

ISMP Canada Safety Bulletin

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A Mix-up between Short- and Long-Acting Medications Administered by Injection: When Does the “Salt” Matter?

Medications may be formulated as salts or esters (collectively referred to as “salts”), usually to improve the properties of the therapeutic moiety (e.g., its stability, bioavailability, or duration of action). In most cases, the type of salt does not influence how the drug is therapeutically used. In some cases, however, the particular salt significantly affects the drug’s pharmacological properties. Depot medications are one such group of drugs. These agents are typically formulated as various salts that are used differently from their short-acting counterparts. ISMP Canada recently received a report of an incident in which a short-acting (immediate-release) intramuscular (IM) form of an antipsychotic was administered by injection to a patient instead of the prescribed long-acting (depot) formulation. This bulletin is shared to increase awareness of the various salt formulations of these drugs and to offer system-based changes to prevent these types of incidents from recurring.

Medication Incident

An older patient had been receiving IM haloperidol decanoate 25 mg every month for many years. Because of a medication shortage, this product was not available at the patient’s ambulatory health centre, so a nurse called several pharmacies in the area in an attempt to procure the drug. Staff at one pharmacy suggested using haloperidol lactate

5 mg/mL for injection. The nurse sent the prescription for “haloperidol LA 25 mg IM monthly” to the pharmacy. The pharmacist dispensed 5 ampoules of the short-acting haloperidol lactate 5 mg/mL to make up the 25 mg dose, which was subsequently administered to the patient. Following the injection, the patient’s family noticed that he was extremely sedated, was much less alert, and had a “dazed” look, symptoms that lasted 3 days. Fortunately, the patient recovered without any long-term consequences.

Background

Depot antipsychotics are commonly used in mental health care settings, for example, for maintenance treatment of schizophrenia. Their main advantage is low frequency of administration (every 1 to 4 weeks), which facilitates adherence with treatment.¹

In most depot formulations of antipsychotics, the active ingredient is available as the decanoate or palmitate ester, which is dissolved in a vehicle such as sesame oil.² These formulations are designed to be deposited via deep IM injection to provide prolonged therapeutic action as the drug is slowly absorbed from its oily “depot” within the muscle into the bloodstream. Haloperidol decanoate is one such drug, and it is typically administered every 4 weeks.³

Injectable haloperidol is also available in an immediate-release formulation (haloperidol USP, as the lactate salt in a water-based formulation).³

Compared with haloperidol decanoate, the immediate-release formulation has a much faster onset and shorter duration of action, which makes it useful in the treatment of psychiatric emergencies.

In Canada, haloperidol is the only antipsychotic available in both depot and immediate-release formulations. However, another antipsychotic, zuclopenthixol, is available in 2 different depot formulations (an acetate ester and a decanoate ester), with varied durations of action and dosing regimens.

Discussion

Errors involving mix ups between short- and long-acting forms of IM medications can result in harm. A depot dose is typically much higher than a dose of the same drug administered in a short-acting immediate-release form, because the former is designed to be slowly released into the body over an extended period. If the same high dose of a short-acting formulation is given by mistake, very high plasma levels of the drug may result, putting the patient at significant risk of overdose. As an example, symptoms of haloperidol overdose include severe extrapyramidal side effects, such as akathisia, acute dystonia, and parkinsonian symptoms.³ Also possible are increases in the risks of electrical disturbances of the heart, hypotension, hypokalemia, seizures, respiratory depression, and coma.³

In this incident, in which short-acting haloperidol was given instead of the long-acting formulation, several possible contributing factors were identified:

- A drug shortage meant that the usual supply of haloperidol decanoate was unavailable in the clinic.
- Healthcare professionals were unfamiliar with the differences between the 2 formulations and did not understand that they are not interchangeable. Such misconceptions may occur because for many medications, the particular salt of the drug does not influence its properties and has no clinical consequences.
- The abbreviation “LA”, which was used in the prescription to mean “long-acting”, might have led

to confirmation bias, if it was mistakenly interpreted as meaning “lactate” (the salt present in the short-acting formulation).

Recommendations

Prescribers

With the growing number of marketed products with varied formulations available for selection, prescription clarity is becoming increasingly important.

- Consider using the entire name of depot medications, including the salt, ester, or other complex for medications available in more than one formulation, and state the desired strength; for example, “haloperidol decanoate 100 mg/mL long-acting injection (or depot)” instead of “haloperidol LA”.

Front-Line Pharmacy and Nursing Staff

- Contact the prescriber when the presence or absence of a medication name suffix (salt, ester, or other complex) fails to align with the prescribed dose. For example, a prescription for “haloperidol 100 mg” should be questioned, as the salt (formulation) is not specified and the dose appears to align with the depot formulation.⁴
- When multiple vials or ampoules or larger-than-anticipated volumes are needed for a given dose, healthcare professionals should question whether the correct product has been supplied. In the incident described in this bulletin, five 1 mL ampoules of haloperidol lactate 5 mg/mL were needed for the prescribed dose of 25 mg; this necessitated 2 IM injections to deliver the total 5 mL volume. In contrast, the decanoate formulation for depot administration is available in concentrations of 50 mg/mL and 100 mg/mL, and the intended product would have required administration of less than 1 mL total volume.
- If the viscosity of the medication seems unusual compared with previous doses when aspirating medication into the syringe, verify that the correct formulation is being prepared. Depot medications are typically more viscous than their short-acting counterparts.

Pharmacies, Ambulatory Clinics, and Hospitals

- Consider how the name of the drug will appear in the pharmacy computer system and on the product label with the end user in mind. When expressing a generic name, do not include the salt of the chemical unless the medication is available in multiple salt formulations.⁵
- Add alerts in pharmacy information systems, electronic prescribing systems, and automated dispensing cabinets for injectable medications that are available in more than one formulation.
- Place labels on the shelves where these products are stored to alert practitioners of the availability of the different formulations.
- Add depot injectable medications to the organization's list of medications requiring an independent double check before administration, where possible. For facilities and other practice settings that carry both short- and long-acting dosage forms of a particular medication, the short-acting form should also require an independent double check. If a second practitioner is not available to do the check, consider having the patient or a caregiver participate in the checking process, in appropriate situations.¹
- Proactively alert staff about drug shortages and provide anticipatory guidance about alternative medications and any increases in risk with use of unfamiliar or substitute products.
- Provide education for staff in psychiatric clinics and other settings where these products are used. Address the various formulations of antipsychotic medications and the differences between the formulations, including pharmacokinetic properties and therapeutic uses.

Manufacturers and Distributors

- Improve labelling on product packaging with the end user in mind. A new Good Label and Package Practices Guide is being developed by Health Canada and ISMP Canada to provide guidance regarding safe packaging and labelling of these products. The guide will include recommendations about how to accurately communicate the drug name to practitioners.
- Proactively alert pharmacies and prescribers about drug shortages and provide anticipatory guidance

about alternative medications and any increases in risk with use of unfamiliar or substitute products.

Information System Vendors

- Ensure that sufficient character spaces are available in drug description fields and in pharmacy label formats to display the full generic name of all drugs, including the salt, ester, or other complex, when needed.
- Ensure that information systems support the use of mixed case lettering in drug selection screens and label formats.

Conclusion

The variation in salts for drugs is clinically important in certain situations, such as differentiation between short-acting and depot formulations containing the same active medication. Mix-ups between formulations with different pharmacokinetic properties can lead to harm. Communicating drug names with the end user in mind is becoming increasingly important with the growing number of drugs and the existence of varied formulations. Manufacturers, information system vendors, facilities, pharmacies, and healthcare practitioners all have a role in preventing incidents related to confusion between formulations of the same medication.

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Invitation to Participate in a Delphi Method Survey on Medication Safety Pictograms for Healthcare Workers

We would like to invite healthcare professionals to participate in the development of a set of pictograms for medication safety. In this first phase, we are seeking assistance to identify the top issues where the development of a pictogram might provide a visual aid and warning cue to help prevent selected medication errors.

Ultimately, the use of a small set of medication safety pictograms could be considered when labelling, dispensing, or administering medications.

This collaborative research project is being led by Dr. Regis Vaillancourt, Pharmacy Director at the Children's Hospital of Eastern Ontario, and aims to involve pharmacists, pharmacy technicians, nurses, physicians, and specialists such as anesthesiologists.

We have chosen to organize a Delphi consultation by email. The Delphi method is designed as a group communication process which aims to achieve a convergence of opinions on a specific real-world issue. The Delphi consists of three rounds, and each round should take approximately **10-15 minutes** of your time to complete. After each round, a summary of the responses will be sent to an expert group. The first Delphi round will include structured, as well as open-ended questions to facilitate discussion. In addition, new topics provided by responses to the open-ended questions will be disseminated to all Delphi participants in the second round.

Research ethics board approval was obtained for the study from the Children's Hospital of Eastern Ontario (January 23, 2014). Your privacy and anonymity will be guaranteed and only the project coordinators will have access to the raw information gathered, and to any personal information provided.

Please send an email to rvallancourt@cheo.on.ca if you would like to participate in this project.

This segment of the bulletin describes a recent SafeMedicationUse.ca publication from ISMP Canada's consumer program.

December 2014 – Newsletter

Medication Appearance and Markings Support Safety

Consumers need to be familiar with the identification marks and general appearance of each of their medications and any medications they administer to others.

SafeMedicationUse.ca received an incident report about a mix-up that occurred in a community pharmacy between a consumer's prescriptions for 2 medications: the antibiotic ciprofloxacin (to be used in treating a lung infection) and ranitidine (to be used on an as-needed basis for indigestion). The error resulted in the ciprofloxacin tablets being placed in the vial labelled "ranitidine" and the ranitidine tablets in the vial labelled "ciprofloxacin". For 6 days, the consumer took 3 ranitidine tablets a day and did not take any ciprofloxacin. As a result, her infection was not treated properly and lasted longer than expected. Fortunately, the consumer had some awareness of the markings of the ranitidine tablets. This helped her to discover the error, which in turn helped her to eventually get the correct treatment for her infection.

The SafeMedicationUse.ca newsletter advises consumers to take an active role in their health by being familiar with the appearance (e.g., colour, shape, markings) of the medicines they take, by checking their prescriptions before leaving the pharmacy, and by reviewing the details of new prescriptions with the prescriber. Consumers are encouraged to read more about checking prescriptions at: www.safemedicationuse.ca/newsletter/newsletter_CheckYourPrescription.html

To further support the consumer in this role, practitioners are encouraged to spend some time with the consumer at the time of prescription pick-up, opening the vials, reviewing each product's appearance, and informing the consumer of any changes to the medications' appearance.

For additional information about safe practices for consumers and practitioners, read the complete newsletter at: www.safemedicationuse.ca/newsletter/newsletter_MedicationAppearance.html



**Consumers Can Help Prevent
Harmful Medication Incidents**

SafeMedicationUse.ca



The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.



The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.



The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada's mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

Report Medication Incidents

(Including near misses)

Online: www.ismp-canada.org/err_index.htm

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.

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www.ismp-canada.org/stayinformed

This bulletin shares information about safe medication practices, is noncommercial, and is therefore exempt from Canadian anti-spam legislation.

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