For the Honourable Jane Philpott, The Federal Minister of Health &
The House of Commons Standing Committee on Health (HESA)

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POLICY BRIEF

Combating codeine misuse: Repeal of Section 36 from the Narcotic Control Regulations of the Controlled Drug and Substances Act.

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To: **The House of Commons Standing Committee on Health (HESA)**

From: Canadian Health Professionals for Evidence-Based Drug Policy

Subject: Combating codeine misuse: Repeal of Section 36 from the Narcotic Control Regulations of the Controlled Drug and Substances Act.

Non-prescription access to codeine is contributing to Canada's opioid problem. In practice, the pharmacy profession has proven unable to prevent misuse of these products.[1-3] Access to these drugs without physician oversight risks opioid addiction, overdose, and hospitalization.[1,4] In addition, current clinical evidence demonstrates that these products have no benefit over safer, over-the-counter pain-killers.[5-7] Removing section 36 from the Narcotic Control Regulations stands to prevent harm to Canadians without reducing access and quality of care.

Codeine

- An opioid analgesic/antitussive in the same family as fentanyl that carries abuse potential and safety concerns.[1]
- At doses above 8mg per tablet, its prescriptive requirements are controlled by federal and provincial regulations due to its abuse potential.
- Adverse effects include sedation, addiction, respiratory depression and death.
- Addiction, resulting from euphoric side effects or uncontrolled pain, often leads to dose escalation and migration to more potent opiates (such as heroin or fentanyl).[8]

Exempted Codeine Products (ECPs) are available without a prescription. Defined in the Narcotic Control Regulations (see Appendix I), ECPs contain no more than 8mg of codeine per tablet, combined with two or three additional non-controlled substances in therapeutic proportions. This is a subtherapeutic dose of codeine; the minimum effective dose in adults is 30mg. One can only attain a therapeutic dose by taking higher than recommended doses (4 tablets) and overdosing on the other components within the preparation. These products attempt to leverage the risk of overdose of the non-narcotic components in order to prevent dose-escalation of codeine.

1. Nielsen, S., et al. "Over the counter codeine dependence." Melbourne: Turning Point Alcohol and Drug Centre (2010).
2. Yang, Jennifer, and Diana Zlomislic. "Star Investigation: Canada's Invisible Codeine Problem." The Toronto Star 12 Nov. 2015.
3. Russell, Jennie. "Investigation Finds Pharmacies Failed to Ask Questions Critical to Patient Safety." *CBC News.* 22 Jan. 2015.
4. MHRA. "PUBLIC ASSESSMENT REPORT: Codeine and Dihydrocodeine-containing Medicines: Minimising the Risk of Addiction." Medicines and Healthcare Products Regulatory Agency. Nov. 2009.
5. Beaver, W. T. "Aspirin and acetaminophen as constituents of analgesic combinations." Archives of internal medicine 141.3 (1981): 293.
6. Charles, Christopher S, et al. "A comparison of ibuprofen versus acetaminophen with codeine in the young tonsillectomy patient." Otolaryngology - Head and Neck Surgery 117.1 (1997): 76-82.
7. Drendel, Amy L., et al. "A randomized clinical trial of ibuprofen versus acetaminophen with codeine for acute pediatric arm fracture pain." Annals of Emergency Medicine 54.4 (2009): 553-560.
8. Miller, Norman S., and Mark S. Gold. "Prescription Opioids and Addiction."Psychiatric Annals 45.10 (2015): 516-521.

The most commonly used ECPs are combined with acetaminophen (Tylenol No.1®) while others contain ASA (222s®), antihistamines or muscle relaxants. These additional drugs each have unique risks as well as safety concerns and overdose can lead to hospitalization.[9,10] In addition, codeine itself is a drug with safety hazards, besides addiction risk. For a significant portion of the population, they metabolize codeine dysfunctionally and risk overdose even from regular doses (representing more than 700,000 Canadians).[11,12]

As not all pharmacies track sales of ECPs in their provincial pharmacy databases, patients can visit multiple pharmacies, acquiring large amounts from each.[2] One 200 tablet bottle contains 1600 mg of codeine, equivalent to 890µg of IV fentanyl (enough to harm a regular adult).[13]

Considerations

Most studies concerning this subject come from Australia, where many codeine products have already been removed from non-prescription designations.[14] There, nearly 1 in 5 non-prescription codeine users were identified as dependent with two thirds of this population overdosing regularly.[1] Previous modifications of regulation (explicit labelling, limiting the size of packages) while maintaining product non-prescription designation has not proven to reduce misuse.[15]

Removal of clause 36 from the Narcotic Control Regulations would result in the requirement of physician oversight and a prescription for access to all codeine products, including ECPs. This would be in line with current clinical guidelines recommending that codeine use should only be used with physician oversight.[14,16]

While there are those benefiting from ECP use without any adverse consequence, there are alternatives on the market that are available without a prescription, with equally demonstrated clinical efficacy and superior safety profiles.[6,7] Switching analgesics would be a simple transition for retail pharmacies to undertake as the alternatives are similar in cost; this would not burden the public healthcare system nor contribute to suboptimal pain management.

9. Lane, Joshua E., et al. "Chronic acetaminophen toxicity: a case report and review of the literature." The Journal of Emergency Medicine 23.3 (2002): 253-256.
10. Temple, Anthony R. "Acute and chronic effects of aspirin toxicity and their treatment." Archives of internal medicine 141.3 (1981): 364.
11. Crews, K. R., et al. "Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P450 2D6 (CYP2D6) genotype." Clinical pharmacology and therapeutics 91.2 (2012): 321.
12. MacDonald, Noni, and Stuart M. MacLeod. "Has the time come to phase out codeine?." Canadian Medical Association Journal 182.17 (2010): 1825-1825.
13. Anderson, Robert, et al. "Accuracy in equianalgesic dosing: conversion dilemmas." Journal of pain and symptom management 21.5 (2001): 397-406.
14. "Interim Decisions on Matters Referred to an Expert Advisory Committee (1.1 Codeine)." *Therapeutic Goods Administration (TGA),* Australian Department of Health. 01 Oct. 2015.
15. Cairns, Rose, Jared Brown, and Nicholas Buckley. "The impact of codeine re-scheduling on misuse: a retrospective review of calls to Australia's largest poisons centre." Addiction (2016).
16. "AMA Supports TGA's Call for Codeine Upscheduling." *Australian Medical Association.* 21 Oct. 2015. Web.

The onus is currently on the pharmacist to refuse sale of ECPs if misuse is suspected. Pharmacy regulation has been the concentration of policymakers,[17] though it is unrealistic to expect pharmacists to limit sales. There are three major limitations that affect unchecked ECP release:

- ➢ Business interests to sell more product.
- ➢ Insufficient human resource allotment for interviewing patients in busy pharmacies.[18]
- ➢ Retail pharmacists are not positioned to recognize nor assess opiate abuse and addiction.

Patients are furthermore easily able to bypass the pharmacist with pre-rehearsed scripts or they may resort to aggression or intimidation even if a pharmacist is vigilant in their assessment.[17] Not surprisingly, as proven by investigative journalism, abusers are still able to acquire ECPs.[2]

In addition to codeine risks, acetaminophen, the most common additional ingredient in ECPs, is the leading cause of acute liver failure in Canada.[19] Those that abuse these ECPs do so despite risk and negative consequence[20] and are at risk for costly hospital stays. For every case of acetaminophen induced liver failure prevented, the public health budget stands to save $2,123.[21] According to a recent Health Canada safety review, acetaminophen-codeine combination products are often directly responsible for acetaminophen overdoses and acute liver failure.[22] In addition, many experts have called for a lower daily dose limit of 2600 mg of acetaminophen, a dose easily surpassed in ECP abuse. With such risks with acetaminophen, it surely should not be combined with a drug with such abuse potential like codeine and made available without a prescription.

Media scrutiny of opioid abuse is increasing in frequency and the public is looking to their government to take strategic action. In response, the Federal Minister of Health, the Honourable Jane Philpott, spoke at the 2nd Charting the Future of Drug Policy in Canada Conference in June 2016. She has explicitly endeavoured to delist non-prescription codeine from legislation.[23]

17. Van Hout, Marie-Claire, and Ian Norman. "Misuse of non-prescription codeine containing products: recommendations for detection and reduction of risk in community pharmacies." International journal of drug policy 27 (2016): 17-22.
18. Resnik, David B., Paul L. Ranelli, and Susan P. Resnik. "The conflict between ethics and business in community pharmacy: what about patient counseling?." Journal of Business Ethics 28.2 (2000): 179-186.
19. Osterweil, Neil. "Acetaminophen Is Leading Cause of Acute Liver Failure." MedPage Today. 30 Nov. 2005. Website.
20. Everitt, Barry J., and Trevor W. Robbins. "Drug addiction: updating actions to habits to compulsions ten years on." Annual Review of Psychology 67 (2016): 23-50.
21. Myers, Robert P., et al. "Impact of liver disease, alcohol abuse, and unintentional ingestions on the outcomes of acetaminophen overdose."*Clinical Gastroenterology and Hepatology* 6.8 (2008): 918-925.
22. "Acetaminophen Special Project: Acetaminophen Overdose and Liver Injury in the Canadian Context." Health Canada: Marketed Health Products Directorate, Health Products and Foods Branch. 17 January 2014.
23. "Speaking Notes for the Honourable Jane Philpott, Minister of Health - 2nd Charting the Future of Drug Policy in Canada Conference." Health Canada. Government of Canada, 17 June 2016.

Conclusion

With prescribing regulation of opiates becoming more strict in Alberta and British Columbia, non-prescription codeine deserves similar attention. Removal of section 36 from the Narcotic Control Regulations will address Canada's battle with opioid misuse and realize Health Canada's mandate to protect the Canadian public. This will represent a progressive approach to protecting the Canadian public from the risks of opioids. We believe that amending the Narcotic Control Regulations is the best way to solve the problem by setting a national standard for all codeine containing products.

Amendment of the Narcotic Control Regulations will ensure that a physician is consulted before release of any codeine preparation and pharmacies will be relied upon to transition ECP users to equally efficacious, safer, over-the-counter alternatives. This can be achieved without sacrificing care and public healthcare budgets will stand to benefit from fewer social and hospital costs associated with misuse and addiction.

Appendix 1 - Legislation for Removal

CONTROLLED DRUGS AND SUBSTANCES ACT
Narcotic Control Regulations C.R.C., c. 1041

36 (1) Subject to subsection (2), a pharmacist may, without a prescription, sell or provide a preparation containing not more than 8 mg or its equivalent of codeine phosphate per tablet or per unit in other solid form or not more than 20 mg or its equivalent of codeine phosphate per 30 mL in a liquid preparation if

- (a) the preparation contains
    - (i) two additional medicinal ingredients other than a narcotic in a quantity of not less than the regular minimum single dose for one such ingredient or one-half the regular minimum single dose for each such ingredient, or
    - (ii) three additional medicinal ingredients other than a narcotic in a quantity of not less than the regular minimum single dose for one such ingredient or one-third the regular minimum single dose for each such ingredient; and
- (b) there is legibly and conspicuously printed on the inner label and the outer label, as those terms are defined in section A.01.010 of the Food and Drug Regulations, a caution to the following effect:
- "This preparation contains codeine and should not be administered to children except on the advice of a physician, dentist or nurse practitioner."

(2) No pharmacist shall sell or provide a preparation referred to in subsection (1) if the pharmacist has reasonable grounds to believe that the preparation is to be used for purposes other than recognized medical or dental purposes.

SOR/78-154, s. 5; SOR/85-588, s. 13; SOR/2004-237, s. 16; SOR/2012-230, s. 21.