ProHance® (Gadoteridol) Injection, 279.3 mg/mL
and
ProHance® Multipack™ (Gadoteridol) Injection, 279.3 mg/mL

Indications and Usage:
CENTRAL NERVOUS SYSTEM
ProHance is indicated for use in MRI in adults and pediatric patients including term neonates to visualize lesions with disrupted blood-brain barrier and/or abnormal vascularity in the brain (intracranial lesions), spine, and associated tissues.

EXTRACRANIAL/EXTRASPINAL TISSUES
ProHance is indicated for use in MRI in adults to visualize lesions in the head and neck.

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. ProHance 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 systemic 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/1.73m^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, or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended ProHance dose and allow a sufficient period of time for elimination of the drug from the body prior to re-administration.**

CONTRAINDICATIONS
Contraindicated in patients with known allergic or hypersensitivity reactions to ProHance.

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

ProHance have not been established with intrathecal use and ProHance 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 administration and resolved with prompt emergency treatment. Prior to ProHance administration, ensure the availability of trained personnel and medications to treat hypersensitivity reactions. Consider these risks, 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. Linear GBCAs cause more retention than 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.

Acute Kidney Injury: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.

ADVERSE REACTIONS

The most commonly reported adverse reactions are nausea and taste perversion with an incidence ≥ 0.9%.

POST-MARKETING EVENTS

The following adverse reactions have been identified during post approval use of Prohance 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 are no data on the presence in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.

Pediatric Use: The safety and effectiveness of ProHance have been established for use with MRI 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 17 years of age. Adverse

reactions in pediatric patients were similar to those reported in adults. No case of NSF associated with ProHance or any other GBCA has been identified in pediatric patients ages 6 years and younger.

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 full Prescribing Information and Patient Medication Guide for additional safety information for ProHance (Gadoteridol) Injection, 279.3 mg/mL.

Please click here for full Prescribing Information and Patient Medication Guide for additional safety information for ProHance Multipack.

ProHance is manufactured for Bracco Diagnostics Inc. by BIPSO GmbH – 78224 Singen (Germany).

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