CRISM-ICRAS

Canadian Research Initiative in Substance Misuse

Initiative Canadienne de Recherche en Abus de Substance

Did you know?
SLOW-RELEASE ORAL MORPHINE

The CRISM National Guideline for the Clinical Management of Opioid Use Disorder recommends treatment with slow-release oral morphine—prescribed as once-daily witnessed doses—**can be considered** for patients who have not benefited from treatment with first-line and second-line treatment options (i.e., buprenorphine/naloxone and methadone) **for opioid use disorder.**

Slow-release oral morphine (24-hour formulation, brand name Kadian®)* is approved in Canada for pain management, and there is a growing evidence base for its use in the treatment of opioid use disorder in patients who have not benefited from methadone or buprenorphine/naloxone.

What the Research Says:

- Clinical trials have found that slow-release oral morphine is as effective as methadone in reducing non-medical opioid use and retaining individuals in treatment, and superior to methadone in terms of overall treatment satisfaction and improvements in dysthymic symptoms.[1-4]
- For patients who are intolerant to or not responding well to methadone, research shows that the transition to slow-release oral morphine is well-tolerated and relatively easy, results in reduced withdrawal symptoms and cravings, and may lead to physical and psychological improvements.[2-6]
- Unlike methadone, slow-release oral morphine does not prolong the QTc interval, and may have **safety advantages** for treatment of patients with pre-existing or emergent cardiovascular risks (e.g., cardiac arrhythmia, Torsades de Pointes) or who are taking other medications known to prolong QTc (e.g., antipsychotics, antidepressants, antimicrobials).[2]

Considerations for Prescribing and Dispensing:

- Although approved for clinical use in several European countries, in Canada, the use of slow-release oral morphine to treat patients with opioid use disorder is considered **off-label**, and requires careful review of risks and benefits, fully informed consent of the patient, and rigorous clinical documentation.
- When prescribing slow-release oral morphine for the treatment of opioid use disorder, careful assessment and monitoring is essential to optimize patient safety. Special care and precaution must be taken during dose induction and titration phases, and when managing missed doses.
- The Guideline recommends that in most cases, slow-release oral morphine should be prescribed as daily witnessed doses. Include specific instructions for pharmacy staff to open the capsule and sprinkle pellets into a medicine cup or onto soft food (applesauce, jam) for witnessed ingestion on every dispensation of the medication. Prescribers are encouraged to review these instructions for witnessed ingestion with the dispensing pharmacy.
- **Important Safety Notice: Pellets must be swallowed whole**. Crushing, chewing, or dissolving slow-release oral morphine pellets can cause rapid release and absorption of a potentially fatal dose of morphine sulphate.

Urine Drug Testing

- Immunoassay-based urine drug tests cannot be used to distinguish ongoing use of heroin or some prescription opioids (i.e., morphine) from slow-release oral morphine treatment.
- Local and hospital testing laboratories can assist with details on available options and interpretation.

Regulatory information for prescribers

- The Guideline recommends that clinicians who wish to prescribe slow-release oral morphine for the treatment of opioid use disorder should hold *a methadone exemption.* **Regardless of methadone exemption status, any care provider who does not have experience prescribing slow-release oral morphine for OUD should seek specialist consultation prior to initiating treatment**.
- Kadian® slow-release oral morphine is eligible for coverage under Health Canada's Non-Insured Health Benefits (NIHB) Program as a limited use medication for the treatment of opioid use disorder.
- Please check your provincial drug formulary for benefits and coverage policies.

For further reading:

- CRISM National Guideline for the Clinical Management of Opioid Use Disorder: https://crism.ca/wp-content/uploads/2018/03/CRISM_NationalGuideline_OUD-ENG.pdf
- Eligibility, assessment, and dosing recommendations from the BC Guideline for Clinical Management of Opioid Use Disorder: http://www.bccsu.ca/wp-content/uploads/2017/06/BC-OUD-Guidelines_June2017.pdf#page=49
- Take-home dosing recommendations from the BC Guideline for Clinical Management of Opioid Use Disorder: http://www.bccsu.ca/wp-content/uploads/2017/06/BC-OUD-Guidelines_June2017.pdf#page=55
- Guidance from the College of Physicians and Surgeons of Alberta: http://www.cpsa.ca/wp-content/uploads/2017/09/Slow-release-oral-morphine.pdf

**Only the once-daily, 24-hour formulation of slow-release oral morphine has been studied in clinical trials for the treatment of opioid use disorder. Other formulations of oral morphine, such as twice-daily, 12-hour sustained- or extended-release formulations (brand name M-Eslon®), have not been empirically studied in this context and are not recommended for treatment of opioid use disorder.*

1. Ferri M, et al. 2013 *Cochrane Database Syst Rev.* Jun 5;(6):CD009879.
2. Hammig R, et al. 2014 *J Subst Abuse Treat.* 47(4):275-81.
3. Verthein U, et al. 2015 Eur Addict Res. 21(2):97-104.
4. Mitchell TB et al. 2004 *Addiction* 99(8): 940-45.
5. Falcato L et al. 2015 *J Clin Psychopharmacol.* 35(2):150-57.
6. Kastelic A, Dubajic G, Strbad E. 2008 *Addiction* 103(11):1837-46.