October, 2019

Dear Customer:

As a valued partner, we want to inform you that Bayer will no longer be providing Magnevist® (gadopentetate dimeglumine) injection to the U.S. marketplace effective September 2019. This decision is in direct response to evolving market trends, which show continued growth in the use of macrocyclic gadolinium-based contrast agents (GBCAs) and a continued decline in the overall use of linear GBCAs, including Magnevist. To ensure no disruption in patient care, we will be working with our Magnevist customers to help facilitate a transition to Gadavist® (gadobutrol) injection, as appropriate to meet their patient needs.

This decision will allow Bayer to focus its efforts and resources on innovation in our Radiology Portfolio, including new indications and products that advance diagnostic imaging across disease states. **Please note, the decision by Bayer to end commercialization of Magnevist in the U.S. is not a result of safety or effectiveness concerns regarding Magnevist.** Over the past few years, market share and worldwide use of Gadavist have continued to rise and we remain committed to investing in Gadavist and its use across diagnostic therapeutic areas.

We encourage you to speak to your Bayer Sales Representative to discuss how the use of Gadavist can meet your contrast needs, along with determining how to implement Gadavist into your Radiology practice. Gadavist is a 1.0 molar, macrocyclic, high relaxivity GBCA approved for multiple indications.

CNS Indication
Gadavist is indicated for use with magnetic resonance imaging (MRI) in adult and pediatric patients including term neonates to detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system.

Breast Indication
The first and only GBCA indicated for breast MRI (BMR), Gadavist is approved for use with MRI to assess the presence and extent of malignant breast disease in adult patients.

Cardiac Indication
The first and only GBCA indicated for Cardiac Magnetic Resonance Imaging . Gadavist is approved for use in Cardiac MRI to assess myocardial perfusion (stress, rest) and late gadolinium enhancement in adult patients with known or suspected coronary artery disease (CAD).

MRA Indication
The first and only GBCA indicated for magnetic resonance angiography (MRA) of the supra-aortic vasculature, Gadavist is approved for use in MRA to evaluate known or suspected supra-aortic or renal artery disease in adult and pediatric patients including term neonates.

In addition, Gadavist is available in a wide range of presentations to support your patient procedures.

Click here to visit Gadavist.com and view the presentation chart in the Packaging section of the site.

We want to thank you for your support of Magnevist and Bayer through the past years. As a long-time partner in providing your MRI contrast-enhancement needs, we value the trust you have in our products and we want to reinforce our ongoing commitment as we work with you to evolve to the latest in GBCA technology.

Best regards,
Rich Dewit
Head, U.S. Sales & Marketing

Important Safety Information for 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.

Please see additional important safety information for Magnevist®.

Important Safety Information for Gadavist®

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- 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.

Please see additional important safety information for Gadavist®.

INDICATIONS and IMPORTANT SAFETY INFORMATION
Magnevist® (gadopentetate dimeglumine)

INDICATIONS AND USAGE

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

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

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- 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®.

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. 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.

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.

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 Full Prescribing Information for Magnevist® (Vials and Syringes).
Please see Full Prescribing Information for Magnevist® (Pharmacy Bulk Package).

INDICATIONS and IMPORTANT SAFETY INFORMATION
Gadavist® (gadobutrol)

INDICATIONS AND USAGE

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 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).

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

IMPORTANT SAFETY INFORMATION

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. 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 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.

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 (1.7%), nausea (1.2%) and dizziness (0.5%).

Please see Full Prescribing Information for Gadavist® (Vials and Syringes).
Please see Full Prescribing Information for Gadavist® (Pharmacy Bulk Package).

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You are encouraged to report negative side effects or quality complaints of prescription drugs to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.