteers and 11 CAD patients) who received MULTIHANCE vs. 11 subjects (6 volunteers and 5 CAD patients), who received placebo. Prolongations ≥ 61 msec were noted in 6 subjects (2 normal volunteers and 4 CAD patients) who received MULTIHANCE and in 3 subjects (0 volunteers and 3 CAD patients) who received placebo. None of these subjects had associated malignant arrhythmias.

CONTRAINDICATIONS

MULTIHANCE is contraindicated in patients with known allergic or hypersensitivity reactions to gadolinium or any other ingredients, including benzyl alcohol.

WARNINGS

Deoxygenated sickle erythrocytes have been shown in in vitro studies to align perpendicular to a magnetic field which may result in vaso-occlusive complications in vivo. The enhancement of magnetic moment by MULTIHANCE may possibly potentiate sickle erythrocyte alignment. MULTIHANCE has not been studied in patients with sickle cell anemia and other hemoglobinopathies. Patients with other hemolytic anemias have not been adequately evaluated following administration of MULTIHANCE to exclude the possibility of increased hemolysis.

Patients with a history of allergy, drug reactions, or other hypersensitivity-like disorders should be closely observed during the procedure and for several hours after drug administration.
(See PRECAUTIONS - General)

PRECAUTIONS

General

Diagnostic procedures that involve the use of contrast agents should be carried out under direction of a physician with the prerequisite training and a thorough knowledge of the procedure to be performed.

Although more lesions are generally visualized on contrast-enhanced images than on unenhanced images, lesions seen on unenhanced images may not all be seen on contrast-enhanced images. CAUTION SHOULD BE EXERCISED WHEN A CONTRAST-ENHANCED INTERPRETATION IS MADE IN THE ABSENCE OF A COMPANION UNENHANCED MRI.

Appropriate facilities should be available for coping with any complications of the procedures, as well as for emergency treatment of severe reactions to the contrast itself. The possibility of a reaction, including serious, life-threatening, or fatal, anaphylactic or cardiovascular reactions, or other idiosyncratic reactions, should always be considered, especially in those patients with a history of a known clinical hypersensitivity or a history of asthma or other allergic respiratory disorders.

Injection site reactions

In rabbits, perivenous injection of MULTIHANCE provoked more severe local reactions than intravenous injection in rabbits. In these animal experiments, local reactions including eschar and necrosis were noted even on Day 8 post perivenous injection of MULTIHANCE. Therefore, caution should be exercised to avoid local extravasation during intravenous administration of MULTIHANCE. If extravasation occurs, subjects should be monitored and treated as necessary if local reactions develop.

Electrocardiographic Changes

The effects of QTc by dose, other drugs, and medical conditions were not systematically studied. Several atrial and ventricular arrhythmias and atrio-ventricular conduction defects were observed in subjects who received MULTIHANCE. Caution should be exercised in patients who may be using medications or who may have underlying metabolic, cardiac, or other abnormalities that may predispose to cardiac arrhythmias. **(see ADVERSE REACTIONS BELOW).**

Drug Interactions

MULTIHANCE and other drugs may compete for the cannalicular multispecific organic anion transporter (cMOAT also referred to as MRP2 or ABCC2) sites. Therefore appropriate caution should be exercised in those patients who receive drugs such as cisplatin, antracyclines (such as doxorubicin, daunorubicin), vinca alkaloids (such as vincristine), methotrexate, etoposide, tamoxifen, taxol (paciltaxel), or others. Caution should also be exercised in those subjects in whom the cMOAT sites may be affected due to underlying metabolic disorders such as Dubin Johnson syndrome, etc. (see also Laboratory Test Interactions below).

Laboratory Test Interactions

Transient increases in serum ferritin were observed in some patients that were attributed to the underlying disease. In patients with renal disease, transient increases in urine zinc were detected and these changes were shown not to be clinically significant. Transient asymptomatic elevations in bilirubin over baseline were observed in patients with underlying hepatic metabolic disorders such as von Willebrands' disease and Wilsons' disease.

Information for Patients

Patients scheduled to receive MULTIHANCE should be instructed to inform their physician if the patient:

1. is pregnant or breast feeding.
2. has anemia or diseases that affect the red blood cells.
3. has a history of renal disease, heart disease, seizure, hemoglobinopathies, or asthma or allergic respiratory diseases.
4. is taking any medications.
5. has any allergies to any of the ingredients of MULTIHANCE.

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of MULTIHANCE.

The results for MULTIHANCE were negative in the following genetic toxicity studies: 1) in vitro bacteria reverse mutation assays, 2) an in vitro gene mutation assay in mammalian cells, 3) an in vitro chromosomal aberration assay, 4) an in vitro unscheduled DNA synthesis assay, and 5) an in vivo micronucleus assay in rats.

MULTIHANCE had no effect on fertility and reproductive performance at IV doses of up to 2 mmol/kg/day (3 times the human dose on body surface basis) for 13 weeks in male rats and for 32 days in female rats. However, vacuolation in testes and abnormal spermatogenic cells were observed when MULTIHANCE was intravenously administered to male rats at 3 mmol/kg/day (5 times the human dose on body surface basis) for 28 days. The effects were not reversible following 28-day recovery period. The effects were not reported in dog and monkey studies (at doses up to about 11 and 10 times the human dose on body surface basis for dogs (28 days dosing) and monkeys (14 days dosing), respectively).

Pregnancy

Pregnancy Category C

MULTIHANCE has been shown to be teratogenic in rabbits when given intravenously administered at 2 mmol/kg/day (6 times the human dose based on body surface area) during organogenesis (day 6 to 18) inducing microphthalmia / small eye and / or focal retinal fold in 3 fetuses from 3 separate litters. In addition, MULTIHANCE intravenously administered at 3 mmol/kg/day (10 times the human dose based on body surface area) has been shown to increase intrauterine deaths in rabbits. There was no evidence that MULTIHANCE induced teratogenic effects in rats at doses up to 2 mmol/kg/day (3 times the human dose based on body surface area), however, rat dams exhibited no systemic toxicity at this dose. There were no adverse effects on the birth, survival, growth, development and fertility of the F1 generation at doses up to 2 mmol/kg in a rat peri- and post-natal (Segment III) study.

There are no adequate and well-controlled studies in pregnant women. MULTIHANCE should be used during pregnancy only if potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known to what extent gadobenate dimeglumine is excreted in human milk. It is known from rat experiments that less than 0.5% of the administered dose is transferred via milk from mother to neonates. Breast-feeding should be discontinued prior to the administration of MULTIHANCE and should not be restarted until at least 24 hours after the administration of MULTIHANCE.

Geriatric Use

Of the total number of 2982 adult subjects in clinical studies of MULTIHANCE, 27% were 65 and over. No overall differences in safety or effectiveness were observed between these elderly subjects and the younger subjects.

The drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to MULTIHANCE may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function it may be useful to monitor renal function.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

In clinical trials, a total of 2982 adult subjects (119 healthy volunteers and 2863 patients) received MULTIHANCE at doses ranging from 0.005 to 0.4 mmol/kg. There were 1724 (58%) men and 1258 (42%) women with a mean age of 55.1 years (range 18 to 92 years). A total of 2644 (89%) subjects were Caucasian, 84 (3%) Black, 162 (5%) Asian, 29 (1%) Hispanic, 18 (1%) in other racial groups, and for 45 (2%) subjects, race was not reported. Among the 2863 patients, 65 subjects were adult patients who participated in special population pharmacokinetics or cardiac electrophysiology studies (n = 20, renal impairment patients; n = 11, renal dialysis patients; n = 11, hepatic impairment patients; n = 23, ECG cardiovascular patients).

Of the 2982 adult subjects who received MULTIHANCE, 531 (17.8%) reported at least one adverse event. In comparison, 35 (27.6%) of the 127 subjects (38 healthy volunteers and 89 patients) who received placebo in clinical trials reported at least one adverse event.

The most commonly reported adverse events in adult subjects who received MULTIHANCE were headache (2.2%) and nausea (1.8%). Most adverse events were mild to moderate in intensity. Two subjects (0.1 %) died and in 13 additional subjects (0.4%), 15 serious adverse events were reported. The two deaths were attributable to the patients' underlying medical conditions. In four of the 13 subjects who experienced serious adverse events, a causal relationship to MULTIHANCE could not be excluded. One subject with a history of seizures experienced convulsions 17 minutes after the administration of MULTIHANCE. Another subject with a history of recent MI and possibly CHF experienced acute pulmonary edema within 10 minutes after the administration of 30 mL of MULTIHANCE. In the third subject who developed acute necrotizing pancreatitis, sufficient information was not available to exclude a causal relationship to MULTIHANCE. Anaphylactoid reaction was suspected in the fourth subject who experienced laryngismus in conjunction with dyspnea. **(See WARNINGS and PRECAUTIONS, General).** The incidence of adverse events for a subgroup of adult patients with known or suspected lesions of the CNS who participated in Study A was comparable among the 276 patients who received MULTIHANCE (28.6%), and the 134 patients who received an approved gadolinium contrast agent (32.1%). The most commonly reported adverse events in patients who received MULTIHANCE for CNS imaging were headache (5.8%), dizziness (3.6%), and taste perversion (3.3%). The other adverse events that were reported in patients who received MULTIHANCE are similar in nature to those reported in the adult population as a whole. Adverse events that occurred in at least 0.5% of 2982 adult subjects who received MULTIHANCE are listed below in related categories, in decreasing order of occurrence within each system, and regardless of causality. The incidence for placebo-treated subjects and the CNS subpopulation are also shown for purposes of comparison.

TABLE 2: ADVERSE EVENTS REPORTED IN ≥ 0.5% OF ADULT SUBJECTS WHO RECEIVED MULTIHANCE IN CLINICAL TRIALS

	All Adult Subjects		CNS Studies
	Placebo	MULTIHANCE	MULTIHANCE
Number of subjects dosed	127	2982	659
Number of subjects with any adverse event	35 (27.6%)	531 (17.8%)	148 (22.5%)
Body as a Whole			
Headache	6 (4.7%)	67 (2.2%)	25 (3.8%)
Injection site reaction	4 (3.1%)	44 (1.5%)	8 (1.2%)
Pain	0	19 (0.6%)	2 (0.3%)
Cardiovascular System			
Hypertension	4 (3.1%)	22 (0.7%)	2 (0.3%)
Tachycardia	1 (0.8%)	14 (0.5%)	2 (0.3%)
Digestive System			
Nausea	2 (1.6%)	55 (1.8%)	12 (1.8%)
Vomiting	1 (0.8%)	16 (0.5%)	4 (0.6%)
Diarrhea	3 (2.4%)	14 (0.5%)	1 (0.2%)
Hemic and Lymphatic System			
Anemia	0	16 (0.5%)	3 (0.5%)
Nervous System			
Vasodilatation	1 (0.8%)	31 (1. 0%)	8 (1.2%)
Paresthesia	2 (1.6%)	24 (0.8%)	3 (0.5%)
Dizziness	2 (1.6%)	22 (0.7%)	10 (1.5%)
Skin and Appendages			
Rash	2 (1.6%)	21 (0.7%)	4 (0.6%)
Special Senses			
Taste perversion	3 (2.4%)	25 (0.8%)	9 (1.4%)

Adverse reactions that occurred in less than 0.5% of the 2982 adult subjects who received MULTIHANCE included:

Body as a Whole: Abdominal pain, anaphylactic reaction, asthenia, back pain, chest pain, chills, facial edema, fever, infection, infiltration of contrast, injection site inflammation, injection site pain, malaise.

Cardiovascular System: Acute pulmonary edema, arrhythmia, atrial fibrillation, bradycardia, ECG abnormality (includes bundle branch block, complete AV block, first-degree AV block, inverted T wave, prolonged PR interval, prolonged QT interval, shortened QT interval), hypotension, myocardial ischemia, palpitations, supraventricular extrasystoles, syncope, ventricular arrhythmia, ventricular extrasystoles **(See PRECAUTIONS).**

Digestive System: Constipation, dyspepsia, fecal incontinence, acute necrotizing pancreatitis, increased pruritus in patients with cirrhosis.

Hemic and Lymphatic System: Basophilia, hemolysis, leukocytosis, leukopenia.

Metabolic and Nutritional System: Abnormal laboratory test (includes changes in CPK, creatinine, ferritin, transferrin, total iron binding capacity), bilirubinemia, hyperglycemia, hyperkalemia, hyperlipemia, hypocalcemia, hypoglycemia, hyponatremia, hypoproteinemia, increased alkaline phosphatase, increased GGT, increased LDH, increased serum iron, increased SGOT, increased SGPT, peripheral edema, thirst.

Musculoskeletal System: Myalgia, myositis.

Nervous System: Cold feeling, convulsion, dry mouth, hemiplegia, hypertonia, hypesthesia, increased salivation, paralysis, stupor, tremor, aphasia.

Respiratory System: Dyspnea, hyperventilation, increased cough, laryngismus, lung edema, rhinitis, pulmonary embolus.

Skin and Appendages: Pruritus, sweating, urticaria.

Special Senses: Abnormal vision, ear pain, eye disorder, parosmia, tinnitus.

Urogenital System: Albuminuria, glycosuria, hematuria, urinary frequency, urinary incontinence, urinary tract infection, urinary urgency.

Non US Post Marketing Experience:

There were reports of anaphylactoid reactions (characterized by cardiovascular, respiratory, and/or cutaneous symptoms) anaphylactic shock, and loss of consciousness. Because these 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.

OVERDOSAGE

Clinical consequences of overdosage with MULTIHANCE have not been reported. Treatment of an overdosage should be directed toward support of vital functions and prompt institution of symptomatic therapy. In a Phase I clinical study, doses up to 0.4 mmol/kg were administered to patients. MULTIHANCE has been shown to be dialyzable. **(See CLINICAL PHARMACOLOGY Pharmacokinetics.)**

DOSAGE AND ADMINISTRATION

The recommended dose of MULTIHANCE is 0.1 mmol/kg (0.2 mL/kg) administered as a rapid bolus intravenous injection.

To ensure complete injection of the contrast medium, the injection should be followed by a saline flush of at least 5 mL. It is important to ensure that the i.v. needle or cannula is correctly inserted into a vein.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration. Do not use the solution if it is discolored or particulate matter is present. Concurrent medications or parenteral nutrition should not be physically mixed with contrast agents and should not be administered in the same intravenous line because of the potential for chemical incompatibility.

When MULTIHANCE injection is to be injected using plastic disposable syringes, the contrast should be drawn into the syringe and used immediately.

MULTIHANCE injection should be drawn into the syringe and administered using sterile technique. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents. Any residual product must be discarded in accordance with regulations dealing with the disposal of such materials.

Rx only
US Patent No. 4,916,246
Manufactured for Bracco Diagnostics Inc. - Princeton, NJ 08543
By ALTANA Pharma AG - 78224 Singen (Germany)

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