



# The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use

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Key Points

Diagnosis

Treatment

- ASAM defines addiction as “a primary, chronic disease of brain reward, motivation, memory, and related circuitry,” with a “dysfunction in these circuits” being reflected in “an individual pathologically pursuing reward and/or relief by substance use and other behaviors.”
  - The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) uses the term “opioid use disorder” (OUD).
- According to the 2013 National Survey on Drug Use and Health, 4.5 million individuals in the United States were current (past month), nonmedical users of prescription opioids and 289,000 were current (past month) users of heroin.
- The leading causes of death in people using opioids for nonmedical purposes are overdose and trauma.
- The injection route use (intravenous or even intramuscular) of opioids or other drugs increases the risk of being exposed to HIV, viral hepatitis, and other infectious agents.
- Recommendations using the term “buprenorphine” will refer to the combination buprenorphine/naloxone formulations. When buprenorphine only is recommended it will be referred to as “buprenorphine monoprodukt.” When recommendations differ by product, the formulation will be described.
- This ASAM Practice Guideline pocket card is intended to aid clinicians in their clinical decision-making and patient management. The Practice Guideline pocket card strives to identify and define clinical decision making junctures that meet the needs of most patients in most circumstances. Clinical decision-making should involve consideration of the quality and availability of expertise and services in the community wherein care is provided. In circumstances in which the Practice Guideline pocket card is being used as the basis for regulatory or payer decisions, improvement in quality of care should be the goal.

### Assessment

- The first clinical priority should be given to identifying and making appropriate referral for any urgent or emergent medical or psychiatric problem(s), including drug-related impairment or overdose.
- Completion of the patient’s medical history should include screening for concomitant medical conditions, including infectious diseases (hepatitis, HIV, and TB), acute trauma, and pregnancy.
- A physical examination should be completed as a component of the comprehensive assessment process. The prescriber (the clinician authorizing the use of a medication for the treatment of OUD) may conduct this physical examination him/herself, or, in accordance with the ASAM Standards<sup>1</sup>, ensure that a current physical examination is contained within the patient medical record before a patient is started on a new medication for the treatment of his/her addiction.
- Initial laboratory testing should include a complete blood count, liver function tests, and tests for hepatitis A, B, C and HIV. Testing for TB and sexually transmitted infections should also be considered. Hepatitis A and B vaccination should be offered, for those who are pregnant and the general population.
- The assessment of females presents special considerations regarding their reproductive health. Women of childbearing age should be tested for pregnancy, and all women of childbearing potential and age should be queried regarding methods of contraception given the increase in fertility that results from effective OUD treatment.
- Patients being evaluated for addiction involving opioid use, and/or for possible medication use in the treatment of OUD, should undergo (or have completed) an assessment of mental health status and possible psychiatric disorders (as outlined in the ASAM Standards of Care<sup>2</sup>).
- Opioid use is often co-occurring with other substance related disorders. An evaluation of past and current substance use as well as a determination of the totality of substances that surround the addiction should be conducted.
- The use of marijuana, stimulants, or other addictive drugs should not be a reason to suspend OUD treatment. However, evidence demonstrates that patients who are actively using substances during OUD treatment have a poorer prognosis.
  - The use of alcohol, benzodiazepines and other sedative hypnotics may be a reason to suspend agonist treatment because of safety concerns related to respiratory depression.

→ A tobacco use query and counseling on cessation of tobacco products and electronic nicotine delivery devices should be completed routinely for all patients, including those who present for evaluation and treatment of OUD.

→ An assessment of social and environmental factors should be conducted (as outlined in the ASAM Standards) to identify facilitators and barriers to addiction treatment, and specifically to pharmacotherapy.

- Before a decision is made to initiate a course of pharmacotherapy for the patient with OUD, the patient should receive a multidimensional assessment in fidelity with The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions (the “ASAM Criteria”<sup>3</sup>). Addiction should be considered a bio-psycho-social-spiritual illness, for which the use of medication(s) is only one component of overall treatment.

### Diagnosis

→ Other clinicians may diagnose OUD, but confirmation of the diagnosis by the provider with prescribing authority, and who recommends medication use, must be obtained before pharmacotherapy for OUD commences.

→ OUD is primarily diagnosed on the basis of the history provided by the patient and a comprehensive assessment that includes a physical examination.

→ Validated clinical scales that measure withdrawal symptoms may be used to assist in the evaluation of patients with OUD: Examples include<sup>4</sup>:

- the Objective Opioid Withdrawal Scale (OOWS)<sup>4</sup>
- the Subjective Opioid Withdrawal Scale (SOWS)<sup>4</sup>
- the Clinical Opioid Withdrawal Scale (COWS)<sup>4</sup>

<sup>4</sup> Visit [www.GuidelineCentral.com/OUD](http://www.GuidelineCentral.com/OUD) for calculators

→ Urine drug testing during the comprehensive assessment process, and frequently during treatment, is recommended. The frequency of drug testing is determined by a number of factors including: the stability of the patient, the type of treatment, and the treatment setting.

**Table 1. Common Signs of Opioid Intoxication and Withdrawal**

Intoxication Signs		
• Drooping eyelids	• Scratching (due to histamine release)	
• Constricted pupils	• Head nodding	
• Reduced respiratory rate		
Withdrawal Signs		
OOWS	SOWS	COWS
<ul style="list-style-type: none"> <li>• Yawning</li> <li>• Rhinorrhoea</li> <li>• Piloerection (observe arm)</li> <li>• Perspiration</li> <li>• Lacrimation</li> <li>• Tremor (hands)</li> <li>• Mydriasis</li> <li>• Hot and cold flushes</li> <li>• Restlessness</li> <li>• Vomiting</li> <li>• Muscle twitches</li> <li>• Abdominal cramps</li> <li>• Anxiety</li> </ul>	<ul style="list-style-type: none"> <li>• I feel anxious.</li> <li>• I feel like yawning.</li> <li>• I’m perspiring.</li> <li>• My eyes are tearing.</li> <li>• My nose is running.</li> <li>• I have goose flesh.</li> <li>• I am shaking.</li> <li>• I have hot flashes.</li> <li>• I have cold flashes.</li> <li>• My bones and muscles ache.</li> <li>• I feel restless.</li> <li>• I feel nauseous.</li> <li>• I feel like vomiting.</li> <li>• My muscles twitch.</li> <li>• I have cramps in my stomach.</li> <li>• I feel like shooting up now.</li> </ul>	<ul style="list-style-type: none"> <li>• Pulse</li> <li>• Sweating</li> <li>• Restlessness</li> <li>• Pupil size</li> <li>• Bone or joint aches</li> <li>• Rhinorrhoea</li> <li>• Tearing</li> <li>• GI upset</li> <li>• Tremor of outstretched hands</li> <li>• Yawning</li> <li>• Anxiety or irritability</li> <li>• Gooseflesh skin</li> </ul>

**Table 2. Related Physical Exam Findings in Substance Use Disorders**

System	Findings
Dermatologic	Abscesses, rashes, cellulitis, thrombosed veins, jaundice, scars, track marks, pock marks from skin popping
Ear, nose, throat and eyes	Pupils pinpoint or dilated, yellow sclera, conjunctivitis, rhinorrhea, rhinitis, excoriation or perforation of nasal septum, epistaxis, sinusitis, hoarseness or laryngitis
Mouth	Poor dentition, gum disease, abscesses
Cardiovascular	Murmurs, arrhythmias
Respiratory	Asthma, dyspnea, rales, chronic cough, hematemesis
Musculoskeletal and extremities	Pitting edema, broken bones, traumatic amputations, burns on fingers
Gastrointestinal	Hepatomegaly, hernias

### Treatment Setting

- **The choice of available treatment options for addiction involving opioid use should be a shared decision between clinician and patient.**
- **Clinicians should consider the patient's preferences, past treatment history, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone in the treatment of addiction involving opioid use.**
  - The treatment setting described as Level 1 treatment in the ASAM Criteria may be a general outpatient location such as a clinician's practice site.
  - The setting as described as Level 2 in the ASAM Criteria may be an intensive outpatient treatment or partial hospitalization program housed in a specialty addiction treatment facility, a community mental health center, or another setting.
  - The ASAM Criteria describes Level 3 or Level 4 treatment respectively as a residential addiction treatment facility or hospital.
- **The venue in which treatment is provided is as important as the specific medication selected.**
  - Opioid Treatment Programs offer daily supervised dosing of methadone, and increasingly of buprenorphine.
  - Naltrexone can be prescribed in any setting by any clinician with the authority to prescribe any medication.
  - In accordance with federal law (21 CFR §1306.07), Office-Based Opioid Treatment (OBOT), which provides medication on a prescribed weekly or monthly basis, is limited to buprenorphine.
  - Clinicians should consider a patient's psychosocial situation, co-occurring disorders, and risk of diversion when determining whether Opioid Treatment Programs (OTP) or OBOT is most appropriate.
- **OBOT may not be suitable for patients with active alcohol use disorder or sedative, hypnotic, or anxiolytic use disorder (or who are in the treatment of addiction involving the use of alcohol or other sedative drugs, including benzodiazepines or benzodiazepine receptor agonists). It may also be unsuitable for persons who are regularly using alcohol or other sedatives but do not have addiction or a specific substance use disorder related to that class of drugs.**
  - The prescribing of benzodiazepines or other sedative-hypnotics should be used with extreme caution in patients who are prescribed methadone or buprenorphine for the treatment of an OUD.
- **Methadone is recommended for patients who may benefit from daily dosing and supervision in an OTP, or for patients for whom buprenorphine for the treatment of OUD has been used unsuccessfully in an OTP or OBOT setting.**

- **Oral naltrexone for the treatment of OUD is often adversely affected by poor medication adherence.**
  - Clinicians should reserve its use for patients who would be able to comply with special techniques to enhance their adherence; e.g. observed dosing. Extended-release injectable naltrexone reduces, but does not eliminate, issues with medication adherence.

### Treating Opioid Withdrawal

- **Using medications for opioid withdrawal management is recommended over abrupt cessation of opioids. Abrupt cessation of opioids may lead to strong cravings, which can lead to continued use.**
- **Patients should be advised about risk of relapse and other safety concerns from using opioid withdrawal management as standalone treatment for OUD.**
  - Opioid withdrawal management on its own is not a treatment method.
- **Assessment of a patient undergoing opioid withdrawal management should include a thorough medical history and physical examination focusing on signs and symptoms associated with opioid withdrawal.**
- **Opioid withdrawal management in cases in which methadone is used to manage withdrawal symptoms must be done in an inpatient setting or in an OTP.**
  - For short acting opioids, tapering schedules that decrease in daily doses of prescribed methadone should begin with doses between 20–30 mg per day and should be completed in 6–10 days.
- **Opioid withdrawal management in cases in which buprenorphine is used to manage withdrawal symptoms should not be initiated until 12–18 hours after the last dose of a short-acting agonist such as heroin or oxycodone, and 24–48 hours after the last dose of a long-acting agonist such as methadone.**
  - A dose of buprenorphine sufficient to suppress withdrawal symptoms is given (this can be 4–16 mg per day) and then the dose is tapered. The duration of the tapering schedule can be as brief as 3–5 days or as long as 30 days or more.
- **The Guideline Committee recommends the inclusion of clonidine as a practice to support opioid withdrawal.**
  - Clonidine is not FDA-approved for the treatment of opioid withdrawal but it has been extensively used off-label for this purpose. Clonidine may be used orally or trans-dermally at doses of 0.1–0.3 mg every 6–8 hours with a maximum dose of 1.2 mg daily to assist in the management of opioid withdrawal symptoms. Its hypotensive effects often limit the amount that can be used. Clonidine can be combined with other non-narcotic medications targeting specific opioid withdrawal symptoms such as benzodiazepines for anxiety, loperamide for diarrhea, acetaminophen or nonsteroidal antiinflammatory medications (NSAIDs) for pain, and ondansetron or other agents for nausea.

- Opioid withdrawal management using anesthesia ultra-rapid opioid detoxification (UROD) is **NOT** recommended due to high risk for adverse events or death.
  - Naltrexone-facilitated opioid withdrawal management can be a safe and effective approach but should be used only by clinicians experienced with this clinical method, and in cases in which anesthesia or conscious sedation are not being employed.
- The use of combinations of buprenorphine and low doses of oral naltrexone to manage withdrawal and facilitate the accelerated introduction of extended-release injectable naltrexone has shown promise. More research will be needed before this can be accepted as standard practice.

### Methadone

- Methadone is a treatment option recommended for patients who are physiologically dependent on opioids, able to give informed consent, and who have no specific contraindications for agonist treatment when it is prescribed in the context of an appropriate plan that includes psychosocial intervention.
  - The recommended initial dose ranges for methadone are from 10–30 mg with reassessment in 3–4 hours, and a second dose not to exceed 10 mg on the first day if withdrawal symptoms are persisting.
  - The usual daily dosage of methadone ranges from 60–120 mg. Some patients may respond to lower doses, and some patients may need higher doses.
  - Dosage increases in 5–10 mg increments applied no more frequently than every 7 days (depending on clinical response) are necessary to avoid over-sedation, toxicity, or even iatrogenic overdose deaths.
- The administration of methadone should be monitored because unsupervised administration can lead to misuse and diversion. OTP regulations require monitored medication administration until the patient's clinical response and behavior demonstrates that the prescribing of non-monitored doses is appropriate.
- Psychosocial treatment, though sometimes minimally needed, should be implemented in conjunction with the use of methadone in the treatment of OUD.
- Methadone should be reinstated immediately if relapse occurs, or when an assessment determines that the risk of relapse is high for patients who previously received methadone in the treatment of OUD but who are no longer prescribed such treatment.
- Strategies directed at relapse prevention are an important part of comprehensive addiction treatment and should be included in any plan of care for a patient receiving active opioid treatment or ongoing monitoring of the status of their addictive disease.

- Switching from methadone to another medication for the treatment of OUD may be appropriate if the patient experiences intolerable side effects or is not successful in attaining or maintaining treatment goals through the use of methadone.
- Patients switching from methadone to buprenorphine in the treatment of OUD should be on low doses of methadone prior to switching medications.
  - Patients on low doses of methadone (30–40 mg per day or less) generally tolerate transition to buprenorphine with minimal discomfort, whereas patients on higher doses of methadone may experience significant discomfort in switching medications.
- Patients switching from methadone to oral naltrexone or extended-release injectable naltrexone must be completely withdrawn from methadone and other opioids, before they can receive naltrexone.
  - The only exception would apply when an experienced clinician receives consent from the patient to embark on a plan of naltrexone-facilitated opioid withdrawal management.
- Patients who discontinue agonist therapy with methadone or buprenorphine and then resume opioid use should be made aware of the risks associated with opioid overdose, and especially the increased risk of death.

### Buprenorphine

- Opioid-dependent patients should wait until they are experiencing mild to moderate opioid withdrawal before taking the first dose of buprenorphine to reduce the risk of precipitated withdrawal.
  - Generally, buprenorphine initiation should occur at least 6–12 hours after the last use of heroin or other short-acting opioids, or 24–72 hours after their last use of long-acting opioids such as methadone.
- Induction of buprenorphine should start with a dose of 2–4 mg. Dosages may be increased in increments of 2–4 mg.
- Clinicians should observe patients in their offices during induction. However, home buprenorphine induction may be considered.
  - Home-based induction is recommended only if the patient or prescribing physician is experienced with the use of buprenorphine.
- Buprenorphine doses after induction and titration should be, on average, ≥8 mg per day. However, if patients are continuing to use opioids, consideration should be given to increasing the dose by 4–8 mg (daily doses of 12–16 mg or higher).
  - The FDA approves dosing to a limit of 24 mg per day, and there is limited evidence regarding the relative efficacy of higher doses. In addition, the use of higher doses may increase the risk of diversion.
- Psychosocial treatment should be implemented in conjunction with the use of buprenorphine in the treatment of OUD.

→ **Clinicians should take steps to reduce the chance of buprenorphine diversion.**

- Recommended strategies include frequent office visits (weekly in early treatment), urine drug testing, including testing for buprenorphine and metabolites, and recall visits for pill counts.

→ **Patients should be tested frequently for buprenorphine, other substances, and prescription medications.**

→ **Accessing Prescription Drug Monitoring Program (PDMP) data may be useful for monitoring.**

→ **Patients should be seen frequently at the beginning of their treatment. Weekly visits (at least) are recommended until patients are determined to be stable.**

- There is no recommended time limit for treatment.

→ **Buprenorphine taper and discontinuation is a slow process and close monitoring is recommended.**

- Buprenorphine tapering is generally accomplished over several months. Patients should be encouraged to remain in treatment for ongoing monitoring past the point of discontinuation.

→ **When considering a switch from buprenorphine to naltrexone, 7–14 days should elapse between the last dose of buprenorphine and the start of naltrexone to ensure that the patient is not physically dependent on opioids prior to starting naltrexone.**

→ **When considering a switch from buprenorphine to methadone, there is no required time delay since the addition of a full mu-opioid agonist to a partial agonist does not typically result in any type of adverse reaction.**

→ **Patients who discontinue agonist therapy and resume opioid use should be made aware of the risks associated with an opioid overdose, and especially the increased risk of death.**

### Naltrexone

→ **Naltrexone is a recommended treatment in preventing relapse in OUD.**

- Oral formula naltrexone may be considered for patients where adherence can be supervised or enforced. Extended-release injectable naltrexone may be more suitable for patients who have issues with adherence.
- Oral naltrexone should be taken daily in 50 mg doses, or 3 times weekly in two 100 mg doses followed by one 150 mg dose.
- Extended-release injectable naltrexone should be administered every 4 weeks by deep intramuscular injection in the gluteal muscle at a set dosage of 380 mg per injection.

→ **Psychosocial treatment is recommended in conjunction with treatment with naltrexone.**

- The efficacy of naltrexone use in conjunction with psychosocial treatment has been established, whereas the efficacy of extended-release injectable naltrexone without psychosocial treatment has **not** been established.

→ **There is no recommended length of treatment with oral naltrexone or extended-release injectable naltrexone.**

- Duration depends on clinical judgment and the patient's individual circumstances. Because there is no physical dependence associated with naltrexone, it can be stopped abruptly without withdrawal symptoms.

→ **Switching from naltrexone to methadone or buprenorphine should be planned, considered, and monitored.**

- Switching from an antagonist such as naltrexone to a full agonist (methadone) or a partial agonist (buprenorphine) is generally less complicated than switching from a full or partial agonist to an antagonist because there is no physical dependence associated with antagonist treatment and thus no possibility of precipitated withdrawal.
- Patients being switched from naltrexone to buprenorphine or methadone will not have physical dependence on opioids and thus the initial doses of methadone or buprenorphine used should be low.
- Patients should not be switched until a significant amount of the naltrexone is no longer in their system, about 1 day for oral naltrexone or 30 days for extended-release injectable naltrexone.

→ **Patients who discontinue antagonist therapy and resume opioid use should be made aware of the increased risks associated with an opioid overdose, and especially the increased risk of death.**

### Psychosocial Treatment in Conjunction with Medications for the Treatment of OUD

→ **Psychosocial treatment is recommended in conjunction with any pharmacological treatment of OUD.**

- At a minimum, psychosocial treatment should include the following: psychosocial needs assessment, supportive counseling, links to existing family supports, and referrals to community services.

→ **Treatment planning should include collaboration with qualified behavioral health care providers to determine the optimal type and intensity of psychosocial treatment and for renegotiation of the treatment plan for circumstances in which patients do not adhere to recommended plans for, or referrals to, psychosocial treatment.**

→ **Psychosocial treatment is generally recommended for patients who are receiving opioid agonist treatment (methadone or buprenorphine).**

→ **Psychosocial treatment should be offered with oral and extended-release injectable naltrexone.**

- The efficacy of extended-release injectable naltrexone to treat OUD has not been confirmed when it has been used as pharmacotherapy without accompanying psychosocial treatment.

**Table 3. Medications for Treatment of OUD**

Agent	Dose	Dosing
Buprenorphine sublingual film, tablets (generic)	PO: 2 mg, 8 mg film and tablets	<b>Initial:</b> 2–4 mg (Increase by 2–4 mg) <b>Daily:</b> ≥8 mg <b>Max:</b> 24 mg/day
Methadone tablets/liquid (generic)	PO: 5 mg, 10 mg, tablets; 10 mg/mL liquid	<b>Initial:</b> 10-30 mg (Reassess in 3–4 hours; add ≤10 mg PRN) <b>Daily:</b> 60-120 mg <sup>a</sup>
Naltrexone XR injection ( <i>Vivitrol</i> ®)	IV/IM: 380 mg in 4 cc	Every 4 weeks
Naltrexone tablets (generic)	PO: 50 mg	<b>Daily:</b> 50 mg (May give 2–3 daily doses at once on M–W–F)

**Buprenorphine Combination Product (See Table 5)**

<sup>a</sup> The dose should be individualized and may be higher or lower than this usual dosage.

**Table 4. Medication Comparison**

	Methadone	Buprenorphine	Extended Release Naltrexone
<b>Pharmacology</b>	Full agonist	Partial agonist	Full antagonist
<b>Dosing</b>	Daily (but duration often longer)	Daily	<i>q4wks</i>
<b>Setting</b>	Specialty licensed OTP	Office-based or OTP, requires “x” waiver	Any medical setting, requires injection
<b>Induction</b>	No time restriction; start low, go slow	Mild-mod withdrawal: >8-12 hrs after last opioid	>7 days after last opioid
<b>Adherence</b>	Intrinsically reinforcing	Intrinsically reinforcing	Long acting
<b>Side Effect/Safety</b>	Sedation esp early in treatment, constipation. Caution re: concurrent benzos/alcohol overdosing, drug-drug interactions	Lower extremity swelling, urinary hesitancy, constipation. Caution re: concurrent benzos/alcohol	Injection site rxns, nausea, malaise. Caution re: precipitated withdrawal if given before opioid free washout period
<b>Other advantages</b>	Co-morbid pain, high potency, high structure of delivery setting.	Safety compared to methadone, co-morbid pain, dosing flexibility, lower burden of OBOT delivery, simple pharmacy availability	Low diversion, no dependence, verifiable dosing, lower stigma in some settings compared to agonists
<b>Craving reduction</b>	+++	++	+

**Table 5. Bioequivalence of Buprenorphine Formulations**

Available Dosage Strengths	
Buprenorphine sublingual tablets, including generic equivalents:	2 mg buprenorphine 8 mg buprenorphine
Buprenorphine and naloxone sublingual tablets, including generic equivalents:	2 mg buprenorphine / 0.5 mg naloxone 8 mg buprenorphine / 2 mg naloxone
<i>Zubsolv</i> ® (Buprenorphine and naloxone sublingual tablets):	1.4 mg buprenorphine / 0.36 mg naloxone 2.9 mg buprenorphine / 0.7 mg naloxone 5.7 mg buprenorphine / 1.4 mg naloxone 8.6 mg buprenorphine / 2.1 mg naloxone 11.4 mg buprenorphine / 2.6 mg naloxone
<i>Suboxone</i> ® sublingual film (Buprenorphine and naloxone sublingual film):	2 mg buprenorphine / 0.5 mg naloxone 4 mg buprenorphine / 1 mg naloxone 8 mg buprenorphine / 2 mg naloxone 12 mg buprenorphine / 3 mg naloxone
<i>Bunavail</i> ® (Buprenorphine hydrochloride and naloxone hydrochloride buccal film):	2.1 mg buprenorphine / 0.3 mg naloxone 4.2 mg buprenorphine / 0.7 mg naloxone 6.3 mg buprenorphine / 1 mg naloxone

**Corresponding doses of buprenorphine products that contain naloxone**

Buprenorphine and naloxone sublingual tablets, including generic equivalents	<i>Suboxone</i> ® sublingual films	<i>Zubsolv</i> ® sublingual tablets	<i>Bunavail</i> ® buccal films
2 mg buprenorphine / 0.5 mg naloxone	2 mg buprenorphine / 0.5 mg naloxone	1.4 mg buprenorphine / 0.36 mg naloxone	
	4 mg buprenorphine / 1 mg naloxone	2.9 mg buprenorphine / 0.71 mg naloxone	2.1 mg buprenorphine / 0.3 mg naloxone
8 mg buprenorphine / 2 mg naloxone	8 mg buprenorphine / 2 mg naloxone	5.7 mg buprenorphine / 1.4 mg naloxone	4.2 mg buprenorphine / 0.7 mg naloxone
	12 mg buprenorphine / 3 mg naloxone	8.6 mg buprenorphine / 2.1 mg naloxone	6.3 mg buprenorphine / 1 mg naloxone
		11.4 mg buprenorphine / 2.9 mg naloxone	

Adapted from: Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers. Available at: <https://www.btodrems.com>

Figure 1. Evaluation and Treatment

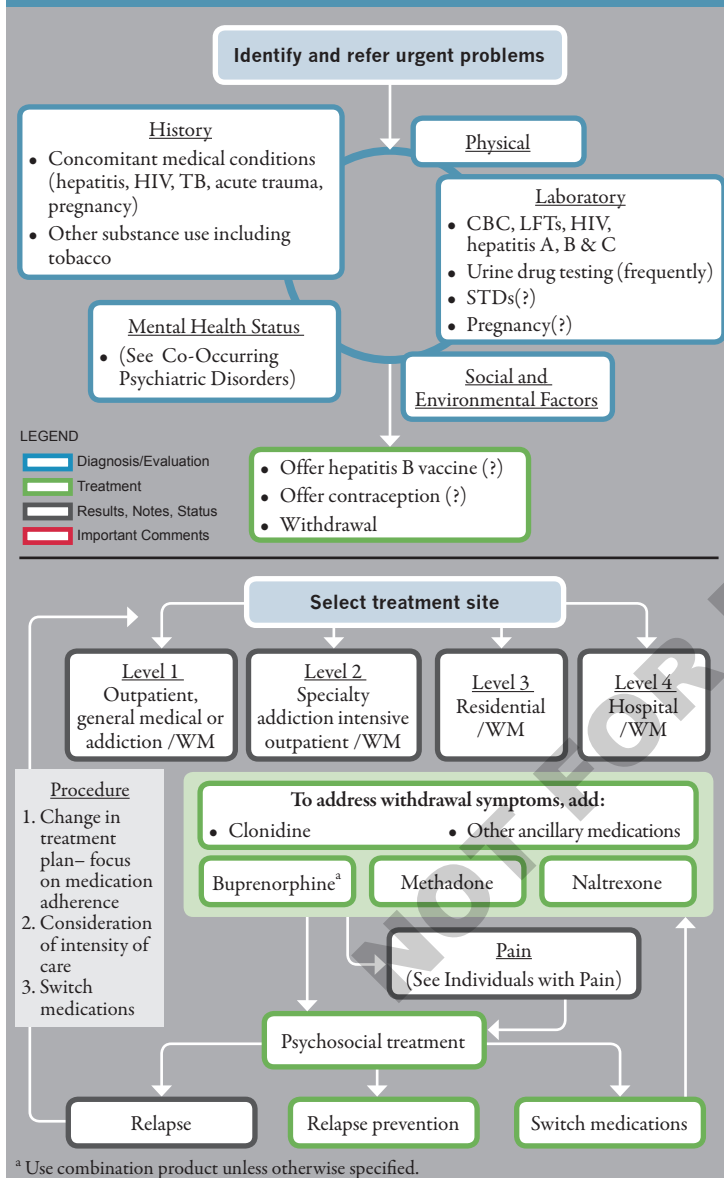
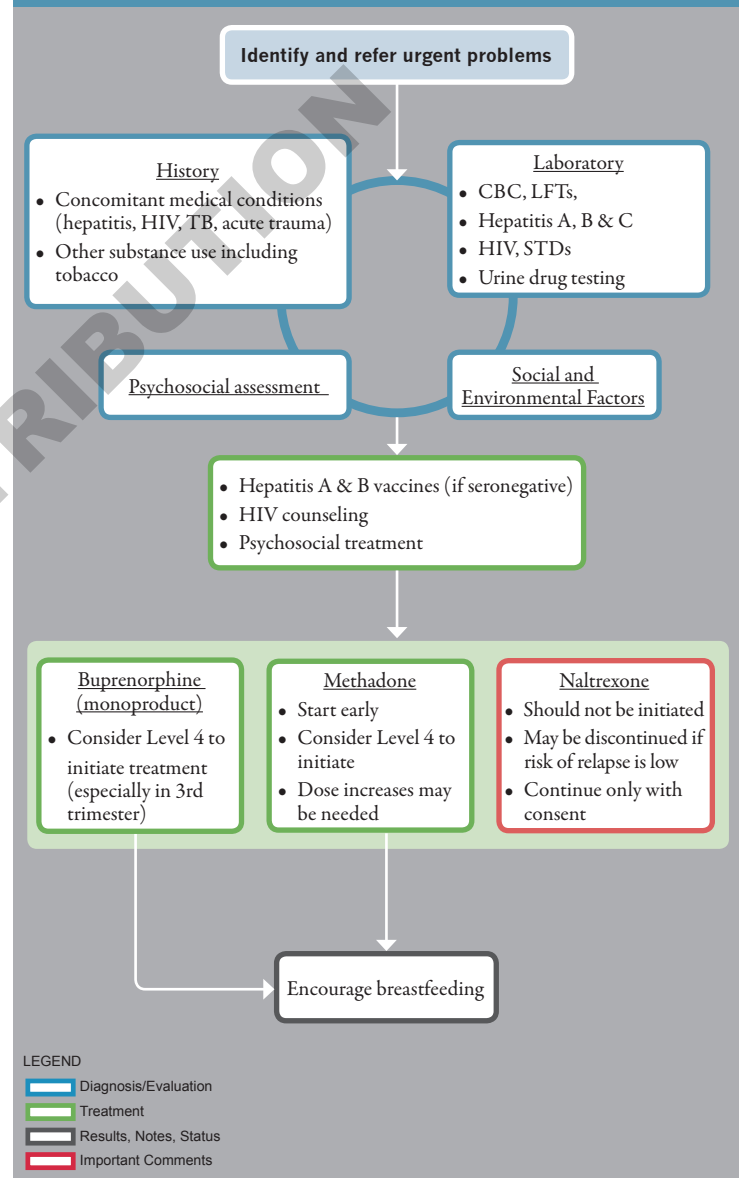


Figure 2. Pregnancy





### Special Populations

#### Pregnant Women

- **The first priority in evaluating pregnant women for OUD should be to identify emergent or urgent medical conditions that require immediate referral for clinical evaluation.**
- **A medical examination and psychosocial assessment is recommended when evaluating pregnant women for OUD.**
- **Obstetricians and gynecologists should be alert to signs and symptoms of OUD.**
  - Pregnant women with OUD are more likely to seek prenatal care late in pregnancy, miss appointments, experience poor weight gain, or exhibit signs of withdrawal or intoxication.
- **Psychosocial treatment is recommended in the treatment of pregnant women with OUD.**
- **Counseling and testing for HIV should be provided in accordance with state law. Tests for hepatitis A, B and C and liver function are also suggested.**
  - Hepatitis A and B vaccination is recommended for those whose hepatitis serology is negative.
- **Urine drug testing may be used to detect or confirm suspected opioid and other drug use with informed consent from the mother, realizing that there may be adverse legal and social consequences of her use.**
  - State laws differ on reporting substance use during pregnancy. Laws that penalize women for use and for obtaining treatment serve to prevent women from obtaining prenatal care and worsen outcomes.
- **Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine monoproduct rather than withdrawal management or abstinence.**
- **Treatment with methadone should be initiated as early as possible during pregnancy.**
  - Hospitalization during initiation of methadone and treatment with buprenorphine may be advisable due to the potential for adverse events, especially in the third trimester.
  - In an inpatient setting, methadone should be initiated at a dose range of 20–30 mg. Incremental doses of 5–10 mg are given every 3–6 hours, as needed, to treat withdrawal symptoms.
  - After induction, clinicians should increase the methadone dose in 5–10 mg increments per week. The goal is to maintain the lowest dose that controls withdrawal symptoms and minimizes the desire to use additional opioids.
  - Twice daily dosing is more effective and has fewer side effects than single dosing but may not be practical because methadone is typically dispensed in an outpatient clinic.

→ **Care for pregnant women with OUD should be co-managed by an obstetrician and an addiction specialist physician.**

- Release of information forms need to be completed to ensure communication among health care providers.

→ **Clinicians should be aware that the pharmacokinetics of methadone are affected by pregnancy.**

- With advancing gestational age, plasma levels of methadone progressively decrease and clearance increases. Increased or split doses may be needed as pregnancy progresses. After child birth, doses may need to be adjusted.

→ **Buprenorphine monoproduct is a reasonable and recommended alternative to methadone for pregnant women.**

- While there is evidence of safety, there is insufficient evidence to recommend the combination buprenorphine/naloxone formulation.

→ **If a woman becomes pregnant while she is receiving naltrexone, it is appropriate to discontinue the medication if the patient and doctor agree that the risk of relapse is low.**

- If the patient is highly concerned about relapse and wishes to continue naltrexone, she should be informed about the risks of staying on naltrexone and provide her consent for ongoing treatment.
- If the patient wishes to discontinue naltrexone but then reports relapse to opioid use, it may be appropriate to consider treatment with methadone or treatment with buprenorphine.

→ **Naloxone is *NOT* recommended for use in pregnant women with OUD except in situations of life threatening overdose.**

→ **Mothers receiving methadone and buprenorphine monoproduct for the treatment of OUDs should be encouraged to breastfeed.**

#### Individuals with Pain

→ **For all patients with pain, it is important that the correct diagnosis be made and that a target suitable for treatment is identified.**

→ **If pharmacological treatment is considered, nonnarcotic medications such as acetaminophen and NSAIDs should be tried first.**

→ **Opioid agonists (methadone or buprenorphine) should be considered for patients with active OUD who are not in treatment.**

→ **Pharmacotherapy in conjunction with psychosocial treatment should be considered for patients with pain who have OUD.**

→ **Patients on methadone for the treatment of OUD will require doses of opioids in addition to their regular daily dose of methadone to manage acute pain.**

- Patients on methadone for the treatment of OUD and who are admitted for surgery may require additional short-acting opioid pain relievers.
  - The dose of pain relievers prescribed may be higher due to tolerance.
- Temporarily increasing buprenorphine dosing may be effective for mild acute pain.
- For severe acute pain, discontinuing buprenorphine and commencing on a high potency opioid (such as fentanyl) is advisable.
  - Monitor patients closely and consider additional interventions such as regional anesthesia.
- The decision to discontinue buprenorphine prior to an elective surgery should be made in consultation with the attending surgeon and anesthesiologist.
  - If it is decided that buprenorphine should be discontinued prior to surgery, this should occur 24–36 hours in advance of surgery and restarted post-operatively when the need for full opioid agonist analgesia has passed.
- Patients on naltrexone will not respond to opioid analgesics in the usual manner. Therefore, it is recommended that mild pain be treated with NSAIDs and moderate to severe pain be treated with ketorolac on a short-term basis.
- Oral naltrexone should be discontinued 72 hours prior to surgery and extended-release injectable naltrexone should be discontinued 30 days prior to an anticipated surgery.

### Adolescents

- Clinicians should consider treating adolescents who have OUD using the full range of treatment options, including pharmacotherapy.
- Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment of OUD in adolescents.
  - Age is a consideration in treatment, and federal laws and FDA approvals need to be considered for patients under age 18.
- Psychosocial treatment is recommended in the treatment of adolescents with OUD.
- Concurrent practices to reduce infection (e.g., sexual risk reduction interventions), are recommended as components of comprehensive treatment for the prevention of sexually transmitted infections and blood-borne viruses.
- Adolescents may benefit from treatment in specialized treatment facilities that provide multidimensional services.

### Co-Occurring Psychiatric Disorders

- A comprehensive assessment including determination of mental health status should evaluate whether the patient is stable.
    - Patients with suicidal or homicidal ideation should be referred immediately for treatment and possibly hospitalization.
  - Management of patients at risk for suicide should include:
    - a. reducing immediate risk
    - b. managing underlying factors associated with suicidal intent and
    - c. monitoring and follow-up.
  - All patients with psychiatric disorders should be asked about suicidal ideation and behavior.
    - Patients with a history of suicidal ideation or attempts should have OUD, and psychiatric medication use, monitored.
  - Assessment for psychiatric disorder should occur at the onset of agonist or antagonist treatment.
    - Reassessment using a detailed mental status examination should occur after stabilization with methadone, buprenorphine or naltrexone.
  - Pharmacotherapy in conjunction with psychosocial treatment should be considered for patients with OUD and a co-occurring psychiatric disorder.
  - Clinicians should be aware of potential interactions between medications used to treat co-occurring psychiatric conditions and OUD.
  - Assertive community treatment should be considered for patients with co-occurring schizophrenia and OUD who have a recent history of, or are at risk of, repeated hospitalization or homelessness.
- ### Individuals in the Criminal Justice System
- Pharmacotherapy for the continued treatment of OUDs, or the initiation of pharmacotherapy, has been shown to be effective and is recommended for prisoners and parolees regardless of the length of their sentenced term.
  - Individuals with OUD who are within the criminal justice system should be treated with some type of pharmacotherapy in addition to psychosocial treatment.
  - Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment.
    - There is insufficient evidence to recommend any one treatment as superior to another for prisoners or parolees.
  - Pharmacotherapy should be initiated a minimum of 30 days prior to release from prison.

## Naloxone for the Treatment of Opioid Overdose

- Naloxone should be given in case of opioid overdose.
- Naloxone can and should be administered to pregnant women in cases of overdose in order to save the mother's life.
- The Guideline Committee, based on consensus opinion, recommends that patients who are being treated for OUD and their family members/significant others be given prescriptions for naloxone. Patients and family members/significant others should be trained in the use of naloxone in overdose.
- The Guideline Committee, based on consensus opinion, recommends that first responders such as emergency medical services personnel, police officers, and firefighters be trained in and authorized to administer naloxone.

**Table 6. Opioid Overdose Medications**

Agent	Dose	Indication
Naloxone injection		
<i>Evszio</i> ® (auto-injector)	0.4 mg/0.4 mL	For emergency treatment of overdose
<i>Narcan</i> ®, generic <sup>a</sup>	(various)	Opioid depression, diagnosis of suspected opioid overdose, ↓ BP in septic shock

<sup>a</sup> There is not yet an FDA-approved intranasal formulation. There are only kits made available to deliver the injectable formulation intranasally.

**Table 7. Switching Drugs**

FROM \ TO	Buprenorphine	Methadone	Naltrexone
Buprenorphine		No delay needed	7–14 days after last dose of buprenorphine
Methadone	Better tolerated when on <30–40 mg of methadone		Must be completely withdrawn from opioids
Naltrexone	Wait 1 day for oral naltrexone and 30 days for extended-release naltrexone	Wait 1 day for oral naltrexone and 30 days for extended-release naltrexone. Use low initial dose of methadone	

## Figure 3. Overdose

### Step 1: Call for Help (Dial 911)

AN OPIOID OVERDOSE NEEDS IMMEDIATE MEDICAL ATTENTION.

### Step 2: Recognize Overdose

- Extreme sleepiness inability to awaken verbally or upon sternal rub.
- Breathing problems can range from slow to shallow breathing in a patient that cannot be awakened.
- Fingernails or lips turning blue/purple.
- Extremely small pupils – “pinpoint pupils.”
- Slow heartbeat and/or low blood pressure.

### Step 3: Support Respiration

- Verify that the airway is clear.
- With one hand on the patient's chin, tilt the head back and pinch the nose closed.
- Place your mouth over the patient's mouth to make a seal and give 2 slow breaths (the patient's chest should rise, but not the stomach).
- Follow up with one breath every 5 seconds.

### Step 4: Administer Naloxone

- The most rapid onset of action is achieved by intravenous administration, which is recommended in emergency situations.
- The intramuscular route of administration may be more suitable for patients with a history of opioid dependence because it provides a slower onset of action and a prolonged duration of effect, which may minimize rapid onset of withdrawal symptoms.
- The product *Evszio*® is specifically designed for intramuscular use but may also be administered subcutaneously.
- The intramuscular or subcutaneous route of administration may be more suitable for patients with a history of opioid dependence because it provides a slower onset of action and a prolonged duration of effect, which may minimize rapid onset of withdrawal symptoms.
- There is not yet an FDA-approved intranasal formulation – there are only kits made available to deliver the injectable formulation intranasally. Despite the intranasal formulation's current lack of FDA approval, it is being used off-label by first responders.

### Step 5: Monitor the Patient's Response

- Most patients respond to naloxone by returning to spontaneous breathing, with mild withdrawal symptoms. The response generally occurs within 3–5 minutes of naloxone administration. (Rescue breathing should continue while waiting for the naloxone to take effect.)
- The duration of effect of naloxone is 30–90 minutes depending on dose and route of administration. Patients should be observed after that time for re-emergence of overdose symptoms. More than one dose of naloxone may be required to revive the patient.
- *The goal of naloxone therapy should be restoration of adequate spontaneous breathing, but not necessarily complete arousal.*

Adapted from Substance Abuse and Mental Health Services Administration. *SAMHSA Opioid Overdose Prevention Toolkit*. HHS Publication No. (SMA) 14-4742. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2014.

**Table 8. Summary of Special Population Recommendations**

Condition	Testing	Psychosocial Rx	Agonist Rx	Antagonist Rx	Rx Adjustments	Setting	Notes
Pregnancy	HIV; hepatitis A, B, and C; STD testing and prevention, urine drugs	✓	Methadone or buprenorphine monoprodu <sup>3</sup>	Naltrexone should not be initiated May be discontinued if risk of relapse is low Continue only with consent	Dose increase as pregnancy advances	Level 4 for methadone induction and buprenorphine Rx	Encourage breast feeding
Pain	HIV; hepatitis A, B, and C; STD testing and prevention, urine drugs	✓	Methadone or buprenorphine	Naltrexone XR or oral	<b>Mild:</b> NSAIDs or acetaminophen <b>Moderate:</b> Increase agonist or add opioid <b>Severe:</b> Discontinue buprenorphine; add a high potency opioid (fentanyl)	All	Discontinue oral naltrexone 72 hrs (or 30 days for extended-release) before surgery
Adolescents	HIV; hepatitis A, B, and C; STD testing and prevention, urine drugs	✓	Methadone or buprenorphine	Naltrexone XR or oral	N/A	All	Legal requirements and FDA approvals for under age 18
Psychiatric Disorders	HIV; hepatitis A, B, and C; STD testing and prevention, urine drugs; suicide potential	✓	Methadone or buprenorphine	Naltrexone XR or oral	Manage drug interactions	Consider Levels 1 or 2 for coincident schizophrenia	
Incarceration	HIV; hepatitis A, B, and C; STD testing and prevention, urine drugs	✓	Methadone or buprenorphine	Naltrexone XR		Prison or parolee Levels 1–4	Initiate Rx ≥30 days before release

<sup>3</sup> The guidelines specifically promote buprenorphine monotherapy

## Abbreviations

**AIDS**, Acquired Immunodeficiency Syndrome; **ASAM**, American Society of Addiction Medicine; **COWS**, Clinical Opioid Withdrawal Scale; **DSM-5**, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; **FDA**, Food and Drug Administration; **HIV**, Human Immunodeficiency Virus; **NSAIDs**, Non-Steroidal Anti-Inflammatory Drugs; **OBOT**, Office-Based Opioid Treatment; **OD**, Opioid use disorder; **OOWS**, Objective Opioid Withdrawal Scale; **OTP**, Opioid Treatment Program; **SOWS**, Subjective Opioid Withdrawal Scale; **TB**, Tuberculosis; **UROD**, Ultra-Rapid Opioid Detoxification; **WM**, withdrawal management

## Resources

<sup>1</sup> <http://www.asam.org/docs/default-source/practice-support/quality-improvement/asam-standards-of-care.pdf>

<sup>2</sup> <http://www.asam.org/docs/default-source/practice-support/quality-improvement/asam-standards-of-care.pdf>

<sup>3</sup> <http://www.asam.org/publications/the-asam-criteria>

<sup>4</sup> [www.GuidelineCentral.com/OUC](http://www.GuidelineCentral.com/OUC) for Calculators

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## Source

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## Disclaimer

*This Guideline attempts to define principles of practice that should produce high-quality patient care. It is applicable to specialists, primary care, and providers at all levels. This Guideline should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation.*

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