11th December 2024

(Reference 24_153_GHE)

Direct Healthcare Professional Communication (DHPC)

Hydroxocobalamin - Cyanokit® 5 g powder for solution for infusion: – Important information regarding batch 2404 in a product shortage context.

Dear Healthcare Professional,

The marketing authorisation holder SERB SA in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- **The manufacturing of Cyanokit® has been suspended due to an investigation of a deviation related to a risk of microbial contamination. The product is in short supply in the UK and all major global markets.**
- **Cyanokit® batch 2404 was manufactured during the time period covered by this deviation. Batch 2404 is the only batch manufactured within this period which has been imported to the UK.**
- **While the risk of contamination of batch 2404 cannot be totally excluded, it is minimal and outweighed by the benefit of Cyanokit® used in situations where there is acute suspected cyanide intoxication.**
- **Use of Cyanokit® batch 2404 presents a minimal but not zero risk of exposure of patients to microorganisms.**
- **In this context, SERB Pharmaceuticals draw the attention of Healthcare Professionals (HCP) likely to use Cyanokit® batch 2404 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 signs of hypoxia.**

➢ **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) is currently suspended due to an investigation of a deviation related to a risk of microbial contamination. Several product batches, including batch 2404 were manufactured during the period impacted by this issue.

Batch 2404 met the registered specifications for release, including sterility and endotoxin tests, and no deviations linked to the event were identified during manufacture of this batch.

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 potentially impacted, which includes batch 2404. 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 as the risk to patients created by non-availability of potentially impacted product is considered a greater risk to public health than making these batches available within the market.

No safety signals in relation with this quality defect have been reported at this stage. SERB Pharmaceuticals 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 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 resumed for several weeks.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

Please report:

- All suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- All suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

You can report via:

- The Yellow Card website
- The free Yellow Card app available from the Apple App Store or Google Play Store
- Some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

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 about the above listed risks 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 (see SmPC)."

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

Company contact points

Healthcare Professionals should report any adverse reactions suspected of being due to Cyanokit® to SERB Pharmaceuticals:

- Postal address: SERB SA, Avenue Louise 480, 1050 Brussels (Belgium)
- Email: safety@serb.com
- Phone: +33 1 73 03 20 00

If you have any questions, please contact SERB Pharmaceuticals Quality department at: quality@serb.eu

If you require further medical information, please contact SERB Pharmaceuticals Medical Information department**:**

- Email: infomed@serb.eu
- Phone: +33 1 73 03 20 00
- Website : www.serb.com

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SERB Pharmaceuticals

Electronically signed by: Guillaume Henry Reason: I approve this document. Date: 11-Dec-2024 12:08 GMT+1

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Electronically signed by: Marc Buchet Reason: I approve this document. Date: 11-Dec-2024 13:53 GMT+1