A focus on high-alert drugs: Methotrexate medication incidents

"A set of blister packages were prepared for a patient. The methotrexate tablets, intended as a once weekly dose, were dispensed as once daily dosing. The error was found after the patient had taken two extra doses."

By Melody Truong and Certina Ho

As a folate analogue, methotrexate exhibits cytotoxic effects through its interference of DNA synthesis, replication and repair. These effects result in an overall poor safety profile, with potential toxicities involving multiple organ systems. The heightened risk of harm associated with its use in error is the basis behind methotrexate's presence on ISMP's List of High-Alert Medications (https://www.ismp.org/tools/highalertmedicationLists.asp). The scenario above illustrates one example where a medication incident involving methotrexate had the potential to cause serious patient harm.

Prescribed for medical conditions in and out of oncology, it is not uncommon to see methotrexate in community and hospital settings. Regardless of practice site, the risk of error when handling the medication is precipitated by several factors, including methotrexate's varying indications, dosage regimens, strengths and formulations. For instance, while methotrexate may be taken as a once weekly dose in rheumatoid arthritis, the medication is taken on predefined days of each cycle in most cancers.

To examine medication incidents in the community related to methotrexate, the Institute for Safe Medication Practices Canada (ISMP Canada) performed a multi-incident analysis to identify contributing factors from reported incidents. Voluntary reports of medication incidents were extracted from the Community Pharmacy Incident Reporting (CPhIR) program, a database designed by ISMP Canada with support from the Ontario Ministry of Health and Long-Term Care.

After evaluation of 137 medication incidents, each were categorized into three themes based on shared characteristics. The themes were further divided into 3 – 4 subthemes (see Table 1).

The results of the analysis demonstrated three key areas for which system-based solutions may be implemented to reduce error when dealing with methotrexate. These include:

1. Standardization of prescribing practices (ex. pre-defined order sets)
2. Implementation of safeguards in the community pharmacy (ex. independent double checks)
3. Fostering a culture of patient-centered care (ex. patient education and follow-up)

Overall, it is important to remember that while methotrexate is indicated in a broad range of medical conditions, the medication poses significant harm to patient safety when handled in error. This applies to all stages of the medication-use process, with the probability of error increased when contributing factors are present. It is therefore ISMP Canada's ongoing initiative to advocate for the reporting, sharing and learning from incident reports – ultimately allowing for continuous quality improvement in medication safety. H

Table 1: Themes and subthemes of the methotrexate multi-incident analysis

THEMES	SUBTHEMES
Associated Medications (Medication incidents were related to the association of methotrexate with other drugs.)	Drug Interactions Look-alike/Sound-alike Drug Names Concomitant Drugs (Note: Some drugs may be concurrently prescribed with methotrexate. For example, folic acid and methotrexate are commonly prescribed together to reduce toxicity.)
Dosing Complexities (Medication incidents were related to the complexities involving methotrexate's varying indications, dosing regimens, strengths and formulations.)	Calculation Error Frequency Error Parenteral Route Multi-Medication Compliance Aids (Note: Compliance aids present with additional intricacies that may facilitate medication errors, independent of the handling of methotrexate.)
Medication-Use Process (Medication incidents were related to the involvement of methotrexate within the stages of the medication-use process.)	Prescribing Order Entry Preparation/Dispensing

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