FRESENIUS KABI

FDA-approved, cost-effective generic

Gadolinium-Based Contrast Agents

Providing you with two MRI contrast options so you may choose what's right for you and your patients.

Now you have a choice.

Please see Indications and Important Safety Information including Boxed Warning on the following pages.

Gadobutrol Injection

- **FDA-approved, AP Rated**
- **High Relaxivity[1,2]**
- **Macrocyclic Bond[1,2]**
- **High Concentration GBCA[1,2]**
- **Preservative Free[1,2]**
- **The container closure is not made with natural rubber latex**
- **Bioequivalent and fully substitutable to Gadavist®***

Unit of Sale NDC	Description	Concentration	Fill Volume (mL)	Unit of Sale
65219-281-02	Single Dose Vial	1 mmol per mL	2 mL	15
65219-281-07	Single Dose Vial	1 mmol per mL	7.5 mL	20
65219-281-10	Single Dose Vial	1 mmol per mL	10 mL	20
65219-281-15	Single Dose Vial	1 mmol per mL	15 mL	20
65219-287-30	Imaging Bulk Package	1 mmol per mL	30 mL	10
65219-289-65	Imaging Bulk Package	1 mmol per mL	65 mL	10

1. Gadobutrol Injection Single Dose Vial Package Insert, September 2024
2. Gadobutrol Injection Imaging Bulk Package Insert, September 2024

*Gadavist® is a registered trademark of Bayer.

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. Gadobutrol injection is not approved for intrathecal use.

Nephrogenic Systemic Fibrosis

GBCAs increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of gadobutrol injection 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/1.73m^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 (for example, 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 gadobutrol injection dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications: Gadobutrol Injection is contraindicated in patients with history of severe hypersensitivity reaction to Gadobutrol Injection.

Hypersensitivity Reactions: Anaphylactic and other hypersensitivity reactions with cardiovascular, respiratory, or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following Gadobutrol Injection administration. Before Gadobutrol Injection administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Gadobutrol Injection. Administer Gadobutrol Injection only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.

Gadolinium Retention: Gadolinium is retained for months or years in brain, bone, and other organs. Linear GBCAs cause more retention than macrocyclic GBCAs. 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. While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent and minimize repetitive GBCA studies, when possible.

Acute Kidney Injury: In patients with chronic renal impairment, acute kidney injury sometimes requiring dialysis has been observed with the use of GBCAs. Do not exceed the recommended dose; the risk of acute kidney injury may increase with higher than recommended doses.

Extravasation and Injection Site Reactions: Ensure catheter and venous patency before the injection of Gadobutrol Injection. Extravasation into tissues during Gadobutrol Injection administration may result in moderate irritation.

Overestimation of Extent of Malignant Disease in MRI of the Breast: Gadobutrol Injection MRI of the breast overestimated the histologically confirmed extent of malignancy in the diseased breast in up to 50% of the patients.

Low Sensitivity for Significant Arterial Stenosis: The performance of Gadobutrol Injection MRA for detecting arterial segments with significant stenosis (>50% renal, >70% supra-aortic) has not been shown to exceed 55%. Therefore, a negative MRA study alone should not be used to rule out significant stenosis.

Adverse Events: The most frequent (≥ 0.5%) adverse reactions associated with Gadobutrol Injection in clinical studies were headache (1.7%), nausea (1.2%) and dizziness (0.5%).

The following additional adverse reactions have been reported during postmarketing use of Gadobutrol Injection: Cardiac Arrest; Nephrogenic Systemic Fibrosis (NSF); Hypersensitivity reactions (anaphylactic shock, circulatory collapse, respiratory arrest, pulmonary edema, bronchospasm, cyanosis, oropharyngeal swelling, laryngeal edema, blood pressure increased, chest pain, angioedema, conjunctivitis, hyperhidrosis, cough, sneezing, burning sensation, and pallor); General Disorders and Administration Site Conditions: fatigue, asthenia, pain syndromes, and heterogeneous clusters of symptoms in the neurological, cutaneous, and musculoskeletal systems; Skin: Gadolinium associated plaques, Gastrointestinal Disorders: Acute pancreatitis with onset within 48 hours after GBCA administration.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Pregnancy: GBCAs cross the placenta and result in fetal exposure and gadolinium retention. Because of the potential risks of gadolinium to the fetus, use Gadobutrol Injection only if imaging is essential during pregnancy and cannot be delayed.

INDICATIONS AND USAGE

Gadobutrol Injection is a gadolinium-based contrast agent indicated for use with magnetic resonance imaging (MRI):

- To detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system in adult and pediatric patients, including term neonates.
- To assess the presence and extent of malignant breast disease in adult patients.
- To assess myocardial perfusion (stress, rest) and late gadolinium enhancement in adult patients with known or suspected coronary artery disease (CAD).

Gadobutrol Injection is indicated for use in magnetic resonance angiography (MRA):

- To evaluate known or suspected supra-aortic or renal artery disease in adult and pediatric patients, including term neonates.

This Important Safety Information does not include all the information needed to use Gadobutrol Injection safely and effectively. Please see accompanying full prescribing information, including BOXED WARNING, for Gadobutrol Injection Single Dose Vials and Imaging Bulk Package. Full prescribing information is also available at www.fresenius-kabi.com/us.

Gadoterate Meglumine Injection, USP

- **FDA-approved, AP Rated**
- **Macrocyclic[3,4]**
- **Ionic[3,4]**
- **Preservative Free[3,4]**
- **The container closure is not made with natural rubber latex**
- **Bioequivalent and fully substitutable to Dotarem®***

Unit of Sale NDC	Description	Concentration	Fill Volume (mL)	Unit of Sale
65219-080-05	Single Dose Vial	0.5 mmol per mL	5 mL	10
65219-082-10	Single Dose Vial	0.5 mmol per mL	10 mL	10
65219-084-15	Single Dose Vial	0.5 mmol per mL	15 mL	10
65219-086-20	Single Dose Vial	0.5 mmol per mL	20 mL	10
65219-088-50	Pharmacy Bulk Package	0.5 mmol per mL	100 mL	6

3. Gadoterate Meglumine Injection, USP Single Dose Vial Package Insert, August 2024
4. Gadoterate Meglumine Injection, USP Pharmacy Bulk Package Insert, August 2024
*Dotarem® is a registered trademark of Guerbet.

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. Gadoterate Meglumine Injection is not approved for intrathecal use.

Nephrogenic Systemic Fibrosis
GBCAs increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of Gadoterate Meglumine Injection 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/1.73m^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, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended Gadoterate Meglumine Injection dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications
Gadoterate Meglumine Injection is contraindicated in patients with history of clinically important hypersensitivity reactions to Gadoterate Meglumine Injection.

Warning 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 Gadoterate Meglumine Injection have not been established with intrathecal use. Gadoterate Meglumine Injection is not approved for intrathecal use.

Nephrogenic Systemic Fibrosis: GBCAs increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of Gadoterate Meglumine Injection among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities.

Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported with Gadoterate Meglumine Injection, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. Monitor patients closely for need of emergency cardiorespiratory support.

Before Gadoterate Meglumine Injection administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Gadoterate Meglumine Injection.

Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by other organs (e.g. brain, skin, kidney, liver and spleen). While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.

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.

Extravasation and Injection Site Reactions: Ensure catheter and venous patency before the injection of Gadoterate Meglumine Injection. Extravasation into tissues during Gadoterate Meglumine Injection administration may result in tissue irritation.

Adverse Reactions
The most frequent (≥ 0.2%) adverse reactions in clinical studies were nausea, headache, injection site pain, injection site coldness, and rash.

Serious adverse reactions in the Postmarketing experience have been reported with Gadoterate Meglumine Injection. These serious adverse reactions include but are not limited to arrhythmia, cardiac arrest, respiratory arrest, pharyngeal edema, laryngospasm, bronchospasm, coma, convulsion, and acute pancreatitis with onset within 48 hours after GBCA administration.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176, option 5, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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 of gadoterate 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 of Gadoterate Meglumine Injection has not been established in preterm neonates. No dosage adjustment according to age is necessary in pediatric patients.

Geriatric Use: Use of Gadoterate Meglumine Injection in elderly patients should be cautious, reflecting the greater frequency of impaired renal function and concomitant disease or other drug therapy. No age-related dosage adjustment is necessary.

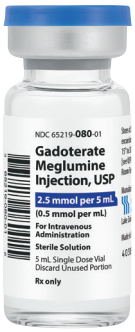
Renal Impairment: No dosage adjustment is recommended for patients with renal impairment

INDICATIONS AND USAGE
Gadoterate Meglumine Injection is a prescription gadolinium-based contrast agent indicated for intravenous use with magnetic resonance imaging (MRI) in brain (intracranial), spine and associated tissues in adult and pediatric patients (including term neonates) to detect and visualize areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

This Important Safety Information does not include all the information needed to use Gadoterate Meglumine Injection, USP safely and effectively. Please see full prescribing information, including BOXED WARNING, for Gadoterate Meglumine Injection, USP Single Dose Vials and Pharmacy Bulk Package Vials at www.fresenius-kabi.com/us.

To learn more about our **Gadolinium-Based Contrast Agents Portfolio,** please visit **GenericContrastAgents.com.**

Gadobutrol Injection



Gadoterate Meglumine Injection, USP

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- **For patients at highest risk for NSF, do not exceed the recommended gadobutrol injection dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Please see additional Important Safety Information inside.

IMPORTANT SAFETY INFORMATION

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Please see additional Important Safety Information inside.

A Cost-Effective Option from an Experienced, Reliable Supplier

Committed to Helping You

Our commitment is to provide you with choice and value — by continuing to grow our portfolio of cost-effective, high-quality generic contrast agents.

Fresenius Kabi is a global healthcare company that specializes in lifesaving medicines and technologies for infusion, transfusion and clinical nutrition – with a comprehensive portfolio of injectable drugs and delivery systems used to treat a broad spectrum of patients. As a leading provider of generic medications, we leverage our 100-year history to deliver innovative therapies that are safe, effective and affordable. **That's how Fresenius Kabi brings confidence within reach.**

Ordering Information

Please contact your account representative or our Customer Service Department Monday through Friday, 7:00AM – 6:00PM (CST) at:

Toll-Free: (888) 386-1300
Fax: (800) 743-7082
E-mail: customerservice.usa@fresenius-kabi.com
For more information visit: GenericContrastAgents.com

FRESENIUS KABI

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