Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Dear Healthcare Professional

Gadolinium contrast agents and risk of tissue accumulation—removal of Omniscan and intravenous Magnevist from February; restrictions to use of other linear agents

With effect from 1 February 2018 the following gadolinium-containing contrast agents will no longer be licensed and any remaining stock will be recalled from the market:

Product Licence (PL) number	Active agent	Product name	Marketing authorisation holder (MAH)	Pharmaceutical form
PL 00637/0015	Gadodiamide	Omniscan injection 0.5 mmol/mL (287 mg/mL)	GE Healthcare AS	Solution for intravenous injection
PL 00637/0030	Gadodiamide	Omniscan 0.5mmol/mL solution for injection	GE Healthcare AS	Solution for intravenous injection
PL 00010/0542	Gadopentetic acid*	Magnevist injection	Bayer PLC	Solution for intravenous injection
PL 00010/0543	Gadopentetic acid*	Magnevist injection	Bayer PLC	Solution for intravenous injection
PL 19206/0004	Gadopentetic acid*	Magnetolux 500 micromol/mL solution for injection	Sanochemia Pharmazeutika AG	Solution for intravenous injection

*also known as gadopentetate dimeglumine

Summary

- There is evidence that gadolinium can be retained in the brain and in other organs after administration of gadolinium-containing contrast agents (GdCAs). Linear GdCAs are associated with higher retention of gadolinium in the brain than macrocyclic GdCAs

- The licences for gadodiamide (Omniscan) and intravenous gadopentetic acid (also known as gadopentetate dimeglumine, Magnevist) will be suspended as of 1 February 2018

- The authorised indication of the linear agents gadobenic acid (also known as gadobenate dimeglumine, MultiHance) and gadoxetic acid (Primovist) will be limited to delayed phase liver imaging only

- Macrocyclic agents, gadoteridol (Prohance), gadobutrol (Gadovist) and gadoteric acid (Dotarem, Clariscan, Dotagraf, Cyclolux) will remain authorised, as will gadopentetic acid for intra-articular use

- Healthcare professionals are advised to replace any use of gadodiamide (Omniscan) and intravenous gadopentetic acid (Magnevist) with suitable alternative GdCAs by 1 February 2018

- Use GdCAs only when diagnostic information is essential and not available with unenhanced magnetic resonance imaging (MRI); do not exceed the recommended dose per kilogram of body weight and use the lowest dose that is effective for diagnosis

Background

Gadolinium-containing contrast agents (GdCAs) are indicated for the enhancement of magnetic resonance imaging (MRI). GdCAs contain gadolinium bound to a ligand molecule and can be divided into two groups based on their chemical structure — linear GdCAs and macrocyclic GdCAs.

A European-level scientific review of gadolinium retention in the brain and other tissues has now completed. Gadolinium deposition in the brain has been confirmed by mass spectrometry and studies of MRI data. Data on stability, as well as in-vitro and non-clinical studies, show that macrocyclic agents have a significantly lower potential to cause retention of gadolinium in the body. This is because they are more stable and do not release gadolinium to any significant extent from the ligand molecule.

Linear GdCAs are already known to have a higher risk than macrocyclic agents of causing nephrogenic systemic fibrosis (NSF) in patients with impaired renal function. In view of the evidence of retention of gadolinium in brain and other tissues following exposure to these agents, the risks of linear agents gadodiamide and gadopentetic acid for intravenous use outweigh their benefits.

There is currently no evidence that gadolinium deposition in the brain has caused adverse neurological effects in patients; however, data on long-term effects of gadolinium deposition in brain, or other tissues, are very limited.

Please continue to report suspected adverse drug reactions to the MHRA through the Yellow Card Scheme: https://yellowcard.mhra.gov.uk/

Yours faithfully,

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