

# Health Canada's Approach to Prescription Opioid Risk Management

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Andrew Slot – Health Canada



# Overview

- High-level description of select Health Canada initiatives to address problematic opioid use
- Specific Health Canada actions on prescription opioids related to safe use, prescribing and advertising
- Prescription opioid Risk Management Plans
- Challenges and next steps

# Overview of Canadian Federal Actions on Opioids

- Regulatory Actions
  - Supporting the establishment of [supervised consumption sites](#) and drug checking technologies
  - [Regulatory amendments](#) to facilitate methadone prescribing and use of medical diacetylmorphine
  - Regulatory amendments to facilitate access to [drugs for urgent public health needs](#)
  - Proposed regulatory amendments to schedule [tramadol](#)
  - Intent to make all [low-dose codeine](#) products prescription-only medications
  - Enacted [legislation](#) to protect individuals who seek emergency assistance for overdose

# Overview of Canadian Federal Actions on Opioids

- Non-regulatory actions
  - Key funding initiatives through the Substance Use and Addictions Program ([SUAP](#))
  - Supporting the development of [treatment guidelines](#) for Opioid Use Disorder (OUD)
  - Facilitated access to [naloxone](#)
  - Coordinating national data collection and publishing [quarterly reports](#)

# Health Canada Actions on Prescription Opioids in the Post-market Space

1. Updated product monographs for opioids
2. Mandatory pharmacy stickers and patient information handouts
3. Stronger stance on opioid advertising and promotional activities
4. Mandatory Canadian Specific Opioid – targeted Risk Management Plans (CSO-tRMP)

# 1. Updates to the Product Monograph

- In conjunction with recommendations from a [Scientific Advisory Panel on Opioid Use and Contraindications](#), the following updates were implemented:
  - Recommendation for a **daily opioid threshold dose** for the management of chronic non-cancer, non-palliative pain
  - Recommendation to **limit the quantity of opioids prescribed for acute pain**
  - Clarification of warnings, including those for special populations such as pregnant women and patients with a history of dependence or substance use disorder
- More recently, advisements have gone out to avoid the use of opioid-containing cough and cold medications in children.

## 2. Stickers and Handouts

- Canadians should have access to needed opioids but with the appropriate knowledge about their safe use and risks
  - New Federal requirement as of October 20<sup>th</sup> 2018
  - All prescription opioids dispensed to patients at the pharmacy-level included in [Part A](#) of the List of Opioids as published on the Health Canada website
  - Evaluation of the impact and effectiveness is needed
  - Monitoring, compliance and enforcement will be carried out by Health Canada



# Opioid Medicines

## Information for Patients and Families

You have been prescribed an opioid medicine for the treatment of pain or for another condition.

Talk to the health professional who prescribed your opioid, or your pharmacist if you:

- Have questions about your opioid medicine.
- Do not understand the instructions for using the opioid medicine given to you.
- Develop side effects or your condition worsens.

### SERIOUS WARNINGS

- **Opioid overdose can lead to death.** Overdose is more likely to happen at higher doses, or if you take opioids with alcohol or with other sedating drugs (such as sleeping pills, anxiety medication, anti-depressants, muscle relaxants).
- **Addiction** may occur, even when opioids are used as prescribed.
- **Physical dependence** can occur when opioids are used every day. This can make it hard to stop using them.
- **Life-threatening breathing problems or reduced blood pressure** may occur with opioid use. Talk to the health professional who prescribed your opioid about whether any health conditions you have may increase your risk.
- **Your pain may worsen** with long-term opioid use or at higher doses. You may not feel pain relief with further increases in your dose. Talk to the health professional who prescribed your opioid if this happens to you, as a lower dose or a change in treatment may be required.
- **Withdrawal symptoms**, such as widespread pain, irritability, agitation, flu-like symptoms and trouble sleeping, are common when you stop or reduce the use of opioids.
- **Babies born to mothers taking opioids** may develop life-threatening withdrawal symptoms.
- **Use only as directed.** Crushing, cutting, breaking, chewing or dissolving opioids before consuming them can cause serious harm, including death.

### SIGNS OF OVERDOSE

- Hallucinations
- Confusion
- Difficulty walking
- Extreme drowsiness/dizziness
- Slow or unusual breathing
- Unable to be woken up
- Cold and clammy skin

**Call 911 or your local emergency response provider right away if you suspect an opioid overdose or think you may have taken too much. \***

\* Naloxone has been approved by Health Canada to temporarily reverse known or suspected opioid overdoses.

### POSSIBLE SIDE EFFECTS

- Reduced physical and/or mental abilities, depression
- Drowsiness, dizziness, risks of falls/fractures
- Heart palpitations, irregular heartbeat
- Problems sleeping, may cause or worsen sleep apnea
- Vision problems, headache
- Low sex drive, erectile dysfunction, infertility
- Severe constipation, nausea, vomiting

### YOUR OPIOIDS MAY BE FATAL TO OTHERS

- **Never give your opioid medicine to anyone.**
- Store opioids (including used patches) in a secure place to prevent theft, problematic use or accidental exposure.
- Keep opioids out of sight and reach of children and pets. Taking even one dose by accident can be fatal.
- Never throw opioids (including used patches) into household trash where children and pets may find them.
- Return expired, unused or used opioids (including patches) to a pharmacy for proper disposal.

**This handout is a summary and will not tell you everything about opioid medicines.**

More information about the opioid you have been prescribed (or naloxone) can be found online in the Product Monograph: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>

Date: 2019/03/15



### 3. Promotion and Advertising

- In June 2018, a [public consultation](#) was launched on the Government of Canada's intention to restrict prescription opioid marketing and advertising
  - Also included a voluntary call on opioid manufacturers and distributors to immediately cease opioid marketing activities to health care professionals in Canada
- New “[Stop Illegal Marketing of Drugs and Devices](#)” platform launched in March, 2019

# Help stop illegal marketing of drugs and devices

## YOU REPORT • YOU PROTECT

As health experts, you work hard to help and protect your patients. Don't let your prescriptions be influenced by illegal marketing practices.

By reporting this type of marketing, you can help Health Canada in our efforts to stop illegal marketing of drugs and devices.



## YOU CAN HELP BY

-  **LEARNING** about Illegal Marketing of Drugs and Devices in Canada at [canada.ca/drug-device-marketing](https://canada.ca/drug-device-marketing)
-  **REPORTING** illegal marketing practices at [drug-device-marketing@canada.ca](mailto:drug-device-marketing@canada.ca)

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### 3. Promotion and Advertising

- Health Canada is now:
  - proactively monitoring, by identifying and responding rapidly to non-compliance, and continuing to address complaints received;
  - monitoring advertising trends;
  - making it easier to [report](#) suspect industry advertising activities; and
  - requiring preclearance of opioid-related advertising and detailing materials through existing pre-clearance agencies.

### 3. Promotion and Advertising

- Under the Terms and Conditions, all opioid-related materials that would be provided to health care professionals must be precleared by an external advertising preclearance agency (e.g. Pharmaceutical Advertising Advisory Board; PAAB)
- This pre-clearance would verify that advertising of opioids:
  - Presents balanced information on benefits and risks
  - Aligns with the Product Monograph
  - Is not false or misleading

### 3. Promotion and Advertising

- Health Canada recently announced that, as of June 2019, new Terms and Conditions will be applied on what information can be included in promotional materials
  - This would restrict all advertising materials of Class B opioids provided to health care professionals to only statements that have been authorized by Health Canada in the Product Monograph.
  - Specifically, only information contained in the Product Monograph would be permitted in such advertising materials and would have to be presented *verbatim* while meeting the requirements for a fair and balanced representation of the benefits and risks.

## 4. Post-market Risk Management Plans

- Under the Terms and Conditions authorities all marketed prescription opioid-containing products included on [Part B](#) of the List of Opioids published on the Health Canada website require a Canadian specific opioid risk management plan, except:
  - Hospital-use only surgical anaesthetics (e.g. sufentanil, remifentanil)
  - Products already subject to controlled distribution and direct administration by a healthcare professional (e.g. Probuphine)

## 4. Post-market Risk Management Plans

- Terms and Conditions were issued to opioid manufacturers based on priority:
  1. High-potency mu agonists (e.g. fentanyl, hydromorphone, oxycodone, morphine, etc.)
  2. Codeine and tramadol
  3. Remaining products (weak or mixed/partial agonists, including meperidine, pentazocine, butorphanol, etc.)
- Companies received a 30 day Notice, followed by a Terms and Conditions letter providing them 90 days to submit the required documents.

## 4. Post-market Risk Management Plans

- Companies had various resources to help them prepare the mandatory risk management plans
  - The Health Canada [Guidance](#) on the Submission of Risk Management Plans outlines the basic requirements for an RMP
  - The Health Canada [Guidance](#) on the Submission of targeted risk management plans and follow-up commitments for prescription opioid-containing products outlines more specific considerations for the RMP
  - Further clarification was offered by contacting the Marketed Health Products Directorate (MHPD) directly



## 4. Post-market Risk Management Plans

- Manufactures were required to submit their risk management plan by the specified deadline, which included all required sections
  - Any missing components would require full justification from the market authorization holder
- Health Canada encouraged companies to work together
  - There has been some voluntary collaboration to date

## 4. Post-market Risk Management Plans

- The desired outcomes of carrying out the activities described in the Opioid RMP Guidance were to:
  - standardize and strengthen the rigor of post-market surveillance of prescription opioids, allowing quantification of the risks associated with opioid-related harms in the Canadian population
  - put in place targeted risk minimization activities to prevent or decrease prescription opioid-related harms in Canada

## Current Status

- The Department has reviewed the first wave of RMPs and provided feedback to industry
- The second and third waves of reviews are nearing completion
- Health Canada expects that this will be an iterative approach to fine-tune what works best for both parties

## Safety Specifications – Health Canada’s Observations

- Most companies had difficulty identifying data to implicate their products directly with opioid-related harms.
  - Data are predominantly by active ingredient
- The majority of companies indicated there was a lot of knowledge about how these products are used, but often limited epidemiological data was presented to support the indicated populations, at risk populations, and general risk factors for opioid-related harms.

# Safety Specification – Health Canada’s Expectations

Risk type	Safety concern
Identified risk	<ul style="list-style-type: none"><li>• Misuse</li><li>• Abuse</li><li>• Opioid use disorder</li><li>• Tolerance and physical dependence</li><li>• Drug withdrawal (including neonatal opioid withdrawal syndrome)</li><li>• Fatal overdose</li><li>• Life-threatening respiratory depression</li><li>• Interactions with other CNS depressants (including benzodiazepines, alcohol, gabapentinoids, etc.)</li></ul>
Potential risk	<ul style="list-style-type: none"><li>• Medication errors</li><li>• Off-label use</li><li>• Accidental exposure</li></ul>
Missing information	<ul style="list-style-type: none"><li>• Safety and efficacy in long-term use (including lack of efficacy and hyperalgesia)</li></ul>

## Pharmacovigilance Proposals – Health Canada’s Observations

- Larger companies have proposed:
  - RADARS-type surveillance approaches
  - Administrative database studies
    - Linked prescription and hospitalization data
  - Funding of academic research
    - Would be administered by third party
  - Surveys to assess health care professionals’ thoughts on the current educational materials
- Smaller companies have proposed:
  - Modified routine surveillance activities
    - Specific disproportionality reporting

## Risk Minimization Proposals – Health Canada’s Observations

- All companies have proposed strengthening access to educational materials, including:
  - Issuing Dear Health Care Professional letters
  - Providing single-window access to third party-made and -endorsed educational materials
  - Continuing Medical Education (CME)

## Controlled Distribution

- The only products with controlled distribution are implantable and injectable buprenorphine products.
  - The controlled distribution plans were implemented to mitigate risks associated with procedural complications or teratogenic concerns with excipients
  - Product would be available to prescriber upon successful completion of training
    - Product to be administered by prescriber only – no direct patient access to product prior to administration



## Challenges

- Concerns from industry on the added financial burden, which for smaller companies may lead to a business decision to discontinue products
  - Possible unintended consequence of reducing patient access to certain medications
  - Becomes challenging to work with smaller companies to ensure continued patient access but to also receive meaningful data
  - At the same time there is a government initiative to reduce drug costs in Canada and mandatory tests or studies are seen as counter to that direction
- No authority to mandate collaboration between companies
- Most proposals received to date were early drafts, and final versions were not available

## Next Steps

- All of the RMPs are to be resubmitted for review, including final protocols, educational tools/ physician aids, etc.
- Preliminary data will be received later in 2019.
- Will continue to chart data gaps and possible intervention points
- Will continue to seek new data sources and partnerships