10-Mar-2025

Hydroxocobalamin - Cyanokit® 5 g powder for solution for infusion – Important information regarding Cyanokit® in a context of shortage.

Dear Healthcare Professional,

The marketing authorisation holder, SERB SA, in agreement with Methapharm Inc. and Health Canada would like to inform you of the following:

Summary

The manufacturing of Cyanokit® was under investigation for a deviation related to a risk of microbial contamination. In January 2025, when manufacturing was temporarily suspended and to alleviate the drug shortage in Canada, a batch of Cyanokit, Lot 2413, which was in scope of the event was distributed in Canada. Currently, another Cyanokit lot 2413A also in scope of the event is being distributed in Canada to mitigate potential for drug shortage of Cyanokit.

- **Although the risk of contamination of the affected batches cannot be completely excluded, it is minimal and outweighed by the benefits of using Cyanokit® in cases of acute suspected cyanide intoxication.**

- **In this context, SERB and Methapharm draw the attention of Healthcare Professionals likely to use a potentially impacted batch of Cyanokit® to the following points:**
  - **Cyanokit® should be reserved for patients presenting clinical signs of acute intoxication in a context suggestive of exposure to cyanide (inhalation of fire smoke or ingestion of a cyanide salt or cyanogenic product), including the following signs: cardiac arrest, shock, respiratory distress, coma, high lactic acidemia (>8 mmol/L).**
  - **Cyanokit® should not be used in the absence of clinical signs of hypoxia mentioned above.**
  - **Any sign or symptoms suggestive of systemic infection or sepsis (e.g. fever, persistent hypotension suggestive of shock) should trigger blood cultures and empiric antibiotic therapy to be adjusted to the identification of the pathogen and results of susceptibility testing.**

Background on the safety concern

Cyanokit® is an antidote for the treatment of known or suspected cyanide poisoning in all age ranges. Cyanokit® is to be administered together with appropriate decontamination and supportive measures.

The manufacturing of Cyanokit® 5 g powder for solution for infusion (hydroxocobalamin) was previously suspended due to an investigation of a deviation related to a risk of microbial contamination. Product batches in the table below were manufactured during the period impacted by this issue and are potentially impacted.

Batch number	Expiry date	Market
2413A	31-Dec-2026	Canada

The above-mentioned batches met the registered specifications for release, including sterility and endotoxin tests, and no deviations that could be linked to the event have been identified during their manufacture.

SERB Pharmaceuticals have generated a risk assessment, which demonstrated that it is not possible to eliminate all of the sterility assurance risk for the batches reviewed. However, it is concluded that based on the detailed batch by batch assessment, benefit of the product to patients, which is considered as critical in multiple markets, the potentially impacted batches should be made available for use.

This decision has been reached that the risk to patients created by the non-availability of potentially impacted product is considered a greater risk to public health versus making these batches available to the market.

No safety signals in relation with this quality defect have been reported at this stage. SERB Pharmaceuticals and Methapharm will continue to monitor the risk presented by this event using pharmacovigilance, customer complaint and medical information processes.

Since a risk of contamination, while minimal, cannot be fully ruled out, the purpose of this communication is to advise Healthcare Professionals to:

- Reserve Cyanokit® for patients presenting clinical signs of acute intoxication in a context suggestive of exposure to cyanide.
- Avoid using Cyanokit® in the absence of clinical signs of hypoxia.
- Trigger blood cultures and empiric antibiotic therapy (to be adjusted to the identification of the pathogen and results of susceptibility testing) in presence of any sign or symptoms suggestive of systemic infection or sepsis (e.g. fever, persistent hypotension suggestive of shock).

Due to the time needed to implement corrective and preventive actions, normal manufacturing of Cyanokit® will not be able to resume for several weeks.

Call for reporting

Healthcare Professionals should report any adverse reactions suspected of being due to Cyanokit® to Methapharm Inc at:

Email: medinfo@methapharm.com

Phone: (+1)519-751-3602 Ext. 7804

Address: 81 Sinclair Blvd, Brantford, Ontario, N3S 76X, Canada

Healthcare professionals in Canada should report any suspected adverse reactions to the **Canada Vigilance Program**. This program is managed by Health Canada and is responsible for monitoring the safety of health products marketed in Canada.

1) **Online**: Submit a report through the MedEffect Canada website. Report a side effect of a health product, drug or medical device - Canada.ca
2) **Phone**: Call toll-free at **1-866-234-2345**

3) **Mail or Fax**: Complete a reporting form and send it by postage-paid mail or fax toll-free to **1-866-678-6789**

If you need more details on how to report, you can visit the MedEffect Canada section on the Health Canada website Adverse Reaction Reporting and Health Product Safety Information - Guide for Health Professionals - Canada.ca

Note: Cyanokit® is subject to additional monitoring for the risks "Clinical consequences of red coloration induced by hydroxocobalamin", "Laboratory test interferences" and "Device interaction".

The objective of this additional monitoring is to inform the Healthcare Professionals (HCP) about the above-listed risks and to improve their management.

This additional monitoring is an HCP educational sticker which is inside the Cyanokit® pack and includes the following wording: "To be attached to the patient's medical record: Cyanokit® has been administered in this patient. Cyanokit® may interfere with burn assessment (red coloration of skin) and laboratory tests and may lead to shut down of haemodialysis machines.

The current worldwide distribution of the Cyanokit® pack includes the same HCP educational sticker for all zones, in 25 languages.

Company contact points

If you have any questions, or require further medical information, please contact Methapharm Inc., Medical Information at:

Email: medinfo@methapharm.com

Phone: (+1)519-751-3602 Ext. 7804