



Clinical Pharmacology & Toxicology Pearl of the Week

~ High-alert medications ~

Case:

- A 65 year old female is diagnosed with new rheumatoid arthritis. After discussing risks and benefits of various medication options, she is started on methotrexate 10 mg po once weekly, and folic acid 1 mg po once daily, six days per week (on non-methotrexate days).
- She brings her new prescription to the pharmacy and her blister packs are updated with the two new medications.
- Six weeks later, she presents to her family physician with one week history of diarrhea - now slightly bloody - and mouth ulcerations. The family physician notes that the patient appears clinically dehydrated and she is directed to the emergency department.
- In the emergency department, the pharmacist conducts a medication review and finds the blister pack loaded with methotrexate 10 mg once daily and folic acid 1 mg once daily.
- Bloodwork shows pancytopenia and mild AKI. Her methotrexate level is 5.5 umol/L. She is started on IV leucovorin. The patient is admitted to MTU with concerns for methotrexate toxicity, with hematology and medical toxicology consulting.

Background:

- High-alert medications are medications that bear a heightened risk of causing significant patient harm when they are used in error.
- Although mistakes may not be more common in the use of these medications, when errors do occur, the impact on the patient can be significant.
- A medication error is different than an adverse drug reaction (ADR), because ADRs are unwanted effects that happen when drugs are used under normal conditions. ADRs don't involve mistakes, and typically can't be prevented.

Medication errors are reported to **Canadian Medication Incident Reporting and Prevention System (CMIRPS)** via the **Institute of Safe Medication Practices Canada (ISMP-Canada)**. <https://ismpcanada.ca>

Adverse drug reactions are reported to Health Canada's **Canada Vigilance Program**. <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/canada-vigilance-program.html>

Characteristics of high-alert medications:

- Low therapeutic to toxic ratio
- Inherent undesirable effects
- Unique dosing (e.g., units instead of mg)
- Pharmacokinetic/pharmacodynamic interactions
- Look-alike or Sound-alike names
- Newly approved drugs
- Off label uses
- Vulnerable patients (e.g., geriatrics - multiple meds, e.g., pediatrics - wt. based dosing)

A new Canadian-specific list of high alert medications

Historic lists provided by ISMP-Canada have been largely based on US data. A Canadian list recognizes contextual differences between countries, such as health system and practice pattern variations and drug supply and availability.

For this new list, candidate medications were identified through consultation with Canadian stakeholders, analysis of local incident reports from 2018-2022, and an environmental scan of Canadian and international high-alert lists, safety reports, and literature. A formal review of candidate medications was completed by an expert panel and ISMPC team, representing a broad cross section of Canadians and multiple health disciplines.

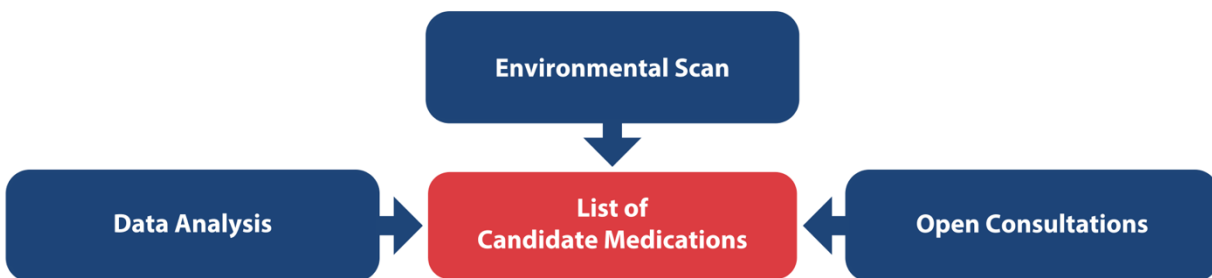


FIGURE 2. Information flow for identifying candidate medications.

ISMP Canada safety bulletin. ISMP Canada. Feb 2024. 24:1 <https://ismpcanada.ca/wp-content/uploads/ISMPCSB2024-i1-High-Alert-Medications.pdf>

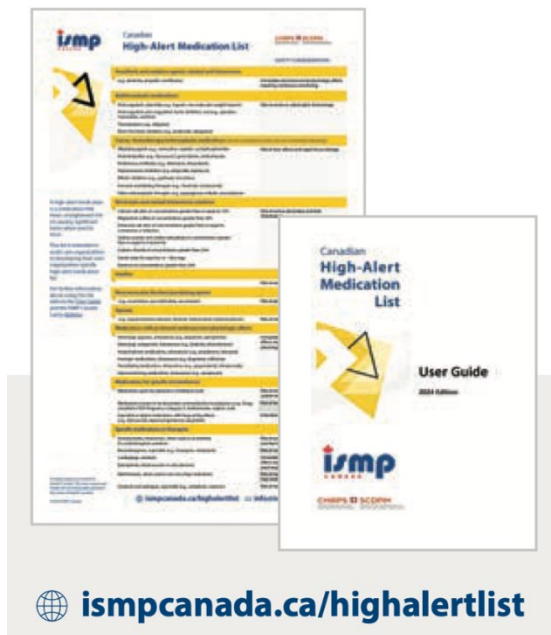
The new Canadian list is intended to apply to all health care settings, but it is recommended that individual providers and organizations familiarize themselves with the list and adapt it to their unique organizational needs. If organizations identify medications in their local context that warrant inclusion on their organization specific high-alert list, they are encouraged to share this with ISMPC to inform future revisions.

The Canadian High-Alert Medication List is intended to assist care organizations in developing their own organization-specific high-alert medication list, based upon a review and/or risk assessment of medications in use, as well as the population(s) served. This Canadian list is not intended to be adopted in its entirety as an organization-specific list.

Canadian list of high-alert medications (see ISMPC website for details):

- Anesthetics – inhaled and intravenous
- Antithrombotic and thrombolytics
- Chemotherapy and antineoplastic medications
- Electrolytes and related infusions
- Insulins

- Neuromuscular blockers
- Opioids
- Benzodiazepines
- Medications with profound cardiovascular/physiologic effects (e.g., adrenergic agonists/antagonists, antiarrhythmics, vasoactive medications)
- Medications by unique routes (e.g., epidural/intrathecal routes, depot injectables)
- Teratogens
- Specific medications (e.g., acetylcysteine, epinephrine, methotrexate, oxytocin)



Report Medication Incidents

(Including near misses)

Online: www.ismpcanada.ca/report/

Phone: 1-866-544-7672

ISMP Canada strives to ensure confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications.

ismpcanada.ca/highalertlist

Strategies to mitigate risk:

Multiple and layered strategies should be used to enhance safety, prioritizing interventions with superior effectiveness and those that address the underlying cause of known incidents.

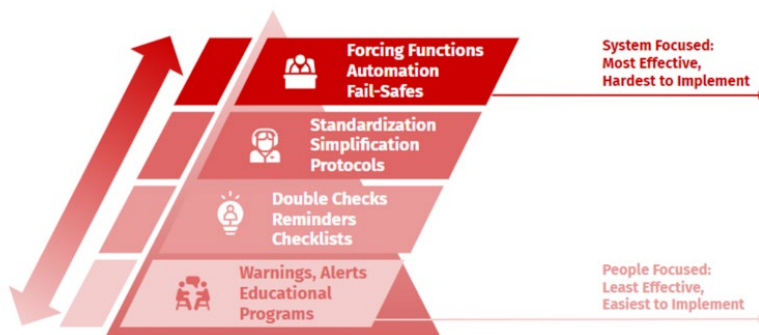


Figure 1. The Hierarchy of Effectiveness of Patient Safety Interventions.

Chan A. Checklists and the hierarchy of effectiveness. Canadiem. Feb 2021. <https://canadiem.org/checklists-and-the-hierarchy-of-effectiveness/>

Strategy Examples:

- Standardized order sets
- Dose calculators
- Smart-pump programming
- Computerized order entry with validation
- Tall-Man lettering
- Acquisition of accurate patient weights
- Organ function and falls assessment in geriatrics
- Avoiding acronyms/prohibited abbreviations and trailing zeros in prescription writing
- Clear division of prescribing, dispensing and administration roles

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Calgary Zone Specialist Link. Click [HERE](#) for more details.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK).

References:

1. Chan A. Checklists and the hierarchy of effectiveness. Canadiem. Feb 2021. <https://canadiem.org/checklists-and-the-hierarchy-of-effectiveness/>
2. ISMP Canada safety bulletin. ISMP Canada. Feb 2024. 24:1 <https://ismpcanada.ca/wp-content/uploads/ISMPCSB2024-i1-High-Alert-Medications.pdf>
3. Benjamin, D. Journal of Clinical Pharmacology, 2003;43:768-783
4. Lin et al. Potentially high-risk medication categories and unplanned hospitalizations: a case-time-control study. Scientific Reports | 7:41035 | DOI: 10.1038/srep41035.
5. ISMP Canada. Medications Most Frequently Reported in Harm Incidents over the Past 5 Years (2015–2020). December 22, 2020. Available at <https://www.ismp-canada.org/download/safetyBulletins/2020/ISMPCSB2020-i11-Medications-Reported-Harm.pdf>
ISMP Canada, 2020