

Important Safety Information on Iodinated Contrast Media- Potential Risk of Hypothyroidism



Guerbet | A small graphic consisting of a vertical line followed by a 3x3 grid of squares, with the bottom-right square colored orange.

2017/04/24

Audience

Healthcare professionals (radiologists, general internists, endocrinologists, pediatricians, neonatologists, family physicians) and radiology departments / clinics

Key messages

- **Rare cases of hypothyroidism following Iodinated Contrast Media (ICM) exposure have been reported, particularly in term and preterm infants.**
- **Hypothyroidism in infants may be harmful for growth and development, including mental development.**
- **Healthcare professionals are encouraged to evaluate and monitor thyroid function in infants exposed to ICM, and if abnormal, continue to monitor until it has normalized.**
- **Health Canada is currently working with the ICM manufacturers to update and harmonize the prescribing information for all ICM products to include this safety information.**

What is the issue?

There have been rare cases of hypothyroidism in patients, particularly term and preterm infants, exposed to ICM reported internationally. No Canadian cases of hypothyroidism related to ICM exposure have been identified to date.

Products affected

Product	Medicinal Ingredient	Company
Gastrografin - LIQ ORL	Diatrizoate Meglumine and Diatrizoate Sodium Solution	Bracco Imaging Canada

Product	Medicinal Ingredient	Company
Sinografin LIQ IU	Diatrizoate Meglumine and Iodipamide Meglumine Injection	Bracco Imaging Canada
Isovue 200, 300, 370 Injection / Isovue Multipack -300, 370	Iopamidol Injection	Bracco Imaging Canada
Cholografin Meglumine INJ.-LIQ IV	Meglumine Iodipamide Injection	Bracco Imaging Canada
Visipaque 270, 320	Iodixanol Injection	GE Healthcare Canada Inc.
Omnipaque 180, 240, 300,350	Iohexol Injection	GE Healthcare Canada Inc.
Ultravist 240, 300, 370	Iopromide Injection	Bayer Inc.
Conray 30, 43, 60	Iothalamate Meglumine Injection	Liebel-Flarsheim Canada Inc.
Cysto-Conray II	Iothalamate Meglumine Injection	Liebel-Flarsheim Canada Inc.
Optiray 240, 300, 320, 350	Ioversol Injection	Liebel-Flarsheim Canada Inc.
Telebrix 38 Oral	Meglumine Ioxitalamate and Sodium Ioxitalamate Oral Solution	Liebel-Flarsheim Canada Inc.

Background information

ICM products are generally used for enhancing visualization of various body parts with radiography. In Canada, ICM products are mostly administered intravascularly and are mainly used for angiography, excretory urography, computed tomography, and ventriculography; some are also used subarachnoidally for lumbar, thoracic, and cervical myelography.

In 2015, the United States Food and Drug Administration issued a class labelling request to all ICM manufacturers to include information related to rare cases of hypothyroidism reported in infants following the use of ICM products.¹

Health Canada has evaluated the possible association between exposure to ICM products and development of hypothyroidism in adult and pediatric patients.

Health Canada identified 10 international cases of hypothyroidism following ICM exposure and determined causal association to be probable in 3 cases and possible in 7 cases. While a causal association could be found at any age, preterm infants and neonates accounted for most of the cases (2 probable and 4 possible cases). Of the 10 international cases the 3 probable cases are considered "recovered" but 2 cases are considered "not recovered" and 5 cases are unknown. All 10 cases were considered serious. The assessment also examined other published scientific literature and found further evidence of a link between ICM use and the potential risk of hypothyroidism.²⁻⁴ Most reports involved infants but some involved adults.

The review of the published scientific literature identified a mechanism by which ICM exposure might lead to hypothyroidism in sensitive populations (e.g., infants and especially pre-terms, the elderly and those with underlying thyroid disease). Hypothyroidism following ICM administration may result from an acute body autoregulatory mechanism (Wolff-Chaikoff effect) as defence against a rapid increase in serum iodide. The Wolff-Chaikoff effect generally occurs within the first 24-48 hours after the excess iodine load and failure to escape this mechanism may result in transient or potentially permanent hypothyroidism.⁴

Health Canada's assessment concluded that there is a rare potential risk of hypothyroidism following exposure to ICM particularly in infants.

Information for consumers

Iodinated Contrast Media or ICM are medical imaging dyes given to patients in some X-ray procedures, including computed tomography (CT) scans. These dyes help healthcare professionals better see internal body structures (such as blood vessels) and organs on medical images. The detailed images help healthcare professionals make a diagnosis.

ICM products contain iodine. Iodine is a chemical element needed for hormone production in a gland in the neck called the thyroid. Too little or too much iodine can cause improper thyroid function. Thyroid hormones are important for proper growth and development (including mental development) in infants and for proper metabolic activity in children and adults. Cases of underactive thyroid (hypothyroidism) have been rarely reported in patients, mainly in infants, following the use of ICM products. Premature infants are more likely to develop underactive thyroid when exposed to ICM. Infants usually do not show any visible signs of underactive thyroid.

Parents and caregivers should contact their healthcare professional for additional information or if they have questions or concerns about their infant's treatment with ICM products.

Information for healthcare professionals

Considering the potentially serious consequences of hypothyroidism on infant growth and mental development, healthcare professionals are encouraged to monitor the thyroid function in infants exposed to ICM, and to continue to monitor abnormal function until it has normalized.

Action taken by Health Canada

Health Canada is working with the ICM manufacturers to update the safety information for all ICM products to inform about this potential risk. Health Canada continues to monitor the situation and will take further action as deemed necessary.

Health Canada is communicating this important safety information update to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication update will be further

distributed through the MedEffect™ e-Notice email notification system.

Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of hypothyroidism or other serious or unexpected side effects in patients receiving ICM products should be reported to the appropriate manufacturer (see "Products affected") or to Health Canada.

Bayer Inc.
2920 Matheson Blvd. E.
Mississauga, ON, L4W 5R6
1-800-265-7382
canada.medinfo@bayer.com

Bracco Imaging Canada
11065 boul. Louis-H-Lafontaine
Montréal, QC, H1J 2Z4
1-800-465-5820
adverse.events@diag.bracco.com

GE Healthcare Canada Inc.
2300 Meadowvale Blvd.
Mississauga, ON, L5N 5P9
1-800-387-7146
canadainfo@ge.com

Liebel-Flarsheim Canada Inc.
7500 Transcanada Hwy
Pointe-Claire, QC, H9R 5H8
1-844-208-7620

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Product Directorate
E-mail: mhpd_dpse@hc-sc.gc.ca
Telephone: 613-964-6522
Fax: 613-952-7738

References

1. [FDA Drug Safety Communication: FDA advises of rare cases of underactive thyroid in infants given iodine-containing contrast agents for medical imaging](http://www.fda.gov/Drugs/DrugSafety/ucm423701.htm). Silver Spring (MD): US Food and Drug Administration; 2015 Nov 17. (Accessed 2017 Mar 28)
2. Ahmet A, Lawson ML, Babyn P, et al. Hypothyroidism in neonates post-iodinated contrast media: a systematic review. *Acta Paediatr* 2009;98(10):1568-74.
3. l'Allemand D, Gruters A, Beyer P et al. Iodine in contrast agents and skin disinfectants is the major cause for hypothyroidism in premature infants during intensive care. *Horm Res* 1987;28(1):42-9.
4. Barr ML, Chiu HK, Li N, et al. Thyroid dysfunction in children exposed to iodinated contrast media. *J Clin Endocrinol Metab* 2016;101(6):2366-70.

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