

SAMHSA

Opioid Overdose Prevention

TOOLKIT

Information for Prescribers



SAMHSA
Substance Abuse and Mental Health
Services Administration

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Opioid overdose is a major public health problem. In 2016, more than 42,000 people died of an opioid-related overdose.¹ Overdoses are experienced by both men and women of all ages, ethnicities, and demographic and socioeconomic characteristics and involve both illicit opioids such as heroin and illicitly manufactured fentanyl and prescription opioid analgesics such as oxycodone, hydrocodone, fentanyl, and methadone.¹

Health care providers can reduce the toll of opioid overdose through:

- Opioid stewardship and implementing the opioid prescribing guidelines of the Centers for Disease Control and Prevention (CDC; <https://www.cdc.gov/drugoverdose/prescribing/guideline.html>).
- Offering risk reduction messaging and prescribing naloxone when potentially dangerous behaviors or opioid doses are identified.
- Treating opioid use disorder (OUD) when individuals screen positive for the disorder and when their substance use histories and further examination indicate a current OUD.
- Treating opioid overdose emergencies.

Federally funded Substance Abuse and Mental Health Services Administration (SAMHSA) continuing medical education courses are available at no charge at <https://pcssnow.org/> and <https://www.OpioidPrescribing.com>.

OPIOID STEWARDSHIP

The CDC developed guidelines to improve communication between prescribers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including OUD, overdose, and death.² The 12 recommendations

for prescribing opioids for adults with chronic pain outside of active cancer, palliative, and end-of-life care are targeted toward primary care providers and are organized into three overarching categories.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety. If these goals are not met, then the opioid therapy should be tapered and stopped and other approaches should be considered.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy as well as patient and clinician responsibilities for managing therapy.

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should

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carefully reassess evidence of individual benefits and risks when increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to more than 90 MME/day or carefully justify a decision to titrate dosage to more than 90 MME/day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three or fewer days will often be sufficient; more than 7 days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate these into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (more than 50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using

state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every time a prescription is written to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for use of prescribed medications as well as use of other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with OUD.

RISK REDUCTION MESSAGING, OVERDOSE PREVENTION EDUCATION, AND NALOXONE PRESCRIPTION

When potentially harmful behaviors are identified (e.g., high-volume use of opioids; taking opioids in combination with alcohol, benzodiazepines, or other respiratory depressants; using illicit opioids where contents of substance cannot be confirmed), it is important to offer education that can reduce that individual's risk for overdose. Providing basic risk reduction messaging, overdose prevention education, and a naloxone prescription can be lifesaving interventions.

Risk reduction messaging from a prescriber may include information about which other medications a patient is taking that are respiratory depressants; benzodiazepines, anti-seizure medications, and many psychiatric

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medications are respiratory depressants. Letting the patient know that mixing these substances with opioids or taking more than prescribed in combination with opioids may increase his or her risk of overdose.

Naloxone competitively binds opioid receptors and is the antidote to acute opioid toxicity. Naloxone will not reverse alcohol, benzodiazepine, or other types of toxicity because it attaches only to the opioid receptors. Community-based naloxone distribution programs have not been shown to increase drug use and have, in fact, been shown to increase treatment engagement. Most patients respond positively to naloxone prescriptions, and some report additional positive behavioral changes following overdose education and naloxone prescription.³ Naloxone prescriptions could be (1) a naloxone kit containing naloxone vials, syringes, and needles; (2) intranasal naloxone spray, which delivers a single dose of naloxone into one nostril via a prefilled intranasal spray; or (3) a naloxone auto-injector, which delivers a single dose of naloxone to the outer thigh via a handheld auto-injector.⁴

Patients who are candidates for naloxone include individuals:²

- With a history of overdose.
- With a history of substance use disorder.
- Who are taking benzodiazepines with opioids.
- Who are at risk for returning to a high dose to which they are no longer tolerant (e.g., former inmates recently released from prison, patients leaving detoxification facilities).
- Who are taking higher dosages of opioids (more than 50 MME/day).

It may also be advisable to suggest that the at-risk patient create an “overdose plan” to share with friends, partners, and/or caregivers. Such a plan would contain information on the signs of overdose and how to administer naloxone or

otherwise provide emergency care (as by calling 911). Examples of patient handouts in seven languages are available from the State of California Department of Consumer Affairs and can be found at http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml.

OUD TREATMENT

If a patient has an OUD, arrange for and/or provide treatment. Treating OUD with Food and Drug Administration (FDA)-approved medications (methadone, buprenorphine with or without naloxone, and naltrexone) is an evidence-based approach. Methadone treatment for OUD can be provided only in licensed opioid treatment programs (OTPs). Buprenorphine can be prescribed by physicians, nurse practitioners, and physician assistants who have completed additional training and have obtained a waiver to prescribe this medication. Naltrexone is an injectable medication that can be prescribed by any provider with prescribing authority. It is recommended that each medication be prescribed in conjunction with behavioral and psychosocial treatment.⁵ For more information on these medications, see SAMHSA’s *Medication-Assisted Treatment of Opioid Use Disorder Pocket Guide* in the resources section or visit <https://store.samhsa.gov/product/Medication-Assisted-Treatment-of-Opioid-Use-Disorder-Pocket-Guide/SMA16-4892PG>. To identify treatment providers in your area, visit SAMHSA’s Behavioral Treatment Services Locator at <https://findtreatment.samhsa.gov/> or SAMHSA’s Buprenorphine Treatment Practitioner Locator at <https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator>.

TREATING OPIOID OVERDOSE

In the time it takes for an overdose to become fatal, it is possible to reverse the respiratory depression and other effects of opioids through respiratory support and administration of the opioid antagonist naloxone.⁶

Naloxone is approved by the FDA and has been used for decades to reverse overdose and resuscitate individuals who have overdosed on opioids. The routes of administration for naloxone are intravenous, intranasal, intramuscular, and subcutaneous. All naloxone products are effective in reversing opioid overdose, including fentanyl-involved opioid overdoses, although fentanyl-involved overdoses may require more naloxone.

The safety profile of naloxone is remarkably high, especially when used in low doses and titrated to effect.⁷ If given to individuals who are not opioid intoxicated or opioid dependent, naloxone produces no clinical effects, even at high doses. Moreover, although rapid opioid withdrawal in opioid-tolerant patients may be unpleasant, it is not life threatening.

Naloxone should be part of an overall approach to known or suspected opioid overdose that incorporates the steps below.

RECOGNIZE THE SIGNS OF OVERDOSE. An opioid overdose requires rapid diagnosis. The most common signs of overdose include:⁶

- Unconsciousness or inability to awaken orally or upon sternal rub.
- Slow or shallow breathing or breathing difficulty such as choking sounds or a gurgling/snoring noise from a patient who cannot be awakened.
- Fingernails or lips turning blue/purple.
- Slow heartbeat and/or low blood pressure.

SUPPORT RESPIRATION. Supporting respiration is a critical intervention for opioid overdose and may be lifesaving on its own. Begin CPR (technique based on rescuer's level of training).⁸ Ideally, individuals who are experiencing opioid overdose should be ventilated with oxygen before naloxone is administered to reduce the risk of acute lung injury.⁷

ADMINISTER NALOXONE. Naloxone competitively binds opioid receptors and is the antagonist of choice for the reversal of acute opioid toxicity. Naloxone should be administered to anyone who presents with signs of opioid overdose or when opioid overdose is suspected. Naloxone can be given by injection intranasally, intramuscularly, subcutaneously, or intravenously.⁴

PREGNANT PATIENTS. Naloxone can be used in life-threatening opioid overdose circumstances in pregnant women.⁹

MONITOR THE PATIENT'S RESPONSE.

Patients should be monitored for reemergence of signs and symptoms of opioid toxicity for at least 4 hours following the last dose of naloxone; however, patients who have overdosed on long-acting opioids require more prolonged monitoring.^{7,10}

Most patients respond to naloxone by returning to spontaneous breathing, with mild withdrawal symptoms.⁷ The response generally occurs within 2 to 3 minutes of naloxone administration. Continue rescue breathing while waiting for the naloxone to take effect.

The duration of effect of naloxone depends on dose and route of administration and is shorter than the effects of some opioids. Patients should be observed after administration for reemergence of overdose symptoms. The goal of naloxone therapy should be restoration of adequate spontaneous breathing, but not necessarily complete arousal.¹¹

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More than one dose of naloxone may be required to revive the patient. Those who have taken longer-acting opioids or opioid partial agonists may require additional doses, additional intravenous bolus doses, or an infusion of naloxone.¹⁰ Therefore, it is essential to get the person to an emergency department or other source of acute care as quickly as possible, even if the person revives after the initial dose of naloxone and seems to feel better.

SIGNS OF OPIOID WITHDRAWAL.

Withdrawal triggered by naloxone can feel unpleasant. Some people may become agitated or confused, which may improve by providing reassurance and explaining what is happening. The signs and symptoms of opioid withdrawal in an individual who is physically dependent on opioids may include body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection (gooseflesh), sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness, tearing, insomnia, opioid craving, dilated pupils, and increased blood pressure.¹² These symptoms are uncomfortable, but not life threatening unless vomiting and diarrhea result in extreme dehydration. After an overdose, a person dependent on opioids should be medically monitored for safety and offered treatment for OUD.

NO RESPONSE TO NALOXONE. If a patient does not respond to naloxone, an alternative explanation for the clinical symptoms should be considered. The most likely explanation is that the person is not overdosing on an opioid but rather some other substance or may even be experiencing a non-overdose medical emergency.

Support of ventilation, oxygenation, and blood pressure should be sufficient to prevent the complications of opioid overdose and should be given the highest

priority if the patient's response to naloxone is not prompt.

FENTANYL-INVOLVED OVERDOSE.

Suspected opioid overdoses, including suspected fentanyl-involved overdoses, should be treated according to standard protocols.^{13,14} However, because of the higher potency of fentanyl and fentanyl analogs compared to that of heroin, larger doses of naloxone may be required to reverse the opioid-induced respiratory depression from a fentanyl-involved overdose.^{5,13,14,15}

Many anecdotal accounts report more rapid respiratory depression with fentanyl than with heroin, although other reports do not reflect such rapid depression.¹⁴

Because of these effects, quicker oxygenation efforts and naloxone delivery may be warranted compared to heroin-only overdose. However, naloxone is an appropriate response for all opioid overdoses, including fentanyl-involved overdoses.

NOTE: All naloxone products have an expiration date. It is important to check the expiration date and obtain replacement naloxone as needed.

LEGAL AND LIABILITY CONSIDERATIONS

Health care professionals who are concerned about legal risks associated with prescribing naloxone may be reassured that prescribing naloxone to manage opioid overdose is consistent with the drug's FDA-approved indication, resulting in no increased liability so long as the prescriber adheres to general rules of professional conduct. Most state laws and regulations now permit physicians to prescribe naloxone to a third party, such as a caregiver. More information on state policies is available from the Prescription Drug Abuse Policy System's Naloxone Overdose Prevention Laws web page (<http://www.pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139>) or from individual state medical boards.

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CLAIMS CODING AND BILLING

Most private health insurance plans, Medicare, and Medicaid cover naloxone for the treatment of opioid overdose, but policies vary by state. The cost of take-home naloxone should not be a prohibitive factor. Many community pharmacies stock naloxone routinely, and those that do not can always order it. If you are caring for a large population of patients who are likely to benefit from naloxone, you may wish to notify the pharmacy when you implement naloxone prescribing as a routine practice.

The codes for Screening, Brief Intervention, and Referral to Treatment (SBIRT) can be used to bill time for counseling a patient about how to recognize overdose and how to administer naloxone. Billing codes for SBIRT are as follows:

- Commercial Insurance: CPT 99408 (15 to 30 minutes), 99409 (greater than 30 minutes)
- Medicare: G0396 (15 to 30 minutes), G0397 (greater than 30 minutes)

- Medicaid: H0049 (alcohol and/or drug screening), H0050 (alcohol and/or drug screening, brief intervention, per 15 minutes)

For counseling and instruction on the safe use of opioids, including the use of naloxone outside the context of SBIRT services, the provider should document the time spent in medication education and use the E&M (Evaluation and Management) code that accurately captures the time and complexity. For example, for new patients deemed appropriate for opioid pharmacotherapy and when a substantial and an appropriate amount of additional time is used to provide a separate service such as behavioral counseling (e.g., opioid overdose risk assessment, naloxone administration training), consider using modifier–25 in addition to the E&M code.

In addition, when using an evidence-based opioid use disorder or overdose risk factor assessment tool/screening instrument, CPT Code 99420 (Administration and interpretation of health risk assessment instrument) can be used for patients with commercial insurance.

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RESOURCES FOR PRESCRIBERS

Additional information on prescribing opioids for chronic pain is available at the following websites:

- <https://www.opioidprescribing.com>: Sponsored by the Boston University School of Medicine, with support from SAMHSA, the OpioidPrescribing.org site presents course modules on various aspects of prescribing opioids for chronic pain. Continuing medical education credits are available at no charge.
- <https://pcssnow.org/>: Sponsored by the American Academy of Addiction Psychiatry in collaboration with other specialty societies and with support from SAMHSA, the Providers Clinical Support System offers multiple resources related to opioid prescribing and the diagnosis and management of OUD. The site also is the source for Drug Addiction Treatment Act of 2000 waiver education requirements.
- <https://www.drugabuse.gov/nidamed-medical-health-professionals/cmece-activities#opioids>: NIDAMED's mission is to disseminate science-based resources to health professionals on the causes and consequences of drug use and addiction, and advances in pain management. Continuing medical education credits are available at no charge.
- <https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm163647.htm>: The Risk Evaluation and Mitigation Strategy website provides physician training and patient education on OUD treatment medications as required by the FDA for extended-release and long-acting opioid analgesics.
- <http://prescribetoprevent.org>: Compiled by prescribers, pharmacists, public health workers, lawyers, and researchers working on overdose prevention and naloxone access, this privately funded site provides health care providers with resources to educate patients on how to reduce overdose risk and provide naloxone rescue kits to patients.
- <https://store.samhsa.gov/product/Medication-Assisted-Treatment-of-Opioid-Use-Disorder-Pocket-Guide/SMA16-4892PG>: SAMHSA's *Medication-Assisted Treatment for Opioid Use Disorder Pocket Guide* provides practical information for clinicians on medications to treat OUD.
- <https://store.samhsa.gov/product/SMA18-5063FULLDOC>: SAMHSA's Treatment Improvement Protocol 63: *Medications for Opioid Use Disorders* provides in-depth information for health care and addiction professionals, policymakers, patients, and families.

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