MultiHance® (gadobenate dimeglumine) injection, 529 mg/mL
and
MultiHance® Multipack™ (gadobenate dimeglumine) injection, 529 mg/mL

Indications and Usage:
MultiHance® (gadobenate dimeglumine) injection, 529 mg/mL is a gadolinium-based contrast agent indicated for intravenous use in:

- Magnetic resonance imaging (MRI) of the central nervous system (CNS) in adults and pediatric patients (including term neonates) to visualize lesions with abnormal blood-brain barrier or abnormal vascularity of the brain, spine, and associated tissues
- Magnetic resonance angiography (MRA) to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease

IMPORTANT SAFETY INFORMATION

WARNING: RISK ASSOCIATED WITH INTRATHECAL USE and NEPHROGENIC SYSTEMIC FIBROSIS

Risk Associated with Intrathecal Use

Intrathecal administration of gadolinium-based contrast agents (GBCAs) can cause serious adverse reactions including death, coma, encephalopathy, and seizures. MultiHance is not approved for intrathecal use.

NEPHROGENIC SYSTEMIC FIBROSIS

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR < 30 mL/min/1.73 m^2), or**
  - **Acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended MultiHance dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

CONTRAINDICATIONS

MultiHance is contraindicated in patients with known allergic or hypersensitivity reactions to gadolinium-based contrast agents.

WARNINGS AND PRECAUTIONS

Risk Associated with Intrathecal Use: Intrathecal administration of GBCAs can cause serious adverse reactions including death, coma, encephalopathy, and seizures. The safety and

effectiveness of MultiHance have not been established with intrathecal use and MultiHance is not approved for intrathecal use.

Nephrogenic Systemic Fibrosis: NSF has occurred in patients with impaired elimination of GBCAs. Higher than recommended dosing or repeated dosing appears to increase risk.

Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of MultiHance administration and resolved with prompt emergency treatment. Consider the risk for hypersensitivity reactions, especially in patients with a history of hypersensitivity reactions or a history of asthma or other allergic disorders.

Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver, and spleen. At equivalent doses, retention varies among the linear agents. Retention is lowest and similar among the macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established, but they have been established in the skin and other organs in patients with impaired renal function. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.

Acute Renal Failure: In patients with renal insufficiency, acute renal failure requiring dialysis or worsening renal function have occurred with the use of GBCAs. The risk of renal failure may increase with increasing dose of the contrast agent. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests.

Extravasation and Injection Site Reactions: Extravasation of MultiHance may lead to injection site reactions, characterized by local pain or burning sensation, swelling, blistering, and necrosis. Exercise caution to avoid local extravasation during intravenous administration of MultiHance.

Cardiac Arrhythmias: Cardiac arrhythmias have been observed in patients receiving MultiHance in clinical trials. Assess patients for underlying conditions or medications that predispose to arrhythmias. The effects on QTc by MultiHance dose, other drugs, and medical conditions were not systematically studied.

Interference with Visualization of Certain Lesions: Certain lesions seen on non-contrast images may not be seen on contrast images. Exercise caution when interpreting contrast MR images in the absence of companion non-contrast MR images.

ADVERSE REACTIONS

The most commonly reported adverse reactions are nausea (1.3%) and headache (1.2%).

POST-MARKETING EVENTS

The following adverse reactions have been identified during post approval use of MultiHance or other GBCAs:

Acute pancreatitis within 48 hours of GBCA administration has been reported.

Respiratory, Thoracic and Mediastinal Disorders: Acute respiratory distress syndrome, pulmonary edema.

USE IN SPECIFIC POPULATIONS

Pregnancy: GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. Use only if imaging is essential during pregnancy and cannot be delayed.

Lactation: There is no information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. However, limited literature reports that breastfeeding after MultiHance administration to the mother would result in the infant receiving an oral dose of 0.001%-0.04% of the maternal dose.

Pediatric Use: MultiHance is approved for intravenous use for MRI of the CNS to visualize lesions with abnormal blood brain barrier or abnormal vascularity of the brain, spine, and associated tissues in pediatric patients from birth, including term neonates, to less than 17 years of age. Adverse reactions in pediatric patients were similar to those reported in adults. No dose adjustment according to age is necessary in pediatric patients two years of age and older. For pediatric patients, less than 2 years of age, the recommended dosage range is 0.1 to 0.2 mL/kg. The safety of MultiHance has not been established in preterm neonates.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please click here for Prescribing Information and Patient Medication Guide for additional important safety information for/regarding MultiHance (gadobenate dimeglumine) injection, 529 mg/mL.

Please click here for Prescribing Information and Patient Medication Guide for additional important safety information for/regarding MultiHance Multipack.

MultiHance is manufactured for Bracco Diagnostics Inc. by BIPSO GmbH – 78224 Singen (Germany) and by Patheon Italia S.p.A., Ferentino, Italy.

Bracco Diagnostics Inc.
510 Carnegie Center
Suite 300
Princeton, NJ 08540 USA
Phone: 609-514-2200
Toll-Free: 1-800-631-5245 (U.S. only)
Fax: 609-514-2424