



IMPORTANT DRUG WARNING

Important Drug Warning for All Gadolinium-Based Contrast Agents

Dotarem[®] (gadoterate meglumine) injection
Eovist[®] (gadoxetate disodium) injection
Gadavist[®] (gadobutrol) injection
Magnevist[®] (gadopentetate dimeglumine) injection
MultiHance[®] (gadobenate dimeglumine) injection
Omniscan[™] (gadodiamide) injection
Optimark[®] (gadoversetamide) injection
ProHance[®] (gadoteridol) injection

**Subject: Gadolinium from gadolinium-based contrast agents (GBCAs) may remain in the body for months to years after injection;
New class warning, patient counseling, and a medication guide**

Dear Health Care Provider:

This letter informs you of important updates to the prescribing information for all the gadolinium-based contrast agents (GBCAs) listed above. GBCAs are approved by the U.S. Food and Drug Administration (FDA) for use in magnetic resonance imaging (MRI). New information about gadolinium retention is provided in the *Warnings and Precautions, Adverse Reactions, Pregnancy, Clinical Pharmacology and Patient Counseling* sections; a medication guide has been added.

New Class Warning

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 (e.g. 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 with Omniscan (gadodiamide) and Optimark (gadoversetamide) causing greater retention than other linear agents [Eovist (gadoxetate disodium), Magnevist (gadopentetate dimeglumine), MultiHance (gadobenate dimeglumine)]. Retention is lowest and similar among the macrocyclic GBCAs [Dotarem (gadoterate meglumine), Gadavist (gadobutrol), ProHance (gadoteridol)].

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 [see Warnings and Precautions]. 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 [see Adverse Reactions].

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.

Prescriber/Dispenser Actions

- Provide the medication guide the first time an outpatient receives a GBCA. The medication guide need not be provided to an inpatient unless requested by the patient or caregiver. A healthcare practitioner can determine that it is not in a particular patient's best interest to receive a medication guide because of significant concerns about the effect of a medication guide. The GBCA manufacturers will contact you with their plans to provide you with the medication guides for distribution.
- Advise patients that gadolinium is retained for months or years in brain, bone, skin, and other organs in patients with normal renal function. The clinical consequences of retention are unknown. Retention is greater following administration of linear GBCAs than following administration of macrocyclic GBCAs.

Reporting Adverse Events

Health care providers and patients are encouraged to report adverse events in patients receiving GBCAs to the respective manufacturer of the suspected GBCA at the phone number listed below. Alternatively, visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

GBCA	Prescribing information*	Manufacturer	Phone
Eovist	www.eovist.com	Bayer HealthCare Pharmaceuticals Inc.	1-888-842-2937
Gadavist	www.gadavist.com		
Magnevist	www.magnevist.com		
MultiHance	https://imaging.bracco.com/us-en/products/magnetic-resonance-imaging/multihance	Bracco Diagnostics Inc.	1-800-257-5181
ProHance	https://imaging.bracco.com/us-en/products/magnetic-resonance-imaging/prohance		
Omniscan	http://www3.gehealthcare.com/en/products/categories/contrast_media/omniscan	GE Healthcare	1-800-654-0118
Dotarem	http://www.guerbet-us.com/products.html	Guerbet LLC	1-877-729-6679
Optimark	http://www.guerbet-us.com/products.html	Guerbet/Liebel-Flarsheim Company LLC	1-877-729-6679

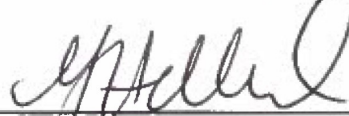
*See the web links above for full prescribing information and medication guide for each GBCA.

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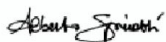
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