

Methadone: A Treatment Option for Chronic Pain But Be Aware of the Following When Prescribing

Recently, the criteria for approval of non-formulary long acting pain medications such as Oxycontin have been strengthened to require failure of two formulary long-acting generic agents, morphine extended release tablets and fentanyl patch. This bullet offers another generic option for treating chronic pain.

Review your Patient's Med List Closely for Potential Interactions

Methadone is the leading cause of accidental death due to opioids

Arrhythmia Risk:

- Methadone has been associated with prolonged QTc and arrhythmias; patients should be informed of the risk of arrhythmia when they are prescribed Methadone, especially at higher doses.
- Patients should be screened for a personal or family history of arrhythmia, syncope, and/or sudden unexplained death.
- In such cases a baseline and follow up ECG should be considered.
- Be aware of other medications that may prolong the QT interval: anti-arrhythmic drugs, flurquinolones, cisapride, macrolides, long acting beta agonists (salmeterol, formoterol).

Drug interactions:

Prescribers must also be aware of drugs which slow the elimination of Methadone, usually due to inhibition or induction of liver enzymes, leading to unpredictably high levels of Methadone.

- Azole antifungals, e.g. ketoconazole
- Macrolide antibiotics
- Sertraline
- Fluvoxamine

Use caution when using Methadone with medications that may induce electrolyte disturbances which may prolong the QT interval (hypomagnesemia, hypokalemia).

- Diuretics
- Laxatives
- Mineralocorticoid hormones- rare

Facts:

- Methadone is an excellent second-line option for patients with chronic non-cancer pain whose opioid requirements are increasing and/or whose side effects are compromising therapy.
- Methadone may be more effective for neuropathic pain compared to other opioids.
- Its effects on NMDA receptors produces analgesia independent of opioid analgesia and also reverses opioid tolerance.
- Methadone commonly has a much greater potency than anticipated, particularly when it is given to a patient who already has been taking another opioid agonist.

Dosing Considerations:

- Initial dosing should be low (2.5-5mg) every 8 hours. OR
- To convert from another opioid, start methadone at a dose that is 25% of the equianalgesic dose of the first opioid, i.e. REDUCE equianalgesic dose by 75%.
- See <http://www.globalrph.com/narcoticonv.htm> to calculate the equianalgesic dose.
- Dosage increases should be no greater than 5-10mg weekly until the desired effect is achieved.
- Special considerations must be made when prescribing methadone because of its:
 - Unique pharmacokinetics
 - Drug interactions
 - Potential for prolonging the QT interval.
- Because of its very long and variable half-life (range between 15 and 55 hours and in some patients up to 120 hours), blood levels may continue to rise and accumulate for 1-2 weeks without a change in dose. Steady state may be achieved in as little as several days to as long as 2 weeks. Because of this, never dose methadone for breakthrough pain or on an as needed basis
- Methadone should not be used in opioid naive patients.
- See patients weekly until stabilized and one week after stabilization to address possible accumulation of methadone.

Common Side Effects (SE):

- While respiratory depression is uncommon, the risk is greatly increased when: taken with benzodiazepines or other depressants, taken with drugs that interact, a dose is increased too quickly, or a dose is given too frequently.
- Similar to other opioid medications, up to 65% of patients report constipation. Tolerance does not usually develop. A scheduled bowel regimen during treatment such as an OTC fiber laxative and stool softener should be considered.
- Somnolence is common during the first few weeks of treatment before tolerance occurs.
- Other CNS SEs include agitation, confusion, disorientation, euphoria, headache, lightheadedness and sedation. Tolerance to these SEs may occur.

R Brown, C Kraus, M Fleming, S Reddy. Methadone: applied pharmacology and use as adjunctive treatment in chronic pain. *Postgrad Med J* 2004; 80:654-659.

R Chou et al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. *The Journal of Pain*. Volume 10, Issue 2, Pages 113-130.