

Update on Recent Guidance and Safety Alerts for Opioid Use in Non-cancer Pain

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Introduction

In 2016, the Centers for Disease Control (CDC) released guidelines for prescribing opioids for chronic pain outside of active cancer treatment, palliative care, or end-of-life care.¹ The goal of these guidelines was to promote patient care and safety in light of the rapidly increasing amount of reported opioid overdoses in the previous decade.² Multiple guidelines emphasized opioid dosage ceilings, avoiding concomitant benzodiazepines, limiting durations for acute pain, and treating opioid use disorder.²⁻⁴ In addition to these guidelines, the Food and Drug Administration (FDA) has published safety alerts regarding the risks of abrupt discontinuation and rapid tapering of opioids in opioid dependent patients.⁵ This newsletter will summarize recent guideline updates and FDA safety alerts.

Guideline Recommendations

With the publication of the 2016 CDC guidelines, multiple national and statewide organizations followed suit, including the American Society of Interventional Pain Physicians (ASIPP), the Department of Veterans Affairs (VA) and the Department of Defense (DoD). Guideline recommendations for chronic pain are outlined in **Table 1**. If opioids are prescribed for acute pain, they should be initiated at the lowest effective dose and patients should be re-evaluated after 3-5 days to assess appropriateness of continuing therapy.⁴

Table 1. Opioid Guideline Prescribing Recommendations

Recommendations	Monitoring
VA/DoD Guideline⁴	
<ul style="list-style-type: none"> ● Use of non-opioid therapy preferred over opioids for chronic pain management ● If opioid is used, use lowest dose and shortest treatment duration ● Avoid concurrent use of benzodiazepines and opioids. 	<ul style="list-style-type: none"> ● Evaluate continuation of opioids every 3 months ● Taper opioids to lowest effective dose or discontinue when medication risks exceed benefit
ASIPP Guideline³	
<ul style="list-style-type: none"> ● Establish appropriate physical and psychological diagnosis ● Stratify patients substance abuse risk (high/medium/low) prior to initiating opioid ● Initiate opioid therapy with low dose, short-acting drugs ● Reserve long-acting therapy for severe intractable pain not relieved by short-acting opioids 	<ul style="list-style-type: none"> ● Monitor for adherence and abuse by urine drug testing ● Assess improvement based upon analgesia relief and patient activity ● Periodically reassess for pain relief and/or functional status improvement of > 30% without adverse consequences

All opioid prescribing guidelines recommend close monitoring and tapering whenever possible. Tapering opioids to the lowest effective dose or discontinuation of therapy is recommended when patient risks exceed benefits. However, careful and slow tapering is essential in patients who are opioid tolerant and/or

physically dependent on opioids. Recently, the US department of Health and Human Services published recommendations for dose reduction or discontinuation of long-term opioid analgesics. This document provides guidance for deciding when to taper, how to individualize the taper, how to treat symptoms of withdrawal, how to provide behavioral support, and guidance for tapering in special populations.⁶ Emphasis is placed on the avoidance of tapering opioids when the benefits outweighs the risk and advising patients on the risk of overdose when there is a rapid return to a previously prescribed dose.⁶

Oregon Health Authority Task Force Guidelines

Chronic Pain

The Oregon Health Authority (OHA) recruited a task force of Oregon-based practitioners in 2016 to develop guidelines for prescribing opioids for acute and chronic pain, for both medical providers and dentists. The guidelines adopted the CDC Guidelines as the foundation for the recommendations while also addressing Oregon-specific concerns.⁷ For management of chronic pain, the task force recommends documentation of clinical justification for doses higher than 50 mg of morphine milligram equivalence (MME) per day and to avoid doses greater than 90 MME.⁷ The guideline also recommends a documented referral for pain management. This can include evaluation by a colleague, discussion with a peer group or multi-disciplinary pain consult team, or referral to a pain and/or addiction mental health specialist.⁷ Providers are also encouraged to use the prescription drug monitoring program (PDMP) to assess for opioid misuse and abuse. If misuse or abuse is identified, the importance of engaging in a discussion with the patient about potential taper plans rather than patient dismissal is emphasized. If substance use disorder is a concern, treatment options and potential referral to a specialist should be explored.⁷

The recommendations strongly advise against co-prescribing opioids and central nervous system (CNS) depressants. Examples of CNS depressants are benzodiazepines, first and second generation antipsychotics, sedatives, and muscle relaxants.⁷ If they are both prescribed, a pain specialist and/or pharmacist should be part of the care team. When misuse, abuse, or co-prescribing are of concern, it is recommended to use clinical tools, such as the PDMP and urine drug screens at least annually. The legalization of recreational marijuana in the state of Oregon and the limited available data for the interaction of marijuana with opioids is also of concern.

Clinicians should prioritize patient safety when patients use cannabinoids and opioids concurrently.⁷

Acute Pain

The goal of the acute pain prescribing recommendations is to improve patient safety while emphasizing effective and compassionate treatment in patients who have had limited exposure to opioids.⁸ In general, opioids should NOT be considered as first-line therapy for mild to moderate pain. Mild to moderate pain can often be treated without opioids by recommending over-the-counter medications, and physical treatments such as ice and immobilization. **Table 2** outlines recommended over the counter (OTC) pain medications. If non-opioid interventions are ineffective, the lowest effective dose of short-acting opioids should be prescribed for less than 3 days. In cases of more severe acute pain, the initial prescription should be limited to less than 7 days.⁸

Table 2: Over-the-counter Pain Medication Options⁹⁻¹¹

Medication	Dosing
Acetaminophen	650-1000 mg every 4-6 hours as needed Max 3000 mg per day ⁹
Ibuprofen	200-400 mg every 6 hours as needed Max 1200 mg per day ¹⁰
Naproxen	220 mg every 8-12 hours as needed Max 1200 mg per day ¹¹

Opioid Tapering

Beginning in March 2019, the OHA convened an expert panel to address guidelines for tapering opioids. This guidance should be publically available in late 2019.

FDA Safety Alerts:

In April of this year, the FDA released a safety statement identifying harm from abrupt discontinuation and/or rapid tapering of opioids in patients who are opioid dependent.⁵ The FDA received reports of rapid opioid discontinuations leading to serious withdrawal symptoms, psychological distress, and suicide.⁵ When patients are tapered off opioids due to a suspicion for substance use disorder, they should have medication assisted therapy (MAT) available. Additionally, a CDC advisory warned that applying the 2016 opioid guidelines to patients with chronic pain associated with cancer or sickle cell anemia increases the risk for harm.²

Federal Legislation

In response to the FDA recommendation to avoid the use of opioids with benzodiazepines and other CNS depressants, the Substance Use Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities (SUPPORT) Act was signed into federal law in October of 2018.¹² This law requires state Medicaid programs to develop a safety review process to monitor opioid doses prescribed in excess of state defined limits (90 MME per day in Oregon) and

monitor concurrent use of opioids with benzodiazepines or antipsychotics. Although the evidence is limited to describe the risks of combining antidepressants and antipsychotics with opioids, it is required that Medicaid agencies monitor these combinations and they should be started at the lowest effective dose if they must be combined. Antidepressants and antipsychotics are frequently involved in opioid overdose. However, underlying mental health conditions increase the risk for opioid and other substance abuse. Evidence related to drug overdoses, highlights that opioid analgesics play a predominant role in pharmaceutical overdose deaths, alone or combined with other therapies.¹³

Oregon Policy Updates

In response to OHA opioid prescribing guidelines, the fee-for-service prior authorization criteria for long-acting opioids has been updated to include new indications and safety considerations. Important policy updates are highlighted below.

OHA Opioid PA Policy Updates

- Approve use of opioids for chronic pain associated with sickle cell disease
- Patient education requirement if opioid is to be used concurrently with a benzodiazepine or CNS depressant
- Restrict use of tramadol or codeine in patients less than 19 years of age based on FDA safety data

Conclusion

CDC guidelines regarding opioid prescribing set a precedent in 2016 to promote care and safety in response to rising opioid abuse and overdoses. Strict enforcement of these guidelines resulted in harm for some patients leading to FDA safety communications to help guide providers to safely manage opioid prescribing. These FDA alerts were accompanied by guideline updates from other major organizations including VA/DoD and OHA task forces. While there are slight differences between the reports from each organization, the overall message of providing safe yet effective pain management is clear. In general, opioids should be reserved for moderate-to-severe pain and in short-term situations whenever possible. It is also important to consider concurrent CNS depressants, especially benzodiazepines, when initiating opioids. Taper schedules should be developed on an individualized basis and should be done slowly for most patients. Overall, the recent changes to guidelines and FDA safety announcements emphasize safe and effective use of opioid medications for only essential indications.

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