ASD Healthcare
AmerisourceBergen

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October 4, 2019

Important: Magnevist® (gadopentetate dimeglumine) injection is no longer FDA-approved in the U.S. marketplace and is being withdrawn at the wholesale level

As of September 15, 2019, Bayer will no longer be providing Magnevist® (gadopentetate dimeglumine) injection to the US marketplace. Once the product is delisted from the FDA Orange Book (Orange Book: Approved Drug Product List), the product will no longer legally be able to be sold and distributed in the U.S., as it will not be a FDA-approved product.

Please note, product that was distributed to the market (hospitals and health systems, imaging centers) before the delisted date is still able to be administered to patients. There is no safety concern with the product. Any product sold or distributed after the end of sale date (September 15, 2019) will not be in accordance with FDA guidelines.

This decision to withdraw the product 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. This will also allow Bayer to focus its efforts and resources on innovation in their Radiology Portfolio, including new indications and products that advance diagnostic imaging across disease states.

For the full Bayer notice, including Important Safety Information and Boxed Warning, please view the attached document on the following pages.

July 2019

Dear Wholesaler:

As previously communicated, Bayer will no longer be providing Magnevist® (gadopentetate dimeglumine) **injection to the US marketplace (estimated end of sale - September 15, 2019). Once the product is delisted from the FDA Orange Book (*Orange Book: Approved Drug Product List)*, the product is no longer legally able to be sold and distributed in the U.S., as it will not be a FDA-approved product.**

Please note: Product that was distributed to the market (hospitals and health systems, imaging centers) before the delisted date is still able to be administered to patients. There is no safety concern with the product. Any product sold or distributed after the end of sale date will not be in accordance with FDA guidelines.

The last day to place orders for the Magnevist product line for wholesalers will be August 16, 2019. As part of this announcement, we will be initiating a buy-back program to our Wholesaler partners to return their remaining Magnevist they have in inventory after September 15, 2019. Wholesalers who return product by October 31, 2019 will be reimbursed at the current WAC price. No Magnevist return reimbursement will be issued after October 31, 2019. If you have any questions regarding the process please contact McKesson Customer Care at 1-877-259-4624.

This decision to withdraw the product 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 for their contrast agent 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. We look forward to continuing to serve your contrast needs.

Please see the Important Safety Information, including Boxed Warning, for Magnevist® below.

Best regards,
Rich Dewit
Head, Sales Execution, Marketing

INDICATIONS AND IMPORTANT SAFETY INFORMATION
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).

Please see the Important Safety Information on the following pages.

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®.

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.

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

IMPORTANT SAFETY INFORMATION: MAGNEVIST® (continued)

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 additional Important Safety Information on the previous pages.

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

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

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.