

CMA response:

HEALTH CANADA CONSULTATION ON REGULATORY AMENDMENTS REGARDING TRAMADOL

August 14, 2018

The Canadian Medical Association (CMA) is the national voice of Canadian physicians. Founded in 1867, the CMA's mission is to empower and care for patients and its vision is to support a vibrant profession and a healthy population.

On behalf of its more than 85,000 members and the Canadian public, the CMA performs a wide variety of functions. Key functions include advocating for health promotion and disease/injury prevention policies and strategies, advocating for access to quality health care, facilitating change within the medical profession, and providing leadership and guidance to physicians to help them influence, manage and adapt to changes in health care delivery.

The CMA is a voluntary professional organization representing the majority of Canada's physicians and comprising 12 provincial and territorial divisions and over 60 national medical organizations.

The Canadian Medical Association (CMA) is pleased to provide this submission in response to Health Canada's notice as published in the Canada Gazette, Part 1 for interested stakeholders to provide comments on Health Canada's intent to amend Schedule 1 to the *Controlled Drugs and Substances Act* (CDSA) and the Schedule to the *Narcotic Control Regulations* (NCR) to include tramadol, its salts, isomers and derivatives and the salts and isomers of its derivatives.¹

Tramadol has been marketed in Canada since 2005 and is available only by prescription.¹ The CMA is concerned that, despite tramadol being judged low-risk in terms of addiction, it is nevertheless an opioid and should be placed in the *Controlled Drugs and Substances Act*, under Schedule 1.²

The Canadian Institute for Health Information reports that tramadol is one of six opioids accounting for 96% of all opioid prescriptions between 2012 and 2016.³ The report noted that there was a significant increase in tramadol prescriptions and Defined Daily Doses (DDDs) in that same 2012 to 2016 timeframe that may have been due in part to a decrease in prescriptions and DDDs for codeine.

Tramadol is considered a weak opioid and is used to treat "moderate pain that has not responded to first-line treatments."⁴ It is regarded as having a lower rate of overdose, misuse and addiction than more powerful opioids.⁴

However, it is not without risks. The addition of tramadol to the CDSA, Schedule 1, is important because, as with any opioid, dependence on tramadol can occur with use over prolonged periods. According to the World Health Organization "dependence to tramadol may occur when used within the recommended dose range of tramadol but especially when used at supra-therapeutic doses."⁵ Physical dependence is "distinct from addiction, which includes behavioural elements and harm despite continued drug use." Maintenance of patients on opioids sometimes is only to avoid withdrawal symptoms, caused by physical dependence, as opposed to being used to treat pain.⁶ Tramadol must be tapered under supervision from a health professional.

In addition, tramadol's analgesic effect can be unpredictable depending on a person's genetic capacity to metabolize the drug. Success or failure will be predicated "on it being converted by CYP2D6 to an active metabolite, O-desmethyltramadol."⁷ If there is a CYP2D6 inhibitor present or if the person's genetic make-up is such that they do not metabolize the enzyme very well, "conversion can be blocked so that little or none of the metabolite is produced and little analgesic effect is achieved."⁷ These tramadol pathways may also be blocked which could lead to the drug being "present at higher concentrations for longer periods."⁷ As one expert has noted "when a doctor prescribes tramadol, he or she rolls the dice, not knowing whether the patient will get a bit of opioid, a lot of opioid or none at all."⁶

The risks associated with tramadol with respect to children are such that the United States Food and Drug Administration (FDA) recently recommended that tramadol (and codeine) should not be given to children under 12.⁸ Their concern stems from the potential for tramadol (and codeine) to "cause life-threatening breathing problems in children."⁹ The FDA also recommended that breast-feeding women not be given tramadol because of the potential harm to the child. As well, teens 12 to 18 should not be given the drug "if there is a history of obesity, obstructive sleep apnea, or severe lung disease."⁹ Further, it warned that it should not "be given to children or adolescents as a pain medication after surgery to remove the tonsils or adenoids."⁹

It is very important for the health and safety of Canadians that tramadol be placed on CDSA's Schedule 1. As described in the Notice of Intent for this consultation, this change will "prevent diversion of tramadol and protect Canadians from the health risks associated with unauthorized use."¹ Further, pharmacists will not be able to follow verbal prescriptions and or provide refills of tramadol, and other controls outlined in the Narcotic Control Regulations within the Controlled Drugs and Substances Act.¹⁰

In conclusion, the CMA is concerned that, despite tramadol being judged low-risk in terms of addiction, it is nevertheless an opioid and carries dangers similar to its stronger counterparts. Doctors support patients in the management of acute and chronic pain, as well as addictions, and as such we have long been concerned about the harms associated with opioid use. Therefore, as part of our advocacy, the

CMA supports Health Canada's intent to amend Schedule 1 to the *Controlled Drugs and Substances Act* (CDSA) and the Schedule to the *Narcotic Control Regulations* (NCR) to include tramadol, its salts, isomers and derivatives and the salts and isomers of its derivatives. By doing so it will "help dispel the perception that it's somehow safer than other opioids."⁶

The CMA continues to urge governments to increase access to services and treatment options for addiction and pain management, as well as harm reduction.¹¹

¹ Controlled Drugs and Substances Act: Notice to interested parties — Proposal to add tramadol to Schedule I to the Controlled Drugs and Substances Act and the Schedule to the Narcotic Control Regulations *Canada Gazette, Part I, 2018 Jun 16 152(24)* Available: <http://www.gazette.gc.ca/rp-pr/p1/2018/2018-06-16/html/notice-avis-eng.html#ne2> (accessed 2018 Jun 25)

² Young JWS, Juurlink DN. Five things to know about Tramadol. *CMAJ* May 2013 185(5) Available: <http://www.cmaj.ca/content/cmaj/185/8/E352.full.pdf> (accessed 2018 Jul 31)

³ Canadian Institute for Health Information. *Pan-Canadian Trends in the Prescribing of Opioids, 2012 to 2016*. Ottawa, ON: CIHI; 2017.

⁴ Kahan M, Mailis-Gagnon A, Wilson L, et al. Canadian guideline for safe and effective use of opioids for chronic noncancer pain; clinical summary for family physician. Part 1: general population. *Can Fam Physician* November 2011 011;57:1257-66. Available: <http://www.cfp.ca/content/cfp/57/11/1257.full.pdf> (accessed 2018 Jul 30)

⁵ World Health Organization. *Tramadol Update Review Report* Expert Committee on Drug Dependence. Thirty-sixth Meeting Geneva, 16-20 June 2014 Available: http://www.who.int/medicines/areas/quality_safety/6_1_Update.pdf (accessed: 2018 Aug 1)

⁶ Juurlink DN. Why Health Canada must reclassify tramadol as an opioid. *The Globe and Mail* November 27, 2017

⁷ Flint, A., Merali, Z., and Vaccarino, F. (Eds.). (2018). *Substance use in Canada: improving quality of life: substance use and aging*. Ottawa, Ont: Canadian Centre on Substance Use and Addiction. Available:

<http://www.ccsa.ca/Resource%20Library/CCSA-Substance-Use-and-Aging-Report-2018-en.pdf#search=all%28aging%29> (accessed 2018 Aug 1)

⁸ Jin J. Risks of Codeine and Tramadol in Children. *JAMA* 2017;318(15):1514. doi:10.1001/jama.2017.13534 Available: <https://jamanetwork.com/journals/jama/fullarticle/2657378> (accessed: 2018 Aug 2)

⁹ United States Food and Drug Administration. Codeine and Tramadol Can Cause Breathing Problems for Children. *Consumer Update* April 20, 2017 Available: <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm315497.htm> (accessed: 2018 Aug 14)

¹⁰ Minister of Justice. Narcotic Control Regulations C.R.C., c. 1041. Current to July 5, 2018. Last amended on May 20, 2018 Available: http://laws-lois.justice.gc.ca/PDF/C.R.C.,_c._1041.pdf (accessed: 2018 Aug 14)

¹¹ Canadian Medical Association. *Harms Associated with Opioids and Other Psychoactive Prescription Drugs*. CMA Policy, 2015. Ottawa: The Association; 2015. Available: https://www.cma.ca/Assets/assets-library/document/en/policies/cma_policy_harms_associated_with_opioids_and_other_psychoactive_prescription_drugs_pd15-06-e.pdf (accessed: 2018 Aug 2).