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(IN REPLY PLEASE QUOTE THIS FILE REF.)

27 Jun 2025

Dear Healthcare Professionals,

Gadolinium-based Contrast Agents: Assessing the potential risk of serious adverse reactions, including seizures, encephalopathy, coma and death, with intrathecal use

Your attention is drawn to the following Health Canada's announcement.

Product

Gadolinium-based contrast agents (Dotarem [gadoterate meglumine], Gadovist 1.0 [gadobutrol], Magnevist [gadopentetate dimeglumine], MultiHance [gadobenate dimeglumine], Omniscan [gadodiamide], Primovist [gadoxetate disodium] and ProHance [gadoteridol]) (GBCAs)

Potential Safety Issue

Serious adverse reactions, including seizures, encephalopathy (brain dysfunction), coma and death, with intrathecal (injection into the spinal canal) use

Key Messages

- Health Canada's review found a possible link between the intrathecal use of GBCAs and serious adverse reactions, including seizures, encephalopathy, coma and death.
- Health Canada is working with manufacturers to update the product safety information in the Canadian product monograph (CPM) for all GBCAs to include the risk of serious adverse reactions, including seizures, encephalopathy, coma and death, with off label intrathecal use.

Overview

Health Canada reviewed the potential risk of serious adverse reactions, including seizures, encephalopathy, coma and death with the intrathecal use of GBCAs. The safety review was triggered by a labelling update in the United States for all GBCAs.

Gadolinium-based contrast agents are not authorized in Canada for intrathecal use. However, Health Canada is aware that they have been used off-label for this route of administration.

Use in Canada

- Gadolinium-based contrast agents are authorized for use in magnetic resonance imaging (MRI) to make it easier to view certain body tissues and to help with the diagnosis of various conditions. They are authorized to be given into a vein (intravenously).
- Gadolinium-based contrast agents have been marketed in Canada for over 30 years. There are 7 GBCAs currently marketed under the following brand names: Dotarem, Gadovist 1.0, Magnevist, MultiHance, Omniscan, Primovist and ProHance. A generic version of Gadovist 1.0 is also available.
- From 2019 to 2024, approximately 2.5 million patients in Canada were given GBCAs. However, information on intrathecal usage is not available.

Safety Review Findings

- Health Canada reviewed the available information from the Canada Vigilance database, the scientific literature, and clinical experts.
- Health Canada reviewed 22 cases (1 Canadian and 21 international) of serious adverse reactions, including seizures, encephalopathy, coma and death, in patients who were administered GBCAs intrathecally. Of the 22 cases, 18 (1 Canadian and 17 international) were found to be possibly linked, including 11 from the published literature. The remaining 4 cases could not be assessed due to missing clinical information.
- The dose given was reported in 15 of the 18 cases that were possibly linked to the intrathecal use of GCBAs, and ranged from 1.5 mmol to 12 mmol (median dose 3 mmol).
- All 18 cases that were possibly linked to the intrathecal use of GCBAs involved adult patients. In 17 (1 Canadian) of those cases, the patients recovered or were recovering. A death occurred in the remaining case.
- Health Canada also reviewed the findings from 28 published studies. There were no reports of seizures, encephalopathy, coma or death in patients administered GBCAs intrathecally.

Conclusions and Actions

- Health Canada's review of the available information found a possible link between the intrathecal use of GBCAs and serious adverse reactions, including seizures, encephalopathy, coma and death.
- Health Canada is working with manufacturers to update the CPM for all GBCAs to include the risk of serious adverse reactions, including seizures, encephalopathy, coma and death, with off label intrathecal use.
- Health Canada will continue to monitor safety information involving GBCAs, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should new health risks be identified.

Please refer to the following website in Health Canada for details:
https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SSR1747762855840

In Hong Kong, there are registered pharmaceutical products which belong to gadolinium-based contrast agents containing meglumine gadoterate (10 products), gadobutrol (2 products), gadobenic acid (as meglumine gadobenate or gadobenate dimeglumine) (1 product), sodium gadoxetate (gadoxetate disodium) (1 product). All products are prescription-only medicines and are indicated for intravenous administration only.

So far, according to available information, the Department of Health (DH) has not received case of adverse drug reaction with regard to intrathecal use of the above gadolinium-based contrast agents. In light of the above Health Canada's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Vincent CHIANG)
for Assistant Director (Drug)