20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Ref. RPQ/REG/ISF/Alert N°8/2022 27 December 2022

Medical Product Alert N°8/2022

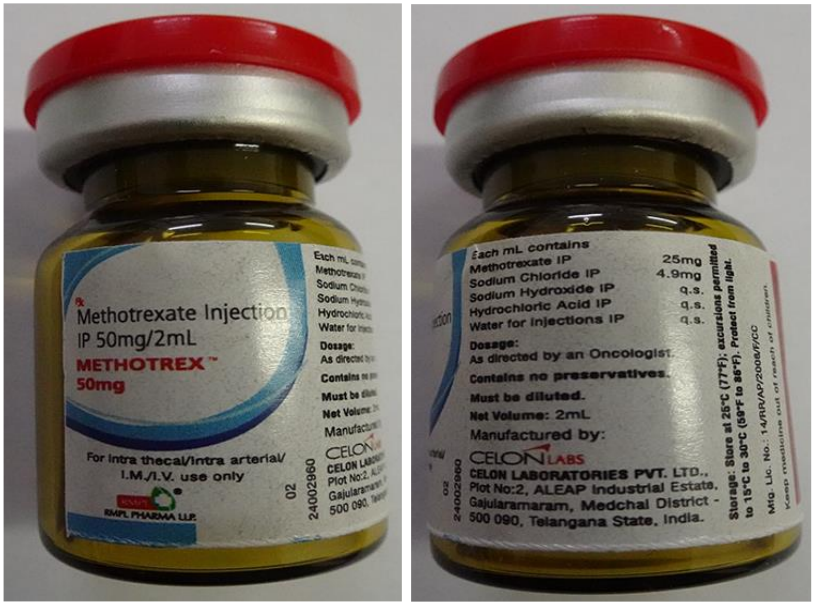
Substandard (contaminated) METHOTREX™ 50mg identified in the WHO Eastern Mediterranean region

Alert Summary

This WHO Medical Product Alert refers to one batch of substandard (contaminated) METHOTREX™ (methotrexate) 50mg, identified in two countries (Yemen and Lebanon) in the WHO Eastern Mediterranean region. Methotrexate is on the WHO model list of essential medicines, and indicated for treatment of cancer and autoimmune diseases.

Substandard medical products are products that fail to meet either their quality standards or specifications and are therefore "out of specification"[1].

Table 1: Methotrexate product referenced in WHO Alert N°8/2022

Product Name	METHOTREX™ 50mg
Declared active ingredient	Methotrexate 50mg/2mL
Stated Manufacturer	CELON LABORATORIES, PVT LTD – Telangana State, India
Stated to be marketed by	RMPL PHARMA LLP – Mumbai
Batch Number	MTI2101BAQ
Expiry Date	12/2022
Date of manufacture	01/2021
Photograph	

Additional photographs are available in the Annex, page 3.

Following adverse events in pediatric patients receiving METHOTREX™ 50mg, the health authorities in both Yemen and Lebanon conducted microbiological testing on the remaining unopened vials of METHOTREX™ 50mg. Results in both countries were positive for *Pseudomonas aeruginosa,* indicating contamination of the products.

The stated manufacturer, CELON Laboratories Pvt Ltd., has confirmed to WHO that the batch number, manufacturing and expiry dates combination referenced above match their internal records. At this stage, they have not had access to samples of the suspect products for their own confirmatory testing.

[1] WHO definitions : https://www.who.int/teams/regulation-prequalification/incidents-and-SF/background/definitions

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Risks

Methotrexate is a chemotherapy agent and immune system suppressant. It may be given by intrathecal, intramuscular, intravenous, or intra-arterial routes. Patients receiving methotrexate treatment may have weakened immune systems and be more vulnerable to opportunistic infections.

Pseudomonas aeruginosa bloodstream infection is a serious infection that may lead to death and any product that has any contamination and is administered directly in the body would present serious risks to patients.

METHOTREX™ 50mg batch MTI2101BAQ was intended to be sold exclusively on the Indian market. METHOTREX™ 50mg batch MTI2101BAQ available in Yemen and Lebanon was procured outside the regulated supply chain. Therefore, the stated manufacturer cannot guarantee the safety of this product which was not destined to these markets.

However, it is likely that this product may have been distributed to other countries through informal markets. It is important to detect and remove this contaminated product from circulation to prevent harm to patients.

Advice to regulatory authorities, manufacturers and the public

WHO requests increased surveillance and diligence within the supply chains of countries and regions likely to be affected by this product. Increased surveillance of the informal/unregulated market is also advised. Competent authorities are advised to immediately notify WHO if this product is discovered in their respective market.

Manufacturers are urged to test for microbial contamination before releasing finished product batches for use.

All medical products must be approved and obtained from authorized/licensed suppliers. The products' authenticity and physical condition should be carefully checked. Seek advice from a healthcare professional when in doubt.

If you are in possession of this product, **please DO NOT use it**.
If you, or someone you know, have used or suffered any adverse reaction/event after use, you are advised to seek immediate medical advice from a qualified healthcare professional and report to the National Regulatory Authority or National Pharmacovigilance Centre.

If you have any information concerning the manufacture or supply of this product, please contact WHO via **rapidalert@who.int .**

Please see annex in page 3 for photographs of the product referenced in Alert N°8/2022.
Alert n°8/2022 may be updated if further relevant information becomes available.

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Annex: Photographs for Alert N°8/2022; Substandard METHOTREX™ 50mg

Note: Below are photographs of the product identified in Yemen. The product identified in Lebanon is visually identical.