

ISMP Canada Safety Bulletin

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Changes in Expression of Strength: Elimination of Ratios on Single-Entity Injectable Products

- *As of May 1, 2016, the USP-NF is eliminating ratios as an acceptable method for expressing the strength of single-entity injectable products (e.g., epinephrine). While it is unknown exactly how these changes will affect Canadian products, it is anticipated that manufacturers of affected products will be required to meet these standards.*
- *The new standards will not apply to combination products (e.g., bupivacaine with epinephrine).*

The standards set by the United States Pharmacopeial Convention, through the United States Pharmacopeia and the National Formulary (USP-NF), are being updated for publication as USP39-NF34. One of the changes in the new edition will be the elimination of ratios as an acceptable method for expressing the strength of single-entity injectable products. The requirement for compliance with this change will take effect in the United States on May 1, 2016. After that date, the strength on the labels for all such products must be expressed only as the amount per unit volume (e.g., mg/mL). If the total volume of a product is less than 1 mL, the amount per fraction of a millilitre should be the only expression of strength (e.g., 1 mg/0.4 mL).¹ Thus, products prepared to a USP standard (e.g., epinephrine injection, USP), will also need to conform to the new standards for expression of strength.

The new USP-NF standards will not affect multi-ingredient local anesthetic with epinephrine products, such as bupivacaine with epinephrine 1:200,000. The concentration of epinephrine in those products may still be expressed as a ratio.¹

The Institute for Safe Medication Practices (ISMP) in the US has published several case reports highlighting potential confusion with ratio expressions, including the death of a teenager who inadvertently received 4 mL of epinephrine 1:1,000 (= 4 mg) by intracavernous injection to treat priapism.² For this procedure, a 1:1,000,000 epinephrine solution is typically prepared by diluting 1 mg of the 1:1,000 strength epinephrine product in 1 litre of normal saline. The corpora cavernosa are then irrigated with 10 to 20 mL of the diluted solution. However, the physician mistakenly thought the ratio expression 1:1,000 on the label meant that the epinephrine was already diluted with 1,000 mL (or 1 litre) of normal saline and injected 4 mL of the undiluted 1:1,000 product.² The following 2 factors contributed to this and similar errors:^{2,3}

- lack of understanding of ratio expression by practitioners; ratio is another method of expressing concentration of a dilute solution (e.g., a 1:1,000 epinephrine strength indicates 1 gram of epinephrine in 1000 mL of solution)
- potential confusion because of apparent similarities in concentrations both when written (i.e., difference of only one zero between “1:1,000” and “1:10,000”) and when spoken (“one-to-one-thousand” sounds like “one-to-ten-thousand”)

Over the past decade, ISMP has been a strong advocate of abolishing ratio expressions for epinephrine. During this period, ISMP Canada received an incident in which the ratio strength expression played a role in the error. In this case, the error was a result of confusion between the 2 concentrations.

ISMP Canada has been in contact with Health Canada about the standard update. While it is unknown exactly how these changes will affect Canadian products, it is anticipated that manufacturers of relevant products will be required to meet these standards.

Products Affected

For many products, the use of the ratio expression is already supplemented with the mg/mL expression of strength (e.g., prefilled epinephrine syringes for emergency use). Epinephrine is the most commonly used medication that will be affected by this change. Isoproterenol and neostigmine are 2 other drugs for which concentration is sometimes expressed as ratio strength. The current Canadian product monographs for both isoproterenol and neostigmine express concentration in terms of amount per unit volume, but existing drug information systems and supporting reference resources may not follow this practice. Table 1 provides the conversions from ratio expression of strength to the equivalent amount per unit volume (i.e., concentration) for these 3 drugs.

Table 1. Equivalent Expressions of Strength

Medication	Ratio	Amount / Volume
Epinephrine	1:1,000	1 mg/mL
	1:10,000	0.1 mg/mL
Isoproterenol	1:5,000	0.2 mg/mL
	1:50,000	0.02 mg/mL
Neostigmine	1:2,000	0.5 mg/mL
	1:1,000	1 mg/mL
	1:400	2.5 mg/mL

Next Steps

For both clarity in dosing and in anticipation of the change in strength expression being implemented in Canada, facilities and organizations should review documentation for the above-mentioned products. Systems, processes and care areas that will be affected by the new USP-NF standard can include the following:

- computerized pharmacy and prescriber order entry systems
- order sets and protocols
- references and reference algorithms used by clinicians (e.g., hospital formulary, Broselow tape)
- dispensing labels and labels for drug storage bins in pharmacy and in automated dispensing cabinets
- drug storage carts for anesthesia, cardiac arrest, and procedures
- stock requisition forms (manual and computerized)

Safe Transition Strategies

The medications affected by this labelling change are mostly high-alert medications, therefore, a multimodal approach, using both higher-leverage strategies and lower-leverage safeguards (such as education), is recommended. The following strategies are suggested to support a safe transition:

- Raise awareness of the labelling transition through educational events, mock code events, safety huddles, and bulletins.
- Ideally, once the change has been implemented, only the amount per unit volume should be expressed throughout the medication system. Post conversion tables, such as Table 1, to support practitioners during the transition.
- Develop a standard process for pharmacists to convert existing “ratio strength” orders to “amount per unit volume” orders for already-admitted patients, so that medication administration records will be consistent with the new labelling standard.
- As products with the new labelling become available, segregate them from products that express strength as a ratio.
 - Ideally, for each affected drug, stock products with only old *or* only new labelling in care areas where they are required.

- Send products with the older labelling to areas of higher usage (e.g., send epinephrine 1:1000 ampoules or vials to the emergency department) where they will be used up quickly, allowing more rapid transition to the new labelling without undue wastage.
- Identify potential opportunities for drug name mix-ups between epinephrine and ePHEDrine.⁵ The drug ePHEDrine has a name that looks and sounds like epinephrine, and is a sympathomimetic agent used to treat hypotension and produce bronchodilation. ISMP has reported at least 2 incidents involving mix-ups between these drugs.⁴ Because ePHEDrine is prescribed in milligrams, the elimination of ratio expression of strength for epinephrine may add to the potential for a look-alike error.
 - Use of TALLman lettering may be an appropriate strategy for differentiating ePHEDrine from epinephrine, as per the Canadian TALLman list of medications.⁵
- After transition to products and systems using only amount per unit volume to express strength, verify all shipments from the supplier and the distributor contain only product with updated labelling.
 - If an alternative supplier's product is purchased due to a drug shortage or other situation, have processes in place to ensure the alternative product expresses strength in the same manner.

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References

1. Labeling. In: United States Pharmacopeia, 39th edition, and National Formulary, 34th edition (USP39-NF34). Rockville (MD): U.S. Pharmacopeial Convention [in preparation].
2. Just say no to ratio! ISMP Med Saf Alert. 2004 [cited 2016 Feb 13];9(15):2. Available from: <https://www.ismp.org/newsletters/acutecare/articles/20040729.asp>
3. Let's stop this "epi"demic!—Preventing errors with epinephrine. PA PSRS Patient Saf Advis. 2006 [cited 2016 Feb 2];3(3):16-7. Available from: <http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2006/Sep3%283%29/Pages/16.aspx>.
4. "Looks" like a problem: ephedrine — epinephrine. ISMP Med Saf Alert. 2003 [cited 2016 Feb 2];8(8):1-2. Available from: https://www.ismp.org/newsletters/acutecare/articles/20030417_2.asp
5. Application of TALLman lettering for selected high-alert drugs in Canada. ISMP Can Saf Bull. 2015 [cited 2016 Feb 2];15(10):1-3. Available from: http://www.ismp-canada.org/download/safetyBulletins/2015/ISMPCSB2015-10_TALLman.pdf

Knowledge Mobilization Tool: Customized Report of Solutions to Help Prevent Medication Errors

When a medication incident occurs, identifying and implementing system-based interventions may prevent recurrence of the error. The online Knowledge Mobilization Tool (KMT) was designed to give healthcare practitioners up-to-date, context-specific medication safety information to support consideration of system improvements.

When conducting a medication incident analysis, the KMT can be used to search medication safety information published in the ISMP Canada Safety Bulletin. Using specific search criteria, the KMT will identify medication safety incidents, contributing factors, and recommendations to inform safety initiatives being considered.

This innovative tool is freely available and will help facilitate learning from medication incidents and support quality improvement initiatives in your organization. Learn more by visiting:

<https://secure.ismp-canada.org/KMT/>

Contact info@ismp-canada.org for more details.



Health Canada's Action to Improve Acetaminophen Safety: An Update

ISMP Canada continues to support Health Canada's efforts to improve acetaminophen safety and to minimize the risk of liver damage. A social media campaign has been launched that focuses on several themes. One of these themes emphasizes that acetaminophen is found in nearly 500 different medication products.

ISMP Canada calls on stakeholder groups, healthcare professionals, and consumers to share and Retweet this information, which can be found by joining the [Healthy Canadians Facebook](#) page and following [Healthy Canadians](#) on Twitter. We also encourage stakeholders to follow and share ISMP Canada's social media postings on [@SafeMedUse](#), [@ISMPCanada](#), and [ISMP Canada's consumer website SafeMedicationUse.ca](#) Facebook page.

For additional information on safe use of acetaminophen and Health Canada's efforts to improve acetaminophen safety, visit [Health Canada's acetaminophen page](#). Additional information on acetaminophen safety is also available at [SafeMedicationUse.ca](#), under [Spotlight on Acetaminophen](#).





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. Medication Safety bulletins contribute to Global Patient Safety Alerts.

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