

ISMP Canada Safety Bulletin

Volume 17 • Issue 4 • April 27, 2017

Acetaminophen: Preventing Harm through Safe Use

- Review the patient's medical and medication-use history to assess whether the patient has risk factors warranting a reduction in the acetaminophen dosage.
- Use the Health Canada guide "[Let's Talk About Acetaminophen](#)" to educate patients on how to use acetaminophen safely.
- Ensure that doses for pediatric patients are calculated using an accurate weight and that an appropriate measuring device is used to administer all liquid doses.

Despite its reputation for safety, acetaminophen has been identified as the leading cause of liver failure in Canada; approximately 4500 Canadians are hospitalized for acetaminophen overdose annually, and about 6% of these patients experience liver injury.¹ Injury to the liver, which has occurred with both intentional and unintentional acetaminophen overdoses, may be irreversible.

Acetaminophen is a commonly used analgesic that is widely available in either single- or multiple-ingredient products. As of early 2017, almost 500 acetaminophen-containing products were marketed in Canada, with over 350 of them available as nonprescription, over-the-counter (OTC) products.² Health Canada recently estimated that 4 billion dosage units of acetaminophen are sold in the country annually.¹

This bulletin highlights, for both healthcare professionals and manufacturers, key safety efforts, important resources, and strategic recommendations based on recent Health Canada initiatives supporting the safe use of acetaminophen in Canada.

Canadian Initiatives to Support Safe Use of Acetaminophen

Health Canada has conducted safety reviews (described in more detail below), issued public advisories, and instituted changes to the labelling requirements for OTC products containing acetaminophen. Practitioners and the public can find links to these and other related resources on a Government of Canada webpage dedicated to [acetaminophen safety](#).³

ISMP Canada's efforts to support the safe use of acetaminophen have included publishing an acetaminophen newsletter as part of its consumer medication safety program at SafeMedicationUse.ca,⁴ launching [Spotlight on Acetaminophen](#),⁵ a webpage dedicated to acetaminophen safety, and publicizing acetaminophen safety strategies on social media.

Health Canada's Acetaminophen Safety Review and Recent Regulatory Changes

In 2009, there was an initial safety review of non-prescription acetaminophen products which led to updated labelling standards that included increased warnings about the potentially serious and possibly fatal risk of liver injury in the event of

acetaminophen overdose with these products.¹ In 2014, Health Canada completed a greater in-depth safety review of acetaminophen,⁶ which showed that although most acetaminophen overdoses are intentional, nearly 20% are unintentional (see Box 1). Furthermore, the proportion of cases of acetaminophen-related injury due to unintentional overdose rose from 27% in 2006 to 45% in 2011. The safety review noted that severe liver injuries were more common in unintentional overdoses and involved either single-entity acetaminophen products or combination prescription medications containing both acetaminophen and an opioid.⁶

Box 1. Possible causes of unintentional acetaminophen overdose

- Belief that over-the-counter medications cannot cause serious harm
- Lack of awareness of the importance of adhering to the maximum daily dose of acetaminophen
- Pediatric dose errors related to:
 - miscalculation of doses
 - incorrect measurement of doses
- Confusion caused by umbrella names (i.e., use of the same brand name for products containing different ingredients)
- Taking more than one product containing acetaminophen at the same time

Although most liver injuries involving acetaminophen are caused by doses higher than 4 grams per day (the recommended daily maximum in Canada), the safety review noted that hepatotoxicity has been reported in patients receiving lower daily doses. Many of these patients had pre-existing liver disease, used alcohol excessively, were malnourished, and/or used acetaminophen for a longer duration than is recommended. In the United States, Johnson & Johnson, the manufacturer of Tylenol brand acetaminophen, voluntarily reduced the labelled daily maximum dose for adults from 4 g to 3 g,⁷ but the company has not implemented this labelling change in Canada.

Table 1 (page 3) outlines selected risk-minimization options considered in the acetaminophen safety review, some of which have been implemented in other jurisdictions, such as the United States (US), the United Kingdom (UK), Australia (AU) and New Zealand (NZ).

To further address the problem of liver damage caused by acetaminophen, in September 2016 Health Canada released an updated [labelling standard](#) for OTC acetaminophen products, as well as an [information update](#) for the general public.⁸ Improvements to the labelling standard are summarized in Box 2.

Box 2. Safety improvements to the Canadian labelling standard for OTC acetaminophen instituted in 2016⁸

- Clearer instructions on packages emphasizing that
 - the lowest effective dose should be used
 - the recommended maximum daily dose should not be exceeded
 - the recommended duration of treatment should not be exceeded
 - precautions must be followed if taken with alcohol
- Enhancement of layout to display that the product contains acetaminophen, by specifying the exact wording, font, and colour to be used, for both single- and multiple-ingredient products.
- Inclusion of a Drug Facts table, to provide instructions, warnings, and other safety information in a consistent, user-friendly format (mandatory by 2021).
- A recommendation that a calibrated dosing device should be provided in all liquid formulation packages and that directions for use should state "Use only the measuring device provided" (recommended, not mandatory).

Links to resource materials, including a fact sheet, "[Let's Talk About Acetaminophen](#)", and an "[Acetaminophen Know Your Dose](#)" poster, were implemented on Health Canada's acetaminophen information webpage in 2016.³ In addition, Health

Table 1. Selected risk-minimization strategies

Risk-Minimization Strategy	Considered in the Acetaminophen Safety Review ⁶	Implemented in Other Jurisdictions
Add warnings to packages and inserts	Yes – to strengthen and improve product labelling	Yes (US, ⁶ UK ⁶)
Use blister packs	No	Yes (UK ⁹)
Limit package size	Yes	Yes (UK, ¹⁰ AU, ¹¹ NZ ⁶)
Limit the amount of acetaminophen contained in prescription products	Yes – limit amount of acetaminophen contained in opioid combination products	Yes (US ¹²)
Include an accurately calibrated dose-delivery device with all pediatric liquid acetaminophen-containing products	Yes – recommended in 2016 guidance ¹³	Yes (US, ¹⁴ UK ⁶)
Reduce the maximum recommended daily dose	Yes – but not implemented as a result of stakeholder feedback	No – not implemented by the FDA, but voluntarily by Johnson & Johnson in the US ⁷
Limit all products to maximum 325 mg acetaminophen per unit dose	Yes – already in place for prescription products, but lacked sufficient support to be implemented for nonprescription products	Yes (US for prescription products) ⁶
Develop and implement an education strategy	Yes	Yes (US, ⁶ UK ⁶)

Canada issued a notice to industry¹⁵ limiting the amount of acetaminophen in prescription combination products to 325 mg per dosage unit.

Analgesic Alternatives to Acetaminophen

Both the public and healthcare professionals are increasingly aware of the potential for harm related to acetaminophen therapy. As such, it might seem to make sense to treat pain with other analgesic options, including nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids; however, these medications carry their own risks and may not be appropriate for use by certain patients. NSAIDs may increase the risk of gastrointestinal, renal, and cardiovascular adverse events. The adverse effects of opioids include sedation and constipation, and use of these drugs is associated with the risk of addiction and overdose.¹⁶

Nonpharmacological strategies, including psychological and sociological interventions and exercise therapy, can be effective for treating chronic pain in some patients.¹⁷ Therefore, the risks and benefits of available therapies must be carefully weighed by the clinician and the patient and/or family, before deciding on a treatment plan.

Recommendations

Healthcare Providers

- Review the patient’s medical and medication-use history before prescribing or recommending acetaminophen, to identify use of any other acetaminophen-containing products and to assess whether the patient has risk factors warranting a dosage reduction.

- Inform patients about using acetaminophen safely; use the Health Canada guide [Let's Talk About Acetaminophen](#) to reinforce this information.¹⁸
- For pediatric patients, assist parents in the following aspects of therapy:
 - calculating the dose of acetaminophen required
 - ensuring the child's weight has been determined accurately, in both pounds and kilograms, given that the Canadian labelling standard permits dosing to be expressed in either of these units (emphasize to parents that they should read the label directions carefully to ascertain the unit of measure for weight, as this unit may vary from one product to another)
 - understanding the amount (dose) to be administered, whether in tablet or liquid form
 - knowing about an appropriate measuring device for liquids and how to use it
- Provide patients with information about nonpharmacological options to treat pain.
- Reduce the labelled maximum daily dose recommendation for acetaminophen, as has been done voluntarily by some manufacturers in other jurisdictions, despite the fact that this labelling change has not been mandated in Canada or elsewhere.
- Although not required by Health Canada, eliminate the use of umbrella names. This measure, as well as the requirement to indicate "contains acetaminophen" on the primary display panel, can inform consumers and reduce confusion among different products.
- When designing package labels, incorporate the recommendations from the Good Label and Package Practices Guides for [Prescription Drugs](#) and [Non Prescription Drugs and Natural Health Products](#), as well as the International Medication Safety Network's statement "Making Medicines Naming, Labeling and Packaging Safer".¹⁹

Manufacturers

- Implement the measures recommended by Health Canada for acetaminophen packages:
 - provide a Drug Facts table, as outlined in the 2016 Health Canada Labelling Standard^{8,13}
 - provide an appropriate, accurately calibrated dosing device for all liquid preparations

Conclusion

In spite of efforts to enhance the safety of acetaminophen use, incidents of serious liver injury from acetaminophen continue to be reported in Canada and globally. ISMP Canada supports ongoing monitoring of the incidence of hepatotoxicity from acetaminophen and the continued implementation of safety measures to mitigate the risk of harm from this commonly used medication.

References

1. Summary safety review—Acetaminophen—Liver injury. Ottawa (ON): Health Canada; 2015 Jul 9 [cited 2017 Jan 19]. Available from: <http://www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/acetamino-eng.php>
2. Acetaminophen. In: Drug Product Database. Ottawa (ON): Health Canada; 2017 [cited 2017 Jan 23] [search for "Acetaminophen" under "Active Ingredients"]. Available from: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>
3. Acetaminophen. Ottawa (ON): Government of Canada; 2016 Sep 15 [cited 2017 Feb 26]. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medical-devices/acetaminophen.html>
4. Acetaminophen—Harm from overdose can be prevented. SafeMedicationUse.ca Newsl. 2014 [cited 2017 Jan 19];5(1):1-2. Available from: https://safemedicationuse.ca/newsletter/newsletter_Acetaminophen.html
5. Spotlight on acetaminophen [medication safety tips]. Toronto (ON): Institute for Safe Medication Practices Canada; 2017 [cited 2017 Feb 28]. Available from: https://safemedicationuse.ca/tools_resources/tips_acetaminophen.html
6. Acetaminophen special project: Acetaminophen overdose and liver injury in the Canadian context. Ottawa (ON): Health Canada, Health Products and Foods Branch, Marketed Health Products Directorate; 2014.
7. Tylenol® dosage for adults. New Brunswick (NJ): Johnson & Johnson Consumer Inc.; 2016 [cited 2017 Jan 20]. Available from: <https://www.tylenol.com/safety-dosing/usage/dosage-for-adults>
8. Stronger, clearer labels for over-the-counter acetaminophen products to further address the risk of liver damage. Ottawa (ON): Government of Canada, Health Canada; 2015 Sep 15 [cited 2017 Jan 19]. Available from: <http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/60198a-eng.php>
9. Turvill JL, Burroughs AK, Moore KP. Change in occurrence of paracetamol overdose in UK after introduction of blister packs. *Lancet* 2000;355(9220):2048-9.

10. Hawton K, Bergen H, Simkin S, Dodd S, Pocock P, Bernal W, et al. Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses. *BMJ*. 2013;346:f403. Also available from: <http://www.bmj.com/content/346/bmj.f403>
11. Paracetamol: changes to pack size. Symonston (Australian Capital Territory): Therapeutic Good Administration (Australian Government – Department of Health). 2013 Aug [cited 2017 Feb 28]. Available from: <https://www.tga.gov.au/media-release/paracetamol-changes-pack-size>
12. FDA Consumer Health Information: New steps aimed at cutting risks from acetaminophen. Silver Spring (MD): Food and Drug Administration (US); 2011 Jan [cited 2017 Jan 19]. Available from: <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm239747.htm>
13. Notice: Revised guidance document: Acetaminophen labelling standard. Ottawa (ON): Health Canada, Natural and Non-prescription Health Products Directorate, Health Products and Food Branch; 2016 Sep 15 [cited 2017 Jan 19]. Available from: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/prodpharma/applic-demande/guide-ld/label_stand_guide_ld-2016-eng.pdf
14. Over-the-counter pediatric oral liquid drug products containing acetaminophen: guidance for industry. Silver Spring (MD): U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). 2015 Aug [cited 2017 Jan 19]. Available from: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM417568.pdf>
15. Notice: Limiting the strength of acetaminophen to 325 mg per dosage unit in prescription combination products. Ottawa (ON): Health Canada; [modified 2016 Sep 13; cited 2017 Jan 19]. Available from: <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/announce-annonce/notice-acetaminophen-acetaminophene-avis-eng.php>
16. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioid for chronic pain—United States, 2016. *JAMA*. 2016;315(15):1624-1645.
17. Managing chronic pain: a holistic approach. Surry Hills (NSW): NPSMedicinewise. 2015 May [cited 2017 Feb 28]. Available from: <http://www.nps.org.au/conditions/nervous-system-problems/pain/for-individuals/pain-conditions/chronic-pain/for-health-professionals/management-plan/holistic-care>
18. Let's talk about acetaminophen. Ottawa (ON): Government of Canada, Health Canada; 2016 Apr 22 [cited 2017 Jan 19]. Available from: <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/let-s-talk-about-acetaminophen.html>
19. Position statement: Making medicines naming, labeling and packaging safer. Horsham (PA): International Medication Safety Network; 2013 [cited 2017 Jan 19]. Available from: <http://www.intmedsafe.net/wp-content/uploads/2014/07/Making-Medicines-Naming-Labeling-and-Packaging-Safer-Final-A4-2013.pdf>

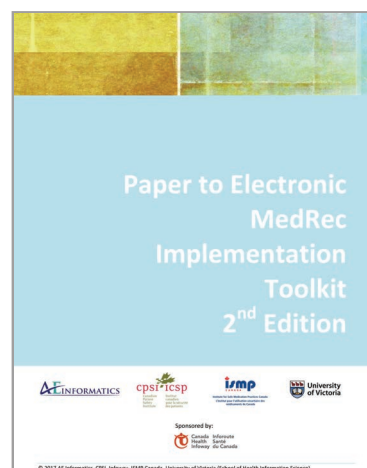
Updated Paper to Electronic MedRec Implementation Toolkit Now Available!

The Institute for Safe Medication Practices Canada, in collaboration with the Canadian Patient Safety Institute and the University of Victoria and with the support of Canada Health Infoway, is pleased to release the second edition of the Paper to Electronic MedRec Implementation Toolkit.

Highlights of this edition:

- evidence for eMedRec to improve patient safety
- eMedRec vignettes to support Health Canada's opioid strategy
- testimonials from early adopters
- improved guidance for evaluating eMedRec
- updated screenshots of exemplary eMedRec solutions
- a comprehensive checklist to support the selection of an eMedRec solution with ideal features

The updated toolkit and checklists can be found at <https://www.ismp-canada.org/medrec/#tab3>



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

March 2017 Newsletter:

Suddenly Stopping a Medication Can Be Harmful

SafeMedicationUse.ca received an incident report describing a patient who was told to stop using her antidepressant but was not given instructions on how to do so safely (i.e., no taper schedule was provided). After abruptly discontinuing her medication, the patient experienced withdrawal symptoms, including tremors and extreme sweating. In the newsletter, consumers are reminded that certain medications must be stopped slowly under the supervision of a healthcare provider, to minimize the risk of withdrawal symptoms and potential harm.

Tips for Practitioners:

- For medications that should not be stopped abruptly (i.e., those that require tapering), apply an auxiliary label alerting the patient to consult a healthcare provider before discontinuing the medication.
- Inform your patients if a medication they are taking needs to be tapered before discontinuation.
- When tapering the dose of a medication, make sure the patient is aware of warning signs that the dose is being reduced too quickly and understands when to seek medical attention.

For more information, read the full newsletter:

https://www.safemedicationuse.ca/newsletter/newsletter_StoppingMedication.html

**Consumers Can Help Prevent
Harmful Medication Incidents**

SafeMedicationUse.ca



Check Out the Updated Medication Reconciliation Kits!

ISMP Canada is delighted to release 2 newly revised medication reconciliation (MedRec) Getting Started Kits. These new kits highlight the most current evidence, knowledge, and practices in both acute care and long-term care settings.

- **Medication Reconciliation in ACUTE CARE Getting Started Kit**
<https://www.ismp-canada.org/download/MedRec/MedRec-AcuteCare-GSK-EN.pdf>
- **Medication Reconciliation in LONG-TERM CARE Getting Started Kit**
<https://www.ismp-canada.org/download/MedRec/MedRec-LTC-GSK-EN.pdf>



More than 100 Endorsements for 5 Questions to Ask!



You can request a customized 5 Questions to Ask about Your Medications poster for your organization by emailing medrec@ismp-canada.org

To date, more than 100 organizations have endorsed 5 Questions to Ask about Your Medications, including international, national, and provincial associations and programs.

For more information, please visit <https://www.ismp-canada.org/medrec/5questions.htm>



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.

Stay Informed

To receive ISMP Canada Safety Bulletins and Newsletters visit:

www.ismp-canada.org/stayinformed/

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

Contact Us

Email: cmirps@ismp-canada.org

Phone: 1-866-544-7672

©2017 Institute for Safe Medication Practices Canada. Permission is granted to subscribers to use material from the ISMP Canada Safety Bulletin for in-house newsletters or other internal communications only. Reproduction by any other process is prohibited without permission from ISMP Canada in writing.