Opioid Therapy and Methadone Use in Primary Care for Chronic Non-cancer Pain

This factsheet accompanies the 2010 VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. It was created to aid with treatment of adult populations. Department of Veterans Affairs (VA) and Department of Defense (DoD) employees who use this information are responsible for considering all applicable regulations and policies throughout the course of care and patient education.

The goal of this factsheet is to make DoD and VA primary care providers aware of the complexities of using methadone opioid therapy (OT) for the treatment of moderate to severe pain. OT is normally administered when a patient presents with moderate to severe non-cancer pain refractory to non-opioid and non-drug therapy. The patient must have no absolute contraindications to OT, and informed consent along with a signed Opioid Pain Care Agreement (OPCA) must be obtained. Contraindications to OT include:

- **Absolute Contraindications:** severe respiratory instability; acute psychiatric instability or uncontrolled suicide risk; diagnosed non-nicotine substance use disorder (DSM criteria) not in remission and not in treatment; true allergy to opioid agents (cannot be resolved by switching agents); co-administration of drug capable of inducing life-limiting drug interaction; corrected QT interval (QTc) > 500 milliseconds for using methadone; active diversion of controlled substances (providing the medication to someone for whom it was not intended); prior adequate trials of specific opioids that were discontinued due to intolerance; serious adverse effects that cannot be treated; and lack of efficacy.

- **Relative Contraindications:** treated substance use disorder; medical condition in which OT may cause harm (e.g., obstructive sleep apnea (OSA) not using CPAP; central sleep apnea; chronic obstructive pulmonary disease (COPD)); QTc interval 450-500 milliseconds (e.g., increased risk of methadone use); paralytic ileus; respiratory depression in unmonitored setting; risk for suicide or unstable psychiatric disorder; complicated pain (e.g., headache not responsive to other pain treatment modalities); conditions that may impact adherence to OT (e.g., cognitively impaired, unwillingness or inability to comply with treatment plan, social instability).

### Patient Education and Follow-up

If OT is undertaken, educate the patient about what to expect while taking the medication. Discuss the addictive potential of OT. Strongly suggest patients avoid alcohol, sedating medications and operation of heavy machinery. Provide education about adverse effects, consequences of non-adherence and the patient’s responsibility to keep medication safe and secure.

<table>
<thead>
<tr>
<th>Table: Risks for Opioid Misuse and Preferred Treatment Settings</th>
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</thead>
<tbody>
<tr>
<td><strong>Risk of Misuse</strong></td>
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<tr>
<td>Low</td>
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<td>Moderate</td>
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<td>High</td>
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</table>
Periodic Follow-up and Re-evaluation

Once OT starts, providers should make sure to follow-up with patients every two to four weeks after any medication or dose change and every one to six months during the maintenance phase. During these visits, providers need to assess pain control, adverse effects, adherence to OT treatment plan, signs of addiction, tolerance, dependence and signs of illegal use. The goal is to determine whether OT is still a safe and beneficial option.

Adverse Effects

For successful opioid therapy, it is critical to ensure patients are provided with a list of common adverse side effects that most commonly occur. Providers can minimize adverse effects through low starting doses, slow titration rates and opioid rotation. Common side effects include:

- confusion
- constipation
- dizziness
- dry mouth
- dyspepsia
- headache
- hyperalgesia
- hypogonadism
- nausea and vomiting
- opioid addiction
- pruritus
- sedation
- sexual dysfunction
- sweating
- tiredness

Methadone Facts

Methadone is a synthetic agent with a long duration of action available in tablet and liquid forms. It is sometimes recommended for continuous chronic pain. The analgesic action lasts six hours or longer, but can take one to two weeks to stabilize. Methadone has a long half-life, with a possibility of accumulation and delayed toxicity without continued analgesic effect. It is also high in toxicity. Methadone is complicated in its pharmacokinetic and pharmacodynamic properties and should be prescribed with caution. Only clinicians who are familiar with methadone’s titration and risks, or those who are able to consult with a pain specialist or clinical pharmacist, should prescribe or make changes to methadone treatment.

Methadone Dosing for Chronic Non-Cancer Pain

- Start low, go slow! Start with low initial dose, adjust conversion ratios to prior opioid use and titrate slowly while patient’s response is monitored.
- For patients not on previous opioids: initial dose is 2.5 mg every eight hours, with titration interval of five to seven days.
- Initial doses of methadone should be small and adjusted to the previous opioid use, using smaller methadone-to-morphine-equivalent conversion ratios (%) the larger the previous morphine-equivalent dose.
- Monitor patients weekly during titration and monthly during maintenance.

<table>
<thead>
<tr>
<th>Dosing strategy</th>
<th>Initial MET dose</th>
<th>Increments</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual titration (For CNCP and situations necessitating less frequent monitoring)</td>
<td>2.5 mg every eight hours</td>
<td>2.5 mg every eight hours every five to seven days</td>
<td>As a general rule, start low and go slow</td>
</tr>
</tbody>
</table>

CNCP = Chronic non-cancer pain; MET = Methadone

Contraindications

Same as for other opioids.
### Adverse Effects and Caution

- Drowsiness: avoid use with other central nervous system depressants, sedatives and alcohol; advise caution if operating a motor vehicle.
- Respiratory depression: extreme caution with asthma, COPD, cor pulmonale, severe obesity and/or OSA.
- QTc prolongation: monitor patients with increased risk of dysrhythmia, conduction abnormalities or medication affecting cardiac conduction.
- Additional caution in elderly (> 65) and patients with liver and renal disease.

### Methadone Patient Education

- Explain to patients that the initial dose may not provide optimum pain relief, but is chosen in order to reduce the chance of adverse effects. A pain diary should be kept to monitor the patient’s response.
- Reassure patients that the dose will be titrated to achieve adequate analgesia.
- When applicable, explain how to use the short-acting opioid during methadone dose titration and advise not to use methadone on an as-needed basis.
- Advise patients that the effect of methadone is not immediate but will strengthen by the end of the week following dose increase. Pain relief during the last few days of that week will be greater than the first few days of the week.
- Remind patients about the need for frequent monitoring during the titration and maintenance periods. Provide patients with instructions on what to do if they develop increasing or intolerable adverse effects.
- Advise patients to avoid abrupt discontinuation of their opioid medication without first consulting their physician. Educate patients about possible withdrawal symptoms.
- Some patients may worry that others will perceive their use of methadone as evidence of a possible addiction to or dependence on opiates. Explain the difference between the therapeutic use of methadone and addiction or dependence.
- It is up to the provider to tell the patient that the overall goal of treatment is not limited to the reduction of pain, but is also to improve physical, emotional and/or social functioning. The provider may also want to inform the patient that the elimination of pain may not be possible.