Opioids and Chronic Pain

A GUIDE FOR PRIMARY CARE PROVIDERS
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Managing chronic non-cancer pain

**Integrative therapies**
- Manual medicine
- Chiropractic, acupuncture
- Herbs, supplements, anti-inflammatory eating
- Yoga, Tai Chi, mindful movement
- Mind-body therapies

**Movement-based therapies**
- Physical/occupational therapy
- Supervised/graded physical activity

**Behavioral therapies**
- Depression/anxiety group
- Health/pain group
- Social engagement plan
- Cognitive Behavioral Therapy (CBT)
- Acceptance and Commitment Therapy (ACT)

**Medication**
- NSAIDs/Acetaminophen
- Anticonvulsants
- Antidepressants
- Topical (lidocaine, capsaicin)
- Immune modulators
- Muscle relaxants
- Cannabinoids
- **Lowest effective opioid dose**

**Procedures**
- Ice/heat
- Injections (joint, trigger point, epidural)
- Transcutaneous electrical nerve stimulation (TENS)
- Referrals (orthopedics, neurosurgery, procedural pain clinic)

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**If an opioid medication is part of the treatment plan, take the following steps:**

- **ASSESSMENT OF RISK, ADHERENCE, FUNCTION AND PAIN:** at least annually
- **INFORMED CONSENT OR CONTROLLED SUBSTANCE AGREEMENT:** at least annually
- **CONTROLLED SUBSTANCE MONITORING PROGRAM:** check CURES every 4 months
- **PRESCRIBE NALOXONE:** at least every two years

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**If managing opioid use disorder, options include:**

- Start buprenorphine, methadone maintenance, or extended-release naltrexone
- Arrange for outpatient or residential treatment
- Consider behavioral health and other referrals

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Non-pharmacologic treatment of chronic pain

The Agency for Healthcare Research and Quality conducted a systematic review of noninvasive non-pharmacological treatment for chronic pain and found the following interventions led to significant improvement in function and pain outcomes at least 1 month after completion of treatment:

**Chronic tension headache:**
- Spinal manipulation

**Chronic neck pain:**
- Exercise
- Low-level laser therapy
- Alexander Technique
- Acupuncture

**Chronic low back pain:**
- Exercise
- Psychological therapies, primarily cognitive behavioral therapy (CBT)
- Spinal manipulation
- Low-level laser therapy
- Massage
- Mindfulness-based stress reduction
- Yoga
- Acupuncture
- Multidisciplinary rehabilitation (MDR)

**Fibromyalgia:**
- Exercise
- CBT
- Myofascial release massage
- Tai chi
- Qigong
- Acupuncture
- Monopolar Dialectic Radiofrequency

**Hip osteoarthritis:**
- Exercise
- Manual therapies

**Knee osteoarthritis:**
- Exercise
- Ultrasound
Non-opioid pharmacologic treatment of chronic pain

Use a systematic approach to initiating pharmacologic therapy for pain:

1. Record history and physical, pain description, function/social assessment.
2. Determine mechanism of pain.
3. Consider non-pharmacologic options.
4. Consider pharmacologic options that may help.
5. Reassess response at regular intervals and modify treatment accordingly.

The Agency for Healthcare Research and Quality (AHRQ) evaluated the impact of non-opioid medications on chronic pain measures from 184 randomized controlled trials.

AHRQ EVIDENCE FOR NON-OPIOID PHARMACOLOGIC TREATMENTS FOR CHRONIC PAIN

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pain</th>
<th>Function</th>
<th>Quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathic pain</td>
<td>SHORT-TERM: Duloxetine</td>
<td>SHORT TERM: Duloxetine</td>
<td>SHORT TERM: Duloxetine</td>
</tr>
<tr>
<td></td>
<td>INTERMEDIATE TERM:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duloxetine, Pregabalin,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gabapentin, Oxcarbazepine</td>
<td></td>
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</tr>
<tr>
<td>Fibromyalgia</td>
<td>SHORT TERM: Duloxetine</td>
<td>SHORT TERM: Duloxetine</td>
<td>SHORT TERM: Duloxetine</td>
</tr>
<tr>
<td></td>
<td>INTERMEDIATE TERM:</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Duloxetine, Pregabalin,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gabapentin, Memantine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower back pain</td>
<td>SHORT TERM: Duloxetine</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>SHORT TERM: Duloxetine,</td>
<td>SHORT TERM: Duloxetine</td>
<td>SHORT TERM: Duloxetine</td>
</tr>
<tr>
<td></td>
<td>NSAIDs, Diclofenac</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory Arthritis</td>
<td>SHORT OR LONG TERM:</td>
<td>SHORT OR INTERMEDIATE TERM:</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td>NSAIDs</td>
<td></td>
</tr>
</tbody>
</table>

Pain scores were abstracted from Visual Analog Scale or Numerical Rating Scale; improvement defined as greater than or equal to 30% improvement. Function and quality of life outcomes abstracted data from validated scales including WOMAC function subscale, EuroQol-5 Dimensions, and Short Form-36. Short term = 3-6 mo; Intermediate term = 6-12 mo; Long term ≥ 12 mo.
Considering opioids for pain management

Avoid opioids as first-line therapy for chronic, non-cancer pain.

Patients randomized to opioids had similar pain-related function and greater pain intensity compared to those randomized to non-opioid medications.³

When should a provider consider opioids for chronic conditions?

- When other therapies are contraindicated
- When other therapy trials were implemented and unsuccessful
- After a full assessment and discussion of risks and benefits

*Pain scores measured by Brief Pain Inventory (BPI) Interference and Severity Scales. Patients had no contraindications to acetaminophen or NSAIDs.
Opioid dose considerations

CALCULATING MORPHINE MILLIGRAM EQUIVALENTS (MME)

<table>
<thead>
<tr>
<th>Opioid (doses in mg/day except where noted)</th>
<th>Conversion factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Morphine</td>
<td>1</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1.5</td>
</tr>
<tr>
<td>Fentanyl transdermal (in mcg/hr)</td>
<td>2.4</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
</tr>
<tr>
<td>1-20 mg/day</td>
<td>4</td>
</tr>
<tr>
<td>21-40 mg/day</td>
<td>8</td>
</tr>
<tr>
<td>41-60 mg/day</td>
<td>10</td>
</tr>
<tr>
<td>≥61 mg/day</td>
<td>12</td>
</tr>
</tbody>
</table>

Higher opioid dose = higher risk of overdose\(^5\)

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Conversion factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 MME</td>
<td>2.0-8.9x higher risk (compared to &lt;20MME)</td>
</tr>
<tr>
<td>20 MME</td>
<td>1.9-4.6x higher risk (compared to &lt;20MME)</td>
</tr>
<tr>
<td>0 MME</td>
<td>Baseline/lower risk</td>
</tr>
</tbody>
</table>

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics. Some opioids, including methadone and fentanyl, have complex conversion factors and require expertise to manage.

If opioids are appropriate, consider using episodic, short-acting opioids and keep at the lowest effective dose—low and slow.

Exercise caution:
- Doses ≥ 50 MME
- Concurrent use of a benzodiazepine, alcohol or methadone for pain

Avoid if possible:
- Dose ≥ 90 MME
- Opioid prescription > 3 months

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Managing patients on opioids

INHERITING PATIENTS ALREADY ON OPIOID THERAPY CAN BE COMPLEX

- When possible, discuss patient’s history with former provider
- Complete baseline assessments
- Establish expectations for opioid prescribing
- Engage in opioid use disorder treatment if appropriate

PATIENT ENGAGEMENT

- Recognize patient (e.g. psychosocial stressors), provider (e.g. time pressure, burnout), and environmental factors (e.g. regulatory changes) that lead to challenging conversations.
- Stigma can have a negative impact on the patient-provider relationship and a patient’s mental health. Use patient-first language.

<table>
<thead>
<tr>
<th>Instead of these terms:</th>
<th>Use these:</th>
</tr>
</thead>
<tbody>
<tr>
<td>addict</td>
<td>person with a substance use disorder</td>
</tr>
<tr>
<td>dirty urine</td>
<td>unexpected results</td>
</tr>
<tr>
<td>abuse</td>
<td>problematic use</td>
</tr>
</tbody>
</table>

- Use motivational interviewing techniques

For more information, go to: motivationalinterviewing.org
Preparing to reduce opioid dose

Tapering opioids may improve pain, based on a systematic review of 20 studies demonstrating improved or similar pain after a successful taper.7

HOWEVER, THERE ARE RISKS TO REDUCING OPIOID THERAPY:

• **Complex persistent dependence:**
  Patients living with chronic pain may experience neuroplastic effects from long-term opioid use, which may cause increased pain, decreased function, and psychological distress.8

• **Increased illicit substance use:** Stopping prescribed opioids increased the chance of more frequent heroin and illicit opioid pain reliever use.9

• **Opioid-related adverse events:**
  Approximately half of Medicaid patients in Vermont had an opioid-related ED visit or hospitalization following discontinuation of high-dose opioids. Speed of taper and substance use disorder diagnosis were the strongest predictors.10

• **Mortality:** In a study of 1,394,102 patients in the VA, patients were at greater risk of fatal overdose or suicide after stopping opioid treatment, with increasing risk the longer patients had been treated before stopping.11 Other studies have shown similar findings.12

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1. Preparing to reduce opioid dose
   - Tapering opioids may improve pain, based on a systematic review of 20 studies demonstrating improved or similar pain after a successful taper.
   - HOWEVER, THERE ARE RISKS TO REDUCING OPIOID THERAPY:
     - Complex persistent dependence:
       - Patients living with chronic pain may experience neuroplastic effects from long-term opioid use, which may cause increased pain, decreased function, and psychological distress.
     - Increased illicit substance use: Stopping prescribed opioids increased the chance of more frequent heroin and illicit opioid pain reliever use.
     - Opioid-related adverse events:
       - Approximately half of Medicaid patients in Vermont had an opioid-related ED visit or hospitalization following discontinuation of high-dose opioids. Speed of taper and substance use disorder diagnosis were the strongest predictors.
     - Mortality: In a study of 1,394,102 patients in the VA, patients were at greater risk of fatal overdose or suicide after stopping opioid treatment, with increasing risk the longer patients had been treated before stopping. Other studies have shown similar findings.

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**AFTER STOPPING OPIOIDS**

- Heroin use: 1.57
- Illicit opioid pain reliever use: 1.75

Adjusted odds ratio of increased use: 1.0

**Hazard ratio for risk of fatal overdose or suicide**

- ≤30 days: 1.67
- 31-90 days: 2.80
- 91-400 days: 3.95
- >400 days: 6.77

**Duration of opioid treatment in VA study**

[FDA and CDC recommend opioid prescribing be individualized for each patient to modulate the risks of changing dose. Go to: bit.ly/CDC_opioidguide and bit.ly/FDA_opioidguide](#)
Shared decision-making for opioid therapy

Avoid making a decision without an individualized conversation with the patient.

1. **Ask the patient to describe perceived risks and benefits.**

   **Patients may identify scenarios with limited benefit or increasing risk such as:**
   - On opioids after pain condition addressed
   - No evidence of pain/function improvement
   - Very high dose of opioids
   - Other risky medications (e.g. benzodiazepines)
   - Adverse effects (constipation, overdose, etc.)
   - Worsening comorbidities
   - Active opioid use disorder

2. **Develop a plan with the patient.**

   **Communication techniques:**
   - Validate patient’s pain and experience
   - Recognize power dynamics
   - Empower patient to participate in treatment planning
   - Don’t judge
   - Be flexible
   - Prepare for emotion

3. **Before implementing change, review and develop a plan for:**

   - Social issues (e.g. housing, finances, intimate partner violence)
   - Alternative pain management strategy (other medication and non-medication strategies)
   - Mental health services
   - Social support
   - Withdrawal medications
   - Changes in tolerance and overdose risk
Mechanics of a taper

BUILD THE CASE

1. Get to know the patient’s stressors, needs, and pain:
   — don’t rush to start a taper immediately: patient buy-in is important
   — individualize the taper plan (see “Example tapers for opioids”)

2. Discuss the risks of tapering.

3. Involve patient in the selection of a taper speed and frequency of dose reduction (see “Example tapers for opioids”).

4. Tapering should not result in withdrawal. However, in some circumstances, you may prescribe adjunctive medications to treat withdrawal symptoms.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold sweats, chills, feeling “jittery”</td>
<td>Clonidine: 0.1 mg tablet</td>
</tr>
<tr>
<td>Anxiety, problems sleeping</td>
<td>Hydroxyzine: 50 mg tablet</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>Ondansetron: 4 mg tablet</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Loperamide: 2 mg tablet</td>
</tr>
<tr>
<td>Body aches or muscle pain</td>
<td>NSAIDS or Acetaminophen</td>
</tr>
</tbody>
</table>

TAPER GOALS

Most commonly, opioid tapers will involve dose reduction of 5-20% of original dose every 4 weeks

Successful tapers look different for each patient and often include pauses, stops, and dynamic goals. Any reduction may be considered a success.

Abrupt tapers (>20% of original dose) should be avoided whenever possible.
## Example tapers for opioids

### Slowest taper (over years)

Reduce by 2% to 10% every 4 to 8 weeks with pauses in taper as needed. Consider for patients taking high doses of long-acting opioids for many years.

Ex: morphine SR 90 mg q8h = 270 MED

- **Month 1:** 90 mg SR qAM, 75 mg noon, 90 mg qPM [5% reduction]a
- **Month 2:** 75 mg SR qAM, 75 mg noon, 90 mg qPM
- **Month 3:** 75 mg SR (60 mg+15 mg) q8h
- **Month 4:** 75 mg SR qAM, 60 mg noon, 75 mg qPM
- **Month 5:** 60 mg SR qAM, 60 mg noon, 75 mg qPM
- **Month 6:** 60 mg SR q8h
- **Month 7:** 60 mg SR qAM, 45 mg noon, 60 mg qPM
- **Month 8:** 45 mg SR qAM, 45 mg noon, 60 mg qPM
- **Month 9:** 45 mg SR q8h b

### Standard taper (over months or years) — MOST COMMON

Reduce by 5% to 20% every 4 weeks with pauses in taper as needed.

Ex: morphine SR 90 mg q8h = 270 MED

- **Month 1:** 75 mg (60 mg+15 mg) SR q8h [16% reduction]
- **Month 2:** 60 mg SR q8h; **Month 3:** 45 mg SR q8h
- **Month 4:** 30 mg SR q8h; **Month 5:** 15 mg SR q8h
- **Month 6:** 15 mg SR q12h; **Month 7:** 15 mg SR qhs, then stop

### Faster taper (over weeks)

Reduce by 10% to 20% every week.

Ex: morphine SR 90 mg q8h = 270 MED

- **Week 1:** 75 mg SR q8h [16% reduction]
- **Week 2:** 60 mg SR (15 mg x 4) q8h; **Week 3:** 45 mg SR (15 mg x 3) q8h
- **Week 4:** 30 mg SR (15 mg x 2) q8h; **Week 5:** 15 mg SR q8h
- **Week 6:** 15 mg SR q12h; **Week 7:** 15 mg SR qhs x 7 days, then stop

### Rapid taper (over days) — RARELY INDICATED

Reduce by 20% to 50% of first dose if needed, then reduce by 10% to 20% every day.

Ex: morphine SR 90 mg q8h = 270 MED

- **Day 1:** 60 mg SR (15 mg x 4) q8h [33% reduction]
- **Day 2:** 45 mg SR (15 mg x 3) q8h; **Day 3:** 30 mg SR (15 mg x 2) q8h
- **Day 4:** 15 mg SR q8h; Days 5-7: 15 mg SR q12h
- Days 8-11: 15 mg SR qhs, then stop

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a Continue the taper based on patient response.
b Continue following this rate of taper until off the morphine or the desired dose of opioid is reached.

*MED = morphine equivalent dose
Opioid stewardship
Pain and function assessments

Assessments should focus on both pain and function.

- Assessments are essential when initiating opioid treatment or seeing a new patient already on long-term opioid therapy.
- Reassessments should take place at regular intervals to ensure benefit and evaluate adverse events.

PAIN, ENJOYMENT, GENERAL ACTIVITY (PEG) SCALE FOR ASSESSING PAIN INTENSITY AND INTERFERENCE: A SIMPLE, 3-QUESTION TOOL

1. What number best describes your pain on average in the past week:
   - 0: No pain
   - 10: Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?
   - 0: Does not interfere
   - 10: Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?
   - 0: Does not interfere
   - 10: Completely interferes

The PEG is as valid and reliable as the longer Brief Pain Inventory scale and is sensitive to changes in pain.16

CAUTION

Among racial and ethnic minority groups, women, and patients who are elderly or have cognitive impairment, pain can be underrecognized and inadequately treated.14,15
Risk factor assessment

Once you have determined that opioids are indicated for a patient, assessing for risk of opioid use disorder may help guide how closely you monitor.

A systematic review found that **the following may be associated with increased risk of use disorder due to prescribed opioids:**

- History of Opioid Use Disorder (OUD)
- Concomitant prescription of some psychiatric medications
- Certain mental health diagnoses, such as personality disorders
- History of Substance Use Disorder (SUD)

Screening tools (e.g. Opioid Risk Tool) are often used in protocols, but do not accurately predict outcomes.

In the presence of risk factors, consider increasing the frequency of:

- Pain/function assessments
- Urine drug screening
- Checking controlled substance monitoring program (CSMP)
- Screening for opioid use disorder
Urine drug screening (UDS)

Goal of UDS: Support patient care

<table>
<thead>
<tr>
<th>UDS does:</th>
<th>UDS does not:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support patient care</td>
<td>Prevent opioid-related problems among patients with chronic pain</td>
</tr>
<tr>
<td>Detect whether a substance has been used in a particular window of time</td>
<td>Diagnose addiction, dependence or diversion of controlled substances</td>
</tr>
<tr>
<td>Guide optimal care, like hemoglobin A1c</td>
<td>Singlehandedly provide justification to stop prescribing opioids for patients</td>
</tr>
</tbody>
</table>

HOW FREQUENTLY SHOULD I ORDER UDS FOR MY PATIENTS?

- CDC recommends UDS at first opioid prescription and at least annually thereafter.
- Most clinics adopt a uniform testing policy to prevent unintentional bias.
- Some facilities establish UDS frequency and timing independently of clinicians.

EXAMPLE

Use risk assessment to guide urine drug screening frequency.
- Low risk: every 12 mo
- Higher risk or opioid dose > 120 MME/day: consider more frequent screening
Interpreting UDS

Most UDS is in the form of immunoassays:
- Point-of-care
- Qualitative
- Show both metabolites and parent drug

**LIMITATIONS:**
- Do not test for all substances
- Methadone, buprenorphine, and fentanyl often require a separate test
- Many false positives/negatives

**Know your lab’s standard testing panel/options.**

**OPIOID METABOLIC PATHWAYS**

**EXAMPLE:**
- **Prescription:** Morphine
- **UDS results:** hydromorphone + morphine
- **Interpretation:** a) Patient most likely taking morphine only; b) Patient could be taking morphine + hydromorphone

**If UDS results are hard to explain:**
- Talk with the patient
- Contact the lab
- Consider mass spectrometry (GC/MS or LC-MS):
  - Lab-based
  - Quantitative
  - Fewer false positives/negatives
  - More expensive

**If UDS results are negative, consider:**
- Is the patient taking the medication?
- Is the patient taking a lower dose of the medication, or more infrequently?
- Are negative results due to duration of use, body mass, hydration, etc.?

*If long-term suspicion for diversion or SUD, engage with patient to create a plan (e.g. OUD treatment, tapering, referrals).

Always discuss results with patient before drawing conclusions; avoid changing therapy based on one unexpected result.
Informed consent and treatment agreements

- **Informed consent** is a joint, documented discussion between provider and patient to address risks associated with opioids and clarify expectations.

- **Controlled substance agreements** are written documents, similar to and possibly replacing informed consent, which include expectations of both the patient and provider. They are generally signed by the patient and renewed annually.

**CONTROLLED SUBSTANCE PATIENT-PROVIDER AGREEMENT**

The use of opioid pain medication is only one part of treatment for chronic pain.

The goals for using this medicine are:
- To improve my ability to work or function at home.
- To help my problem as much as possible.

<table>
<thead>
<tr>
<th>Provider’s Responsibilities</th>
<th>Patient Responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Refills                      Privacy

Prescriptions from Other Providers

Stopping the Medication

I have been told about the possible risks and benefits of this medicine.

<table>
<thead>
<tr>
<th>Patient’s name and signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Provider’s name and signature</th>
<th>Date</th>
</tr>
</thead>
</table>

At a minimum, providers should offer written information to patients about the benefits and risks of opioid therapy and document patients’ understanding and agreement.

Controlled substance agreement templates are available online: [bit.ly/PA_form](https://bit.ly/PA_form)

Additional considerations

- Remind patients to keep opioids in a locked and safe place.
- Encourage safe disposal of drugs, like take-back programs.
Controlled substance monitoring

California’s controlled substance monitoring program (CURES) is an online system used by prescribers to review prescriptions for controlled substances.

All California licensed prescribers and pharmacists who are authorized to prescribe, order, administer, or dispense scheduled drugs must register for CURES, check it when starting controlled substances and re-check it every 4 months.

FEATURES OF CURES

- **Save search list:** Save patient searches so they are easily available next time you log in.
- **Peer-to-peer communication:** Send communications securely to providers about mutual patients.
- **Alerts/messaging:** Receive daily alerts with information on patients who reach prescribing thresholds.

CURES CONTACT INFO:
Email: CURES@doj.ca.gov
Phone: (916) 210-3187
To register: oag.ca.gov/cures

CURES alerts prescribers to patients with multiple prescribers, high-dose opioid prescriptions, concomitant opioids and benzodiazepines, and daily opioids over 90 days.
Overdose prevention

Prior opioid overdose is a major risk for future overdose.

A patient who has previously overdosed is greater than seven times more likely to overdose in the subsequent year.19

OTHER FACTORS THAT INCREASE RISK OF OVERDOSE

- Reduced tolerance: after a period of abstinence, dose change, or release from incarceration
- Genetic predisposition
- Concomitant use of substances: benzodiazepines, alcohol

Some patients have overdosed and don’t realize it.

In one study, out of 60 patients on opioid therapy for pain, 37% had stopped breathing or required help to be woken up due to opioids.20

45% of those patients denied overdosing, calling it a bad reaction.

The word “overdose” may have negative connotations and prescription opioid users may not relate to it. Instead of using the word “overdose”, consider language like “accidental overdose” or “bad reaction”, or talk about “opioid safety”.

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Naloxone is effective as overdose prevention

GIVING NALOXONE TO PEOPLE WHO USE DRUGS IS ASSOCIATED WITH REDUCED OVERDOSE MORTALITY

FATAL OPIOID OVERDOSE RATES BY NALOXONE IMPLEMENTATION IN MASSACHUSETTS²¹

Overdose education and nasal naloxone distribution programs trained 2912 potential bystanders who reported 327 rescues. Compared to communities that did not implement these programs, both groups had significantly reduced adjusted rate ratios (p < 0.01). The adjusted odds ratio measured the incidence of overdoses, controlling for confounding variables.

NALOXONE MAY REDUCE OPIOID-RELATED ADVERSE EVENTS

OPIOID-RELATED EMERGENCY DEPARTMENT VISITS BY RECIPIENT OF NALOXONE PRESCRIPTION AMONG PRIMARY CARE PATIENTS ON OPIOID THERAPY FOR CHRONIC PAIN²²**

Prescribing naloxone to 29 patients averted 1 opioid-related emergency department visit in the following year.

*Ratios with 95% confidence intervals, adjusted for population age <18, male, race/ethnicity, below poverty level, medically supervised inpatient withdrawal, methadone and buprenorphine treatment, prescriptions to doctor shoppers, year.

**In a population with a rate of opioid-related emergency department visits of 7/1000 person years.
Indications for naloxone prescribing

**CDC recommends**

- Prescribing naloxone for patients on prescribed opioids with:
  - Opioid use ≥50 MMEs/day
  - Benzodiazepine use
  - History of substance use disorder
  - History of opioid overdose
  - Other factors that increase overdose risk, including comorbidities or concomitant medications

**Also offer naloxone to patients:**

- With any illicit substance use
- At risk of witnessing an opioid overdose

Naloxone is NOT a controlled substance. **Any licensed healthcare prescriber can prescribe naloxone.** California law provides additional protections to encourage naloxone prescribing and distribution.

**NALOXONE CO-PRESCRIBING (AB2760)**

- Prescribers in California are required to offer a prescription for naloxone to a patient who is receiving 90 MME or higher per day, receiving concurrent benzodiazepine, or at risk of overdose.

**PHARMACIST PROVISION OF NALOXONE (CA AB1535)**

- Pharmacists are allowed to directly prescribe and dispense naloxone to patients at risk of experiencing or witnessing an opioid overdose.
Naloxone formulations

Naloxone mechanism of action

- Highly specific, high-affinity opioid antagonist used to reverse the effects of opioids
- Lasts 30-90 minutes
- Virtually no side effects

INTRANASAL

- Naloxone 4mg #1 two pack, use PRN for suspected opioid overdose

AUTO-INJECTOR

- Naloxone auto-injector 2mg #1 two pack, use PRN for suspected opioid overdose

If the above devices are not optimal or accessible, a prescription can be written for a naloxone vial and syringe. In this situation, education should be provided directly to the patient.

INJECTABLE

- Naloxone 0.4mg IM #2, use PRN for suspected overdose, IM syringe (3ml 25g 1” syringe) #2

SBIRT CODES

To bill time for naloxone training (per 15 min intervals)

<table>
<thead>
<tr>
<th></th>
<th>Medicare:</th>
<th>MediCal:</th>
<th>Commercial:</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0396</td>
<td>H0050</td>
<td>CPT99408</td>
<td></td>
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</tbody>
</table>

SBIRT: Screening, Brief Intervention, and Referral to Treatment

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Opioid use disorder management
Recognizing opioid use disorder (OUD)

Ask non-judgmental, open-ended questions about patterns of drug use and how use affects the patient’s life.

**DSM-5 CRITERIA FOR SUBSTANCE USE DISORDER (SUD)***

**USE PATTERNS:**
- More/longer use than intended
- Unable to stop or cut down
- Excessive time dealing with opioids
- Craving

**CONTINUED USE EVEN WHEN:**
- Responsibilities not fulfilled
- Social and interpersonal problems
- Activities reduced
- Physical hazards from use
- Health problems patient knows are caused by opioids

**DRUG EFFECTS (ONLY IF NOT PRESCRIBED):**
- Tolerance: requiring more to achieve effect
- Withdrawal symptoms if opioids are stopped

* Used to diagnose OUD as well as other SUDs.

**SCORING**

Give 1 point for each domain endorsed by the patient or observed by the clinician.

Mild SUD = 2-3
Moderate SUD = 4-5
Severe SUD = 6 or more
Managing OUD

- If your patient has OUD, it is essential to arrange for treatment.
- **Treatment with medications has the best evidence for managing OUD** and should be considered for all patients.
- When therapy for OUD is stopped, the risk of death increases.

**FDA-APPROVED MEDICATION TREATMENT OPTIONS**
- Buprenorphine (with or without naloxone)
- Methadone
- Extended-release naltrexone

**BEHAVIORAL/PSYCHOLOGICAL INTERVENTIONS**
- Outpatient or inpatient rehabilitation and counseling
- Support groups such as Narcotics Anonymous

**If not personally providing OUD treatment, a warm hand-off to other providers is critical.**
Buprenorphine overview and safety profile

SAFETY PROFILE

• Due to the “ceiling effect” of a partial agonist, buprenorphine has:
  — Low potential for misuse and diversion
  — Low risk of respiratory depression or overdose
  — Ability to reduce craving and withdrawal without the euphoria of full agonist

• Maintenance is critical: OUD requires long-term care.
• Buprenorphine treatment is safe and effective during pregnancy.24
• Most buprenorphine for OUD treatment is co-formulated with naloxone to discourage diversion or injection of the product.

STUDIES ALSO SUPPORT USE OF BUPRENORPHINE FOR CHRONIC PAIN25

In a study of 35 patients on 200–1,370 morphine equivalent milligrams of opioids for chronic pain, after two months of sublingual buprenorphine:

Pain scores reduced from 7.2 to 3.5 (p<0.001)

Quality of life scores increased from 6.1 to 7.1 (p=0.005)

Range of pain scores = 0-10
Buprenorphine is an effective medication to treat OUD in primary care

ROUTINE MEDICATION MANAGEMENT CAN BE AS EFFECTIVE AS COMBINING BUPRENORPHINE WITH COUNSELING

While counseling should be sought if available, lack of access should not be a barrier to treatment.\(^{26}\)

PATIENTS CAN BE STARTED ON BUPRENORPHINE IN THE OFFICE OR AT HOME

Reductions in opioid use are similar when patients start therapy themselves at home compared to office-based settings.\(^{27}\)
Obtaining the DATA 2000 waiver to prescribe buprenorphine for OUD

• The DATA 2000 waiver or “X” number is a separate DEA registration number that must be used when buprenorphine is prescribed for OUD. Prescribing buprenorphine ONLY for pain does NOT require an “X” number, but may require prior authorization.

• After getting an “X” number, you can prescribe:
  — ≤30 patients in year one
  — ≤100 patients in subsequent years upon notifying SAMHSA
  — OR in year one if you meet the criteria in the SUPPORT Act (i.e. work in qualified practice setting or boarded in addiction medicine)

• MDs and DOs can apply to treat ≤275 patients after treating 100 patients for a year.

1 Complete free training: bit.ly/X-waiver

- If you are a licensed MD or DO: 8-hour training (or have substance use disorder treatment experience)
- If you are a licensed NP, PA, CNM, CNS or CNRA: 24-hour training

2 Complete and submit online buprenorphine waiver notification form.

3 Receive second DEA registration card with your “X” number.

For more information, contact SAMHSA:
866-BUP-CSAT (866-287-2728) or infobuprenorphine@samhsa.hhs.gov
Planning for buprenorphine

Formulations

- Keep buprenorphine tablet or film under tongue until dissolved (5-15 min). DO NOT SWALLOW.
- OK to cut film in half or quarter pieces.
- Therapy usually involves buprenorphine with naloxone, although the monoformulated product can also be used.

### BUPRENORPHINE/NALOXONE (CO-FORMULATED)
- Sublingual tablets
- Sublingual film

### MONOFORMULATED BUPRENORPHINE
- Sublingual tablets
- Subcutaneous injection
- Transdermal patch

Patient education and considerations

- Manage withdrawal symptoms when starting
- **Side effects:** fatigue, agitation, headache (from naloxone), nausea
  - **Precipitated withdrawal:** too large a dose started too soon after last opioid agonist (patient should call provider or go to the emergency department if severe symptoms present).
- Treatment is as long as needed; longer is usually better, and lifelong is normal

Not contraindications:

- Pregnancy
- Benzodiazepines
- Stimulants/other illicit drugs
- Alcohol

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Starting buprenorphine

Have patient sign a consent form for treatment

Make sure patient is in withdrawal
12-48 hours after last opioid dose, COWS score > 8, and at least one objective sign

Decide on induction location and timing
Home, clinic or hospital

HOME OR CLINIC

DAY 1
Usual first dose: 4mg
If still in withdrawal, repeat dose every 1-2 hours until stable.
Max dose Day 1 = 12mg

DAY 2
Start total Day 1 dose (or less if sedated).
Max dose Day 2 = 16mg

HOSPITAL

DAY 1
Usual first dose, either: 4mg or 8mg
Assess every hour. If still in withdrawal but symptoms improving, repeat dose until stable.
Max dose day 1 = 16mg

DAY 2
Start total Day 1 dose (or less if sedated).
Max dose Day 2 = 32mg

Subsequent days
Follow similar protocol. Usual final dose = 8-24mg

CHECK COWS:
Higher score = less risk of precipitated withdrawal

Clinical Opioid Withdrawal Scale (COWS): mdcalc.com/cows-score-opiate-withdrawal
COWS has 11 items and up to 48 points.

Look for subjective symptoms AND at least one objective sign.

- **Subjective:** insomnia, vomiting, diarrhea, restlessness, anxiety, abdominal cramps, diaphoresis, myalgias/arthralgias, hot flashes, dizziness, tearing, goosebumps, shaking, yawning, twitching, sweating
- **Objective:** restlessness, shivering, rhinorrhea, dilated pupils, tachycardia, yawning, piloerection, tremor, sweating, hypertension
Continuing buprenorphine

- Document OUD in chart.
- **Optimal dose varies by patient.**
  ≥16mg/day may aid in retention, block other opioids, and reduce relapse, pain, and dysphoria.
- **Follow-up visits:** tailor frequency to patient stability. Weekly visits at start of treatment or when unstable; monthly or longer when stable.

**Review:**
- Buprenorphine adherence, illicit opioid use, UDS, CSMP
- Mental health and comorbid substance use disorders
- Healthcare maintenance
- If unsuccessful, consider other OUD medications such as methadone or extended-release naltrexone.

**Remember that buprenorphine:**
- Gives patients control over opioid use.
- **Lowers overdose risk,** even if still using illicit opioids, by binding very tightly to μ receptors.
- Does not treat other substance use disorders.

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**FOR PAIN**
- Any formulation can be used, including the transdermal patch.
- Prior authorization may be required.
- No “X” number or waiver required.
- Medication is generally administered 2-3 times daily.
- **Acute pain:** May require a temporary dose increase.
- **Peri-operative pain:** Usually continue buprenorphine (Project Shout has a helpful template: [bit.ly/PainControl](http://bit.ly/PainControl))
Substance use disorder (SUD) therapies

- **Screening for substance use and SUD**: Ask about type, frequency, amount, route, complications and withdrawal symptoms.

- **Diagnosing SUD**: Use DSM-5 criteria—the criteria apply across substances. The use disorder is considered mild, moderate or severe based on the number of criteria a patient meets.

- Assess the patient’s readiness to change.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Screening tools</th>
<th>Medications</th>
<th>Behavioral interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine</td>
<td>AAR</td>
<td>Nicotine replacement, Varenicline, Bupropion</td>
<td>CBT, Smoking cessation</td>
</tr>
<tr>
<td>Alcohol</td>
<td>CAGE(-AID), AUDIT</td>
<td>Naltrexone IR or ER, Acamprosate, Disulfiram, Gabapentin, Topiramate</td>
<td>CBT, AA, Mindfulness, MI</td>
</tr>
<tr>
<td>Opioids</td>
<td>TAPS, DAST-10</td>
<td>Buprenorphine, Methadone, ER Naltrexone</td>
<td>CBT, NA, Mindfulness-oriented recovery enhancement</td>
</tr>
<tr>
<td>Stimulants</td>
<td>NM ASSIST, TAPS, DAST-10</td>
<td>For methamphetamine: Mirtazapine, Bupropion</td>
<td>CBT, Contingency management</td>
</tr>
</tbody>
</table>

*SBIRT can be used to screen for all substances: bit.ly/SBIRT_screen; off-label use; CBT, Mindfulness and MI target both use disorder and depression symptoms.*

Urine drug screening can help assess whether or not a substance has been used but do not diagnose substance use disorders.
Additional medical care for patients who use drugs

Due to increased risk for various complications, patients who use drugs should also be considered for:

<table>
<thead>
<tr>
<th>+ Screen for infections such as HIV, hepatitis B, hepatitis C, sexually-transmitted infections and tuberculosis (at least annually for most patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>🧑‍⚕️ Vaccinations such as hepatitis A, hepatitis B, human papillomavirus, tetanus-diphtheria-pertussis, influenza and pneumococcus</td>
</tr>
<tr>
<td>⚒️ Management of cardiac risk factors, particularly for people who use stimulants or tobacco, including blood pressure and lipid control, as well as smoking cessation</td>
</tr>
<tr>
<td>🕊️ Treatment of other comorbid substance use disorders, including tobacco and alcohol use disorders</td>
</tr>
<tr>
<td>🧠 Treatment of comorbid psychiatric disorders</td>
</tr>
<tr>
<td>🎯 Education about safe injection practices and provision of clean injection equipment</td>
</tr>
<tr>
<td>💉 Naloxone to reverse the effects of an opioid overdose</td>
</tr>
<tr>
<td>🎯 Pre- and post-exposure prophylaxis (PrEP and PEP) for HIV prevention</td>
</tr>
</tbody>
</table>
References


About this publication

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The recommendations contained in this brochure are general and informational only; specific clinical decisions should be made by providers on an individual case basis.