

## Using Methadone to Treat Pain: Information for Health Care Providers

### What is methadone?

- Methadone is a synthetic opioid analgesic developed in the 1940s, with NMDA receptor antagonism as well as mu-opioid receptor agonism.
- While methadone is a synthetic opioid medication used to treat opioid drug addiction, this information relates to the use of methadone as analgesia in the management of non-cancer and cancer pain.

### Why choose methadone?

- Methadone is a long-acting opioid that comes in various forms (liquid, tablets, injectable) and may be considered for patients with:
  - Tolerance, toxicity, or allergy to other opioids
  - Renal failure and/or dialysis
  - Opioid-induced hyperalgesia
  - Neuropathic pain

### What are the advantages of using methadone?

- It is effective for treating neuropathic and bone pain.
- It is a N-methyl-D-aspartate (NMDA) receptor antagonist, attenuating opioid tolerance.
- It is metabolized in the liver with no known active metabolites, and does not accumulate in renal insufficiency.
- It can be titrated in small increments.
- Methadone is lipophilic and readily absorbed from the gastrointestinal tract. Therefore it has a high oral bioavailability of 80-90% and appears in plasma within 30 minutes of administration.
- Liquid methadone can be given via sublingual or buccal routes if difficulty swallowing.

### What should health care providers know about methadone?

- Methadone is not appropriate for the management of acute, unstable pain.
- Methadone is contraindicated in severe liver disease, allergy to methadone or its formulation components, acute respiratory failure.
- Warnings and special precautions apply when prescribing methadone to patients with COPD, sleep apnea and prolonged QTc interval.
- Methadone's half-life averages approximately 24 hours; it takes about 5 days to reach steady state after a dose change. Dose changes should generally not occur more frequently than once per week.
- Follow-up and vigilance regarding analgesic effect and adverse side effects is required during methadone dose initiation and titration (particularly if other opioid medications are also being adjusted).
- A short-acting PRN analgesic medication such as immediate-release morphine or hydromorphone should be prescribed to use for breakthrough pain.
- Methadone has the greatest number of drug interactions reported for opioids. There are extensive and diverse potential interactions with a wide variety of medications related to: enzyme induction or inhibition; displacement from plasma proteins; and additive effects on the QTc interval, serotonergic tone, sedation, or respiratory depression. Methadone is also affected by certain foods such as grapefruit. Consult with pharmacists to review current and new medication prescriptions.

### What are the side effects of taking methadone?

- Methadone can cause drowsiness/sleepiness. This is more common during the first few days after methadone is started or after a methadone dose increase. This usually improves as tolerance develops. When taking methadone, advise patients to:
  - Avoid drinking alcohol.
  - Avoid driving a vehicle or operating equipment/heavy machinery until a stable dose is reached or at any time he/she feels drowsy or sleepy.
- Like other opioid similar medications, methadone may cause nausea or constipation. It is important to proactively address these potential symptoms (e.g. prescribe laxatives concurrently).
- Methadone may cause itchiness. This is usually not due to an allergic reaction, but if the patient develops a rash, swelling or difficulty breathing, they should stop taking the methadone and seek medical attention immediately.
- As with other opioids, excessive dosing may cause respiratory depression. If reversal is indicated, repeated naloxone doses are generally required due to methadone's long elimination half-life.
- In very rare cases, patients using high doses of methadone may experience the potentially fatal ventricular arrhythmia torsades de pointes.

### Will the patient become addicted to methadone?

- Addiction to methadone prescribed for pain is not common.
- As with all opioids, methadone tolerance may develop and require a dose increase to produce the same effect, and physical dependence (with withdrawal symptoms if abruptly discontinued) will occur with sustained use; these are not the same as addiction, which has behavioural and social features.

### Who can prescribe methadone?

- The prescribing of methadone is federally regulated, requiring special exemption from Health Canada.

### What individuals and families need to know when taking methadone?

- Methadone should be taken on a scheduled basis **regardless** of the intensity of pain.
- The best relief happens if methadone is taken at regular, evenly spaced intervals around the clock.
- A breakthrough medication is usually prescribed in addition to the regularly scheduled medication. Patients should report if they need more than 2-3 doses per day of the prescribed breakthrough medication, as this may indicate the need for titrating the scheduled dose.
- Methadone takes time to reach its full effect. Breakthrough doses of short acting analgesia may be required while methadone reaches its full effect.
- Ask your patient to monitor and report his/her response to the methadone and any possible side effects (i.e. patients should document breakthrough doses in a pain diary).
- Advise patients to never stop, start, or adjust the methadone dose without doctor's approval.
- Methadone should never be used by someone other than the person for whom it is prescribed. If used incorrectly methadone can have serious consequences such as slowed breathing and sedation.

### How should methadone be stored in home setting?

- Store methadone at room temperature and, away from extremes of heat and moisture.
- Methadone must be stored in a safe place. Encourage patients and families to consider buying an inexpensive lockable case to store medications.
- Medication no longer required should be returned to a pharmacy for disposal.

### Additional Resources:

Methadone For Pain in Palliative Care Online Course ([www.methadone4pain.ca](http://www.methadone4pain.ca)).

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