Managing Side Effects and Complications of Opioid Therapy for Chronic 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 explain how to properly manage side effects of opioid therapy (OT) in DoD and VA primary care settings. Co-occurring conditions and side effects are common consequences of OT, and may occur during both short-term and long-term treatment. After prescribing opioids, it is important to comprehensively assess the patient for co-occuring conditions and side effects at each subsequent visit. ***Providers should inform patients that side effects are common and should ask patients to tell their providers about any side effects that occur.***

Spectrum of Side Effects

The incidence and severity of side effects range from common and manageable to adverse effects that ***require immediate intervention***. Development of tolerance to some adverse effects may be observed over time. Providers should consider individual levels of tolerability to different opioid agents and should also consider preventive treatment for common side effects, particularly constipation and nausea.

Common and Manageable Side Effects

It is critical for successful OT to make sure patients are aware of common side effects and to provide a list of those that most commonly occur. These side effects include:

- confusion
- constipation
- dizziness
- dry mouth
- dyspepsia
- headache
- hyperalgesia
- nausea and vomiting
- pruritus
- sedation*
- sweating
- sexual dysfunction
- tiredness
- drug tolerance

These side effects may often be diminished by low starting doses, slow titration rates, modifying the dosage regimen, treating side effect symptoms, patient education at the outset of therapy and rotating the type of opioid.

**Sedation is a very common side effect, and it is imperative that the provider strongly suggest avoiding alcohol, sedating medications and the operation of heavy machinery.*

Managing Adverse Effects:

It is imperative that providers discuss possible adverse effects of OT with patients and family members. If adverse effects are unmanageable and therapy is a greater detriment than benefit, as determined by discussion with the patient and family, OT should be discontinued. See the chart below for more information on some of the potential adverse effects.

Adverse Effect	Symptoms	Protocol for Management
Respiratory depression	▪ Drowsiness ▪ Slow or shallow breathing ▪ Difficulty staying awake ▪ Difficulty awakening ▪ Loud or unusual snoring	▪ Administer the lowest effective opioid dose necessary to achieve satisfactory pain control. Start low and go slow. ▪ Avoid other central nervous system (CNS) depressants, especially benzodiazepines because this combination has been identified in opioid-related deaths. ▪ Alert family members or caretakers of the important warning signs to watch for that may indicate that the opioid should be decreased or stopped: – Difficult or slow breathing – Difficulty staying awake – Loud or unusual snoring – Difficulty being awakened
Mental status changes	▪ Confusion ▪ Bad dreams ▪ Hallucinations ▪ Restlessness ▪ Agitation ▪ Dysphoria ▪ Significantly depressed level of consciousness ▪ Seizures	▪ Evaluate underlying cause; consider role of primary therapy. Hallucinations can be due to a variety of causes, including change in surroundings and sleep deprivation. ▪ Evaluation of hallucinations is often performed by “trial and error” techniques. Eliminate nonessential CNS-acting medications (e.g., steroids). ▪ Re-evaluate and treat underlying process if appropriate. ▪ Dysphoria is more common with mixed opioid agonists/antagonists and antidopaminergic medications. ▪ If hallucinations persist: – Consider a trial of an antipsychotic in consultation with behavioral health specialty, or – Switch to another opioid
Opioid-induced endocrinopathy	▪ Loss of libido ▪ Impotence ▪ Fatigue ▪ Mood alterations ▪ Loss of muscle mass and strength ▪ Abnormal menses ▪ Infertility	▪ Ask all patients on opioids about symptoms of opioid-induced endocrinopathy (e.g., hypogonadism) at each visit. ▪ Determine cause of symptoms through lab work and/or consultation with an endocrinologist. ▪ For males, consider testosterone patch therapy, as research indicates it may improve androgen deficiency symptoms, sexual function, mood, depression and hematocrit levels. ▪ NOTE: There is insufficient data to recommend routine laboratory screening for endocrinopathy in asymptomatic patients on OT.
Unmanageable sleep-disordered breathing	▪ Loud snoring ▪ Excessive daytime sleepiness ▪ Fatigue ▪ Morning headaches (cerebral vasodilation) ▪ Depression and/or emotional instability ▪ Short-term memory loss ▪ Impaired concentration ▪ Irregular pauses in breathing	▪ Strongly consider discontinuing OT and obtain sleep studies. ▪ The type of sleep apnea should be evaluated to determine if it is obstructive or central. ▪ Central sleep apnea is a relative contraindication to OT, and discontinuation of OT should be considered if sleep apnea is severe or life-threatening. ▪ Instruct patients to avoid alcohol and medications that cause drowsiness.

Complications of OT for Chronic Pain:

Patients may have complicated pain conditions or other conditions that affect the response to therapy and may warrant consultation with specialty care or referral to a higher level of care with a pain medicine specialist. These co-occurring conditions include:

Opioid-induced hyperalgesia (OIH): This condition is characterized by increased pain or pain sensitivity without a change in medical condition. It may be managed by tapering or discontinuing OT. A paradoxical reduction in pain would be expected to occur with reductions in the opioid dose.

Opioid-induced tolerance: This neuroadaptive condition is characterized by decreased sensitivity to opioids and decreased pain relief at a stable dose of medication. Higher doses are needed to achieve the initial effects of the drug. It does not, in and of itself, imply addiction. Psychological and physiological mechanisms of tolerance include:

- A genetically determined, preexisting relative insensitivity to a medication
- Pharmacokinetic (enzyme induction) modification
- Behavioral modification
- Reduction in number of receptors over time
- Up-regulation and resistance of cAMP pathways to opioid mediated decreases in activity

Note: Patients who have developed tolerance will have improved pain control with increased doses. Medical providers may easily confuse opioid-induced hyperalgesia with opioid tolerance. Opioid tolerance will also present with increased pain at a stable dose of medication. However, patients with OIH may have worsening pain with escalating doses of opioids, while patients who have developed tolerance will have improved pain control with increased doses. Testing of pain and sensory analgesia before and after initiating OT may help to distinguish between OIH and opioid tolerance.