# Provider Pocket Guide

## Opioid Therapy for Chronic Pain

Department of Veterans Affairs and Department of Defense employees who use this information are responsible for considering all applicable regulations and policies throughout the course of care. Every health care professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

# Pocket Guide Tabs

This pocket guide references content and considerations from sections and algorithms within the 2017 VA/DoD Clinical Practice Guideline (CPG) for Opioid Therapy (OT) for Chronic Pain (hereby referred to as 2017 VA/DoD OT for Chronic Pain CPG), and addresses interrelated aspects of care for patients who manage their chronic pain with OT.

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NOTE: The recommendations in the 2017 VA/DoD OT for Chronic Pain CPG and this pocket guide are intended to provide information and assist in decision making. They are not intended to define a standard of care and should not be construed as one. Additionally, they should not be interpreted as prescribing an exclusive course of treatment.

# Introduction

Since the release of the original CPG for management of chronic pain with OT in 2010, there has been growing recognition of an epidemic of opioid misuse and opioid use disorder (OUD) in the U.S., including among veterans. At the same time, there is a mounting body of research expanding our knowledge and understanding of the troublesome effects of long-term opioid therapy (LOT). Consequently, a recommendation to update the 2010 VA/DoD OT for Chronic Pain CPG was initiated in 2015. The updated 2017 VA/DoD OT for Chronic Pain CPG includes objective, evidence-based information on the management of chronic pain. It is intended to assist health care providers in all aspects of patient care, including, but not limited to, diagnosis, treatment and follow-up.

## Overview

This pocket guide is a quick reference tool created for general and specialty health care providers who administer and direct OT treatment services to patients with chronic pain in the Department of Veterans Affairs (VA) or Department of Defense (DoD) health care settings. It was developed directly from the 2017 VA/DoD OT for Chronic Pain CPG. VA and DoD employees who use this information are responsible for considering all applicable regulations and policies throughout the course of care and patient education.

**For more comprehensive information, please refer to the full-length CPG, available at: https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf and https://www.qmo.amedd.army.mil/pguide.htm**

### Target audience:

- Health care providers managing or co-managing patients with chronic pain on or being considered for LOT

### Target patient population:

- Adults (18 or older) with chronic pain conditions who are treated in any VA or DoD clinical setting

### Contraindications:

- Not intended for and does not provide recommendations for the management of pain with LOT in children or adolescents, patients with acute pain or patients receiving end-of-life care

### VA/DoD CPG and Pocket Guide goals:

- Assess the patient's condition, provide education and determine the best treatment methods in collaboration with the patient and a multidisciplinary care team
- Optimize the patient's health outcomes and function, and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

# CPG Recommendations

The following recommendations were made using a systematic approach per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (see 2017 VA/DoD OT for Chronic Pain CPG, Appendix E, for explanation of the GRADE approach).

| # | Recommendation | Strength |
|---|---|---|
| **Initiation and Continuation of Opioids** | | |
| **1.** | a) We recommend against initiation of LOT for chronic pain<br>b) We recommend alternatives to OT such as self-management strategies and other non-pharmacological treatments<br>c) When pharmacologic therapies are used, we recommend non-opioids over opioids | a) Strong against<br>b) Strong for<br>c) Strong for |
| **2.** | If prescribing OT for patients with chronic pain, we recommend a short duration<br>Note: Consideration of OT beyond 90 days requires re-evaluation and discussion with patient of risks and benefits | Strong for |
| **3.** | For patients currently on LOT, we recommend ongoing risk mitigation strategies (see Recommendations 7 – 9), assessment for OUD, and consideration for tapering when risks exceed benefits (see Recommendation 14) | Strong for |
| **4.** | a) We recommend against LOT for pain in patients with untreated substance use disorder (SUD)<br>b) For patients currently on LOT with evidence of untreated SUD, we recommend close monitoring, including engagement in SUD treatment, and discontinuation of OT for pain with appropriate tapering (see Recommendations 14 and 17) | a) Strong against<br>b) Strong for |

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| **5.** | We recommend against the concurrent use of benzodiazepines and opioids<br><br>Note: For patients currently on LOT and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate (see Recommendation 14 and the VA/DoD CPG for the Management of SUDs) | Strong against |
| **6.** | a) We recommend against LOT for patients less than 30 years of age secondary to higher risk of OUD and overdose<br><br>b) For patients less than 30 years of age currently on LOT, we recommend close monitoring and consideration for tapering when risks exceed benefits (see Recommendations 14 and 17) | a) Strong against<br><br>b) Strong for |
| **Risk Mitigation** | | |
| **7.** | We recommend implementing risk mitigation strategies upon initiation of LOT, starting with an informed consent conversation covering the risks and benefits of OT as well as alternative therapies. The strategies and their frequency should be commensurate with risk factors and include:<br>▪ Ongoing, random urine drug testing (UDT) – including appropriate confirmatory testing<br>▪ Checking state prescription drug monitoring programs (PDMP)<br>▪ Monitoring for overdose potential and suicidality<br>▪ Providing overdose education<br>▪ Prescribing of naloxone rescue and accompanying education | Strong for |

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| **8.** | We recommend assessing suicide risk when considering initiating or continuing LOT and intervening when necessary | Strong for |
| **9.** | We recommend evaluating benefits of continued OT and risk for opioid-related adverse events at least every three months | Strong for |
| **Type, Dose, Follow-up and Taper of Opioids** | | |
| **10.** | If prescribing opioids, we recommend prescribing the lowest dose of opioids as indicated by patient-specific risks and benefits<br><br>Note: There is no absolutely safe dose of opioids | Strong for |
| **11.** | As opioid dosage and risk increase, we recommend more frequent monitoring for adverse events including OUD and overdose<br><br>Note:<br>▪ Risks for OUD start at any dose and increase in a dose dependent manner<br>▪ Risks for overdose and death significantly increase at a range of 20 – 50 mg morphine equivalent daily dose (MEDD) | Strong for |
| **12.** | We recommend against opioid doses over 90 mg MEDD daily dose for treating chronic pain<br><br>Note: For patients who are currently prescribed doses over 90 mg MEDD, evaluate for tapering to reduced dose or to discontinuation (see Recommendations 14 and 15) | Strong against |
| **13.** | We recommend against prescribing long-acting opioids for acute pain, as an as-needed medication, or on initiation of LOT | Strong against |

| | | |
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| **14.** | We recommend tapering to reduced dose or to discontinuation of LOT when risks of LOT outweigh benefits<br><br>Note: Abrupt discontinuation should be avoided unless required for immediate safety concerns | Strong for |
| **15.** | We recommend individualizing opioid tapering based on risk assessment and patient needs and characteristics<br><br>Note: There is insufficient evidence to recommend for or against specific tapering strategies and schedules | Strong for |
| **16.** | We recommend interdisciplinary care that addresses pain, SUDs and/or mental health problems for patients presenting with high risk and/or aberrant behavior | Strong for |
| **17.** | We recommend offering medication assisted treatment (MAT) for OUD to patients with chronic pain and OUD<br><br>Note: See the VA/DoD CPG for the Management of SUDs | Strong for |
| **OT for Acute Pain** | | |
| **18.** | a) We recommend alternatives to opioids for mild-to-moderate acute pain<br><br>b) We suggest use of multimodal pain care including non-opioid medications as indicated when opioids are used for acute pain<br><br>c) If take-home opioids are prescribed, we recommend that immediate-release opioids are used at the lowest effective dose with OT reassessment no later than three to five days to determine if adjustments or continuing OT is indicated<br><br>Note: Patient education about opioid risks and alternatives to OT should be offered | a) Strong for<br><br>b) Weak for<br><br>c) Strong for |

# OT for Chronic Pain

# Tab 1 – OT for Chronic Pain

## What is Pain?

- Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage…Pain is always subjective…It is unquestionably a sensation in a part or parts of the body, but it is also always unpleasant and therefore also an emotional experience"[1, 2]
- Pain as a symptom is multifaceted and is described and characterized by many factors such as its quality (e.g., sharp versus dull), intensity, timing, location and whether it is associated with position or movement
- Pain can be acute, subacute or chronic in nature

| Type of Pain | Characteristics |
|---|---|
| **Acute and Subacute** | ▪ Involve primarily nociceptive processing areas in the central nervous system (CNS)<br>▪ Not associated with changes in the CNS |
| **Chronic** | ▪ Pain lasting 3 months or more<br>▪ Often associated with changes in the CNS known as central sensitization<br>▪ Often associated with alterations in brain centers involved with emotions, reward and executive function as well as central sensitization of nociceptive pathways across several CNS areas |

- Patients with chronic pain may report:
  - — Worsened quality of life
  - — Sleep disturbances
  - — Reduced immune system functioning
  - — Psychological complaints (e.g., depression, anxiety, poor general emotional functioning, poor self-efficacy)
  - — Changes in employment status
  - — Impaired personal relationships

# Underlying Mechanisms of Chronic Pain

### There are many causes of chronic pain:

- Pain arising from persistent peripheral stimulation could be mechanical or chemical/inflammatory in nature, typically leading to well-localized nociceptive mechanism of pain
- Mechanical or inflammatory pain with a visceral origin may produce a less localized pain

A comprehensive pain assessment including biopsychosocial interview and focused physical exam is required to determine the pain profile.

- Neuropathic pain due to injury or disease of the central or peripheral nervous system (e.g., spinal cord injury, diabetic neuropathy, radiculopathy) may lead to poorly localized symptoms such as diffuse pain, burning, numbness or a feeling of skin sensitivity

# A Paradigm Shift in Pain and its Treatment

- Chronic pain is among the most common, costly and disabling chronic medical conditions in the U.S.; however, there has been limited research on the effectiveness of long-term opioid therapy (LOT) for non-end-of-life pain
- There is mounting evidence of the ill effects of LOT, including increased mortality, opioid use disorder (OUD), overdose, sexual dysfunction, fractures, myocardial infarction, constipation and sleep-disordered breathing
- The increasing use of opioids as well as the accompanying rise in morbidity and mortality associated with opioid use has called attention to the need for a paradigm shift in pain and in the way it is treated

The accumulation of evidence of harms and the limited evidence of long-term benefits has warranted a newly cautious approach to LOT that prioritizes safety. This approach coupled with the evidence of both the safety and efficacy for non-pharmacologic and non-opioid pharmacologic pain therapies has led to the current transformation in the way in which pain is viewed and treated.

The U.S. is in the midst of a cultural transformation in the way pain is viewed and treated – moving away from the biomedical model of pain to the biopsychosocial model of pain, which views pain and treatment options holistically and prioritizes safe opioid prescribing practices.

| Biomedical model of pain | Biopsychosocial model of pain |
|---|---|
| ▪ Prevailed during the 1990s and early 2000s<br>▪ The pain experience is reduced to a pain generator<br>▪ Treatment is aimed at fixing or numbing the pain with medications, interventions or surgery<br>▪ Despite the absence of long-term safety or efficacy data, OT for chronic non-terminal pain became common practice | ▪ Current model that grew out of observational and epidemiologic data of harm from LOT<br>▪ Pain is a complex multidimensional experience that requires multimodal and integrated care approaches<br>▪ Emphasizes safety<br>▪ Non-pharmacologic treatments and non-opioid medications are the preferred treatments for chronic non-terminal pain<br>▪ OT has a limited role, primarily in the treatment of severe acute pain, post-operative pain and end-of-life pain |

## Chronic Pain Treatment Options

Treatment of chronic pain with LOT in general is associated with considerable risk and must be justified by attainment of benefit that outweighs those risks in any individual patient. Non-pharmacologic therapies and non-opioid pharmacologic therapies are preferred and should be optimized.

### Known risks and lack of benefit of OT for chronic pain:

- There is a rapidly growing understanding of the significant harms of LOT (e.g., overdose, OUD)
- There is a lack of high quality evidence that LOT improves pain, function and/or quality of life

- Given the lack of evidence showing sustained functional benefit of LOT and moderate evidence outlining harms, non-opioid treatments are preferred for chronic pain
- When considering the initiation or continuation of LOT, it is important to consider patient values, goals, concerns and preferences, and whether LOT will result in clinically meaningful improvements in function (e.g., readiness to return to work/duty, measurable improvement in other areas of function) such that the benefits of LOT outweigh the potential harms

### Preferred chronic pain treatment:

- Psychological therapies (e.g., cognitive behavioral interventions such as cognitive behavioral therapy [CBT] and biofeedback), exercise treatments (e.g., aerobic exercise, physical therapy [PT]) and multidisciplinary psychosocial rehabilitation (described as a combination of a physical intervention such as graded exercise and a psychological, social or occupational intervention) have been found to be effective for reducing pain
- These interventions are safe and have not been shown to increase morbidity or mortality – there is insufficient evidence to recommend psychological over physical therapies or vice versa; the choice of which to try first should be individualized based on patient assessment and a shared decision making process
- Considering the low harms associated with exercise and psychological therapies when compared with LOT, these treatments are preferred over LOT and should be offered to all patients with chronic pain, including those currently receiving LOT
- In addition to non-pharmacological therapies (e.g., exercise, CBT), appropriate mechanism and condition-specific non-opioid pharmacologic agents should be tried and optimized before consideration of opioid medications

# Risk Factors for Adverse Outcomes of OT

It is important to consider patients' values and concerns, address misconceptions, express empathy and fully explain to patients with one or more risk factors that they may not benefit from and may even be harmed by treatment with OT.

## Selected significant risk factors

The risk factors with the greatest impact for development of opioid-related adverse events are the **duration** and **dose** of opioid analgesic use. Factors that increase the risk of adverse outcomes and that must be considered prior to initiating or continuing OT include:

- Duration and dose
- Severe respiratory instability
- Sleep disordered breathing (e.g., sleep apnea)
- Acute psychiatric instability (e.g., severe depression, unstable bipolar disorder, unstable psychotic disorder)
- Intermediate to high acute suicide risk
- Current or history of substance use disorder (SUD)
- Current or history of depression
- Generalized anxiety disorder
- Borderline personality disorder
- Antisocial personality disorder
- Posttraumatic stress disorder (PTSD)
- History of drug overdose
- Under 30 years of age
- Co-administration of a drug capable of inducing fatal drug-drug interactions
- QTc interval >450 milliseconds (ms) for using methadone
- Evidence for or history of diversion of controlled substances
- Intolerance, serious adverse effects or a history of inadequate beneficial response to opioids
- Impaired bowel motility unresponsive to therapy
- Traumatic brain injury
- Pain conditions worsened by opioids (e.g., fibromyalgia, headache)
- True allergy to opioid agents (that cannot be resolved by switching agents)

# Patient-centered Care and Shared Decision Making

## Patient-centered care

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is tailored to the patient's capabilities, needs, goals, prior treatment experience and preferences.

- To further promote safety and patient-centered care, the Veterans Health Administration (VHA) issued a policy in 2014 requiring standardized education and signature informed consent for all patients receiving LOT for non-cancer pain (see page 58 for a copy or go to https://www.va.gov/vaforms/)
- Regardless of setting, all patients in the health care system should be offered access to evidence-based interventions appropriate to that patient
- When properly executed, patient-centered care may decrease patient anxiety, increase trust in clinicians and improve treatment adherence
- Improved patient-clinician communication through patient-centered care can be used to convey openness to discuss any future concerns
- As part of the patient-centered care approach, clinicians should:
    - Review the patient's history, including previous treatment approaches, their results and any other outcomes with the patient
    - Ask the patient about his/her willingness to accept a referral to an addiction or other behavioral health specialist when appropriate
    - Involve the patient in prioritizing problems to be addressed and in setting specific goals regardless of the selected setting or level of care

## Shared decision making

The shared decision making process for chronic pain treatment planning is based on the foundation of a patient-centered assessment of risks and benefits and a clinical synthesis performed by the provider. As illustrated in Figure 1, Shared Decision Making for Chronic Pain Treatment and LOT, the shared decision making process culminates in a patient-centered pain care plan with the patient selecting from the clinically appropriate treatment options (for additional information on shared decision making, please see Module E, Patient-Provider Shared Decision Making, and Shared Decision Making: A Guide for Busy Clinicians[3] available at https://www.healthquality.va.gov/ and https://www.qmo.amedd.army.mil).

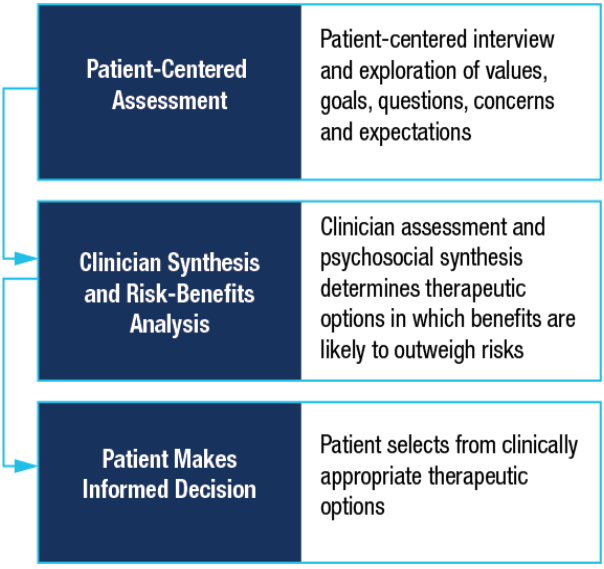


Figure 1. Shared Decision Making for Chronic Pain Treatment and LOT

# Stepped Care Model for Pain Management

The Stepped Care Model for Pain Management, developed by the VA, has been implemented within the VHA and Military Health System with the aim of providing a continuum of effective, coordinated and patient-centered treatment to patients with pain.

### The Stepped Care Model for Pain Management:

- Uses education, self-care and whole-health approaches to wellness as the foundation
- Provides progressively more intensive biopsychosocial care within increasingly specialized settings as patients become more complex, have a greater degree of co-morbidity and present higher risk
- Incorporates psychological, physical, complementary and alternative as well as medication therapies to create a multimodal pain care plan
- The goals of the Stepped Care Model for Pain Management, as illustrated in Figure 2, include:
    - Functional rehabilitation
    - Improvement in quality of life
    - Prevention of the pain becoming chronic and associated deterioration in function

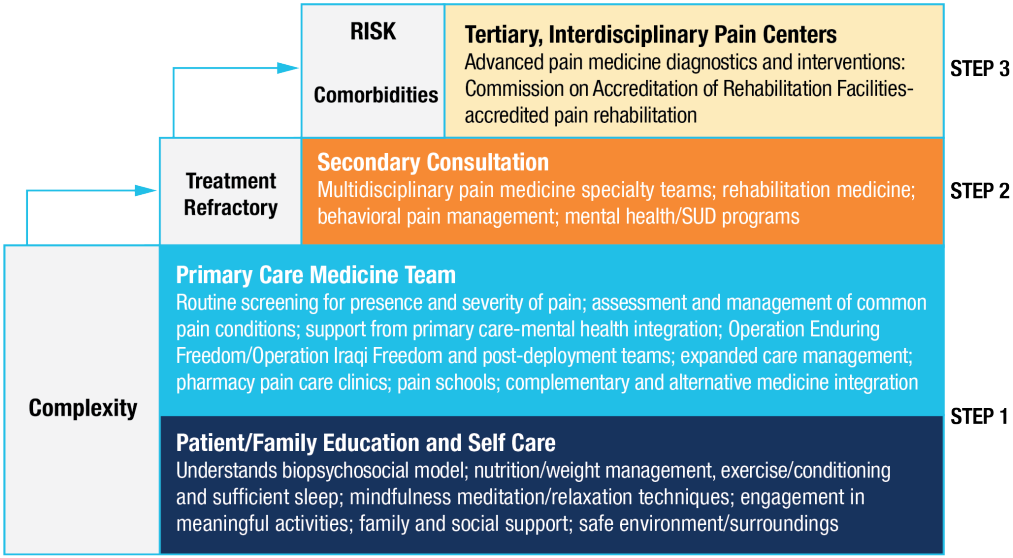


Figure 2. The Stepped Care Model for Pain Management Adapted from the Interagency Pain Research Coordinating Committee's National Pain Strategy[4]

# Transfer of Care

As the entire medical community is moving toward a greater understanding of the need for opioid safety, it is possible that a provider may receive, as a result of a transfer of care, a patient on a high risk opioid regimen that raises concerns related to the provider's and patient's current understanding of opioid risks.

Universal approaches should be used in the management of care for the patient regardless of the location from which that patient is transferred. Providers should:

1. **Provide each new patient with a full evaluation.** Chronic pain is a complex process that requires a comprehensive assessment of the whole individual as well as their social circumstances.
   - This process should build a therapeutic relationship as well as facilitate behavior change when necessary
   - It is important to understand the situation from the patient's perspective, elicit a pain-specific history to aid in establishing the correct pain diagnosis, identify patient-specific coping strategies, identify patient-specific pain interference with functioning and identify important co-occurring conditions
   - The transferring provider should also communicate the patient's medical history to the receiving provider to ensure it is taken into account along with the patient's perspective – this can aid the provider in synthesizing the full biopsychosocial history
2. **Review previous medical records** to determine what diagnostic and therapeutic options have already been tried as previous medical records can help to:
   - Determine the patient's risk of a non-overdose opioid-related adverse event, overdose risk and risk of having developed or developing OUD
   - Determine co-occurring conditions that will need to be evaluated and treated in order to put together a comprehensive approach to the patient's pain
3. **Determine what the patient knows about current concerns related to OT** and how comfortable he or she is with an approach that will address opioid safety along with an integrated whole person approach to pain.
4. **Offer all new patients a physical exam** to help determine the cause of the pain as well as co-occurring conditions that may complicate pain symptoms and/or treatment.
5. **Provide each patient an assessment** that outlines the specifics related to opioid safety:
   - What is the diagnosis for which opioids are prescribed?
   - What non-opioid therapies have been tried and/or is the patient currently using?
   - Are there co-occurring conditions or medication dose/combinations that would increase risk of OT?
   - Engage patient in shared decision making discussion about assessment and recommendations for a new treatment plan

6. **Use standard opioid risk mitigation strategies such as:**
   - Checking the prescription drug monitoring programs (PDMP)
   - Making sure the patient has participated in shared decision making about OT and understands and signs the opioid informed consent
   - Obtaining consent for and performing urine drug tesing (UDT)

## Patients transferred from within the VA and/or DoD system

For patients transferred from within the VA and/or DoD system who request to transfer an opioid prescription that the receiving provider has determined to be too risky to continue, providers should:

- Employ risk stratified tapering strategies
- Engage patients in shared decision making, including consideration of the patient's values, goals, concerns and preferences, prior to tapering
- Assess and treat for OUD when present

## Patients transferring from outside the VA and/or DoD system

For patients who are transferring from outside of the VA and/or DoD, there may be some unique issues to consider:

- Are complete medical records available that would inform treatment planning?
  - Until full record review and communication with the previous prescriber are completed, there are significant risks of assuming responsibility for opioid prescribing even if it is with intent to taper
- Has the new plan of care been communicated to the previous prescriber and the patient?
  - If it is felt that the regimen is too risky with the resources available, then it is important to communicate this to the patient as well as the previous prescriber, so that they can begin an exit plan for the patient as indicated
  - If the new provider feels comfortable assuming responsibility for the OT, even if it is to start a taper, then this needs to be communicated to the previous prescriber as soon as possible to avoid duplication of prescriptions

# OT for Acute Pain

This pocket guide addresses LOT for chronic pain – the use of opioids for acute pain is not reviewed in detail and is strongly recommended against. Patient education about opioid risks and alternatives to OT should be offered.

- Prescribing long-acting opioids for acute pain is not recommended (with exception of oxycodone/acetaminophen extended-release tablets)
- Alternatives to opioids for mild to moderate acute pain are recommended (**CPG Recommendation 18a**)
- Multimodal pain care, including non-opioid medications as indicated when opioids are used for acute pain (**CPG Recommendation 18b**)
- If take-home opioids are prescribed, immediate-release opioids used at the lowest effective dose are recommended with OT, reassessment no later than three to five days to determine if adjustment or continuing OT is indicated (**CPG Recommendation 18c**)


**The risk of overdose includes the use of opioids for acute pain.** Factors that increase overdose risk when opioids are used for acute pain include high prescribed dose, history of SUD and history of mental health concerns. While the risk of overdose increases at doses above 20 mg MEDD, this risk increases even further as doses increase to over 50 or 100 mg MEDD.

## Discussion of risks of acute OT:

- While it is understood that acute OT for severe pain due to injuries or surgery is the most effective option for many patients, the risks associated with acute therapy must be addressed when opioids are prescribed or considered:
  - There is a risk of opioid-related overdose even during acute OT
  - Patient education about opioid risks and alternatives to OT should be offered
- The risks of acute OT extending into LOT are increased in patients with mood disorders, patients who refill the initial prescription, those using a higher prescribed dose (greater than 120 mg MEDD) or those using long-acting opioids
- The risk of acute post-operative OT progressing into LOT is increased when the patient presents with complicating factors, such as, history of depression, SUD, higher preoperative total body pain or preoperative use of sedative-hypnotics or antidepressants
- There are situations in which opioids may be necessary for acute pain, even when substantial risk factors exist – it is important to incorporate opioid risk mitigation strategies into opioid prescribing for acute pain

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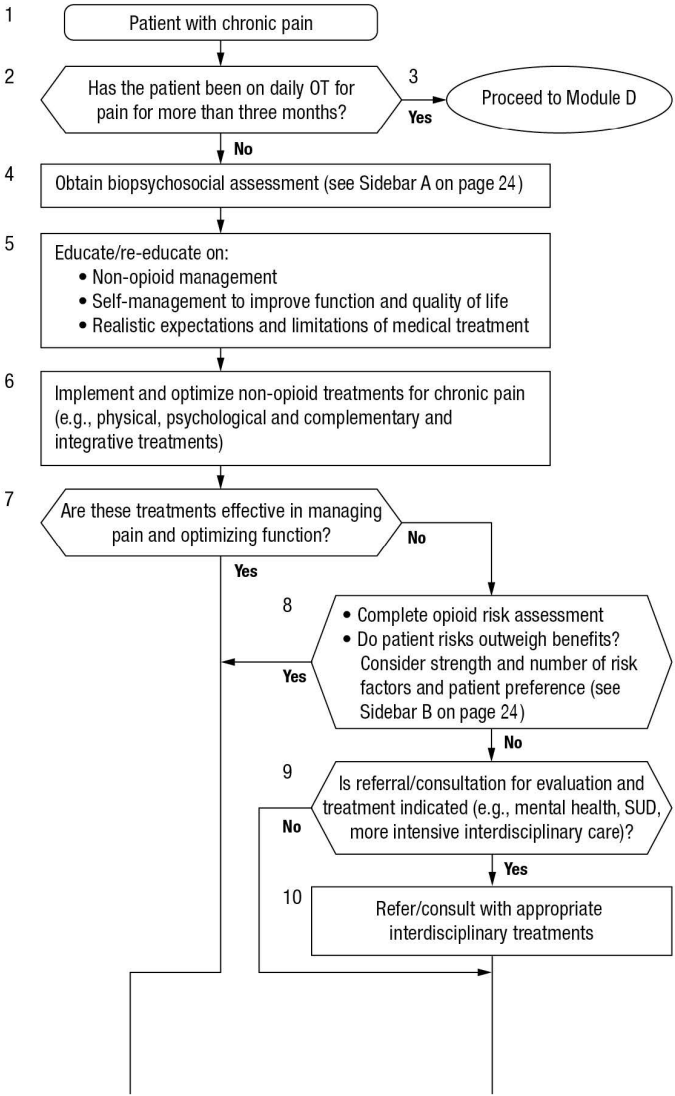
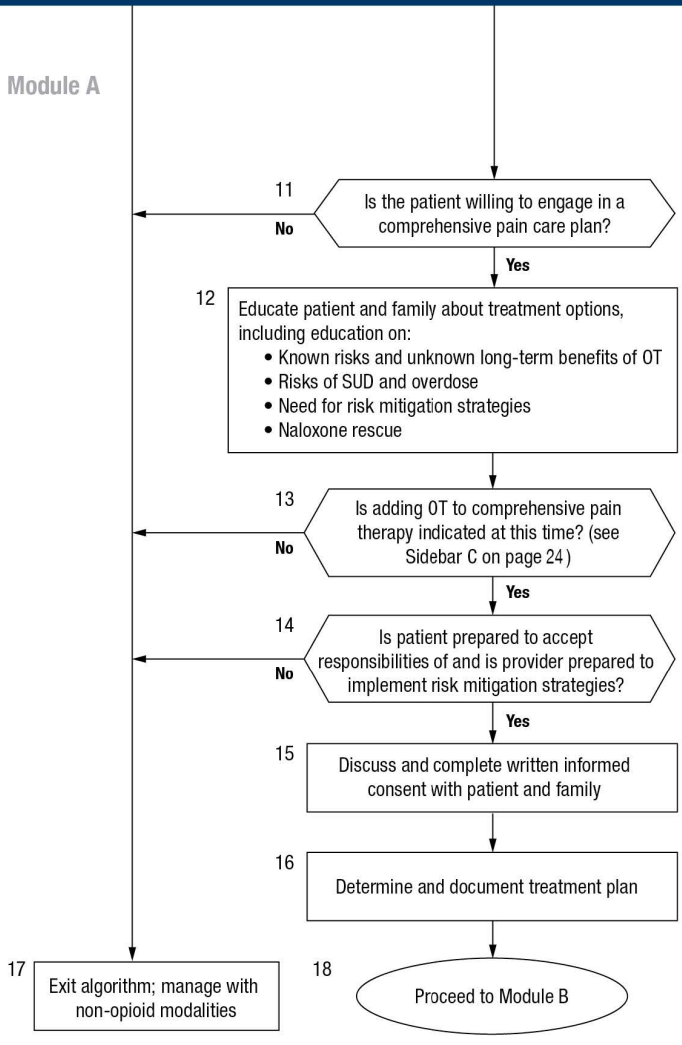
# Algorithms

## Module A: Determination of Appropriateness for Opioid Therapy

Note: Non-pharmacologic and non-opioid pharmacologic therapies are preferred for chronic pain






Abbreviations: LOT: long-term opioid therapy; OT: opioid therapy; PDMP: prescription drug monitoring program; SUD: substance use disorders; UDT: urine drug test; VA/DoD Suicide CPG: VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide

**Sidebar A: Components of Biopsychosocial Assessment**

- Pain assessment including history, physical exam, co-morbidities, previous treatment and medications, duration of symptoms, onset and triggers, location/radiation, previous episodes, intensity and impact, patient perception of symptoms
- Patient functional goals
- Impact of pain on family, work, life
- Review of previous diagnostic studies
- Additional consultations and referrals
- Coexisting illness and treatments and effect on pain
- Significant psychological, social or behavioral factors that may affect treatment
- Family history of chronic pain
- Collateral of family involvement
- Patient beliefs/knowledge of:
  - The cause of their pain
  - Their treatment preferences
  - The perceived efficacy of various treatment options

For patients already on OT, include assessment of psychological factors (e.g., beliefs, expectations, fears) related to continuing vs. tapering OT

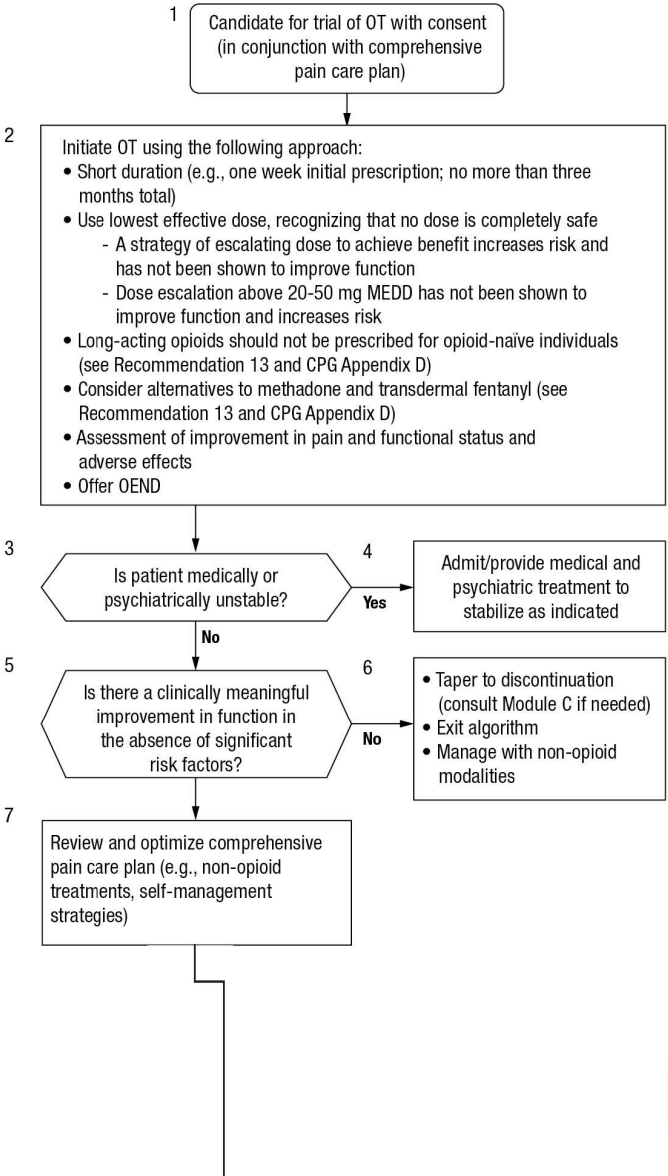
**Sidebar B: Examples of Absolute Contraindications to Initiating Opioid Therapy for Chronic Pain**

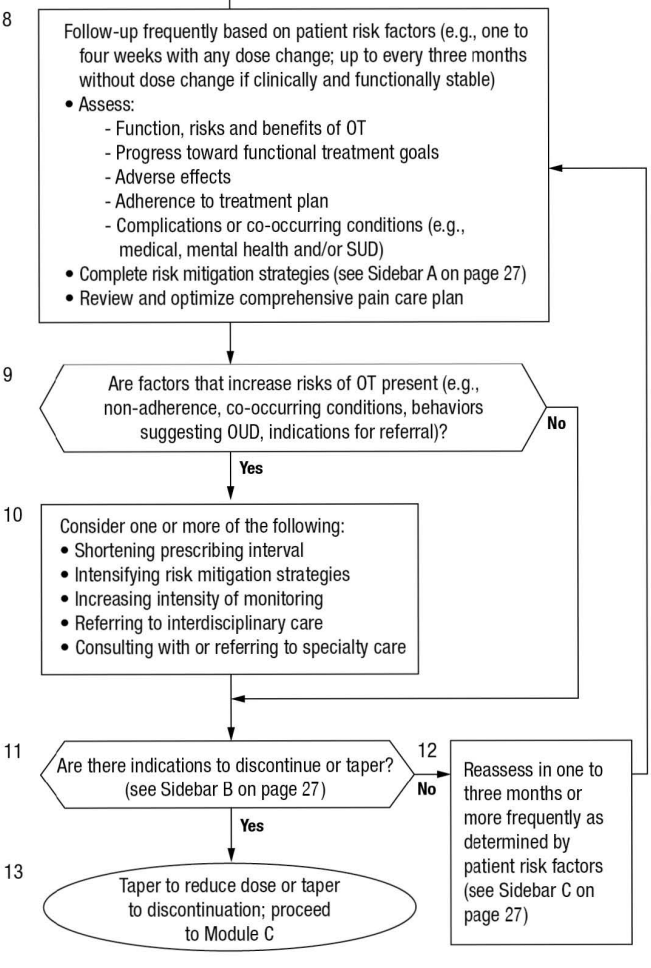
- True life-threatening allergy to opioids
- Active SUD
- Elevated suicide risk (see VA/DoD Suicide CPG)
- Concomitant use of benzodiazepines

**Sidebar C: Consideration Checklist for LOT for Chronic Pain**

- Risks do not outweigh potential modest benefits
- Patient is experiencing severe chronic pain that interferes with function and has failed to adequately respond to indicated non-opioid and non-drug therapeutic interventions
- Patient is willing to continue to engage in comprehensive treatment plan including non-opioid treatments and implementation of learned active strategies that meets his or her needs to be successful with plan of care
- Clear and measurable treatment goals are established
- Patient is able to access adequate follow-up for OT (see Recommendations 7-9)
- PDMP and UDT are concordant with expectations
- Review of recent medical records is concordant with diagnosis and risk assessment
- Patient is fully informed and consents to the therapy

## Module B: Treatment with Opioid Therapy






Abbreviations: MEDD: morphine equivalent daily dose; mg: milligram; MRI: magnetic resonance imaging; OEND: Overdose Education and Naloxone Distribution; OT: opioid therapy; OUD: opioid use disorder; PDMP: Prescription Drug Monitoring Program; SUD: substance use disorder; UDT: urine drug test

**Sidebar A: Necessary Risk Mitigation Strategies**

- OEND
- UDT
- PDMP
- Face-to-face follow-up with frequency determined by risk

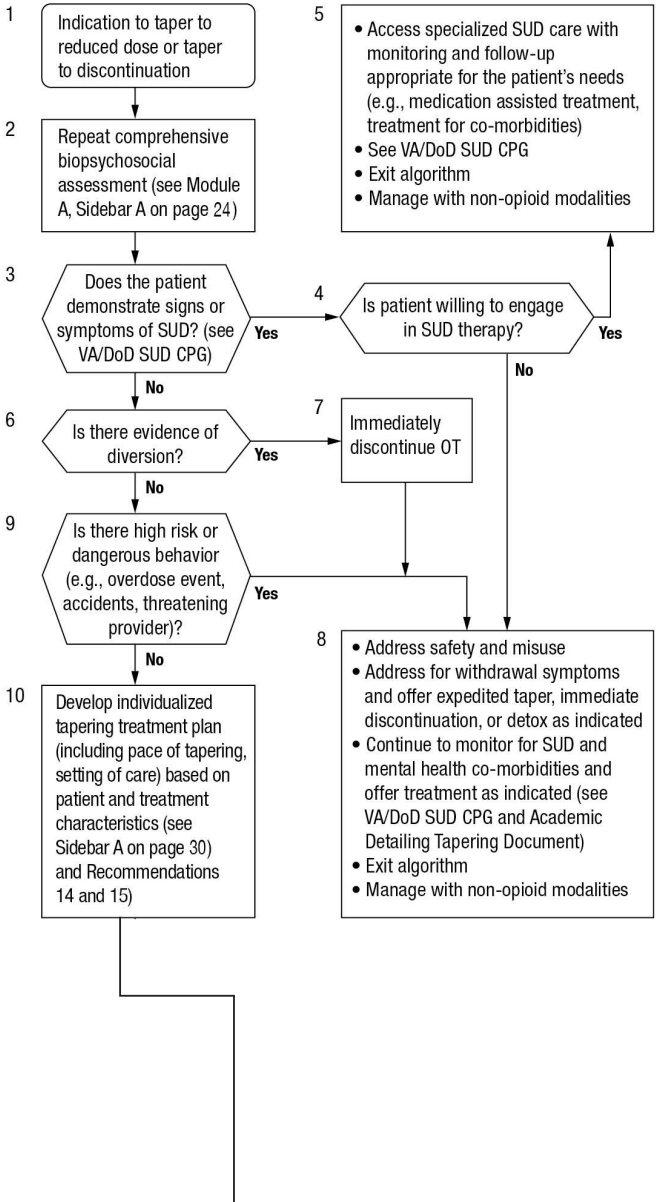
**Sidebar B: Indications for Tapering and Discontinuation**

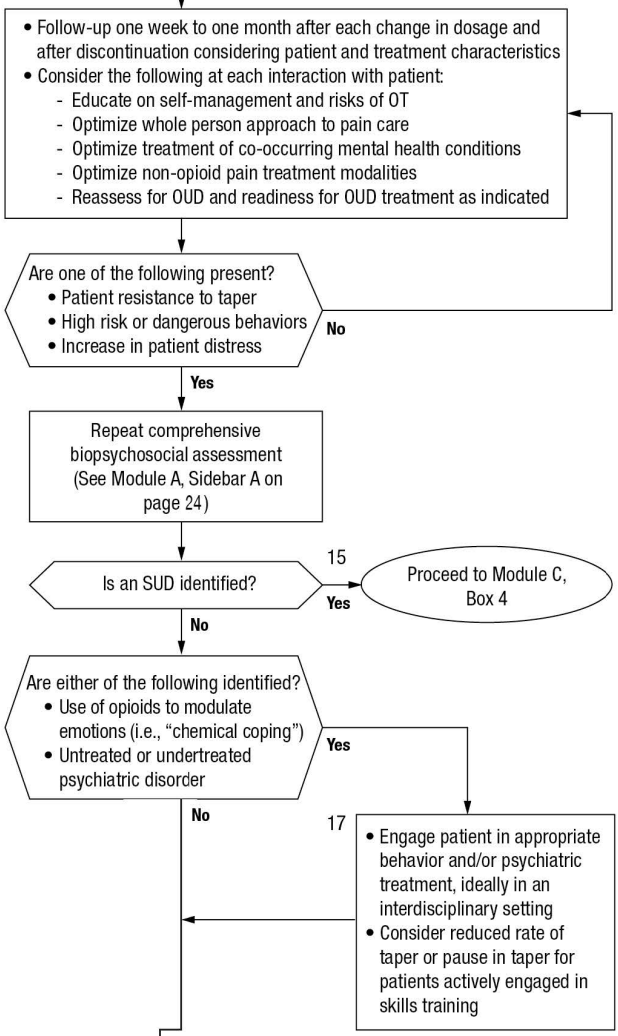
- Risks of OT outweigh benefits
  - Lack of clinically meaningful improvement in function
  - Concomitant use of medications that increase risk of overdose
  - Co-occurring medical or mental health conditions that increase risk
  - Concerns about OUD or other SUD
  - Patient non-compliance with opioid safety measures and opioid risk mitigation strategies
  - Patient non-participation in a comprehensive pain care plan
  - Prescribed dose higher than the maximal recommended dose (which increases risk of adverse events)
  - Pain condition not effectively treated with opioids (e.g., back pain with normal MRI, fibromyalgia)
  - Medical or mental health co-morbidities that increase risk
  - Improvement in the underlying pain condition being treated
  - Unmanageable side effects
- Patient preference
- Diversion

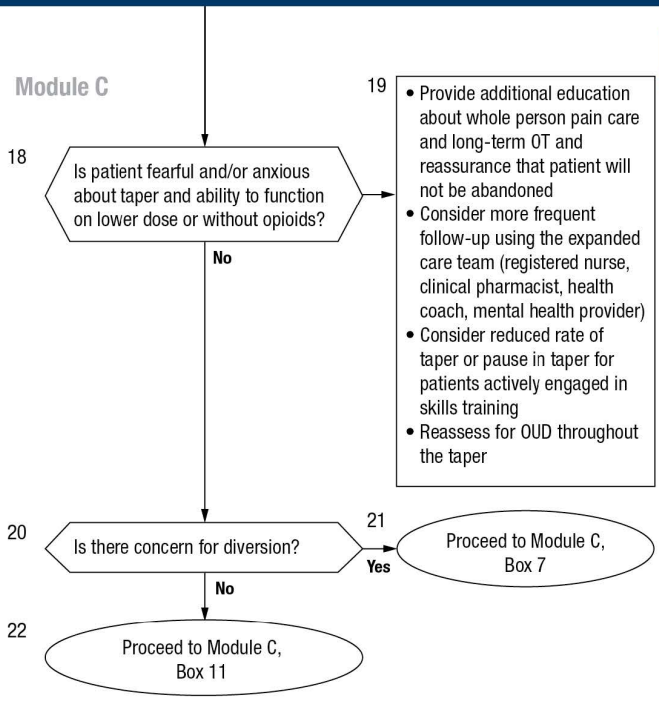
**Sidebar C: Factors That May Indicate Need for More Frequent Follow-up**

- Non-adherence to comprehensive pain care plan (e.g., attendance at appointments)
- Unexpected UDT and PDMP results
- Non-adherence to opioid prescription (e.g., using more than prescribed and/or running out early)
- Higher risk medication characteristics (e.g., high-dose opioids, combination of opioids and benzodiazepines)
- Patients with mental health, medical or SUD co-morbidities that increase risk for adverse outcomes

## Module C: Tapering or Discontinuation of Opioid Therapy




11
• Follow-up one week to one month after each change in dosage and after discontinuation considering patient and treatment characteristics
• Consider the following at each interaction with patient:
- Educate on self-management and risks of OT
- Optimize whole person approach to pain care
- Optimize treatment of co-occurring mental health conditions
- Optimize non-opioid pain treatment modalities
- Reassess for OUD and readiness for OUD treatment as indicated
12
Are one of the following present?
• Patient resistance to taper
• High risk or dangerous behaviors
• Increase in patient distress
No
Yes
13
Repeat comprehensive biopsychosocial assessment (See Module A, Sidebar A on page 24)
14
Is an SUD identified?
15
Yes
Proceed to Module C, Box 4
No
16
Are either of the following identified?
• Use of opioids to modulate emotions (i.e., "chemical coping")
• Untreated or undertreated psychiatric disorder
Yes
No
17
• Engage patient in appropriate behavior and/or psychiatric treatment, ideally in an interdisciplinary setting
• Consider reduced rate of taper or pause in taper for patients actively engaged in skills training




Abbreviations: LOT: long-term opioid therapy; MAT: medication assisted treatment; OT: opioid therapy; OUD: opioid use disorder; SUD: substance use disorder; VA/DoD SUD CPG: VA/DoD Clinical Practice Guideline for the Assessment and Management of Substance Use Disorders

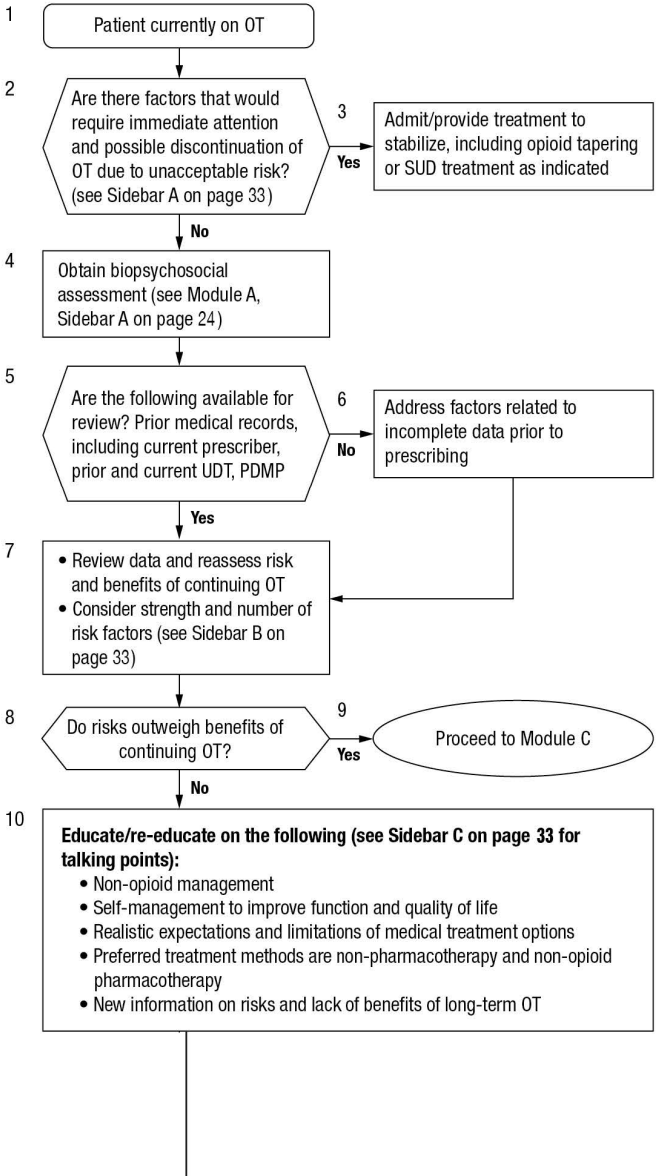
**Sidebar A: Tapering Treatment**

- When safety allows, a gradual taper rate (5-20% reduction every four weeks) allows time for neurobiological, psychological and behavioral adaptations
- When there are concerns regarding risks of tapering (e.g., unmasked OUD, exacerbation of underlying mental health conditions), consider interdisciplinary services that may include mental health, SUD, primary care and specialty pain care
- Address concerns that may negatively impact taper (e.g., inability for adequate follow-up, inability to provide adequate treatment for co-occurring medical and mental health conditions and SUD)

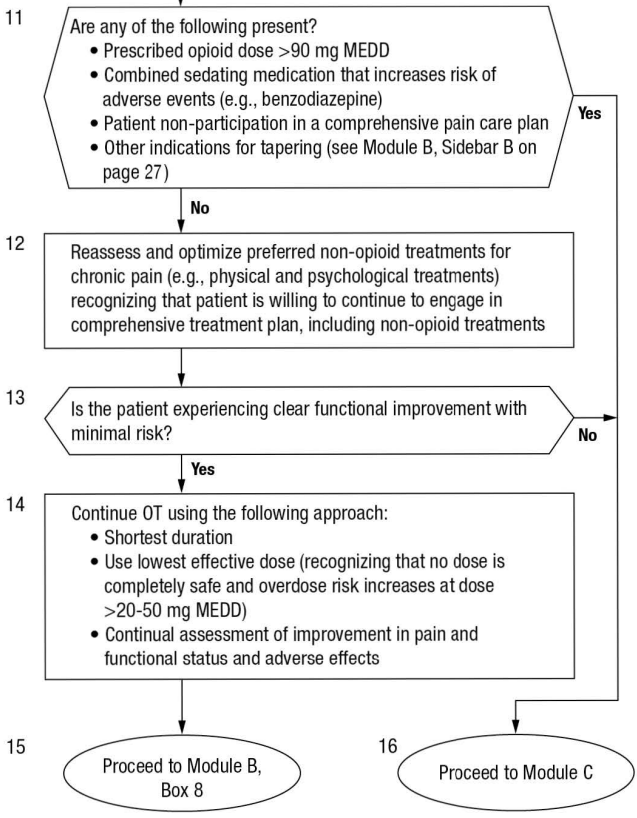
**Patient and Treatment Characteristics to Consider when Determining Tapering Strategy**

- Opioid dose
- Duration of therapy
- Type of opioid formulation
- Psychiatric, medical and SUD co-morbidities
- Other patient risk factors (e.g., non-adherence, high-risk medication-related behavior, strength of social support, coping)

## Module D: Patients Currently on Opioid Therapy



## Module D




Abbreviations: MEDD: morphine equivalent daily dose; mg: milligram; OT: opioid therapy; PDMP: Prescription Drug Monitoring Program; SUD: substance use disorders; UDT: urine drug test; VA/DoD Suicide CPG: VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide

**Sidebar A: Factors Requiring Immediate Attention and Possible Discontinuation**

- Untreated SUD
- Unstable mental health disorder
- Medical condition that acutely increases opioid risks (e.g., compromised or worsening cognitive or cardiopulmonary status)
- Other factors that acutely increase risk of overdose:
  - Recent overdose
  - Current sedation
  - Recent motor vehicle accident
- Acutely elevated suicide risk (see VA/DoD Suicide CPG)

**Sidebar B: Considerations During Reassessment**

Risks:

- Increase risk of all-cause mortality
- Increase risk of unintentional overdose death
- Increase risk of developing OUD
- Risk of developing or worsening:
  - Depression
  - Falls
  - Fractures
  - Sleep disordered breathing
  - Worsening pain
  - Motor vehicle accidents
  - Hypogonadism
  - Prolonged pain
  - Nausea
  - Constipation
  - Dry mouth
  - Sedation
  - Cognitive dysfunction
  - Immune system dysfunction
  - Reduction in function
  - Reduction in quality of life

Benefits:

- Modest short-term improvement in pain
- Possible short-term improvement in function

**Sidebar C: Talking Points for Education and Re-education for Patients Currently on OT**

- "Doctors used to think that opioids were safe and effective when used for long periods of time to treat chronic pain."
- "New information has taught us that long-term opioid use can lead to multiple problems, including loss of pain relieving effects, increased pain, unintentional death, OUD, and problems with sleep, mood, hormonal dysfunction, and immune dysfunction."
- "We now know that the best treatments for chronic pain are not opioids. The best treatments for chronic pain are non-drug treatments such as psychological therapies and rehabilitation therapies and non-opioid medications."

## Key Elements of Shared Decision Making

### ASK

- Apply a patient-centered approach
- Use motivational interviewing

### PRIORITIZE

- Help the patient focus on specific needs

### ASSESS

- Assess the capacity of the decision making process
- Address patient and provider barriers

### ADVISE

- What is the evidence?
- Discuss benefits and risks

### ACKNOWLEDGE

- Agree on what's important for the individual
- Share values, power, expectations

### ASSIST

- Provide tools to help weigh the options
- Promote input from others

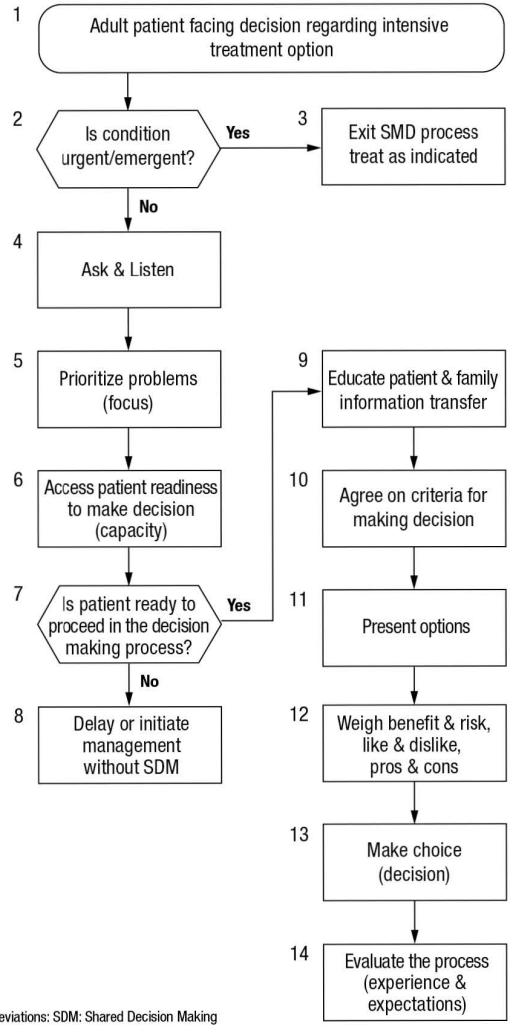
### MAKE DECISION

- If ready, patient makes the choice

### EVALUATE

- Evaluate the process
- Revisit the decision if there are concerns

# Shared Decision Making Algorithm




Abbreviations: SDM: Shared Decision Making

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# Initiation and Continuation of OT

# Tab 3 – INITIATION AND CONTINUATION OF OT

## Initiation of OT for Patients with Chronic Pain

Initiation of LOT for chronic pain is strongly recommended against (**CPG Recommendation 1a**). Alternatives to OT such as self-management strategies and other non-pharmacological treatments are strongly recommended (**CPG Recommendation 1b**). When pharmacologic therapies are used, non-opioid, pharmacologic therapies are strongly recommended over opioids (**CPG Recommendation 1c**).

- Given the lack of evidence showing sustained functional benefit of LOT and moderate evidence outlining harms, non-opioid treatments are preferred for chronic pain
- Alternatives to OT such as self-management strategies and other non-pharmacological treatments are recommended, including:
  - Exercise (e.g., yoga, PT)
  - Psychological therapies (e.g., CBT, biofeedback)
  - Multidisciplinary biopsychosocial rehabilitation
- Patient values, goals, concerns and preferences must be factored into clinical decision making on a case-by-case basis


**Absolute contraindications to initiating OT for chronic pain include:**

- True life-threatening allergy to opioids
- Active SUD
- Elevated suicide risk
- Concomitant use of benzodiazepines

**Patients less than 30 years of age are at risk for adverse events with LOT.**

- When considering initiating or continuing LOT, it is important to consider whether LOT will result in clinically meaningful improvements in function such as readiness to return to work/duty, and/or measurable improvement in other areas of function, such that the benefits outweigh the potential harms
- If a decision is made to initiate LOT, a careful assessment of benefits and risks should be made to ensure that the benefits are expected to outweigh the well-documented risks – in addition, prior to this consideration, a multimodal pain care plan should be integrated into the patient's care
- Once OT is initiated, follow the opioid risk mitigation strategies outlined in this pocket guide

# Is OT Indicated?

The checklist below lists considerations for determining appropriateness of adding LOT for patients presenting with chronic pain.

**Consideration checklist for LOT for chronic pain:**

- ☑ Risks do not outweigh potential modest benefit
- ☑ Patient is experiencing severe chronic pain that interferes with function and has failed to adequately respond to indicated non-opioid and non-drug therapeutic interventions
- ☑ Patient is willing to continue to engage in a pain care management plan, including non-opioid treatments and implementation of learned active strategies that meet his or her needs to be successful with plan of care
- ☑ Clear and measurable treatment goals are established
- ☑ Patient is able to access adequate follow-up for OT
- ☑ Review of recent medical records is concordant with diagnosis and risk assessment
- ☑ PDMP and UDT are concordant with expectations
- ☑ Patient is fully informed and consents to therapy

# Determining Appropriateness for OT

The steps below are drawn from the 2017 VA/DoD OT for Chronic Pain CPG Module A algorithm, which includes: an ordered sequence of steps of care; recommended observations and examinations; decisions to be considered; and actions to be taken by health care providers when determining appropriateness of OT for patients with chronic pain.

**Obtain Biopsychosocial and Opioid Risk Assessments**

- Complete a comprehensive biopsychosocial assessment prior to initiating OT
- Complete an opioid risk assessment, including presence of absolute contraindications to OT
- Determine whether patient risks outweigh the benefits of OT
- Consider strength and number of risk factors and patient preferences

**Educate/Re-educate Patient on Non-opioid Treatment**

- Provide education on:
  - Non-opioid management of pain
  - Self-management to improve function and quality of life
  - Realistic expectations and limitations of medical treatment
- Discuss and implement alternatives to OT, including physical, psychological and complementary and integrative treatments

**Refer/Consult with Appropriate Interdisciplinary Treatments**

- Determine whether referral/consultation for evaluation and treatment is indicated for:
  - Mental health conditions
  - SUD
  - Other conditions requiring more intensive interdisciplinary care or a pain specialist
- Consult with appropriate interdisciplinary care teams and determine whether patient is willing to engage in a comprehensive pain care plan

**Educate/Re-educate Patient about Treatment Options and Risks**

- Provide education to the patient and family on:
  - Known risks and unknown long-term benefits of OT
  - Risks of SUD and overdose
  - Need for risk mitigation strategies
- Naloxone rescue

| | |
|---|---|
| **Determine, Document and Initiate OT for Eligible, Consented Candidates** | ▪ Discuss and complete written informed consent with patient and family<br>— Patient is prepared to accept responsibilities of OT and the provider is prepared to implement risk mitigation strategies<br>▪ Develop and implement an individualized, comprehensive pain care plan |

The 2017 VA/DoD OT for Chronic Pain CPG emphasizes the importance of obtaining a biopsychosocial assessment when determining the appropriateness for OT. The table below lists the components of a biopsychosocial assessment.

## Components of a biopsychosocial assessment

- Pain assessment history including:
  - Physical exam
  - Co-morbidities
  - Previous treatment and medications
  - Duration of symptoms
  - Onset and triggers
  - Location/radiation
  - Previous episodes
  - Intensity and impact
  - Patient perception of symptoms
- Patient functional goals
- Impact of pain on family, work and/or life
- Review of previous diagnostic studies
- Additional consultations and referrals
- Coexisting illness and treatments and effect on pain
- Significant psychological, social or behavioral factors that may affect treatment
- Family history of chronic pain
- Collateral of family involvement
- Patient beliefs/knowledge of:
  - The cause of their pain
  - Their treatment preferences
  - The perceived efficacy of various treatment options
- For patients already on OT, include assessment of psychological factors (e.g., beliefs, expectations, fears) related to continuing versus tapering OT

# Treatment with OT

The steps below are drawn from the 2017 VA/DoD OT for Chronic Pain CPG Module B algorithm, which includes: an ordered sequence of steps of care; recommended observations and examinations; decisions to be considered; and actions to be taken by health care providers when initiating a trial of OT.

If prescribing OT for patients with chronic pain, a short duration is strongly recommended (**CPG Recommendation 2**). Consideration of OT beyond 90 days requires re-evaluation and discussion with patient of risks and benefits. For patients currently on LOT, there are strong recommendations for ongoing risk mitigation strategies, assessment for OUD and consideration for tapering when risks exceed benefits (**CPG Recommendation 3**).

**Initiate OT**

- Initiate OT using the following approach:
  - Short duration (e.g., one-week initial prescription; no more than three months total)
  - Use lowest effective dose – recognizing no dose is completely safe
- Long-acting opioids should not be prescribed for opioid-naïve individuals
- Consider alternatives to methadone and transdermal fentanyl
- Assess improvement in pain, functional status and adverse effects

**Implement Risk Mitigation Strategies**

- Implement necessary risk mitigation strategies including:
  - Opioid overdose education and naloxone distribution (OEND)
  - Urine drug testing (UDT)
  - Prescription drug monitoring programs (PDMP)
- Face-to-face follow-up with frequency determined by risk

| | |
|---|---|
| **Follow-up** | ▪ Follow-up frequently based on patient risk factors (one to four weeks with any dose change; up to every three months without dose change if clinically and functionally stable)<br>▪ Assess:<br>— Function, risks and benefits of OT<br>— Progress towards functional treatment goals<br>— Adverse effects<br>— Adherence to pain care plan<br>— Complication or co-occurring conditions (e.g., medical, mental health, SUD)<br>▪ Complete risk mitigation strategies<br>▪ Review and optimize comprehensive pain care plan<br>▪ If factors that increase risks of OT are present (e.g., non-adherence, co-occurring conditions, behaviors suggesting OUD, indications for referral), consider:<br>— Shortening prescribing interval<br>— Intensifying risk mitigation strategies<br>— Increasing intensity of monitoring<br>— Referring to interdisciplinary care<br>— Consulting with or referring to specialty care |

# Patient Groups at High Risk for Adverse Events with LOT

## Patients with untreated SUD

LOT for pain in patients with untreated SUD is strongly recommended against (**CPG Recommendation 4a**). Harms may outweigh the benefits for LOT in these patient populations. For patients on LOT with untreated SUD, there are strong recommendations for close monitoring, including engagement in SUD treatment and discontinuation of OT for pain with appropriate tapering (**CPG Recommendation 4b**).

- Opioids carry a significant risk for OUD, overdose and death, especially among patients with untreated SUD
- Some patients with SUD may disagree with the recommendation to use non-opioid modalities in lieu of LOT to treat their pain
- The lack of evidence of efficacy of LOT and considerable evidence of significant harms of overdose, death from overdose and increased risk of suicide outweigh any potential modest benefit of prescribing LOT in this population

## Patients concurrently using benzodiazepines

Concurrent use of benzodiazepines and opioids is strongly recommended against (**CPG Recommendation 5**). For patients currently on LOT and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate.

- Concurrent use of benzodiazepines with prescription opioids increases the risk of overdose and overdose death and use should be weighed heavily in the risk-benefit evaluation for tapering versus continuing one or both agents
- Once initiated, benzodiazepines can be challenging to discontinue due to symptoms related to benzodiazepine dependence, exacerbations of PTSD and/or anxiety
- Tapering benzodiazepines should be performed with caution and within a team environment when possible
- Due to the difficulty of tapering or discontinuing benzodiazepines, particular caution should be used when considering initiating benzodiazepines for patients with PTSD who have co-occurring chronic pain


**Abrupt discontinuation of benzodiazepines should be avoided.** It can lead to serious adverse effects, including seizures and death.

### Patients less than 30 years of age

There is a strong recommendation against LOT for patients less than 30 years of age secondary to higher risk of OUD and overdose (**CPG Recommendation 6a**). For patients less than 30 years of age currently on LOT, close monitoring and consideration for tapering when risks exceed benefits are strongly recommended (**CPG Recommendation 6b**).

- All patients who take opioids chronically are at risk for OUD and overdose, but especially those who are younger than 30 years of age
- Age less than 30 years is not an absolute contraindication to LOT – there may be some situations where the benefits of LOT clearly outweigh the risks of OUD and overdose – in those cases, LOT may be appropriate only if risk mitigation strategies are employed, including prescribing of naloxone rescue with accompanying education and patients are titrated off LOT as soon as it is appropriate

## Duration of OT

OT should only be used for a short duration – of utmost concern is the heightened risk for developing OUD in patients who receive OT beyond 90 days.

- Similar to other risk factors, continuing OT beyond 90 days duration should be weighed heavily in the risk-benefit calculus for LOT
- Continuing OT for longer than 90 days is not an absolute contraindication to LOT – there may be some situations where the benefits of LOT clearly outweigh the risks and that must be determined through individual clinical assessment
- Patients should be informed that progression from acute to LOT is associated with little evidence for sustained analgesic efficacy but a substantial increase in risk for OUD

**CAUTION**

Providers should discuss this information with patients at initiation of OT and continuously thereafter to ensure that the patient understands the associated risks and benefits of LOT – when fully informed, some patients may desire continuation of OT while others may decline its continued provision.

- The relationship between OUD and duration of therapy is magnified when patients have a history of previous opioid or non-opioid SUD

## Dose of OT

If prescribing opioids, prescribing the lowest dose as indicated by patient-specific risks is strongly recommended (**CPG Recommendation 10**). There is absolutely no safe dose of opioids. As opioid dosage and risk increase, more frequent monitoring for adverse events, including OUD and overdose, are strongly recommended (**CPG Recommendation 11**). Risks for OUD start at any dose and increase in a dose-dependent manner. Risks for overdose and death significantly increase at a range of 20 to 50 mg MEDD. Prescribing opioid doses >90 mg MEDD for treating chronic pain

is strongly recommended against (**CPG Recommendation 12**). For patients who are currently prescribed doses >90 mg MEDD, evaluate for tapering to reduced dose or to discontinuation.

- The risk of prescription opioid overdose and overdose death exists even at low opioid dosage levels and increases as dosage increases
- Risk continues to increase at higher dosage ranges (≥100 mg MEDD)
- Although it is widely accepted that progressively higher doses of prescribed opioids result in correspondingly higher risks of opioid overdose, patients using any dose of opioids can still experience life-threatening respiratory or CNS depression, especially when opioid-naïve


Dosing determinations should be individualized based upon patient characteristics and preferences, with the goal of using the lowest dose of opioids for the shortest period of time to achieve well-defined functional treatment goals.

- The risk of life-threatening respiratory or CNS depression begins to increase with as low as 20 to 50 mg MEDD – risk is further increased when certain concomitant demographic factors, co-occurring medical or psychiatric conditions or interacting medications or substances exist
- There will be greater mortality, co-occurring medical conditions and other adverse events in patients who require higher doses of opioids, even in those who benefit from such therapy
- When closer follow-up is needed, health care resources and patient adherence should be considered

## Type of OT and Route of Administration

Long-acting opioids should not be used for treatment of acute pain, on an as-needed basis or during initiation of LOT (**CPG Recommendation 13**). There is insufficient evidence to recommend for or against any specific opioid or delivery system. There are several considerations when determining type and route of administration of OT, specifically the following:

- Short-acting versus long-acting opioids (for LOT for chronic pain)
- Route of administration/delivery among alternatives such as transdermal, buccal, sublingual or pumps
- Abuse deterrent formulations of opioids compared to non-abuse deterrent formulations
- Tramadol and other dual-mechanism opioids
- Buprenorphine for pain (compared to other opioids)
- Methadone (with QT [time interval from the start of the Q wave to the end of the T wave] monitoring)

## Short- and long-acting opioids:

- No single opioid or opioid formulation is preferred over the others
- There is concern for additional overdose risk associated with long-acting versus short-acting opioids
- Individuals may have a better response, degree of safety or tolerability depending on their individual characteristics and preferences

## Route of administration/delivery:

- The concomitant use of oral and transdermal opioids or oral and intrathecal pumps should be approached with extreme caution and warrants specialty consultation (discussions of intrathecal pumps are beyond the scope of this pocket guide)
- Although some patients may prefer either transdermal or buccal opioid delivery for opioids, there is significant potential for harm from OT with these delivery mechanisms, with no evidence of benefit over traditional opioid delivery systems in patients with chronic pain

**Fentanyl transdermal delivery system (or patch):**

- Providers need to be especially aware of the risks associated with a fentanyl transdermal delivery system (or patch):
  - Unique pharmacokinetic profile
  - Continuous delivery, even after the patch is removed due to depot effect
  - Increased rate of delivery
  - Unpredictable variation in rate of delivery:
    - Due to alterations in temperature due to external heat, skin integrity and amount of adipose tissue
    - Among patients with fever, skin damage or cachexia

**Specific safety precautions that all providers should be aware of regarding transdermal fentanyl include:**

- Transdermal fentanyl should not be used in opioid-naïve patients
- Patients need to be informed that:
  - Heat (e.g., sun exposure, heating pad, febrile condition) can increase the rate and quantity of absorption
  - Proper application includes: being sure to take old patch off; never applying damaged patch or a patch to non-intact skin; proper disposal to avoid exposure to children and pets, and precautions taken against possible diversion of remaining drug in used patch
  - Adjusted dose (decreased patch size) should be used in patients with renal or hepatic insufficiency and considered in elderly patients and those with febrile illness


Given the potential serious risks with starting fentanyl and challenges with tapering, providers intent on prescribing transdermal fentanyl for chronic pain are encouraged to consult with other providers (e.g., pain specialists, pharmacists) and to be familiar with the unique properties of fentanyl.

## Abuse deterrent formulation of opioids:

- Abuse deterrent formulations for LOT are neither recommended for or against
- The aim of most abuse deterrent formulations is to present a physical barrier to prevent chewing, crushing, cutting, grating or grinding of the dosage form, or present a chemical barrier, such as a gelling agent, that will resist extraction of the opioid with use of a common solvent
- Alternatively, an opioid antagonist (naloxone or naltrexone) can be added to interfere with, reduce or defeat the euphoria associated with abuse of an agent intended for oral use when taken nasally or parenterally
- While these properties deter abuse, they do not fully prevent abuse – no opioid formulation prevents consumption of a large number of intact capsules or tablets, which continues to be the most common method of abuse
- Future research is needed to ascertain whether abuse deterrent formulations actually reduce OUD when used for chronic pain, and whether said formulations differ across clinical outcomes such as pain, function and adverse events

## Dual mechanism opioids:

- Dual mechanism opioids for LOT are neither recommended for or against
- Dual-mechanism opioids include formulations of an opioid medication with a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI)
- Dual-mechanism opioid medications have additional considerations as a result of their dual action – they include a lowering of seizure threshold in susceptible patients and the risk of serotonin syndrome
- Two common examples are tramadol and tapentadol – while both are dual-mechanism opioids, they differ in their affinity for the mu opioid receptor, resulting in partial versus full agonist effects

## Buprenorphine for chronic pain:

- There is insufficient evidence to recommend buprenorphine over other opioids for the treatment of chronic pain
- Buprenorphine has several properties that make it potentially desirable as an analgesic:
  - It is a synthetic opioid analgesic with partial mu opioid agonist and kappa opioid antagonist properties
  - It has high affinity to the opiate receptor and a long duration of action (24 to 72 hours)
  - It is a partial agonist agent and, as such, may be associated with less euphoria and easier withdrawal
- Buprenorphine should not be added to patients that are on a full mu agonist as it will precipitate withdrawal – in addition, caution should be exercised when adding full mu agonists to patients on buprenorphine as the efficacy and side effect profiles may vary

- Consideration should be given to specialty consultation when patients on buprenorphine have acute or post-operative pain conditions
- Practitioners who prescribe sublingual (SL) buprenorphine or SL buprenorphine/naloxone for pain are not required to have an X Drug Enforcement Administration (DEA) number – practitioners do not need an X DEA license to prescribe buprenorphine patches labeled for pain
- When buprenorphine is used for pain, higher doses should be used with caution in opioid-naïve patients
- Split dosing is often preferred as the duration of pain relief may be eight to 12 hours

## Buprenorphine formulations

| Route | Dosage Form | Strengths | Brand Name | Use |
|---|---|---|---|---|
| **Topical** | Transdermal System | 5 mcg/hour<br>7.5 mcg/hour<br>10 mcg/hour<br>15 mcg/hour<br>20 mcg/hour | Butrans® | Management of pain severe enough to require around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate |
| **Buccal** | Film | 75 mcg<br>150 mcg<br>300 mcg<br>450 mcg<br>600 mcg<br>750 mcg<br>900 mcg | Bulbuca® | Management of pain severe enough to require around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate |
| **Parenteral** | Injection | 0.3 mg/mL | Buprenex® | Management of moderate-to-severe pain |
| **Sublingual** | Tablets | 2 mg<br>8 mg | Subutex® | Treatment of opioid dependence |

## Methadone for chronic pain:

- The unique pharmacologic properties of methadone make it particularly risky to prescribe
- Methadone carries a risk of cardiac arrhythmia and risk assessment for QT prolongation and electrocardiographic monitoring is essential
- Methadone has a variable half-life with peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect – dose escalation to improve pain relief may lead to unintentional intoxication and corresponding respiratory depression or arrest
- The metabolism of methadone varies by dose and individual, making dosing unpredictable


Only providers who are experienced with methadone and who are prepared to implement appropriate precautions, risk mitigation strategies and patient/caregiver education should initiate, titrate or taper methadone for chronic pain.

## Methadone prescribing checklist:

- ☑ Inform patients of arrhythmia risk
- ☑ Ask patients about heart disease, arrhythmia, syncope and sleep apnea
- ☑ Educate patients about drug interactions
- ☑ Obtain baseline electrocardiogram (ECG) and regularly thereafter in intervals appropriate to risk/dosage
- ☑ Re-evaluate and discuss with the patient the potential risks and benefits of therapy and the need for monitoring the QTc more frequently
- ☑ Discontinue or taper the methadone dose and consider using an alternative therapy if the QTc interval exceeds 500 ms; whenever possible, eliminate other contributing factors, such as drugs that cause hypokalemia or QT prolongation
- ☑ Be aware of interactions between methadone and other drugs that may prolong QTc interval or slow the elimination of methadone, and educate patients about potential drug interactions
- ☑ Implement a conservative dosing strategy:
  - — Methadone should not be initiated in opioid-naïve patients in the outpatient setting
  - — Primary care providers should never rotate from another opioid to methadone without guidance from an experienced provider regarding the starting dose of methadone
  - — When initiating or increasing dosage, close follow-up is recommended (e.g., within five to seven days) to assess signs of methadone toxicity, such as excess sedation or delirium
  - — Wait at least one week on a particular dose of methadone before increasing dosage to make sure that the full effects of the previous dosage are evident

# Continuing OT

The steps below are drawn from the 2017 VA/DoD OT for Chronic Pain CPG Module D algorithm, which includes: an ordered sequence of steps of care; recommended observations and examinations; decisions to be considered; and actions to be taken by providers when treating patients currently on OT.

**Obtain Biopsychosocial Assessment**

- Complete a comprehensive biopsychosocial assessment (see page 41)
- Determine presence of factors requiring immediate attention and possible discontinuation of OT due to unacceptable risk

**Review Data and Reassess Risks and Benefits of OT**

- Review data and reassess risks and benefits of continuing OT
- Consider strength and number of risk factors
- Determine presence of any of the following:
  - Prescribed opioid >90 mg MEDD
  - Combined sedating medication (e.g., benzodiazepine) that increases risk of adverse events
  - Patient non-participation in a comprehensive pain care plan
  - Other indications for tapering
- Reassess and optimize preferred non-opioid treatments for chronic pain (e.g., physical and psychological treatments)
- Determine whether the patient is experiencing clear functional improvement with minimal risk

| | |
|---|---|
| **Educate/ Re-educate the Patient** | ▪ Educate or re-educate the patient on:<br>— Non-opioid management<br>— Self-management to improve function and quality of life<br>— Realistic expectations and limitations of medical treatment options<br>— Preferred non-pharmacological and non-opioid pharmacotherapy<br>▪ Review any new information on risks and lack of benefit of LOT |
| **Continue OT** | ▪ Continue OT using the following approach:<br>— Shortest duration<br>— Lowest effective dose – recognizing that no dose is completely safe and overdose risk increases at doses >20 to 50 mg MEDD<br>▪ Continual assessment of improvement in pain and functional status and adverse effects |

During initial assessment of patients currently on OT, providers should determine presence of factors requiring immediate attention and possible discontinuation of OT due to unacceptable risk.

**STOP** **Factors requiring immediate attention and possible discontinuation of OT in patients currently on OT:**

- Untreated SUD
- Unstable mental health disorder
- Medical condition that acutely increases opioid risks (e.g., compromised or worsening cognitive or cardiopulmonary status)
- Other factors that acutely increase risk of overdose:
  - Recent overdose
  - Current sedation
  - Recent motor vehicle accident
- Acutely elevated suicide risk

During the reassessment of patients currently on OT, providers should reassess the following risks and benefits of continuing OT and consider the strength and number of risk factors.

### Risks:

- Increased risk of all-cause mortality
- Increased risk of unintentional overdose death
- Increased risk of developing OUD
- Risk of developing or worsening:
  - Depression
  - Falls
  - Fractures
  - Sleep-disordered breathing
  - Worsening pain
  - Motor vehicle accidents
  - Hypogonadism
  - Prolonged pain
  - Nausea
  - Constipation
  - Dry mouth
  - Sedation
  - Cognitive dysfunction
  - Immune system dysfunction
  - Reduction in function
  - Reduction in quality of life

### Benefits:

- Modest short-term improvement in pain
- Possible short-term improvement in function

When educating or re-educating patients currently on LOT, providers can use the following talking points to share important information about the safety of OT for chronic pain.

### Talking points for education and re-education for patients currently on OT

- "Doctors used to think that opioids were safe and effective when used for long periods of time to treat chronic pain"
- "New information has taught us that long-term opioid use can lead to multiple problems, including loss of pain-relieving effects, increased pain, unintentional death, OUD, and problems with sleep, mood, hormonal dysfunction and immune dysfunction"
- "We now know that the best treatments for chronic pain are not opioids. The best treatments for chronic pain are non-drug treatments such as psychological therapies, rehabilitation therapies and non-opioid medications"

# Risk Mitigation

# Tab 4 – RISK MITIGATION

There has been a paradigm shift in approaches to ensure and document mutual patient and provider understanding and expectations regarding the risks and benefits of LOT.

The implementation of risk mitigation strategies upon initiation of LOT, starting with an informed consent conversation covering the risks and benefits of OT as well as alternative therapies are strongly recommended (**CPG Recommendation 7**). The strategies and their frequency should be commensurate with risk factors and include: ongoing, random drug testing; checking state prescription drug monitoring programs; and providing overdose education and prescribing of naloxone rescue and accompanying education.

Assessment of suicide risk when considering initiating or continuing LOT, and intervening when necessary is strongly recommended (**CPG Recommendation 8**). Evaluation of benefits of continued OT and risk for opioid-related adverse events at least every three months are strongly recommended (**CPG Recommendation 9**).

- The implementation of more extensive risk mitigation strategies entails an investment of resources – primary care providers may require more time with patients to allow for shared decision making and treatment
- More frequent follow-up of patients on LOT can affect access to care for all empaneled patients
- VHA providers must also follow VHA policy regarding education and signature informed consent when providing LOT for patients with non-cancer pain

| Strategy | Description |
|---|---|
| **Informed Consent** | ▪ Signature informed consent* replaced the prior practice of using opioid treatment agreements<br>▪ Robust, signature informed consent process that is patient-centered and provides patients with information about known benefits and harms of OT and treatment alternatives |
| **Specific Risk Mitigation Strategies** | ▪ UDT<br>▪ PDMP<br>▪ OEND |

| | |
|---|---|
| **Suicide Risk Assessment** | ▪ Opioid medications are potentially lethal and an assessment of current suicide risk should be made at every phase of treatment<br>▪ Some patients on LOT who suffer from chronic pain and co-occurring OUD, depression and/or personality disorders may threaten suicide when providers recommend discontinuation of opioids – in such cases, it is essential to involve a behavioral health provider to assess, monitor and treat a patient who becomes destabilized as a result of a medically-appropriate decision to taper or cease LOT |
| **Follow-up and Re-evaluation** | ▪ An individualized assessment of potential opioid-related harms relative to realistic treatment goals must be completed<br>▪ Frequent visits contribute to the appropriate use and adjustment of the planned therapy<br>▪ Follow-up at least every 3 months or more frequently to re-examine the rationale for continuing the patient on OT<br>▪ The Centers for Disease Control and Prevention (CDC) guideline for OT recommends re-evaluating harms versus benefits within 1 to 4 weeks of starting OT or at any dose change, and at least every 3 months or more frequently if needed<br>▪ Providers should take into account changes in co-occurring conditions, diagnoses/medications and functional status when conducting the risk/benefit analysis for LOT<br>▪ Alcohol use, pregnancy, nursing of infants and lab abnormalities may change the risk/benefit calculus for LOT<br>▪ Ongoing OT prescribing practice may include pharmacy review, informed consent, UDT and checking state PDMP – providers should also be mindful of signs of diversion during follow-up<br>▪ The longer the patient is on opioids, the greater the potential for change in patient status and development of opioid-related harms |

*Department of Veterans Affairs (2009). VHA Handbook 1004.01. Informed Consent for Clinical Treatments and Procedures. Retrieved from: https://www.va.gov/vhapublications/index.cfm.

# Sample VA Signature Informed Consent

**Department of Veterans Affairs** | **Consent for Long-Term Opioid Therapy for Pain**

**A. IDENTIFICATION**

**1. Patient Name, Social Security Number, and Date of Birth:**

Name: Last, First, Middle | Social Security Number | Date of Birth

**2. Decision-making capacity:**

☐ The patient HAS decision-making capacity (skip to item 3).

☐ The patient DOES NOT HAVE decision-making capacity. Enter surrogate name and relationship to the patient. (If the patient's surrogate is not established or available, refer to Handbook 1004.01 for guidance).

**Name: Last, First, Middle** | Relationship

**3. Name of the treatment:** Long-Term Opioid Therapy for Pain

**4. Practitioner obtaining consent:**

Name: Last, First, Middle

**5. Supervising practitioner:** (if applicable)

**Name: Last, First, Middle**

**6. Additional practitioner(s) performing or supervising the treatment:** (if not listed above)

**B. INFORMATION ABOUT THE TREATMENT**

**7. Reason for long-term opioid therapy (diagnosis, condition, or indication):**

**8. Location of pain:**

**9. Goal(s) of long-term opioid therapy (e.g., pain score, functional abilities such as go back to work, climb stairs, walk short distances, sleep through the night, do daily household chores, start a light exercise program):**

**10. Name of current or initial opioid medication(s):**

**11. Brief description of the treatment:**

Opioids are very strong medicines that may be used to treat pain. You may already be taking opioids. Or your provider may try to give you opioids to find out if they will help you. They may try them for a short time or continue them for the rest of your life. Your provider will learn more about your risks and side effects when you are trying the opioids. If the risks and side effects outweigh the benefits, your provider will stop the prescription.

If your provider continues your opioid prescription, the goals of your treatment may change over time. The names and doses of your opioids may also change. You will not need to sign another consent form for these changes. You may be asked to sign another consent form if you seek opioid pain care from another VA provider.

Your provider will monitor your prescription. This may include checking how often you refill and renew your prescription, counting pills, asking you about your symptoms, and testing your urine, saliva, and blood. If you do not take opioids responsibly, your provider may stop your prescription. For example, if you do not let your provider monitor how you are responding to the opioids or tell them if you are taking other drugs that may affect the safety or effectiveness of your opioid treatment, your provider may stop the prescription.

For your safety, your provider and pharmacist will monitor when you renew and refill your opioids within VA. Consistent with state law, they will also monitor this outside of VA. Most states have monitoring programs that track unsafe patterns of prescription drug use. VA and these programs may obtain and share information about you without your specific consent.

Your provider will review with you a Patient Information Guide called "Taking Opioids Responsibly" to make sure that you know how to take your medication safely. You will be given a copy of the guide so that you can use it as a reference

**12. Potential benefits of the treatment:**

Opioids -- when added to other treatments as part of your pain care plan -- may reduce your pain enough for you to feel better and do more. It is unlikely that opioids will eliminate your pain completely. It is possible that you may not receive any benefits from opioid therapy.

**13. Known risks and side effects of the treatment:**

**Possible opioid side effects include:**

- Sleepiness or "slow thinking"
- Mental confusion, bad dreams, or hallucinations
- Constipation
- Intestinal blockage
- Itching
- Sweating
- Nausea or vomiting
- Decreased sex hormones
- Irregular or no menstrual periods
- Depression
- Dry mouth that causes tooth decay
- Allergies

**Other risks of opioid therapy:**

- Withdrawal symptoms if you suddenly stop taking opioids, lower the dose of your opioids too quickly, or take a drug that reverses the effects of your opioids. Withdrawal symptoms are caused by physical dependence that is a normal result of long-term opioid therapy. Some common withdrawal symptoms are runny nose, chills, body aches, diarrhea, sweating, nervousness, nausea, vomiting, mental distress, and trouble sleeping.
- Sleep apnea (abnormal breathing pauses during sleep)
- Worsening of pain
- Impaired driving or impaired ability to safely operate machinery
- Tolerance, which means that you may need a higher dose of opioid to get the same pain relief, resulting in an increase in the likelihood of the other side effects and risks
- Addiction (craving for a substance that gets out of control). Some patients become addicted to opioids even when they take opioids as prescribed.
- Drug interactions (problems when drugs are taken together). Taking small amounts of alcohol, some over-the counter medications, some herbal remedies, and other prescription medications can increase the chance of opioid side effects.
- Risks in pregnancy:
  - **Continued use of opioids during pregnancy can cause your baby to have withdrawal symptoms after birth and require your baby to stay in the hospital longer after birth.**
  - **Stopping opioids <u>suddenly</u> if you are pregnant and physically dependent on opioids can lead to complications during pregnancy.**
  - **Studies have not shown a clear risk for birth defects with opioid use in pregnancy. If there is an increased risk for birth defects in pregnancy with opioid use, it is likely small.**
- Death

**14. Alternatives to the treatment:**

You have the option not to take opioids. Other treatments can be used as part of your pain care plan. Alternatives include:

- Heat and cold therapy (heating pads, ice packs)
- Stretching
- Exercise
- Weight loss
- Massage
- Acupuncture
- Chiropractic
- Nerve Stimulation
- Relaxation or stress reduction training
- Physical therapy
- Occupational therapy
- Mental health treatment
- Self-care techniques
- Counseling and coaching
- Meditation
- Rehabilitation
- Non-opioid pain medicines (Non-steroidal anti-inflammatory drugs, antidepressants, anticonvulsants)
- Injections
- Specialist pain care
- Surgery
- Pain classes
- Support groups
- Attention to proper sleep

**15. Additional Information:**

**16. Comments:**

**C. SIGNATURES**

**Practitioner obtaining consent:**

- All relevant aspects of the treatment and its alternatives (including no treatment) have been discussed with the patient **(or surrogate) in language that s/he could understand. This discussion included the nature, indications, benefits, risks, side effects, monitoring, and likelihood of success of each alternative that was considered.**
- I have discussed all of the information contained in the education document "Taking Opioids Responsibly" with the patient (or surrogate).
- The patient (or surrogate) demonstrated comprehension of the discussion.
- I have given the patient (or surrogate) an opportunity to ask questions.
- I did not use threats, inducements, misleading information, or make any attempt to coerce the patient/surrogate to consent to this **treatment.**
- I have offered the patient (or surrogate) the opportunity to review and receive a printed copy of the consent form.
- If the patient is a woman of childbearing age (ages 15-50), I have discussed the patient's pregnancy status and pregnancy intentions.
  - **If the patient is not considering pregnancy, I have discussed (or referred the patient for) contraceptive counseling.**
  - **If the patient is considering pregnancy, I have discussed (or referred the patient for) preconception counseling.**

Signature _____ Date _____ Time _____

**Patient or surrogate:**

- I understand that to receive long-term opioids I must agree to my opioid treatment plan by signing this consent form.
- Someone has explained the treatment, what it is for, and how it could help me.
- Someone has explained things that could go wrong, including serious side effects and death, particularly if I do not take my medicine as prescribed.
- Someone has told me about other treatments that might be done instead, and what would happen if I have no treatment.
- I have discussed the information in the document "Taking Opioids Responsibly" with my provider.
- I understand the importance of:
  - **telling my provider about side effects.**
  - **telling my provider about changes in my pain and daily function.**
  - **getting my opioids from only my VA provider and no one else.**
  - **not giving away (or selling) my opioids to other people.**
  - **storing my opioids in a safe place away from children, family, friends, and pets.**
  - **safely getting rid of opioids I do not need.**
  - **not drinking alcohol or taking illegal street drugs when I am on opioids.**
  - **for women, telling my provider if I think I might be pregnant, know I am pregnant, or am planning to become pregnant.**

- I plan to use my medications responsibly, and take them as prescribed.
- I understand how to refill my opioid prescription or get a new prescription. I understand that my VA pharmacy may be closed on weekends, holidays, and after regular clinic hours. I understand that my provider might not give me early medication refills or replace doses that are lost or stolen.
- I understand that my provider may order urine or blood drug tests with my consent (separate from this consent). I understand that the results of these tests or my refusal to be tested may cause my provider to talk to me about changing my opioid treatment plan.
- I understand that I may have to stop opioids if my provider thinks that it is unsafe for me to continue.
- Someone has answered all my questions.
- Someone has given me information about how to contact the clinic, if there is a problem and who to call in an emergency.
- I know I may refuse or change my mind about having treatment. If I do refuse or change my mind, I will not lose my health care or any other VA benefits.
- I have been offered the opportunity to review and receive a copy of my consent form.
- I choose to have this treatment.

Signature _____ Date _____ Time _____

**Witnesses:** No witness is required if the patient or surrogate signs their name. Two witnesses are required only when the patient's signature is indicated with an "X" or some other identifying mark.

Witness Name (Please Print) _____

Witness Signature _____ Date _____ Time _____

Witness Name (Please Print) _____

Witness Signature _____ Date _____ Time _____

# Recommended Risk Mitigation Strategies

Risk mitigation should begin before opioid medications are prescribed, concurrently with the therapy and in response to adverse events.

- Certain patients may appreciate the use of risk mitigation strategies, but others may not
- Patients may decline risk mitigation strategies; however, providers should discuss how that may increase the risks of an adverse outcome and thus, likely outweigh the benefit of the treatment
- Clinical decision making should remain patient-centered, including a focus on patient safety – risk mitigation strategies alone or in combination improve patient safety
- The strategies and their frequency should be commensurate with risk factors and include ongoing assessment for co-morbid physical and psychological conditions, including SUD and suicidality, ongoing, random UDT, checking state PDMP and providing OEND

| Strategy | Description |
|---|---|
| **Urine Drug Testing** | ▪ The inaccuracies inherent to patient self-report coupled with the evident mortality and morbidity to the treated patients, their families and others require additional methods to ascertain patient and public safety<br>▪ When used in the appropriate way, UDT helps to address safety, fairness and trust with OT<br>▪ It is critical that the UDT and confirmatory testing be done in a timely, confidential, accurate and easily-available manner to assure the prescribers, patients and public that safety, fairness and trust are being addressed<br>▪ It is important that UDT be viewed in a therapeutic framework so that appropriate follow-up with SUD evaluation and treatment are offered when indicated<br>▪ UDT results are helpful and can help identify active SUD or possible diversion<br>▪ Within the VA, verbal informed consent is required prior to UDT; although a patient can decline to consent to UDT, a provider can factor that declination into their OT safety assessment |

| | |
|---|---|
| | ▪ There are 3 types of UDT currently being used in clinical settings:<br>— Immunoassay (fast and widely available, higher potential for false positives and negatives as well as lack of specificity)<br>— Gas chromatography-mass spectrometry (GCMS) confirmatory testing (highly sensitive and specific; however, expensive and time consuming)<br>— Liquid chromatography-mass spectrometry (LCMS) confirmatory testing (less expensive than GCMS but more expensive than immunoassay, give a confirmation for a large number of medications, substances and drugs at one time, and may be helpful to many patients at initiation of OT, periodically during OT and following cessation of OT if SUD is a possibility)<br>▪ Interpretation of a UDT and confirmatory results requires education and knowledge of the local procedures and clinical scenario |
| **Prescription Drug Monitoring Programs** | ▪ State database queries for detection of multi-sourcing of controlled substances are used throughout the country<br>▪ The CDC currently recommends at least quarterly checks of the state database system |
| **Opioid Overdose Education and Naloxone Distribution** | ▪ Naloxone administration has been identified as a life-saving measure following opioid overdose<br>▪ Clinical efficacy has been established for its use on short-acting opioids, but not for its use on long-acting opioids such as methadone or exceptionally potent opioids<br>▪ Naloxone administration has been efficacious whether given by medical personnel or lay people<br>▪ Providers should discuss prescribing naloxone rescue kits and accompanying education with their LOT patients (and family members) |

| | |
|---|---|
| **Follow-up and Re-evaluation** | ▪ An individualized assessment of potential opioid-related harms relative to realistic treatment goals must be completed<br>▪ Frequent visits contribute to the appropriate use and adjustment of the planned therapy<br>▪ Follow-up at least every 3 months or more frequently to re-examine the rationale for continuing the patient on OT<br>▪ CDC guideline for OT recommends re-evaluating harms versus benefits within 1 – 4 weeks of starting OT or at any dose change, and at least every 3 months or more frequently, if needed<br>▪ Providers should take into account changes in co-occurring conditions, diagnoses/medications and functional status when conducting the risk/benefit analysis for LOT<br>▪ Alcohol use, pregnancy, nursing of infants and lab abnormalities may change the risk/benefit calculus for LOT<br>▪ Ongoing OT prescribing practice may include pharmacy review, informed consent, UDT and checking state PDMP<br>▪ Providers should also be mindful of signs of diversion during follow-up<br>▪ The longer the patient is on opioids, the greater the potential for change in patient status and development of opioid-related harms |

## Other risk mitigation strategies include:

- Take back programs
- Needle exchange programs
- Syringe service programs

# Urine Toxicology Specimen Validity and Normal Characteristics of a Urine Sample

| Urine toxicology specimen validity | Normal characteristics of a urine sample |
|---|---|
| ▪ Urine samples that are adulterated, substituted or diluted may avoid detection of drug use<br>▪ Urine collected in the early morning is most concentrated and most reliable<br>▪ Excessive water intake and diuretic use can lead to diluted urine samples (creatinine <20 mg/dL)<br>▪ THC assays are sensitive to adulterants (e.g., eye drops) | ▪ Temperature within 4 minutes of voiding: 90 – 100$^{0}$F<br>▪ pH: 4.5 – 8.0<br>▪ Creatinine: >20 mg/dL<br>▪ Specific gravity: >1.003<br>▪ Nitrates: <500 mcg/dL<br>▪ Volume: ≥30 mL |

Abbreviations: $^{0}$F: degrees Fahrenheit; dL: deciliter(s); mcg: microgram(s); mg: milligram(s); mL: milliliter(s); THC: tetrahydrocannabinol

# Summary of Agents Potentially Contributing to False Positives

| Agent | Summary of Agents Potentially Contributing to False Positives | | |
|---|---|---|---|
| **Marijuana Metabolites** | ▪ dronabinol<br>▪ efavirenz | ▪ NSAIDs*<br>▪ proton pump inhibitors | ▪ hemp foods: tea, oil† |
| **Cocaine Metabolites** | ▪ cocoa leaf teas | ▪ topical anesthetics containing cocaine | |
| **Opioid Metabolites** | ▪ dextromethorphan<br>▪ fluoroquinolone<br>▪ levofloxacin | ▪ ofloxacin<br>▪ poppy seeds<br>▪ poppy oil | ▪ rifampin<br>▪ quinine |
| **Amphetamines/ Methamphetamines (high rate of false positives)** | ▪ amantadine<br>▪ benzphetamine<br>▪ brompheniramine<br>▪ bupropion<br>▪ chlorpromazine<br>▪ desipramine | ▪ isometheptene<br>▪ isoxsuprine<br>▪ labetalol<br>▪ l-methamphetamine (OTC nasal inhaler)<br>▪ methylphenidate | ▪ propanolamine<br>▪ promethazine<br>▪ pseudoephedrine<br>▪ ranitidine<br>▪ selegiline<br>▪ thioridazine |

| | | | |
|---|---|---|---|
| | ▪ dextroamphetamine<br>▪ doxepin<br>▪ ephedrine<br>▪ fluoxetine | ▪ MDMA<br>▪ phentermine<br>▪ phenylephrine | ▪ trazodone<br>▪ trimethobenzamide<br>▪ trimipramine |
| **Benzodiazepines** | ▪ oxaprozin | ▪ sertraline | |
| **Opioid Metabolites** | ▪ ibuprofen | ▪ naproxen | |
| **Methadone** | ▪ chlorpromazine<br>▪ clomipramine<br>▪ diphenhydramine | ▪ doxylamine<br>▪ ibuprofen<br>▪ quetiapine | ▪ thioridazine<br>▪ verapamil |
| **Alcohol** | ▪ mouthwash | ▪ short-chain alcohols | ▪ OTC cough products (isopropyl alcohol) |

* Detection time for most drugs in urine is 1 – 3 days
†Long-term use of lipid-soluble drugs (THC, diazepam, ketamine) can be detected for a longer period of time
Abbreviations: NSAIDs: non-steroidal anti-inflammatory drugs; MDMA: 3,4-methylenedioxy-methamphetamine; OTC: over the counter; THC: tetrahydrocannabinol

# Interpreting Urine Toxicology Screening

| | Drug or Class | Expected Results | Consideration |
|---|---|---|---|
| **Non-Opioids** | Alcohol | Alcohol | ▪ Testing for ethanol metabolites, ethyl glucuronide or ethyl sulfate, can identify alcohol up to 80 hr after consumption |
| | Amphetamines | **Immunoassay** – Amphetamines, methamphetamines or MDMA<br>**Confirmatory** – Amphetamines, methamphetamines or MDMA | ▪ Immunoassay tests are highly cross-reactive; therefore confirmatory testing is required and can identify which amphetamine is present |
| | Benzodiazepines | **Immunoassay** – Unconjugated oxazepam or its metabolites<br>**Confirmatory** – Alprazolam, diazepam, clonazepam, lorazepam, etc. | ▪ Immunoassays for benzodiazepines have a 28% overall false negative rate<br>▪ Confirmatory testing is needed when use is expected or suspected (alprazolam, clonazepam and lorazepam often not detected by immunoassay) |
| | Barbiturates | **Immunoassay** – Barbiturates | ▪ N/A |

| | | | |
|---|---|---|---|
| | Cocaine metabolites | **Immunoassay** – cocaine or benzoylecgonine | ▪ Cocaine's primary metabolite, benzoylecgonine, has low cross-reactivity with other substances and is highly predictive of cocaine use<br>▪ A positive result should be interpreted as recent exposure to cocaine |
| **Opioids of "Opiates" – Natural (from opium)** | Codeine (Tylenol #2, 3/4) | Opiates Immunoassay – Positive<br>**Confirmatory** – codeine, possibly morphine & hydrocodone | ▪ Immunoassays for "opiates" are responsive to morphine and codeine but do not distinguish which<br>▪ Codeine is metabolized to morphine and small quantities of hydrocodone |
| | Morphine (Avinza®, Embeda®, MS Contin®, Kadian®) | Opiates Immunoassay – Positive<br>**Confirmatory** – morphine, possibly hydromorphone | ▪ Immunoassays for "opiates" are responsive to morphine and codeine but do not distinguish which<br>▪ Morphine (<10%) may be metabolized to hydromorphone |
| | Heroin | Opiates Immunoassay – Positive<br>**Confirmatory** – heroin (6-MAM), morphine, possibly codeine | ▪ 6-MAM is pathognomonic for heroin use, detection 12 – 24 hr<br>▪ Heroin is metabolized to morphine |

| | | | |
|---|---|---|---|
| **Opioid – Semisynthetic (derived from opium)** | Hydrocodone (Lorcet®, Lortab®, Norco®, Vicodin®) | Opiates Immunoassay – Positive<br>**Confirmatory** – hydrocodone, possibly hydromorphone | ▪ "Opiates" immunoassay may detect semisynthetic opioids<br>▪ Hydrocodone > hydromorphone > oxycodone<br>▪ Negative result does not exclude use and confirmatory testing (GCMS) is required<br>▪ Hydrocodone is metabolized in small amounts to hydromorphone, both may be found in urine<br>▪ Oxycodone is metabolized to oxymorphone, both may be found in urine<br>▪ Hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively |
| | Hydromorphone (Dilaudid®, Exalgo®) | Opiates Immunoassay – Positive<br>**Confirmatory** – codeine, possibly morphine & hydrocodone | |
| | Oxycodone (Roxicet®, OxyContin®) | Opiates Immunoassay – May be positive<br>Oxycodone Immunoassay – Positive<br>**Confirmatory** – oxycodone, possibly oxymorphone | |
| | Oxymorphone (Opana®) | Oxycodone Immunoassay – Positive<br>**Confirmatory** – oxymorphone | |

| | | | |
|---|---|---|---|
| **Opioids – Synthetic (man-made)** | Buprenorphine | **Immunoassay** – buprenorphine<br>**LCMS, GCMS** – buprenorphine, norbuprenorphine | ▪ Current “opiates” immunoassays do not detect synthetic opioids<br>▪ Confirmatory testing (GCMS or LCMS) is needed |
| | Fentanyl | **GCMS** – fentanyl, norfentanyl | |
| | Meperidine (Demerol®) | **GCMS** – normeperidine, possibly meperidine | |
| | Methadone (Methadose®) | Methadone Immunoassay – Positive<br>**GCMS** – methadone, EDDP | |

Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

Abbreviations: 6-MAM: 6-monoacetylmorpine; EDDP: 2-ethylidene-1, 5-dimethyl-3, 3-diphenylpyrrolidine; GCMS: gas chromatography-mass spectrometry; hr: hours; LCMS: liquid chromatography-mass spectrometry; MDMA: 3, 4-methylenedioxy-methamphetamine

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# Taper and Discontinuation of OT

# Tab 5 – TAPER AND DISCONTINUATION OF OT

Tapering to reduced dose or to discontinuation of LOT when risks of LOT outweigh benefits is strongly recommended (**CPG Recommendation 14**). Abrupt discontinuation should be avoided unless required for immediate safety concerns. Individualizing opioid tapering based on risk assessment and patient needs and characteristics are strongly recommended (**CPG Recommendation 15**). There is insufficient evidence to recommend for or against specific tapering strategies and schedules.

The steps below are drawn from the 2017 VA/DoD OT for Chronic Pain CPG Module C algorithm, which includes: an ordered sequence of steps of care; recommended observations and examinations; decisions to be considered; and actions to be taken by the providers when tapering or discontinuing OT.

**Repeat Biopsychosocial Assessment**

- Complete a comprehensive biopsychosocial assessment (see page 41) prior to initiation of opioid taper
- Assessment includes evaluation of medical, psychiatric and co-occurring substance use conditions as well as the patient's social support system
- Weigh the risks and benefits of the current opioid regime with the risks and benefits associated with a reduction in opioid dose

**Develop Individualized Tapering Treatment Plan**

- Consider pace of tapering, setting of care and frequency of follow-up when developing the pain care plan
- Individualize the pain care plan based on risk assessment and patient needs and characteristics including:
  - Opioid dose and duration of therapy
  - Opioid formulation
  - Psychiatric, medical and SUD co-morbidities
  - Other patient risk factors

**Follow-up**

- Follow-up one week to one month after change in dosage and after discontinuation considering patient and treatment characteristics

- Determine presence of:
  - Patient resistance to taper
  - High risk or dangerous behaviors
  - Increase in patient distress
- Re-evaluate risks and benefits coupled with repeated biopsychosocial assessment
  - Each follow-up interaction with the patient is an opportunity to provide education about self-management strategies and the risks associated with OT while optimizing whole person approaches to pain care and treatment of co-occurring medical and mental health conditions

## Indications for Tapering and Discontinuing

Providers should reassess the use of LOT in all patients currently receiving the therapy and consider tapering or discontinuing opioids in all patients on LOT when the risks exceed the benefits of therapy.

### Indications for tapering and discontinuation

- Risks of OT outweigh the benefits
- Lack of clinically meaningful improvement in function
- Pain condition not effectively treated with opioids
- Concomitant use of medications that increase risk of overdose
- Medical co-morbidities that increase risk
- Mental health co-morbidities that may worsen with OT
- Concerns about OUD or other SUD
- Patient requests to discontinue therapy
- Patient non-adherence to a comprehensive pain care plan and opioid risk mitigation strategies
- Opioid dosage exceeds 90 mg MEDD
- Improvement in underlying pain condition being treated
- Unmanageable side effects
- Prescribed dose higher than the maximal recommended dose (which increases risk of adverse events)
- Opioid dosage exceeds 90 mg MEDD
- Strong concern for diversion

# Special Considerations

## Benzodiazepines

Abrupt discontinuation of benzodiazepines should be avoided, as it can lead to serious adverse effects, including seizures and death. Tapering benzodiazepines should be performed with caution and within a team environment when possible; even gradual benzodiazepine taper may result in exacerbation of PTSD symptoms.

## OUD

For patients with OUD, sudden discontinuation of opioids due to suspected diversion may place them at high risk for illicit opioid use and resulting opioid overdose. Patients on LOT with OUD are at increased risk of overdose when opioids are either continued or discontinued without appropriate treatment for OUD.

## Abrupt discontinuation of opioids may be justified in certain high risk circumstances

When there is evidence for diversion, the provider may need to discontinue OT, frequently assess for withdrawal symptoms and offer necessary support for withdrawal symptoms and treatment of SUD, if present.

When a patient exhibits dangerous behaviors (e.g., threatening behaviors, persistent and serious disruptive behavior, suicidal ideation or behaviors), the provider may consider abruptly discontinuing OT while providing urgent or emergent psychiatric referral and medical care for the management of opioid withdrawal. When relevant, dangerous or illegal behavior should be documented accurately and completely in the medical record to guide future care.


Low frequency of follow-up in primary care and limited access to comprehensive interdisciplinary specialty pain, rehabilitation, mental health and addiction services may be barriers to tapering LOT that may need to be addressed.

# Tapering Pain Care Plan

The goal of opioid tapering is to improve the balance of risks and clinically meaningful benefits for patients on LOT. The tapering plan should be individualized and should address the pace of tapering, setting of care and frequency of follow-up.

Interdisciplinary care that addresses pain, SUDs and/or mental health problems for patients presenting with high risk and/or aberrant behavior is strongly recommended (**CPG Recommendation 16**). Use of MAT, which includes behavioral approaches, should be offered for patients in whom a diagnosis of OUD is made (**CPG Recommendation 17**). See the VA/DoD CPG for the Management of SUDs.

- The risks and benefits of continuing OT should be evaluated along with the risks and benefits of tapering OT
- If the provider determines a patient to be at significant risk of adverse outcomes due to the use of LOT and if either the patient or the provider is concerned about potential destabilizing effects of opioid tapering, referral to or consultation with specialty services, including mental health, SUD, pain medicine and rehabilitation, should be strongly considered
- It is important to maintain vigilance for symptoms of OUD and/or exacerbation of an underlying mental health condition that may manifest during an opioid taper
- Providers should consider using an interdisciplinary team-based approach that may include primary care, mental health, pain specialty/rehabilitation, pharmacy, PT and/or SUD services during the opioid tapering process and, in particular, for patients with significant risk factors for adverse outcomes, including very high prescribed opioid doses (>90 mg MEDD), combined use of opioids and benzodiazepines, high risk patient behaviors, and the presence of psychiatric, medical or SUD co-morbidities
- Consider referring patients with co-occurring substance use or psychiatric conditions to addiction medicine/psychiatry or other behavioral health specialists – coordination of care between pain care and other specialty care, including SUD clinicians, is advised; however, if structured comprehensive programs are not available, coordination among individual health care providers is essential to address the full range of high risk behaviors
- Chronic pain in general and LOT in particular, require consideration of all of the patient's life problems – if resources do not exist to address co-occurring SUD and psychiatric conditions or if the patient declines to participate, treatment with LOT should be reconsidered
- Mental health and SUD co-morbidities that were previously unrecognized or that may worsen should be assessed and addressed with an interdisciplinary approach
- Interdisciplinary care, including mental health, rehabilitation and SUD treatment services may be necessary to support the tapering process

## Patient and treatment characteristics to consider when determining a tapering strategy

The opioid tapering plan should be individualized based on risk assessment and patient needs and characteristics including:

- Results of biopsychosocial assessment
  - Psychiatric, medical and SUD co-morbidities
- Opioid dose
- Duration of OT
- Type of opioid formulation
- Other patient risk factors that increase potential for harm:
  - Non-adherence
  - High risk medication-related behavior
  - Strength of social support
  - Coping

# Tapering Protocol

Below are the steps and considerations for implementing a tapering pain care plan.

1. When possible, use an interdisciplinary, team-based approach (primary care, mental health, pain specialty, pharmacy and SUD services) that addresses pain, SUD and/or mental health problems.
2. Complete a biopsychosocial assessment, including evaluation of co-occurring medical, psychiatric and co-occurring substance use conditions and patient's social support system.
3. Provide patient education on risks of continued use, along with possible benefits of continued use and discuss other available non-opioid pharmacological therapies.


Strongly caution patients that it takes as little as a week to lose tolerance to their prior opioid dose and that they are at risk of an overdose if they resume their prior dose.

4. Provide patient and family education about acute and protracted opioid withdrawal symptoms and provide treatment strategies to mitigate, as appropriate.
5. Ensure the patient does not feel abandoned during the opioid tapering process.
6. Determine the treatment goal – is the goal to reduce dosage or to discontinue OT?
7. Develop an individualized tapering plan based on the current pain care plan, risk assessment and patient needs and characteristics; include pace of taper, care setting and frequency of follow-up.
8. Determine appropriate care setting based on safety, patient preference and availability of services.
9. If patients are receiving both long-acting and short-acting opioids, determine which formulation is to be tapered first based on patient safety, medical history, mental health conditions and patient preference (tapering both formulations simultaneously may be appropriate).
10. Provide written and verbal instructions to the patient and family members about the taper protocol, possible withdrawal symptoms and the best way to dispose of opioids.
11. Reassess and follow up within a range of one week to one month after any dosage change.

# Speed of Taper

Regardless of the initial speed of taper, the rate of taper may need to be adjusted during the course of lowering the opioid dose. The pace of taper should be re-evaluated after each dose change and the rationale for the taper and taper schedule should be documented in the medical record.

### Gradual and rapid tapering:

- A gradual taper pace of reducing opioid dosage by five to 20 percent every four weeks with the option to pause periodically allows time for neurobiological equilibration as well as the acquisition of new skills to manage pain and emotional distress
- In some patients, a faster taper may be needed when risks are too high to consider a gradual taper; consider tapering the dose by five to 20 percent per week in this patient population
- Regardless of the initial speed of taper, the pace of taper should be re-evaluated frequently and adjusted as needed to maximize safety and patient comfort as safety allows

| Gradual taper | More rapid taper* |
|---|---|
| Higher opioid dose | Non-adherence to pain care plan |
| Longer OT duration – the longer the duration of previous OT, the longer the taper may take | Escalating high risk medication-related behaviors |
| When safety permits, gradual taper is more often tolerated | Drug diversion or illegal activities |
| Can be completed over several months to years | Risks too high to consider gradual taper* |
| **Suggested taper** | **Suggested taper** |
| 5 – 20% every 4 weeks | 5 – 20% per week** |

* When it is determined that patient risks are significantly high to warrant a rapid taper over a period of days or weeks, then specialty consultation should be obtained to determine the rate of taper and resources needed. These patients will need frequent follow-up and re-evaluation of SUD, mental health and/or co-occurring medical conditions with every dose change.

**For patients on LOT, consider changing patient's prescription to an equivalent dose of a long-acting opioid (e.g., methadone), then taper methadone accordingly.

# Opioid Use Disorder

All persons using opioid analgesics are at risk for developing an OUD.

- OUD (also known as opioid addiction, abuse or dependence) is a chronic brain disease that impairs one's ability to control opioid use
- Opioids disrupt the functioning of brain circuits that mediate a complex array of functions involved in obtaining natural rewards such as food and water that are essential for survival – because opioids activate these circuits more powerfully than natural rewards, the primitive brain learns to prioritize attention to and motivation for opioids over other natural rewards


Persons with OUD are at high risk for premature death, not only from opioid overdose, but from other consequences. Thus, providing first-line treatment is important to save lives as well as to improve the quality of life of patients.

- Repeated opioid use over time can lead to OUD – while there are some risk factors such as other substance use or co-occurring mental illness that can increase the risk of developing an OUD among those taking opioid analgesics, by far **the most powerful risk factor for developing OUD is long-term opioid analgesics use**
- Persons who become addicted to opioids gradually become more and more preoccupied with opioid use and spend more of their time seeking the drug, using it, or recovering from its effects and may continue to use opioids (see Diagnostic and Statistical Manual [DSM] diagnostic criteria for OUD on page 82)
- OUD is associated with premature death from opioid overdose and other medical complications such as acquired immunodeficiency syndrome (AIDS), hepatitis C and sepsis
- Consult the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders (VA/DoD SUD CPG) for further information

# DSM-5 Diagnostic Criteria for OUD

The DSM-5 defines OUD as "a problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the symptoms in the table below, occurring within a 12-month period."[5] OUD is classified as mild, moderate or severe depending on the number of presenting symptoms.

**DSM-5 diagnostic criteria for OUD**

1. Craving or strong desire or urge to use opioids
2. Recurrent use in situations that are physically hazardous
3. Tolerance
4. Withdrawal (or opioids are taken to relieve or avoid withdrawal)
5. Using larger amounts of opioids or over a longer period than initially intended
6. Persisting desire or unable to cut down on or control opioid use
7. Spending a lot of time to obtain, use or recover from opioids
8. Continued opioid use despite persistent or recurrent social or interpersonal problems related to opioids
9. Continued use despite physical or psychological problems related to opioids
10. Failure to fulfill obligations at work, school or home due to use
11. Activities are given up or reduced because of use

| Severity of OUD | Number of Symptoms |
|---|---|
| **Mild** | Presence of 2 – 3 symptoms |
| **Moderate** | Presence of 4 – 6 symptoms |
| **Severe** | Presence of 6 or more symptoms |

# Tapering and OUD

It is important to recognize that some patients who are undergoing an opioid taper may experience symptoms of OUD that were not present or had not been previously identified prior to the taper.

- Opioid prescribers and the treatment team should remain vigilant for signs and symptoms of OUD for patients receiving LOT – particular attention is warranted during the tapering process
- When there is concern for OUD or other SUD in a patient undergoing opioid tapering, providers should recommend SUD assessment and treatment to the patient in a setting that corresponds to the patient's level of risk and availability of services, while considering patient preferences
    - Some patients may be able to be seen in the primary care setting while others may be more appropriate for specialty care

> Patients on LOT with OUD are at increased risk of overdose when opioids are either continued or discontinued without appropriate treatment for OUD.

- Overdose education should be provided and naloxone should be offered as an antidote to all patients at risk for an opioid overdose, including those who are in the process of tapering
- During and following an opioid taper, patients may still be using opioids from other sources such as saved opioids, other prescribers, friends and family, as well as illicit sources
    - Continued surveillance for OUD and assessment for naloxone is suggested in patients who are no longer on opioids but who remain at risk for opioid use from unknown sources

## Medication Assisted Treatment

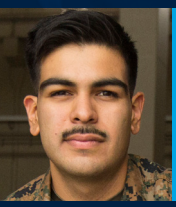
Patients on LOT with OUD are at increased risk of overdose when opioids are either continued or discontinued without appropriate treatment for OUD.

- Providers should offer MAT (e.g., MAT using methadone, buprenorphine/naloxone, or extended-release injectable naltrexone) for patients with OUD with chronic pain
- Treatment of OUD with MAT can occur in SUD programs as well as in primary care, specialty pain care and mental health settings when the necessary resources are available
- In patients with OUD, the opioid prescriber should ensure that opioid overdose education and naloxone distribution (OEND) has been offered
    - The opioid prescriber may consider slowing the taper until a warm hand-off to OUD treatment can be accomplished; however, close monitoring must occur for all patients during this transition process
    - Expediting the taper process and continuing to offer OUD treatment may be appropriate in some situations (e.g., if patient is not adherent to opioid taper and declines OUD treatment)

## Reassessment and Follow-up

Periodic re-evaluation of risks and benefits coupled with a biopsychosocial assessment should occur when implementing an opioid taper and on follow-up.

- Periodic re-evaluation of risks and benefits together with a biopsychosocial assessment within one week to one month after any opioid dosage change is recommended
- The frequency and type of follow-up is determined by the risk assessment conducted by the health care team
- If the initial treatment goal is dose reduction, ongoing assessment of the balance of risks and benefits should be conducted once the original treatment goal is achieved
- Each follow-up interaction with the patient is an opportunity to provide education about self-management strategies and the risks associated with OT while optimizing whole person approaches to pain care and treatment of co-occurring medical and mental health conditions
- Following discontinuation of opioids, consider continuing risk mitigation strategies
- Tapering may unmask underlying mental health and SUD co-morbidities – frequent assessment for these conditions is recommended



# Opioid Medication Table

# Tab 6 – OPIOID MEDICATION TABLE

The opioid medications described in this table are divided into the following sections: long-acting, combination and short-acting medications. Within each section, the medications are alphabetized. The combination opioid medications can be combined with other medications or given alone. Opioids should be used cautiously with elderly or debilitated patients. Additionally, use caution in patients with hepatic or renal dysfunction.

# Short-acting/Immediate-release (IR) Orally Administered Opioid Medications

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Codeine (alone or in combination with acetaminophen [APAP] or aspirin [ASA])<br>▪ Available as 15, 30 or 60 mg tablets<br>▪ Combination products vary in codeine content from 15 – 60 mg/dose unit | ▪ 15 – 30 mg every 4 – 6 hours<br>▪ Initial dose based upon codeine component; maximum dose based upon non-opioid component | ▪ Maximum APAP dose: 4000 mg/d (2000 mg/d in chronic alcoholics or hepatic impairment)<br>▪ Analgesic ceiling effect occurs at doses >60 mg/dose | Yes |

**Contraindications**: Include hypersensitivity to codeine or acetaminophen, respiratory depression in the absence of resuscitative equipment, acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Analgesic Onset (min)**: 15 – 30; **Peak (min)**: 30 – 60; **Duration (hr)**: 4 – 6

**Additional Information**:

- May be less effective in patients with decreased CYP-2D6 activity because of decreased conversion to morphine
- CYP-2D6 ultra-rapid metabolizers can have extensive conversion to morphine with increase in opioid-mediated effects
- Elderly or debilitated: Use with caution
- Hepatic dysfunction: Conversation to active metabolite (morphine) may be reduced in patients with cirrhosis; avoid use in patients with liver disease
- Renal dysfunction: Use lower dosage or an alternative

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Hydrocodone (in combination with APAP, ASA or IBU)<br>▪ Combination products vary in hydrocodone content from 2.5 – 10 mg/dosage unit | ▪ 5 – 10 mg every 6 hours<br>▪ Initial dose based upon hydrocodone component; maximum dose based upon non-opioid component | ▪ Maximum dose: 60 mg/d (4000 mg/d APAP; 2000 mg/d APAP in chronic alcoholics or hepatic impairment) for hydrocodone + APAP<br>▪ 37.5 – 50 mg/d (1000 mg/d IBU) for hydrocodone + IBU | Yes |

**Contraindications**: Include hypersensitivity to hydrocodone or acetaminophen, hypersensitivity to other opioids may exhibit cross-sensitivity to hydrocodone

**Analgesic Onset (min)**: 10 – 20; **Peak (min)**: 60 – 100; **Duration (hr)**: 4 – 8

**Additional Information**:

- May be less effective in patients with decreased CYP-2D6 activity because of decreased conversion to morphine
- CYP-2D6 ultra-rapid metabolizers can have extensive conversion to morphine with increase in opioid-mediated effects
- Elderly or debilitated: Use with caution; start with reduced dose (2.5 – 5 mg) of hydrocodone component
- Hepatic dysfunction: Use with caution

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Hydromorphone<br>▪ Available as 1 mg/ml oral solution<br>▪ Available as 2, 4 or 8 mg tablets | ▪ 2 mg every 4 – 6 hours<br>▪ Initial dose of 4 – 8 mg for severe pain may be given | ▪ There is no optimal or maximum dose of hydromorphone<br>▪ Patients are likely to become tolerant and require doses higher than usual dosage range to maintain desired effect | Yes |

**Contraindications**: Include hypersensitivity to hydromorphone, patients with respiratory depression in the absence of resuscitative equipment, status asthmaticus, obstetrical analgesia

**Analgesic Onset (min)**: 15 – 30; **Peak (min)**: 30 – 60; **Duration (hr)**: 3 – 4

**Additional Information**:

- Use with extreme caution in patients with chronic obstructive pulmonary disease or cor pulmonale, a substantially decreased respiratory reserve, hypoxia, hypercapnia or preexisting respiratory depression
- Elderly or debilitated: Use with caution; start at 25 – 50% of usual dose at low end of dosage range
- Hepatic/Renal dysfunction: Reduce initial dose for moderate impairment; more with severe impairment

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Morphine<br>▪ Available as 10 or 20 mg/5 ml or 100 mg/5 ml oral solution for opioid-tolerant patients<br>▪ Available as 15 or 30 mg tablets | ▪ 10 – 30 mg every 4 hours | ▪ There is no optimal or maximum dose of morphine<br>▪ Patients are likely to become tolerant and require doses higher than usual dosage range to maintain desired effect | Yes |

**Contraindications**: Include hypersensitivity to morphine, respiratory depression in the absence of resuscitative equipment, acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Analgesic Onset (min)**: 30; **Peak (min)**: 60; **Duration (hr)**: 3 – 5

**Additional Information**:

- Morphine has active metabolites (M3G and M6G) which may accumulate in renal impairment and contribute to toxic effects
- Elderly or debilitated: Use with extreme caution and with lower doses in the elderly or debilitated patients
- Hepatic dysfunction: Use carefully in patients with cirrhosis and consider reducing the dose or extend the dosing interval by 1.5 – 2 times
- Renal dysfunction: Reduce the dose in renal impairment and avoid use in severe impairment

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Oxycodone (alone or in combination with APAP or ASA)<br>▪ Single agent oral solution available as 5 mg/5 ml and 20 mg/1 ml<br>▪ Available as 5, 10, 15, 20, 30 mg tablets<br>▪ Combination products vary in oxycodone content from 2.5 – 10 mg per dose unit | ▪ 5 – 15 mg every 4 – 6 hours<br>▪ Initial dose based upon oxycodone component<br>▪ Maximum dose based upon non-opioid component | ▪ For combination products, maximum dose is limited by APAP or ASA (4000 mg/d for both; 2000 mg/d APAP in chronic alcoholics or patients with hepatic impairment<br>▪ There is no optimal or maximum dose of oxycodone<br>▪ Patients are likely to become tolerant and require doses higher than usual dosage range to maintain desired effect | Yes |

**Contraindications**: Include hypersensitivity to oxycodone or acetaminophen, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Analgesic Onset (min)**: 10 – 15; **Peak (min)**: 30 – 60; **Duration (hr)**: 3 – 6

**Additional Information**:

- Must not be taken concomitantly with alcohol; alcohol can cause highly variable effects on peak drug levels, ranging from a decrease of 50% to an increase of 270%
- Elderly or debilitated: Use with caution and start at low end of dosing range; levels are increased 40% in patients >65 years
- Hepatic dysfunction: For mild impairment, use cautiously and start at low end of dosing range; contraindicated for moderate and severe dysfunction
- Renal dysfunction: Bioavailability is increased 57 – 65% in moderate and severe impairment; start at lower doses and adjust slowly

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Oxymorphone<br>▪ Available as 5 or 10 mg tablets | ▪ 5 mg every 4 – 6 hours | ▪ There is no optimal or maximum dose of oxymorphone<br>▪ Patients are likely to become tolerant and require doses higher than usual dosage range to maintain desired effect | No |

**Contraindications**: Include hypersensitivity to oxymorphone or morphine analogs such as codeine, respiratory depression (except in monitored settings and in the presence of resuscitative equipment), acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus, patients with moderate and severe hepatic impairment

**Analgesic Onset (min)**: 30 – 45; **Peak (min)**: N/A; **Duration (hr)**: 4

**Additional Information**:

- Must be taken on an empty stomach at least 1 hour before or 2 hours after a meal – food has been shown to increase peak levels of oxymorphone ER by 38%
- Elderly or debilitated: Use with caution; start at 25 – 50% of usual dose at low end of dosage range
- Hepatic dysfunction: For mild impairment, use cautiously and start at low end of dosing range; contraindicated for moderate and severe impairment
- Renal dysfunction: Bioavailability is increased 57 – 65% in moderate and severe impairment; start at lower doses and adjust slowly

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Tapentadol<br>▪ Available as 50, 75 or 100 mg tablets | ▪ 50 mg every 4 – 6 hours | ▪ Subsequent dose is 50, 75 or 100 mg every 4 – 6 hours, adjusted to analgesia and tolerability<br>▪ Second dose may be given 1 hour after first dose if necessary<br>▪ Maximum recommended dose: 700 mg on first day and 600 mg on subsequent days<br>▪ Patients are likely to become tolerant and require doses higher than usual dosage range to maintain desired effect | Yes |

**Contraindications**: Include impaired pulmonary function (significant respiratory depression, acute or severe bronchial asthma, hypercapnia in unmonitored settings or absence of resuscitative equipment), known or suspected paralytic ileus, concurrent use of or use within 14 days of monoamine oxidase inhibitors (MAOIs)

**Analgesic Onset (min)**: N/A (rapid); **Peak (min)**: 60; **Duration (hr)**: 4 – 6

**Additional Information**:

- Inhibits reuptake of serotonin and norepinephrine; potentially life-threatening serotonin syndrome could result with concomitant use of other serotonergic agents and drugs that impair metabolism of serotonin (e.g., MAOIs)
- Elderly or debilitated: Consider starting at the lowest recommended dose
- Hepatic dysfunction: For moderate impairment, start at 50 mg and give subsequent doses at least 8 hours apart with a maximum of 3 doses in 24 hours; use is not recommended in severe hepatic impairment
- Renal dysfunction: Use is not recommended in severe renal impairment
- Respiratory dysfunction: Use with caution because of respiratory depressant effects and consider non-mu opioid agonist analgesics

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Tramadol (alone or in combination with APAP)<br>▪ Available as 50 mg tablet<br>▪ Available as combination with APAP tablet (325 mg APAP, 37.5 mg tramadol) | ▪ 25 mg every morning | ▪ May increase by 25 mg per day every 3 days to 100 mg tramadol/d (25 mg every 6 hours)<br>▪ Subsequent increments of 50 mg/d may then be made every 3 days to 200 mg/d (50 mg every 6 hours)<br>▪ After titration, may give 50 – 100 mg every 4 – 6 hours<br>▪ Combination product: maximum 4000 mg/d ADAP; 2000mg/d APAP in chronic alcoholics or in hepatic impairment | Yes |

**Contraindications**: Include hypersensitivity to tramadol and any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Analgesic Onset (min)**: <60; **Peak (min)**: 120 – 240; **Duration (hr)**: 6

**Additional Information**:

- U.S. Food and Drug Administration (FDA) warnings for the risk of suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs
- FDA warnings also exist for the risk of overdose
- Slower initiation and titration improves tolerability
- Inhibits reuptake of serotonin and norepinephrine; concomitant use with MAOIs or SSRIs may increase risk of seizures, serotonin syndrome
- Dose carefully or use another agent in patients on serotonergic agents
- Seizures reported within the recommended dosage range; increased risk above recommended dosage range and in patient with seizure disorder, history of seizures, in conditions with increased risk of seizures, or with other drugs that increase seizure risk; observe maximum dose limits
- Serious anaphylactoid reactions reported, often following first dose; patients with a history of anaphylactoid reaction to codeine and other opioids may be at increased risk
- Elderly or debilitated: Use caution; in patients >75 years, give <300 mg/d in divided dose
- Hepatic dysfunction: Decrease dosage to 50 mg once every 12 hours in patients with cirrhosis
- Renal dysfunction: For CrCl <30 ml/min, increase dosing interval to 12 hours and decrease maximum daily dose to 200 mg

# Long-acting/Extended-Release (ER) Opioid Medications

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Buprenorphine buccal film<br>▪ Available in strengths of 75, 150, 300, 450, 600, 750 and 900 mcg/film for twice daily administration | ▪ 75 mcg once or twice daily for at least 4 days, then increase dose to 150 mcg every 12 hours<br>▪ There is potential for buprenorphine to precipitate withdrawal in patients already on opioids; to reduce risk, the dose of other opioid should be tapered to <30 mg morphine equivalent daily dose (MEDD) before initiating buprenorphine | ▪ After initial dosing, dosing changes as necessary can proceed in increments of 150 mcg every 12 hours, no more frequently than every 4 days<br>▪ Patients on prior dose of opioid 30 – 89 mg MEDD may initiate buprenorphine film at 150 mcg every 12 hours, 90 – 160 mg MEDD may initiate at 300 mcg every 12 hours; if prior opioid is >160 mg MEDD – consider an alternative analgesic<br>▪ Time to steady state is approximately 3 days with every 12 hour dosing | Yes |

**Contraindications**: Include hypersensitivity to buprenorphine, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- QTc prolongation reported with recommended doses of buprenorphine; maximum dose of 900 mcg every 12 hours established due to the potential for this adverse effect; avoid in patients with Long QT Syndrome, family history of Long QT Syndrome, or those taking Class IA or Class III antiarrhythmic drugs
- Buprenorphine buccal film is a potential treatment option for patients with significant renal impairment and those with gastrointestinal structural or functional abnormality that interferes with swallowing or absorption of orally administered medications
- Elderly or debilitated: Initiation at the low end of the dosing range is recommended
- Hepatic dysfunction: Patients with severe hepatic impairment should have starting and titration doses reduced by half that of patients with normal liver function

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Buprenorphine Transdermal System (TDS)<br>▪ Available in every 7 day patch formulation that delivers transdermal buprenorphine at the following rates: 5 mcg/hour, 7.5 mcg/hour, 10 mcg/hour, 15 mcg/hour and 20 mcg/hour | ▪ Initiate with 5 mcg/hour patch<br>▪ There is potential for buprenorphine to precipitate withdrawal in patients already on opioids; to reduce risk, the dose of other opioid should be tapered to ≤30 mg MEDD before initiating buprenorphine; the 10 mcg/hour patch may then be initiated at the next dosing interval | ▪ Maximum dose of buprenorphine TDS 20 mcg/hour may not provide adequate analgesia for patients requiring greater than 80 mg MEDD; an alternate analgesic should be considered<br>▪ Steady state achieved in approximately 3 days | Yes |

**Contraindications**: Include hypersensitivity, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus, management of post-operative pain (including outpatient or day surgeries), mild or intermittent pain or use on “as needed” basis

**Additional Information**:

- Dosage does not need to be adjusted in patients with mild or moderate hepatic impairment, renal impairment or the elderly or debilitated
- Buprenorphine TDS is a potential treatment option for patients with significant renal impairment or those with gastrointestinal structural or functional abnormality that interferes with swallowing or absorption of oral medications
- Buprenorphine patch 10 mcg/hour is approximately equivalent to an oral MEDD of 18 – 28 mg; the 20 mcg/hour patch is approximately equivalent to a MEDD of 36 – 55 mg
- Dose of one 20 mcg/hour patch per week should not be exceeded due to risk of QTc prolongation
- Avoid use in patients with Long QT Syndrome, family history of Long QT Syndrome, or those taking Class IA or Class III antiarrhythmic medications
- Advise patients that application of external heat (e.g., hot baths, sunbathing, saunas, heating pads) increases maximum plasma concentration of buprenorphine and risk of fatal overdose

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Fentanyl Transdermal System (TDS)<br>▪ Available in every 3 day patch formulation that delivers transdermal fentanyl at the following rates: 12 mcg/hour, 25 mcg/hour, 50 mcg/hour, 75 mcg/hour and 100 mcg/hour | ▪ 25 mcg/hour applied every 72 hours<br>▪ The 12 mcg/hour dose has not been evaluated as an initial dose | ▪ Must be used only on intact skin<br>▪ Dose change increments should be based on supplemental opioid doses, using a ratio of fentanyl TDS 12 mcg/hour for every 45 mg/24 hours of supplemental oral MEDD<br>▪ Dosing changes, as necessary, should occur at least 3 days after the initial dose; thereafter, not more often than every 6 days | Yes |

**Contraindications**: Include hypersensitivity, patients who are not opioid tolerant, management of acute pain or for short-term treatment, management of post-operative pain, mild pain, or intermittent pain, significant respiratory depression (especially in unmonitored settings), acute or severe bronchial asthma, known or suspected paralytic ileus

**Additional Information**:

- Consider fentanyl TDS in patients with persistent, moderate-to-severe pain who cannot take oral ER morphine or oral ER oxycodone
- Using the fentanyl patch entails special safety considerations – all prescribers should be thoroughly familiar with the product's prescribing information
- Patients must receive a copy of the medication guide
- In order to avoid any confusion, always write fentanyl in mcg/hr
- Should not be used in patients particularly susceptible to intracranial effects of CO2 retention (increased intracranial pressure, impaired consciousness, coma)
- Fentanyl patches should ONLY be used in patients who are already receiving opioid therapy, are opioid-tolerant and require a daily dose at least equivalent to fentanyl 25 mcg/hour
- Rotate to a different opioid either long-acting morphine or methadone in order to taper patient off of the medication; alternatively, taper down to 12 mcg/hour patches and then give a brief supply of oral short-acting opioids to complete the taper
- Avoid application of external heat sources (e.g., heating pads, electric blankets, heat lamps, saunas, hot tubs, hot baths, sunbathing, heated water beds) to the application site while the patch is worn as heat may increase release and speed absorption of fentanyl
- Using damaged or cut fentanyl TDS patches can lead to rapid release of the contents of the patch and fatal overdose
- If leakage of the fentanyl gel occurs, wash any skin that has come in contact with the gel with copious amounts of water only – do not use soap or alcohol
- Use of fentanyl TDS with CYP3A4 inhibitors can result in increased fentanyl plasma concentrations, increased or prolonged opioid effects, including fatal respiratory depression; use extreme caution and frequent monitoring in patients receiving these combinations
- CYP3A4 inducers may increase fentanyl clearance
- Elderly: Patients are twice as sensitive to fentanyl as younger patients; avoid initiation at doses >25 mcg/hour unless patient is already taking >135 mg oral morphine or equivalent
- Hepatic/Renal dysfunction: Reduce dose by 50% in mild-moderate impairment and avoid use if impairment is severe
- Patients with fever: Increased body temperature may increase release of fentanyl from the TDS; monitor patients for opioid adverse effects and modify dosage as necessary

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| **Hydrocodone ER**<br>▪ ER tablets contain 20, 30, 40, 60, 80, 100 or 120 mg hydrocodone for once daily administration<br>▪ ER capsules contain 10, 15, 20, 30, 40 or 50 mg hydrocodone for every 12 hour administration | ▪ **20 mg ER tablet once daily** *(opioid-naïve patients)*<br>▪ **10 mg ER capsule every 12 hours** *(opioid-naïve patients)*<br>▪ **Convert current opioid to equianalgesic daily dose of hydromorphone ER; reduce the calculated amount by 33 – 50%** *(opioid-tolerant patients)* | ▪ *For opioid-experienced, both ER tablets and capsules*: **Convert current opioid to equianalgesic hydrocodone dose, then reduce that dose by 25%; initiate at nearest whole-tablet or capsule strength, rounding down as necessary**<br>▪ *For both tablets and capsules*: **Dose change increments of 20 mg per day may be made every 3 – 7 days**<br>▪ **Steady state achieved in approximately 3 days of dosing** | Yes |

**Contraindications**: Include hypersensitivity to hydrocodone

**Additional Information**:

- CYP3A4 inhibitors may decrease clearance of hydrocodone, increase plasma concentrations and increase risk of overdose; CYP3A4 inducers may increase clearance and reduce opioid effect
- Both ER tablets and ER capsules are formulated with polyethylene oxide which imparts ER properties
- Hydrocodone ER tablets or capsules must be swallowed intact and should not be cut, broken, chewed, crushed or dissolved due to risk of fatal overdose
- ER tablet has abuse deterrent labeling related to resistance to crushing and high viscosity when dissolved in aqueous solution
- ER capsule has abuse deterrent properties but is not FDA-labeled as an abuse deterrent formulation
- Renal dysfunction: Hydrocodone plasma concentrations are increased in moderate or severe impairment; use low initial dose and monitor closely for adverse events such as excessive sedation and respiratory depression; avoid use in severe impairment
- Hepatic dysfunction: No dosage adjustment is required in mild or moderate hepatic impairment; for severe hepatic impairment, start with the lowest dose (10 mg) and monitor closely

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Hydromorphone ER tablets<br>▪ Available as 8, 12, 16 and 32 mg tablets for once daily administration | ▪ Convert current opioid to equianalgesic daily dose of hydromorphone ER; reduce the calculated amount by 33 – 50% *(opioid-tolerant patients)* | ▪ Dosing adjustments may be made in increments of 4 – 8 mg every 3 – 4 days as needed<br>▪ Steady state achieved after 3 – 4 days of once daily dosing | Yes |

**Contraindications**: Include hypersensitivity to hydromorphone or sulfite-containing medications, respiratory depression (except in monitored settings and in the presence of resuscitative equipment), acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus, history of surgical procedures and/or underlying disease resulting in narrowing of the gastrointestinal tract, or have "blind loops" of the gastrointestinal tract or gastrointestinal obstruction, contraindicated in opioid-naïve patients due to risk of respiratory depression

**Additional Information**:

- Hydromorphone ER tablets must be swallowed intact and should not be cut, broken, chewed, crushed or dissolved due to risk of fatal overdose
- Hydromorphone ER contains sulfites
- Hydromorphone ER has abuse deterrent properties but is not FDA-labeled as an abuse deterrent formulation
- Elderly or debilitated: Monitor closely, particularly when initiating or titrating dosage
- Hepatic dysfunction: Start patients with moderate impairment at 25% of usual dose in non-impaired patients
- Renal dysfunction: Start patients with moderate impairment at 50% of usual dose, and patients with severe impairment at 25% of usual dose

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Methadone<br>▪ Available as 5 or 10 mg/5 ml oral solution<br>▪ Available as 5 and 10 mg tablets | ▪ 2.5 mg every 8 – 12 hours | ▪ Start low and go slow<br>▪ May increase every 5 – 7 days by 2.5 mg every 12 hours<br>▪ Delayed analgesia or toxicity may occur because of drug accumulation after repeated doses (e.g., on days 2 – 5) – if the patient has excessive sedation during this timeframe, consider temporarily holding dose(s), lowering the dose and/or slowing the titration rate<br>▪ Once a stable analgesic dose is reached, the dosing interval may be extended to every 8 – 12 hours or longer | Yes |

**Contraindications**: Include hypersensitivity to methadone, any situation where opioids are contraindicated, such as patients with respiratory depression (in absence of resuscitative equipment or in unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- Prescribers of methadone should be thoroughly familiar with its complex pharmacokinetic and pharmacodynamic properties or consult a provider with experience in dosing methadone
- Extended plasma half-life may be longer than the analgesic duration
- Methadone has little cross-tolerance with other opioids; therefore, even patients with a high degree of opioid tolerance may be at risk for overdose when switched to methadone
- The only long-acting opioid available as an oral solution
- May prolong QTc intervals on ECG, risk of torsade de pointes
- Elderly or debilitated: Consider reduced dosing
- Hepatic dysfunction: No dosage adjustments required in patients with stable chronic liver disease or mild-to-moderate hepatic dysfunction; avoid in severe liver disease
- Renal dysfunction: Methadone and its metabolites do not accumulate in patients with renal failure; however, dosage reduction by up to 50 – 75% is recommended in patients with CrCl <10 mL/min

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Morphine CR or SR<br>▪ Available as 15, 30, 60, 100 and 200 mg strengths for every 8 –12 hours<br>▪ Morphine ER capsules available in 10, 20, 30, 40, 50, 60, 70, 80, 100, 130, 150 and 200 mg strengths for once daily administration | ▪ Morphine CR or SR 15 mg every 8 – 12 hours *(opioid-naïve patients)*<br>▪ Morphine ER capsules are not indicated in opioid-naïve patients<br>▪ 30 mg every 24 daily *(non-opioid-tolerant patients)* | ▪ Total daily increments of <30 – 40 mg/day may be made every 2 days<br>▪ Steady state achieved with morphine ER within 24 – 36 hours | Yes |

**Contraindications**: Include hypersensitivity to morphine, respiratory depression in the absence of resuscitative equipment, acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- Controlled-release tablets should be swallowed whole, not broken, chewed or crushed. For patients who have difficulty swallowing, SR and ER capsules may be opened and the pellets may be sprinkled onto a small amount of soft food or administered via 16F gastrostomy tube
- Morphine SR is preferred first-line long-acting agent because of similar efficacy to other long-acting opioids, comparable safety profile, provider familiarity with use and lower cost
- M6G, an active metabolite, may accumulate in renal impairment and contribute to excessive opioid effects
- M3G, a metabolite without analgesic activity, may accumulate in renal impairment; this metabolite has been implicated in morphine-induced neurotoxicity, hyperalgesia and allodynia
- Elderly or debilitated: Use with caution and at lower dose
- Hepatic dysfunction: Clearance decreases and half-life increases; M3G and M6G to morphine ratios are reduced; use carefully in patients with cirrhosis and consider reducing dose or extending dosing interval by 1.5 – 2 times
- Renal dysfunction: Reduce the dose in renal impairment and avoid use in severe renal impairment; bioavailability is increased and clearance is decreased; metabolites M3G and M6G accumulate significantly

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Morphine and Naltrexone ER capsule<br>▪ Available as 20/0.8, 30/1.2, 50/2, 60/2.4, 80/3.2 and 100/4 strengths (mg morphine/mg naltrexone) for once or twice daily administration | ▪ 20 mg/0.8 mg *(opioid-naïve patients)*<br>▪ Convert current opioid to equianalgesic daily dose of morphine; reduce the calculated amount by 33 – 50% *(opioid-tolerant patients)* | ▪ Dose may be up titrated no more frequent than every other day<br>▪ If once daily administration results in inadequate analgesia, may switch to twice daily dosing | Yes |

**Contraindications**: Include hypersensitivity to morphine or naltrexone, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- Morphine/naltrexone must be swallowed whole or the contents of the capsules sprinkled on apple sauce; crushing, dissolving, or chewing pellets may cause a fatal overdose (particularly in the opioid-naïve patient) and the absorption of naltrexone could increase the risk of precipitating withdrawal in opioid tolerant patients
- M6G, an active metabolite, may accumulate in renal impairment and contribute to excessive opioid effects
- M3G, a metabolite without analgesic activity, may accumulate in renal impairment; this metabolite has been implicated in morphine-induced neurotoxicity, hyperalgesia, and allodynia
- Elderly or debilitated: Use with caution and at lower dose
- Hepatic dysfunction: Clearance decreases and half-life increases; M3G and M6G to morphine ratios are reduced; use carefully in patients with cirrhosis and consider reducing dose or extending dosing interval by 1.5 – 2 times
- Renal dysfunction: Reduce the dose in renal impairment and avoid use in severe renal impairment; bioavailability is increased and clearance is decreased; metabolites M3G and M6G accumulate significantly

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Oxycodone ER<br>▪ Tablets available as 10, 15, 20, 30, 40, 60 and 80 mg strengths for every 12 hour administration<br>▪ Capsules available as 9, 13.5, 18, 27 and 36 mg strengths for every 12 hour administration | ▪ 10 mg tablets or 9 mg capsules every 12 hours *(opioid-naïve patients)*<br>▪ Convert current opioid to equianalgesic daily dose of oxycodone; reduce the calculated amount by 33 – 50% *(opioid-tolerant-patients)* | ▪ May increase to 20 mg (tablets) or 18 mg (capsules) every 12 hours after 1 – 2 days; thereafter, the total daily dose may be increased by 25 – 50% of the current dose every 1 – 2 days<br>▪ ER tablets are not bioequivalent to ER capsules; 10 mg oxycodone HCl (ER tablet) = 9 mg oxycodone base (ER capsule)<br>▪ Steady state achieved with tablets or capsules in 24 – 36 hours with repeat dosing | Yes |

**Contraindications**: Include hypersensitivity to oxycodone, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- Recommended for patients who experience intolerable, unmanageable adverse effects to long-acting morphine
- Both ER tablets and ER capsules have abuse-deterrent labeling related to resistance to abuse by intranasal and intravenous means
- ER tablets should be swallowed whole, not broken, chewed or crushed
- ER capsules may be opened and sprinkled on soft food or administered via feeding tube
- Elderly: Plasma concentrations of oxycodone are increased approximately 15% in the elderly; however, usual dosing and dosing intervals may be appropriate
- Hepatic dysfunction: Reduce initial dose to 1/3 – 1/2 of the usual dose and monitor closely
- Renal dysfunction: Plasma concentrations of oxycodone are increased approximately 50% in patients with CrCl <60 ml/min; dose conservatively and adjust according to clinical situation

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Oxycodone/APAP ER<br>▪ Available as tablets containing oxycodone 7.5 mg and APAP 325 mg for every 12 hour administration | ▪ 2 tablets every 12 hours *(opioid-naïve patients)*<br>▪ A standard, single dose consists of 2 tablets totaling 15 mg oxycodone/650 mg APAP<br>▪ This is the only long-acting/ER opioid to have an acute pain indication | ▪ The polyethylene oxide content causes the tablet to swell and become sticky when wet – this has the potential to cause obstruction of the airway or gastrointestinal obstruction<br>▪ Steady state concentration of both components are reached within 24 hours of product initiation | Yes |

**Contraindications**: Include hypersensitivity to oxycodone, any situation where opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations) and patients with acute bronchial asthma or hypercarbia, known or suspected paralytic ileus

**Additional Information**:

- This long-acting/ER opioid is an exception to the risk evaluation and mitigation strategy (REMS) requirements due to the relatively low amount of oxycodone contained in each tablet
- Oxycodone/APAP ER tablets are formulated with polyethylene oxide (PEO) which is responsible for its ER in addition to labeled abuse deterrent properties
- Patients should be instructed not to pre-soak, lick, or otherwise wet tablets prior to swallowing and to take one tablet at a time with adequate water to insure complete and immediate swallowing
- Elderly or debilitated: Take precautions when determining the dosing amount and frequency in geriatric patients since a greater sensitivity to oxycodone may be observed in this patient population when compared to younger patients
- Hepatic/Renal dysfunction: Patients with renal dysfunction (CrCl <60 ml/min) or hepatic dysfunction should initiate therapy with 1 tablet every 12 hours and adjust as needed

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Tapentadol ER<br>▪ Available as tablets containing 50, 100, 150, 200 or 250 mg tapentadol for twice daily administration | ▪ 50 mg twice daily *(opioid-naïve patients)*<br>▪ Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression<br>▪ There are no established conversion ratios for conversion from other opioid to tapentadol ER; convert current opioid to an estimated equianalgesic daily dose of tapentadol; reduce the calculated amount by 33 – 50% for initial daily start dose *(opioid-tolerant patients)* | ▪ May increase dose by no more than 50 mg twice daily every 3 days<br>▪ Maximum daily dose is 500 mg<br>▪ Steady state is achieved after the third dose (24 hours after the first twice daily multiple dose administration) | Yes |

**Contraindications**: Include hypersensitivity to tapentadol or to any other ingredients of the product, concurrent use of or use within 14 days of MAOIs, respiratory depression (except in monitored settings and in the presence of resuscitative equipment), acute or severe bronchial asthma or hypercarbia, known or suspected paralytic ileus, patients with moderate and severe hepatic impairment

**Additional Information**:

- Must not be taken concomitantly with alcohol, which can increase tapentadol concentration and cause fatal overdose
- Inhibits reuptake of serotonin and norepinephrine; potentially life-threatening serotonin syndrome could result with concomitant use of other serotonergic agents and drugs that impair metabolism of serotonin (e.g., MAOIs)
- Tapentadol ER tablets must be taken whole; crushing, chewing or dissolving tablets will result in uncontrolled delivery of tapentadol and can lead to overdose
  or death
- Elderly: Consider starting at the lowest recommended dosage
- Hepatic dysfunction: Use not recommended in severe hepatic impairment
- Renal dysfunction: Use not recommended in severe renal impairment

| Drug | Initial Dose | Additional Dosage Information | Black Box Warning |
|---|---|---|---|
| Tramadol ER<br>▪ Available as 100, 200 or 300 mg tablets for once daily administration | ▪ 100 mg once daily<br>▪ Converting from tramadol IR: start at 24 hour dosage equivalent rounded down to closest 100 mg increment | ▪ Increase by 100 mg every 5 days based on analgesia and tolerability<br>▪ Maximum daily dose is 300 mg | Yes |

**Contraindications**: Include hypersensitivity to tramadol and any situation where opioids are contraindicated, including acute intoxication with any of the following: alcohol, hypnotics, narcotics, centrally acting analgesics, opioids or psychotropic drugs – tramadol hydrochloride ER tablets may worsen CNS and respiratory depression in these patients

**Additional Information**:

- FDA warnings for the risk of suicide for patients who are addiction-prone, taking tranquilizers or antidepressant drugs
- FDA warnings also exist for the risk of over dosage
- Must be swallowed whole and must not be chewed, crushed or split
- Must not be taken concomitantly with alcohol, which can cause highly variable effects on peak drug levels, ranging from a decrease of 50% to an increase of 270%
- Elderly: Start at low end of dosing range; use particular caution in patients >75 years
- Hepatic dysfunction: Should not be used in severe hepatic impairment (Child-Pugh Class C)
- Renal dysfunction: Should not be used if CrCL <30 ml/min

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# Clinical Pearls, References and Resources

# Tab 7 – CLINICAL PEARLS[6], REFERENCES AND RESOURCES

## Clinical pearls for prescribing opioids

- Chronic pain is a complex human experience strongly influenced by psychosocial factors, including the patient's relationship with the health care system
  - When prescribing opioids, provide in-depth and patient-specific education about the goals, methods and responsibilities of chronic pain treatment
  - Teach your patient that self-management pain strategies that may not include medications are the foundation of high quality pain care
- Safety is always more important than urgent pain relief
  - Titrating to effect is not a rational prescribing strategy
  - When risk outweighs benefit or adequate risk mitigation is not possible, opioids should not be used
- As risks increase, mitigation and monitoring increases
  - Opioid risks and benefits can change over time
  - Opioid prescribing requires ongoing evaluation and documentation of risks and benefits
- Generally avoid initiating LOT for chronic pain; however, when opioids are prescribed and when titrating up, start low and go slow
  - Do not exceed 50 mg MEDD unless you are able to closely follow and monitor risks
  - Avoid titrating to doses greater than 90 mg MEDD
- Improved function, not pain relief, is the primary clinical goal
  - Opioids should only be continued when patients demonstrate functional benefit and are reactively engaged in self-management of pain
  - Opioid prescribing should be conducted as an ongoing trial documenting high benefit and low risk
- When your patient does not benefit, is exposed to undue risk, or is misusing, the question is not "if" the patient should be tapered but "how"
  - When tapering down, be clear about the rationale, be specific about the process, be empathic but not apologetic – bad care is not an option
  - Your goal is to ensure safety while supporting and educating your patient
  - Offer alternative pain treatments and be prepared to address other problems such as OUD or suicidality

# References


1 Institute of Medicine Committee on Advancing Pain Research, Care Education. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, D.C.: The National Academies Press

2 Task Force on Taxonomy of the International Association for the Study of Pain. (1994). Classification of Chronic Pain Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, Second Edition. Seattle: IASP Press

3 Shared Decision Making: A Guide for Busy Clinicians. Retrieved from: https://www.healthquality.va.gov/ and https://www.qmo.amedd.army.mil

4 Interagency Pain Research Coordinating Committee (2016). National Pain Strategy: A Comprehensive Population Health-level Strategy for Pain. Retrieved from: https://iprcc.nih.gov/National_Pain_Strategy/NPS_Main.htm

5 American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th Edition). Washington, D.C.: American Psychiatric Publishing

6 U.S. Department of Veterans Affairs and U.S. Department of Defense Evidence-Based Clinical Practice Guideline Work Group. (2017). Clinical Practice Guideline for Opioid Therapy for Chronic Pain: Clinician Summary. Retrieved from: http://www.healthquality.va.gov/ and https://www.qmo.amedd.army.mil

# DoD/VA Resources

**VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain**
https://www.healthquality.va.gov/guidelines/Pain/cot/ VADoDOTCPG022717.pdf and https://www.qmo.amedd.army.mil/pguide.htm

**VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders** https://www.healthquality.va.gov/guidelines/MH/sud/ and https://www.qmo.amedd.army.mil/pguide.htm

**Patient Information Guide: Long-term Opioid Therapy for Chronic Pain**
https://www.healthquality.va.gov/guidelines/Pain/cot/ and https://www.qmo.amedd.army.mil/pguide.htm

**The Opioid Safety Initiative Toolkit**
www.va.gov/PAINMANAGEMENT/Opioid_Safety_Initiative_Toolkit.asp

**Department of Veterans Affairs VHA (2009). Handbook 1004.01. Informed Consent for Clinical Treatments and Procedures**
https://www.va.gov/vhapublications/index.cfm

**Signature Informed Consent**
https://www.va.gov/vaforms

**The VA National Center for Ethics in Health Care**
www.ethics.va.gov

**Veterans Administration Pain Management**
www.va.gov/painmanagement

**Defense and Veterans Center for Integrative Pain Management**
www.dvcipm.org

# External Resources

**National Institute of Neurological Disorders and Stroke: Chronic Pain Information Page**
www.ninds.nih.gov/Disorders/All-Disorders/Chronic-Pain-Information-Page


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