Health Canada Santé Canada

Canada

Health Product InfoWatch

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REPORTING ADVERSE REACTIONS

Canada Vigilance Program
Online: Adverse Reaction and Medical Device Problem Reporting
Telephone: 1-866-234-2345
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To receive the Health Product InfoWatch and notifications of health product advisories electronically, subscribe to MedEffect™ e-Notice or to MedEffect™ Canada RSS feeds.

This monthly publication is intended primarily for healthcare professionals and includes information on pharmaceuticals, biologics, medical devices and natural health products. It provides a summary of key health product safety information published in the previous month by Health Canada, as well as a selection of new health product safety information meant to raise awareness. New information contained in this issue is not comprehensive but rather represents a selection of clinically relevant items warranting enhanced dissemination.

Contents

MONTHLY RECAP OF HEALTH PRODUCT SAFETY INFORMATION

The following is a list of health product advisories, type I drug recalls and summaries of completed safety reviews published in May 2024 by Health Canada.

Iodinated contrast medium

This safety review evaluated the risk of hypothyroidism with the use of iodinated contrast medium products in children under 3 years of age. Health Canada's review of available information concluded that there is a potential risk of hypothyroidism in this age group. Health Canada will work with the manufacturers to update the Canadian product monograph for all iodinated contrast medium products to provide additional information about the risk of hypothyroidism and monitoring recommendations for children under 3 years of age.

Summary Safety Review: Iodinated contrast medium

JAMP Digoxin

JAMP Pharma Corporation recalled one lot of JAMP Digoxin 0.0625 mg tablets as some bottles may contain thicker, oversized tablets. Patients taking an oversized tablet will unexpectedly receive a higher dose than intended, which may pose serious health risks, including overdose.

Advisory: JAMP Digoxin
Type 1 drug recall: JAMP Digoxin

Nexavar (sorafenib)

This safety review evaluated the risk of tumour lysis syndrome with the use of Nexavar. Health Canada's review of available information found a possible link. Health Canada is working with the manufacturer to update the Canadian product monograph for Nexavar to include this risk.

Summary Safety Review: Nexavar (sorafenib)

Reddy-Sapropterin

One lot of Reddy-Sapropterin 100mg powder for solution has been recalled due to the potential for unexpected colour change leading to potential decreased potency.

Type 1 drug recall: Reddy-Sapropterin

Unauthorized Health Products

Health Canada advised Canadians about various unauthorized health products being sold at retail locations across Canada or online that may pose serious health risks.

Advisory: Fake Viagra and Cialis drugs seized from Petro Canada in Vineland, ON
Advisory: Unauthorized sexual enhancement products
Advisory: Unauthorized UMARY Hyaluronic Acid Dietary Supplement

NEW HEALTH PRODUCT SAFETY INFORMATION

The following topics have been selected to raise awareness and encourage reporting of adverse reactions.

Safety Briefs

False-positive human immunodeficiency virus nucleic acid test results in patients receiving lentivirus-based chimeric antigen receptor T-cell therapy

Nucleic acid testing (NAT) devices can detect viral genetic material (ribonucleic acid [RNA]) or viral genetic material that has been integrated into the host deoxyribonucleic acid (DNA).[1] Human Immunodeficiency Virus (HIV) NAT devices licensed in Canada are designed to detect HIV RNA. In Canada, these tests can be indicated for screening blood and tissues, diagnosis, confirmation of diagnosis, and/or clinical management of patients confirmed with HIV diagnosis. HIV NAT devices are commonly used in blood bank screening or in preparation for surgical procedures such as tissue donation or transplantation, where potential donors or recipients are screened for HIV.[2]

An HIV test may be prescribed to patients who receive a lentivirus-based chimeric antigen receptor (CAR) T-cell therapy for the purpose of determining eligibility for a tissue transplant procedure.[3,4] Given the close genetic homology between the lentivirus vectors designed to transfect genes and the HIV virus, there is potential that patients receiving this treatment may also receive a false-positive HIV result.[3] This false-positive HIV result may delay confirmation of eligibility for tissue transplant due to the need for additional testing.[3,4] As a result of its safety review, Health Canada will work with the manufacturers of HIV NAT devices licensed in Canada to include the risk of **potential false-positive HIV NAT results in patients receiving lentiviral-based CAR T-cell therapy** in their instructions for use.

Key messages for healthcare professionals:

- There have been case reports of false-positive HIV NAT results in patients receiving lentivirus-based CAR T-cell therapy.[3,4,5,6,7]
- It was determined that the false-positive HIV NAT results were due to cross-reactivity between these tests and the CAR-T cell therapy.[3,4,5,6,7] The cross-reactivity has been proposed to be the result of the close genetic homology between the lentivirus vectors and the HIV virus.[3]
- A false-positive HIV NAT result in patients receiving lentiviral-based CAR T-cell therapy may result in a delay for tissue transplant procedures due to the need for additional confirmatory testing, or cause the patients to be eliminated from eligible lists for blood products, tissue and organ donation or transplantation.[3,4]
- Positive HIV NAT results in patients who have received CAR-T cell therapy should be subject to additional testing and clinical assessment to confirm the result.

References

1. Ochodo, E.A., et al., *Point-of-care tests detecting HIV nucleic acids for diagnosis of HIV-1 or HIV-2 infection in infants and children aged 18 months or less.* Cochrane Database Syst Rev. 2021 Aug 12;8(8):CD013207.
2. Canadian Blood Services. Accessed May 10, 2024. Available from: Backgrounder: Donor Testing - Human Immunodeficiency Virus (HIV) | Blood.ca
3. Villalba, J.A., et al., *False-Positive Human Immunodeficiency Virus Test Results in Patients Receiving Lentivirus-Based Chimeric Antigen Receptor T-Cell Therapy: Case Report, Review of the Literature, and Proposed Recommendations*. The Journal of Infectious Diseases, 2021. 225(11): p. 1933-1936.
4. Alali, M., et al., *Case Series of False-Positive HIV Test Results in Pediatric Acute Lymphoblastic Leukemia Patients Following Chimeric Antigen Receptor T-Cell Therapy: Guidance on How to Avoid and Resolve Diagnostic Dilemmas.* Journal of the Pediatric Infectious Diseases Society, 2022. 11(8): p. 383-385.
5. Ariza-Heredia, E.J., et al., *False-positive HIV nucleic acid amplification testing during CAR T-cell therapy*. Diagnostic Microbiology and Infectious Disease, 2017. 88(4): p. 305-307.
6. Hauser, J.R., et al., *False-Positive Results for Human Immunodeficiency Virus Type 1 Nucleic Acid Amplification Testing in Chimeric Antigen Receptor T Cell Therapy*. J Clin Microbiol, 2019. 58(1).
7. Hongeng, S., et al., *Wild-type HIV infection after treatment with lentiviral gene therapy for β-thalassemia*. Blood Advances, 2021. 5(13): p. 2701-2706.

Tacrolimus safety reminders

Tacrolimus is an immunosuppressant drug that is used to prevent or treat organ transplant rejection.* Tacrolimus has a narrow therapeutic index, and even minor differences in blood levels have the potential to cause graft rejection and other adverse reactions. There are currently three different oral tacrolimus formulations available in Canada: immediate-release capsules, extended-release capsules and prolonged-release tablets. These formulations are not interchangeable. Inadvertent substitution between oral formulations can lead to dosing errors, which may result in blood levels outside the therapeutic range and patient harm.

Marketed Oral Tacrolimus Formulations Indicated for Prevention/Treatment of Organ Transplant Rejection in Canada**

Brand Name	Strengths	Dosing Frequency	Market Authorization Holder (MAH)
Immediate-release capsules			
Prograf	0.5 mg, 1 mg, and 5 mg	Twice daily	Astellas Pharma Canada Inc.
Sandoz Tacrolimus	0.5 mg, 1 mg, and 5 mg	Twice daily	Sandoz Canada Inc.
ACH-Tacrolimus	0.5 mg, 1 mg, and 5 mg	Twice daily	Accord Healthcare Inc
Extended-release capsules			
Advagraf	0.5 mg, 1 mg, 3 mg and 5 mg	Once daily	Astellas Pharma Canada Inc.
Prolonged-release tablets			
Envarsus PA	0.75 mg, 1 mg, and 4 mg	Once daily	Endo Ventures Ltd Importer: Paladin Labs Inc.

***At the time of publication, Sandoz-Tacrolimus XR and Apo-Tacrolimus are approved but not marketed.*

In 2019, Health Canada communicated on the risks of inadvertent substitution between different oral tacrolimus formulations. Reports of mix-ups between products continue to be received by Health Canada and by the Canadian Medication Incident Reporting and Prevention System (CMIRPS). The majority of reports are from community pharmacies and describe mix-ups during the dispensing process.

* Immediate-release tacrolimus is also indicated for the treatment of active rheumatoid arthritis in adult patients for whom disease modifying anti-rheumatic drug (DMARD) therapy is ineffective or inappropriate. Tacrolimus is to be given once daily when used for this indication.

Analysis of these reports indicate some of the factors contributing to medication errors are:

1. similarities in strength and brand names between the non-interchangeable formulations
2. healthcare professionals' unfamiliarity with oral tacrolimus formulations
3. changes in prescribed dose or formulation, and
4. transitions in care between different healthcare settings/providers

Healthcare professionals are advised of the following strategies to prevent and mitigate medication errors:

- Brand names and modifiers or descriptors (e.g., 'immediate-release', 'extended-release', or 'PA' for prolonged-release) should be used throughout the medication-use process to specify which formulation is intended for the patient.
- During transitions in care consider completing a Best Possible Medication History (BPMH) assessment in collaboration with patients and/or their designated support team as part of the medication reconciliation process. An updated guide to completing a BPMH is available from the Institute for Safe Medication Practices Canada (ISMP Canada).
- Contact the prescriber if the prescription is not clear to ensure the appropriate tacrolimus product and formulation is dispensed.
- Consider an automated alert for computerized prescriber and pharmacy order entry systems, including a warning that these formulations are not interchangeable, as well as a dosing frequency reminder.
- Remind patients to contact their healthcare professional immediately if they notice any changes in the appearance, dose, brand/product name or packaging of their medication.

If a prescriber intends to switch between tacrolimus formulations, careful medical supervision and therapeutic monitoring are required.

Report health or safety concerns

Health Canada encourages the reporting of medication errors to CMIRPS, a collaboration between Health Canada, ISMP Canada, the Canadian Institute for Health Information, Patients for Patient Safety Canada and Healthcare Excellence Canada.

Did you know?

The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a national program that collects, analyzes, and distributes information on medication errors. The knowledge gained through analyzing reports submitted to CMIRPS is used to advance medication safety in all healthcare settings.

Product monograph update

The following safety labelling updates, which were recently made to the Canadian product monographs, have been included for your awareness. A complete list of safety labelling updates for pharmaceuticals is available on Health Canada's Product monograph brand safety updates page. Canadian product monographs can be accessed through Health Canada's Drug Product Database.

Zyvoxam (linezolid)

The *Warnings and Precautions*, *Adverse Reactions (Post-Market Adverse Reactions)* and *Patient Medication Information* sections of the Canadian product monographs for linezolid injectable solution, powder for suspension and tablet formulations have been or will be updated with the risk of **rhabdomyolysis**.

Key messages for healthcare professionals:[1]

- Rhabdomyolysis associated with creatine kinase (CK) elevations has been reported with the use of linezolid. In some cases, rhabdomyolysis led to acute kidney injury.
- Consider regular monitoring of CK levels in patients:
  - with an increased risk of myopathy or rhabdomyolysis
  - who recently received or are currently taking other medications known to be associated with myopathy or rhabdomyolysis
  - who develop any signs or symptoms of rhabdomyolysis, including muscle pain, weakness, or dark urine.
- If signs or symptoms of rhabdomyolysis are observed, linezolid should be discontinued and appropriate therapy initiated.

Reference

1. *Zyvoxam (linezolid)* [product monograph]. Kirkland (QC): Pfizer Canada ULC.; 2023.

Helpful links

- Recalls and Safety Alerts Database
- New Safety and Effectiveness Reviews
- Canada Vigilance Adverse Reaction Online Database
- Drug Product Database
- Medical Devices Active Licence Listing
- Licensed Natural Health Products Database
- The Drug and Health Product Portal
- Drug Shortages Canada
- Medical device shortages
- COVID-19 vaccines and treatments portal

Contact us

Your comments are important to us. Let us know what you think by reaching us at: infowatch-infovigilance@hc-sc.gc.ca

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Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.

Due to time constraints relating to the production of this publication, information published may not reflect the most current information.

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