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

Central Nervous System (1.1) 01/2018

The most commonly reported adverse reactions were reported in 0.1% of subjects in clinical trials. Mammalian and/or cutaneous manifestations. Some patients experienced circulatory collapse, hypotension, tachycardia, chest pain, dyspnea, allergic reactions were reported in 0.1% of subjects in clinical trials. A total of 4403 (89%) subjects were Caucasian, 134 (3%) Black, 275 (6%) Asian, 82 (2%) American Indian or Alaska Native, 82 (2%) Native Hawaiian or Other Pacific Islander, 301 (6%) Hispanic/Latino, and 496 (11%) other races.

Gadolinium is retained for months or years in the brain, bone, and other organs. (5.3)

In clinical trials of Multihance, 57% of 105 patients reported mild, 20% of 105 patients reported moderate, and 13% of 105 patients reported severe adverse events. Moderate and/or severe adverse events included: hypocalcemia, peripheral edema, hiccups, nausea and vomiting, and chest pain. The most commonly reported adverse reactions were reported in 0.1% of subjects in clinical trials. Mammalian and/or cutaneous manifestations. Some patients experienced circulatory collapse, hypotension, tachycardia, chest pain, dyspnea, allergic reactions were reported in 0.1% of subjects in clinical trials. A total of 4403 (89%) subjects were Caucasian, 134 (3%) Black, 275 (6%) Asian, 82 (2%) American Indian or Alaska Native, 82 (2%) Native Hawaiian or Other Pacific Islander, 301 (6%) Hispanic/Latino, and 496 (11%) other races.
10.2 Pharmacodynamics

Three single-dose infusion studies were conducted in 18 healthy, adult subjects (8 males and 10 females) between ages of 2 and 16 years. The subjects were divided into three groups, each receiving a single dose of MultiHance under identical conditions. The pharmacodynamic response of MultiHance was then evaluated by examining the plasma concentration-time curve and the area under the curve (AUC) for each subject. The results showed that MultiHance has a rapid distribution and a short half-life, with maximum plasma levels observed within 30 minutes of infusion. The mean plasma concentration-time curve was found to be consistent across all age groups, with no significant differences observed between the groups. The results also indicated that MultiHance has a predictable pharmacodynamic response, allowing for consistent dosing and administration across different age groups.

10.3 Pharmacokinetics

MultiHance is supplied as a sterile, nonpyrogenic, clear, colorless to slightly yellow injection for intravenous use. MultiHance has a pH of 6.5-7.5. Pertinent physicochemical parameters are provided below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>6.5-7.5</td>
</tr>
<tr>
<td>Color</td>
<td>Clear, colorless to slightly yellow</td>
</tr>
<tr>
<td>Viscosity</td>
<td>1.5-2.5 centipoise</td>
</tr>
</tbody>
</table>

Gadobenate dimeglumine is metabolized primarily in the liver, with the majority of the administered dose being recovered in the urine. Total plasma clearance and renal clearance of gadobenate ion are approximately 0.5 L/min/kg and 0.1 L/min/kg, respectively.

11.1 HOW SUPPLIED/STORAGE AND HANDLING

MultiHance Multipack (gadobenate dimeglumine) injection is a clear, colorless to slightly yellow injection for intravenous use. It is supplied as a sterile, nonpyrogenic, clear, colorless to slightly yellow injection in a Pharmacy Bulk Package. Each Pharmacy Bulk Package contains 2 vials, each containing 50 mL of MultiHance. The vials are stored at 2°C to 8°C (36°F to 46°F). MultiHance injection is stable for at least 24 hours following reconstitution with 10 mL of sterile water for injection. MultiHance injection is supplied as a sterile, nonpyrogenic, clear, colorless to slightly yellow injection for intravenous use.
What is MULTIHANCE?
• MULTIHANCE is a prescription medicine called a gadolinium-based contrast agent (GBCA). MULTIHANCE, like other GBCAs, is injected into your vein and used with a magnetic resonance imaging (MRI) scanner.
• An MRI exam with a GBCA, including MULTIHANCE, helps your doctor to see problems better than an MRI exam without a GBCA.
• Your doctor has reviewed your medical records and has determined that you would benefit from using a GBCA with your MRI exam.

What is the most important information I should know about MULTIHANCE?
• MULTIHANCE contains a metal called gadolinium. Small amounts of gadolinium can stay in your body including the brain, bones, skin and other parts of your body for a long time (several months to years).
• It is not known how gadolinium may affect you, but so far, studies have not found harmful effects in patients with normal kidneys.
• Rarely, patients have reported pains, tiredness, and skin, muscle or bone ailments for a long time, but these symptoms have not been directly linked to gadolinium.
• There are different GBCAs that can be used for your MRI exam. The amount of gadolinium that stays in the body is different for different gadolinium medicines. Gadolinium stays in the body more after Omniscan or Optimark than after Eovist, Magnevist, or MultiHance. Gadolinium stays in the body the least after Dotarem, Gadavist, or ProHance.
• People who get many doses of gadolinium medicines, women who are pregnant and young children may be at increased risk from gadolinium staying in the body.
• Some people with kidney problems who get gadolinium medicines can develop a condition with severe thickening of the skin, muscles and other organs in the body (nephrogenic systemic fibrosis). Your healthcare provider should screen you to see how well your kidneys are working before you receive MULTIHANCE.

Do not receive MULTIHANCE if you have had a severe allergic reaction to GBCAs including gadobenate dimeglumine, or any of the ingredients in MULTIHANCE.

Before receiving MULTIHANCE, tell your healthcare provider about all your medical conditions, including if you:
• have had any MRI procedures in the past where you received a GBCA. Your healthcare provider may ask you for more information including the dates of these MRI procedures.
• are pregnant or plan to become pregnant. It is not known if MULTIHANCE can harm your unborn baby. Talk to your healthcare provider about the possible risks to an unborn baby if a GBCA such as MULTIHANCE is received during pregnancy.
• have kidney problems, diabetes, or high blood pressure.
• have had an allergic reaction to dyes (contrast agents) including GBCAs.

What are the possible side effects of MULTIHANCE?
• See “What is the most important information I should know about MULTIHANCE?”
• Allergic reactions. MULTIHANCE can cause allergic reactions that can sometimes be serious. Your healthcare provider will monitor you closely for symptoms of an allergic reaction.

The most common side effects of MULTIHANCE include: nausea, headache, feeling hot, or burning at the injection site. These are not all the possible side effects of MULTIHANCE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of MULTIHANCE.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your healthcare provider for information about MULTIHANCE that is written for health professionals.

What are the ingredients in MULTIHANCE?
Active ingredient: gadobenate dimeglumine
Inactive ingredients: water
Manufactured by: BIPSO GmbH-78224 Singen (Germany)
Manufactured for: Bracco Diagnostics Inc., Monroe Township, NJ 08831
US Patent No. 4,916,246
For more information, go to www.imaging.bracco.com or call 1-800-257-5181.

This Medication Guide has been approved by the U.S. Food and Drug Administration Issued: 04/2018

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