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. Any unused portion must be discarded in accordance with regulations dealing with the disposal of such materials.

### HOW SUPPLIED

**STORAGE**

ProHance® is a nonionic contrast medium for magnetic resonance imaging (MRI), available as a 0.5M solution of gadoteridol in water for injection. ProHance contains 0.5 mmol/mL gadoteridol. Each mL of solution contains 0.5 mmol gadoteridol; 1.21 mg tromethamine, 0.02 mg sodium citrate, 0.007 mg calcium, 1.21 mg tromethamine and water for injection. ProHance contains no antimicrobial preservative.

ProHance has a pH of 6.5 to 8.0. Pertinent physicochemical data are noted below:

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality (mOsmol/kg water)</td>
<td>285</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>1.075</td>
</tr>
<tr>
<td>Density</td>
<td>1.075</td>
</tr>
</tbody>
</table>

ProHance has an osmolality 2.2 times that of plasma (285 mOsmol/kg water) and is hypertonic under conditions of use.

### CLINICAL PHARMACOLOGY

The pharmacokinetics of intravenously administered gadoteridol in normal subjects conforms to a two-compartment open model. The peak serum concentration of gadoteridol is approximately 700 mg/mL after administration as an intravenous bolus; 250 mg/mL after administration as a rapid intravenous infusion (10 mL/min-60 mL/min); and 100 mg/mL after administration as a slow intravenous infusion (0.1 mL/kg/min).

Gadoteridol is eliminated in the urine with 94.4 ± 4.8% (mean ± SD) of the dose excreted within 24 hours post-injection. It is unknown if biotransformation or decomposition of gadoteridol occurs.

**WARNING: 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 critical and no alternative is available. NSF is a rare but serious complication characterized by the systemic deposition of amorphous extracellular matrix causing fibrosis, typically involving skin, subcutaneous tissues, and deeper organs (e.g., heart, lungs, liver, and kidneys). The risk for NSF appears highest among patients with:

- Chronic, severe kidney disease (GFR < 30 mL/min/1.73 m²) and/or a history of interstitial nephritis or constrictive pericarditis.
- Multiple myeloma or other plasma cell dyscrasias.
- History of kidney transplantation.
- History of chronic kidney disease.
- History of prior NSF.

### DESCRIPTION

ProHance® (Gadoteridol) Injection, 279.3 mg/mL

**WARNINGS**

- Hypersensitivity Reactions: Anaphylaxis and other severe reactions have been reported with ProHance. Use ProHance with caution in patients with a history of drug-related allergy and in those with a history of sensitivity to other gadolinium-containing products.

- Renal Function: For patients with impaired renal function, ProHance dose adjustments according to kidney function may be necessary. ProHance is primarily cleared by the kidneys and is eliminated in the urine.

- Pregnancy: ProHance is Category B with respect to human risk. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, use ProHance during pregnancy only if clearly needed.

- Nursing Mothers: It is unknown if ProHance is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ProHance is administered to a nursing woman.

- Pediatric Use: Safety and efficacy for extracranial/extra-spinal tissues has not been established. Dose adjustments in renal and liver impairment have not been studied.

- Geriatric Use: Use of ProHance in elderly patients is not expected to have a different risk profile from that observed in younger adults.

**ADVERSE REACTIONS**

The most common adverse reactions reported with ProHance include injection site reactions, headache, nausea, and back pain. Other reported adverse reactions include flushing, rash, and angioedema. In isolated cases, mild elevations in liver enzymes have been observed with ProHance. Rare cases of anaphylaxis and other severe reactions have been reported with ProHance.

### CONTRAINDICATIONS

ProHance is indicated for patients with impaired renal function. ProHance is contraindicated for patients with impaired hepatic function.

### DOSAGE AND ADMINISTRATION

- IV injection

The recommended dose of ProHance is 0.1 mmol/kg (0.2 mL/kg) or bolus (> 0.2 mL/kg). The safety and efficacy of doses > 0.1 mmol/kg, and sequential and/or repeat procedures has not been studied.

### PRECAUTIONS

- Vascular Risk

ProHance should be infused only into large veins. Infusion should be given slowly and at a rate sufficient to complete the administration in 1 to 2 minutes.

- Hypersensitivity Reactions

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Use of ProHance in elderly patients is not expected to have a different risk profile from that observed in younger adults.

### CLINICAL TRIALS

ProHance was evaluated in two blinded read trials in a total of 133 adults who had an indication for head and neck imaging. The scans were read by two independent radiologists. The relevance of the findings to disease sensitivity and specificity has not been fully evaluated.

ProHance was evaluated in a multicenter clinical trial of 103 children who had an indication for head and neck imaging. The scans were read by two independent radiologists. The relevance of the findings to disease sensitivity and specificity has not been fully evaluated.

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Patients scheduled to receive ProHance should be instructed to avoid exposure to strong magnetic fields for 24 hours after drug administration. If a reaction occurs, stop ProHance and provide appropriate therapy including resuscitation. (See PRECAUTIONS - General).

Gadoteridol increases the risk for nephrogenic systemic fibrosis (NSF). Patients with impaired renal function should receive ProHance only when the potential benefit justifies the potential risk. Currently, the risk of NSF is greatest for patients with end-stage renal disease on hemodialysis, but cannot be excluded in patients with milder forms of renal impairment or normal renal function. (See WARNINGS - NSF).

Acute Kidney Injury (AKI) has been reported after GBCA administration (See WARNINGS - NSF).

There are rare reports of pathologic skin changes in patients with normal renal function. Adverse events involving skin including localized pruritus, erythema, rash, maculopapular rash, and other skin reactions have been reported in adult patients with normal renal function. Adverse events involving skin have been reported in pediatric patients with normal renal function. (See WARNINGS - Skin Reactions).
What is PROHANCE?
• PROHANCE is a prescription medicine called a gadolinium-based contrast agent (GBCA). PROHANCE, like other GBCAs, is used with a magnetic resonance imaging (MRI) scanner.
• An MRI exam with a GBCA, including PROHANCE, 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 PROHANCE?
• PROHANCE 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 PROHANCE.

Do not receive PROHANCE if you have had a severe allergic reaction to PROHANCE.

Before receiving PROHANCE, 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 PROHANCE can harm your unborn baby. Talk to your healthcare provider about the possible risks to an unborn baby if a GBCA such as PROHANCE 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 PROHANCE?
• See “What is the most important information I should know about PROHANCE?”
• Allergic reactions. PROHANCE 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 PROHANCE include: nausea, taste perversion, headache, feeling hot, or burning at the injection site.

These are not all the possible side effects of PROHANCE. 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 PROHANCE.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your healthcare provider for information about PROHANCE that is written for health professionals.

What are the ingredients in PROHANCE?
Active ingredient: gadoteridol
Inactive ingredients: calteridol calcium, tromethamine
Manufactured by: BIPSO GmbH-78224 Singen (Germany)
Manufactured for: Bracco Diagnostics Inc., Monroe Township, NJ 08831
US Patent No. 5,474,756; 5,846,519; and 6,143,274.
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

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