August 15th, 2018

Dear Valued Customer:

Thank you for your continued patience over the last several months as we have worked to resolve our contrast supply interruption. The purpose of this letter is to provide you with an update to ensure that you have the latest information in order for you to continue to meet your contrast supply needs.

Since January, we have been actively working to increase production, while meeting our high quality manufacturing standards. While there may be some lag time in full product availability, we are pleased to communicate that we will not experience any wide-spread out of stock situations on our most widely used MRI (Magnetic Resonance Imaging) contrast, Gadavist® (gadobutrol) presentations (Gadavist 7.5mL and Gadavist 10mL vials) throughout the remainder of 2018.

As we work to continue to re-stock distribution channels, we may experience varying levels of supply across other Gadavist presentations until the end of the year (other than the 7.5 mL and 10 mL presentations as noted above). Note, these are short-term and temporary. If you are unable to order a certain presentation alternative presentations will be available.

Overview of current supply interruption:

- We are now lifting the maximum order on the following Gadavist presentations, including (**Vials-** 2 mL, 7.5mL, 10mL, **Pharmacy Bulk Pack-** 30 mL, 65 mL.). The Gadavist pre filled syringes and 15 mL vial continue to have a maximum order and we will continue to evaluate increasing ordering capacity on these presentations.
- The release of certain Magnevist (gadopentetate dimeglumine) injection presentations were delayed which caused a short-term supply interruption, which has now been resolved.

We are taking additional steps to increase production capacity across our product lines, including expanding and investing in the production facility where our contrast agents are produced to keep pace with the growing demand for our MRI agents. We are confident that this will enable us to meet increasing customer demands for Gadavist®.

We appreciate your trust and loyalty, and Bayer remains committed to working with you during the supply challenge to minimize any disruption. All customers are encouraged to continue to place orders and work with their wholesalers and Bayer Sales Representative. You may also contact customer support at 1-877-259-4624, or contact us at contrastcustomersupport@bayer.com. When emailing us, please provide a contact telephone number and the best time to reach you and someone from our Support Team will be in contact with you.

Please see Important Safety Information, including Boxed Warnings for Gadavist and Magnevist below.

Best regards,
Rich Dewit
Head, US Sales & Marketing

INDICATIONS AND IMPORTANT SAFETY INFORMATION
INDICATIONS AND USAGE: GADAVIST® (gadobutrol) Injection

Gadavist® (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 (BBB) 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

Gadavist® 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)

Please see the Important Safety Information on the following pages.

IMPORTANT SAFETY INFORMATION: GADAVIST®

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

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 of 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 GADAVIST dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.

Contraindication and Important Information about Hypersensitivity Reactions: Gadavist® is contraindicated in patients with history of severe hypersensitivity reactions to Gadavist®. Anaphylactic and other hypersensitivity reactions with cardiovascular, respiratory, or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following Gadavist® administration. Before Gadavist® 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 Gadavist®.

Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (for example, brain, skin, kidney, liver, and spleen). The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, gadolinium 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. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function. There are rare reports of pathologic skin changes in patients with normal renal function. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention.

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 when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies particularly closely spaced 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 some 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 Gadavist®. Extravasation into tissues during Gadavist® administration may result in moderate irritation.

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

Please see additional Important Safety Information on the previous and following pages.

IMPORTANT SAFETY INFORMATION: GADAVIST® (continued)

Low Sensitivity for Significant Arterial Stenosis: The performance of Gadavist® 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 Reactions: The most frequent (≥0.5%) adverse reactions associated with Gadavist® in clinical studies were headache (1.5%), nausea (1.1%) and dizziness (0.5%).

Please see additional Important Safety Information on the previous and following pages.
Please see the Gadavist® Full Prescribing Information (Vials and Syringes).
Please see the Gadavist® Full Prescribing Information (Pharmacy Bulk Packages).

INDICATIONS AND USAGE: MAGNEVIST® (gadopentetate dimeglumine) Injection

Central Nervous System: Magnevist® (gadopentetate dimeglumine) injection is indicated for the use with magnetic resonance imaging (MRI) in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the brain (intracranial lesions), spine and associated tissues. Magnevist® has been shown to facilitate visualization of intracranial lesions including but not limited to tumors.

Extracranial/Extraspinal Tissues: Magnevist® is indicated for use with MRI in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the head and neck.

Body: Magnevist® is indicated for use with MRI in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the body (excluding the heart).

IMPORTANT SAFETY INFORMATION: MAGNEVIST®

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

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.

- Do not administer MAGNEVIST to 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.

Do not exceed the recommended MAGNEVIST dose and allow a sufficient period of time for elimination of the drug from the body prior to re-administration.

Contraindications: Magnevist® is contraindicated in patients with:

- Chronic, severe kidney disease (glomerular filtration rate, GFR <30 mL/min/1.73m^2), or
- Acute kidney injury, or
- History of severe hypersensitivity reactions to Magnevist®.

Please see additional Important Safety Information on the previous and following pages.

IMPORTANT SAFETY INFORMATION: MAGNEVIST® (continued)

Hypersensitivity Reactions: Anaphylactoid and anaphylactic reactions with cardiovascular, respiratory and/or cutaneous manifestations rarely resulting in death have occurred. The risk of hypersensitivity reactions is higher in patients with a history of reaction to contrast media, bronchial asthma, or allergic disorders. Hypersensitivity reactions can occur with or without prior exposure to GBCAs.

Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (for example, brain, skin, kidney, liver, and spleen). The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, gadolinium 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. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function. There are rare reports of pathologic skin changes in patients with normal renal function. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention.

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 when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies particularly closely spaced studies, when possible.

Renal Failure: In patients with renal impairment, acute renal failure (acute kidney injury) requiring dialysis or worsening renal function has occurred, mostly within 48 hours of Magnevist® Injection. The risk of acute renal failure is higher with increasing dose of contrast. Use the lowest possible dose, evaluate renal function in patients with renal impairment, and allow sufficient time for contrast elimination before re-administration. Elimination half-life in patients with mild or moderate renal impairment is 3 to 4 hours. Elimination half-life in patients with severe renal impairment is about 11 hours. Magnevist® is cleared by glomerular filtration and is dialyzable. After 3 dialysis sessions of 3 hours each, about 97% of the administered dose is eliminated from the body; each dialysis session removes about 70% of the circulating drug.

Injection Site Reaction: Skin and soft tissue necrosis, thrombosis, fasciitis, and compartment syndrome requiring surgical intervention (e.g., compartment release or amputation) have occurred very rarely at the site of the contrast injection or the dosed limb. Total volume and rate of Magnevist® Injection, extravasation of contrast agent, and patient susceptibility might contribute to these reactions. Phlebitis and thrombophlebitis may be observed generally within 24 hours after Magnevist® Injection and resolve with supportive treatment. Determine the patency and integrity of the intravenous line before administration of Magnevist® Injection. Assessment of the dosed limb for the development of injection site reactions is recommended.

Interference with Visualization of Lesions with Non-Contrast MRI: As with any paramagnetic contrast agent, Magnevist® Injection might impair the visualization of lesions seen on non-contrast MRI. Therefore, caution should be exercised when Magnevist® MRI scans are interpreted without a companion non-contrast MRI scan.

Please see additional Important Safety Information on the previous and following pages.

IMPORTANT SAFETY INFORMATION: MAGNEVIST® (continued)

Adverse Reactions: In clinical trials, the most frequently reported adverse reactions (≥1%) included headache (4.8%), nausea (2.7%), injection site coldness/localized coldness (2.3%) and dizziness (1%).

Please see additional Important Safety Information on the previous pages.
Please see the Magnevist® Full Prescribing Information (Vials and Syringes).
Please see the Magnevist® Full Prescribing Information (Pharmacy Bulk Packages).

Bayer HealthCare LLC, 100 Bayer Boulevard, PO Box 915, Whippany, NJ 07981

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