



The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder

2020 Focused Update

Key Points

Diagnosis

Treatment

Special Populations

Key Points

➔ **ASAM defines addiction as “a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual’s life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.”**

- The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) uses the term “opioid use disorder” (OUD).

➔ **According to the 2018 National Survey on Drug Use and Health, an estimated 10.3 million people aged 12 or older misused opioids in the past year, including 9.9 people who misused prescription pain relievers and 808,000 people who used heroin.**

➔ **The leading causes of death in people using opioids for nonmedical purposes are overdose and trauma.**

➔ **Injection (intravenous [IV], or intramuscular [IM]) 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 monoproduct.” When recommendations differ by product, the formulation will be described.**

➔ **This ASAM Practice Guideline pocket guide is intended to aid clinicians in their clinical decision-making and patient management. The Practice Guideline pocket guide 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 guide is being used as the basis for regulatory or payer decisions, improvement in quality of care should be the goal.**

Table 1. Testing/Screening

History	Laboratory	Social and Environmental Factors
• Concomitant medical conditions (hepatitis, HIV, TB, acute trauma, pregnancy) • Alcohol • Other substance use including tobacco	• CBC, LFTs • Hepatitis A, B & C, HIV, STIs • Confirmatory urine drug testing • Pregnancy(?)	• Food insecurity • Housing • Transportation challenges • Domestic violence • Significant mental health issues

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.
- **NEW** – Comprehensive assessment of the patient is critical for treatment planning. However, completion of all assessments should not delay or preclude initiating pharmacotherapy for OUD. If not completed before initiating treatment, assessments should be completed soon thereafter.
- Completion of the patient's medical history should include screening for concomitant medical conditions including psychiatric disorders, infectious diseases (viral hepatitis, HIV, and tuberculosis [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) should ensure that a current physical examination is contained within the patient medical record before (or soon after) a patient is started on pharmacotherapy. (See Table 1)
- Initial laboratory testing should include a complete blood count, liver enzyme tests, and tests for TB, hepatitis B and C, and HIV. Testing for sexually transmitted infections should be strongly considered. Hepatitis A and B vaccinations should be offered, if appropriate.
- Women of childbearing potential should be tested for pregnancy, and all women of childbearing potential should be queried regarding methods of contraception.
- Patients being evaluated for OUD, 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 (such as is outlined in *The ASAM Criteria*¹ and *The ASAM Standards*²). OUD is often co-occurring with other substance use disorders. Evaluation of a patient with OUD should include a detailed history of other past and current substance use and substance use disorders.
- The use of cannabis, stimulants, alcohol, and/or other addictive drugs should not be a reason to withhold or suspend OUD treatment. However, patients who are actively using substances during OUD treatment may require greater support including a more intensive level of care (see *The ASAM Criteria*¹ and *The ASAM Standards*²).

↩ Diagnosis

→ **MAJOR REVISION** –The use of benzodiazepines and other sedative-hypnotics should not be a reason to withhold or suspend treatment with methadone or buprenorphine.

- While the combined use of these medications increases the risk of serious side effects, the harm caused by untreated OUD can outweigh these risks.
- A risk-benefit analysis should be conducted, and greater support should be provided including careful medication management to reduce risks.

→ A nicotine use query should be completed routinely for all patients and counseling on cessation of the use of tobacco products and electronic nicotine delivery devices (e.g., vaping) provided if indicated.

→ As part of comprehensive care, the patient should receive a multidimensional assessment (as described in *The ASAM Criteria*¹), including an assessment of social and environmental factors, to identify facilitators and barriers to addiction treatment and long-term recovery (including pharmacotherapy).

- Addiction is a complex biopsychosocial illness, for which the use of medication(s) is only one component of comprehensive treatment.

Diagnosis

→ Other clinicians may diagnose OUD, but confirmation of the diagnosis must be obtained by the prescriber 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.

→ Drug testing is recommended during the comprehensive assessment process and during treatment to monitor patients for adherence to prescribed medications and use of alcohol, illicit, and controlled substances.

- The frequency of testing is determined by several factors including stability of the patient, type of treatment, and treatment setting. For additional information see *The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine*⁴ guidance document.

Table 2. Common Signs of Opioid Intoxication and Withdrawal

Intoxication Signs	Withdrawal Signs
• Drooping eyelids • Constricted pupils • Reduced respiratory rate • Scratching (due to histamine release) • Head nodding	• Restlessness, irritability, anxiety • Insomnia • Yawning • Abdominal cramps, diarrhea, vomiting • Dilated pupils • Sweating • Piloerection

Table 3. Related Physical Exam Findings in Substance Use Disorders

System	Findings
Dermatologic	Abscesses, rashes, cellulitis, thrombosed veins, jaundice, spider angioma, palmer erythema, scars, track marks, pock marks from skin popping
Ear, nose, throat and eyes	Pupils pinpoint or dilated, yellow sclera, conjunctivitis, ruptured eardrums, otitis media, discharge from ears, 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 Options

➔ **MAJOR REVISION** – All FDA-approved medications for the treatment of OUD should be available to all patients. Clinicians should consider the patient's preferences, past treatment history, current state of illness, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone.

➔ **NEW** – There is no recommended time limit for pharmacological treatment.

➔ **MAJOR REVISION** – Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs.

- However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacotherapy, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing individual needs.

➔ **The venue in which treatment is provided should be carefully considered.**

- Methadone can be provided only in opioid treatment programs (OTPs) and acute care settings (under limited circumstances).
- Buprenorphine can be prescribed by waived clinicians in any setting including OTPs and office based opioid treatment (OBOT) in accordance with Federal law (21 CFR §1301.28).
- Naltrexone can be prescribed in any setting by any clinician with the authority to prescribe medication.
- Clinicians should consider a patient's psychosocial situation, co-occurring disorders, and risk of diversion when determining which treatment setting is most appropriate (see *The ASAM Criteria*¹ for additional guidance).

➔ **Patients with active co-occurring alcohol use disorder or sedative, hypnotic, or anxiolytic use disorder (or who are in treatment for a substance use disorder involving use of alcohol or other sedative drugs including benzodiazepines or benzodiazepine receptor agonists) may need a more intensive level of care than can be provided in an office-based setting.**

- Persons who are regularly using alcohol or other sedatives, but do not meet the criteria for diagnosis of a specific substance use disorder related to that class of drugs, should be carefully monitored.

➔ **MAJOR REVISION** – The prescribing of benzodiazepines or other sedative-hypnotics should be used with caution in patients who are prescribed methadone or buprenorphine for the treatment of an OUD.

- While the combined use of these drugs increases the risk of serious side effects, the harm caused by untreated OUD can outweigh these risks.
- A risk-benefit analysis should be conducted when deciding whether to co-prescribe these medications.

→ 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.

→ **NEW** – Opioid dosing guidelines developed for chronic pain, expressed in morphine milligram equivalents (MME), are not applicable to medications for the treatment of OUDs.

→ Oral naltrexone for the treatment of OUD is often adversely affected by poor medication adherence and should **NOT** be used except under very limited circumstances.

- Clinicians should reserve its use for patients who would be able to comply with special techniques to enhance their adherence, for example, observed dosing.
- Extended-release injectable naltrexone reduces, but does not eliminate, issues with medication adherence.

→ The Prescription Drug Monitoring Program⁵ (PDMP) should be checked regularly for the purpose of confirming medication adherence and to monitor for the prescribing of other controlled substances.

→ **NEW** – Naloxone, for the reversal of opioid overdose, should be provided to patients being treated for, or with a history of, OUD. Patients and family members/significant others should be trained in the use of naloxone in overdose.

Treating Opioid Withdrawal

→ Using methadone or buprenorphine for opioid withdrawal management is recommended over abrupt cessation of opioids. Abrupt cessation of opioids may lead to strong cravings and/or acute withdrawal syndrome, which can put the patient at risk for relapse, overdose, and overdose death.

→ Opioid withdrawal management (i.e., detoxification) on its own, without ongoing treatment for OUD, is not a treatment method for OUD and is **NOT** recommended.

- Patients should be advised about the risk of relapse and other safety concerns, including increased risk of overdose and overdose death.
- Ongoing maintenance medication, in combination with psychosocial treatment appropriate for the patient's needs, is the standard of care for treating OUD.

→ 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.

↩ Treatment

→ **By regulation, opioid withdrawal management with methadone must be done in an OTP or an acute care setting (under limited circumstances).**

- For patients withdrawing from short-acting opioids the initial dose should typically be 20–30mg per day, and the patient may be tapered off in approximately 6–10 days.

→ **MAJOR REVISION** – Opioid withdrawal management with buprenorphine should not be initiated until there are objective signs of opioid withdrawal. (See p. 10–11 for more information on the timing of initiating buprenorphine.)

- Once signs of withdrawal have been objectively confirmed, a dose of buprenorphine sufficient to suppress withdrawal symptoms is given (an initial dose of 2–4mg titrated up as needed to suppress withdrawal symptoms).

→ **MAJOR REVISION** – Alpha-2 adrenergic agonists (e.g., FDA-approved lofexidine and off-label clonidine) are safe and effective for management of opioid withdrawal.

- However, methadone and buprenorphine are more effective in reducing the symptoms of opioid withdrawal, in retaining patients in withdrawal management, and in supporting the completion of withdrawal management.

→ **Opioid withdrawal management using ultra-rapid opioid detoxification (UROD) is *NOT* recommended due to high risk for adverse events or death.**

- Naltrexone-facilitated opioid withdrawal management can be safe and effective but should be used only by clinicians experienced with this clinical method and in cases in which anesthesia or conscious sedation are not employed.

Methadone

→ **Methadone is a recommended treatment for patients with OUD who are able to give informed consent and have no specific contraindication to this treatment.**

→ **MAJOR REVISION** – The recommended initial dose of methadone ranges from 10–30mg with reassessment as clinically indicated (typically in 2–4 hours).

- Use a lower-than-usual initial dose (2.5–10mg) in individuals with no or low opioid tolerance.

→ **MAJOR REVISION** – Following initial withdrawal stabilization, the usual daily dose of methadone ranges from 60–120mg.

- Some patients may respond to lower doses and some may need higher doses.
- Methadone titration should be individualized based on careful assessment of the patient's response and generally should not be increased every day.
- Typically, methadone can be increased by no more than 10mg approximately every 5 days based on the patient's symptoms of opioid withdrawal or sedation.

→ **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.

→ **MAJOR REVISION – Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with methadone in the treatment of OUD.**

- However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay treatment with methadone, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **For patients who previously received methadone for the treatment of OUD, methadone should be reinstituted immediately if relapse occurs or if an assessment determines that the risk of relapse is high (unless contraindicated).**

- Re-initiation of methadone should follow the recommendations above regarding initial dose and titration.

→ **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.**

→ **Strategies directed at relapse prevention are an important part of addiction treatment and should be included in any plan of care for a patient receiving OUD treatment or ongoing monitoring of the status of their disorder.**

→ **Transitioning from methadone to another medication for the treatment of OUD may be appropriate if the patient experiences dangerous or intolerable side effects or is not successful in attaining or maintaining treatment goals through the use of methadone.**

→ **Patients transitioning from methadone to buprenorphine in the treatment of OUD should ideally be on low doses of methadone before making the transition.**

- Patients on low doses of methadone (30–40mg per day or less) generally tolerate transition to buprenorphine with minimal discomfort, whereas patients on higher doses of methadone may experience significant discomfort in transitioning medications.

↗ Treatment

➔ **Patients transitioning from methadone to 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.

➔ **There is no recommended time limit for pharmacological treatment with methadone.**

- Patients who discontinue methadone treatment should be made aware of the risks associated with opioid overdose, and especially the increased risk of overdose death if they return to illicit opioid use.
- Treatment alternatives including buprenorphine (see below) and naltrexone (see p. 12), as well as opioid overdose prevention with naloxone, should be discussed with any patient choosing to discontinue treatment.

Buprenorphine

➔ **NEW** – Buprenorphine is a recommended treatment for patients with OUD who are able to give informed consent and have no specific contraindication for this treatment.

➔ **For patients who are currently opioid dependent, buprenorphine should not be initiated until there are objective signs of opioid withdrawal to reduce the risk of precipitated withdrawal.**

➔ **MAJOR REVISION** – Once objective signs of withdrawal are observed, initiation of buprenorphine should start with a dose of 2–4mg. Dosages may be increased in increments of 2–8mg.

➔ **MAJOR REVISION** – The setting for initiation of buprenorphine should be carefully considered.

- Both office-based and home-based initiation are considered safe and effective when starting buprenorphine treatment.
- Clinical judgement should be used to determine the most appropriate setting for a given patient and may include consideration of the patient's past experience with buprenorphine and assessment of their ability to manage initiation at home.
- Clinicians should observe patients in their offices during induction. However, home buprenorphine induction may be considered.

➔ **MAJOR REVISION** – Following initiation, buprenorphine dose should be titrated to alleviate symptoms.

- To be effective, buprenorphine dose should be sufficient to enable patients to discontinue illicit opioid use.
- Evidence suggests that 16mg per day or more may be more effective than lower doses.
- There is limited evidence regarding the relative efficacy of doses higher than 24mg per day, and the use of higher doses may increase the risk of diversion.

→ **NEW** – The FDA recently approved several new buprenorphine formulations for treatment of OUD.

- Since data regarding the effectiveness of these products are currently limited, clinicians should use these products as indicated and be mindful of emerging evidence as it becomes available.

→ **MAJOR REVISION** – Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with buprenorphine in the treatment of OUD.

- However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay buprenorphine treatment, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

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

- Recommended strategies may include frequent office visits (e.g., weekly in early treatment); drug testing, including testing for buprenorphine and metabolites; and recall visits for medication counts.
- Refer to ASAM's *Sample Diversion Control Policy*³ for additional strategies to reduce the risk for diversion.

→ **Drug testing should be used to monitor patients for adherence to buprenorphine and use of illicit and controlled substances.**

- For additional guidance see *The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine*.⁴

→ **Patients should be seen frequently at the beginning of treatment until they are determined to be stable.**

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

→ **When considering a transition from buprenorphine to methadone, there is no required time delay because the transition to a full mu-opioid agonist from a partial agonist does not typically result in an adverse reaction.**

→ **There is no recommended time limit for pharmacological treatment with buprenorphine.**

- Patients who discontinue buprenorphine treatment should be made aware of the risks associated with opioid overdose, and especially the increased risk of death if they return to illicit opioid use.
- Treatment alternatives including methadone (see p. 8–9) and naltrexone (see p. 12), as well as opioid overdose prevention with naloxone, should be discussed with any patient choosing to discontinue treatment.

↗ Treatment

→ **Buprenorphine taper and discontinuation is a slow process; 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.

Naltrexone

→ **MAJOR REVISION** – Extended-release injectable naltrexone is a recommended treatment for preventing relapse to OUD in patients who are no longer physically dependent on opioids, able to give informed consent, and have no contraindications to this treatment.

→ **MAJOR REVISION** – Extended-release injectable naltrexone should generally be administered every 4 weeks by deep IM injection in the gluteal muscle at the set dosage of 380mg per injection.

→ **MAJOR REVISION** – Oral naltrexone is **NOT** recommended except under limited circumstances (see p. 7 for more details).

→ **Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with extended-release naltrexone.**

- A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay naltrexone treatment, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **There is no recommended length of treatment with 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.

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

- Transitioning from an antagonist such as naltrexone to a full agonist (methadone) or a partial agonist (buprenorphine) is generally less complicated than transitioning 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 transitioned from naltrexone to buprenorphine or methadone will not have physical dependence on opioids, and thus the initial doses of methadone or buprenorphine should be low.
- Patients should not be transitioned until a significant amount of the naltrexone is no longer in their system, about 1 day for oral naltrexone or 28 days for extended-release injectable naltrexone.

→ **Patients who discontinue naltrexone treatment should be made aware of the increased risks associated with opioid overdose, and especially the increased risk of overdose death, if they return to illicit opioid use.**

- Treatment alternatives including methadone (see p. 8–9) and buprenorphine (see p. 10–11), as well as overdose prevention with naloxone (see p. 33), should be discussed with any patient choosing to discontinue treatment.

Psychosocial Treatment in Conjunction with Medications for the Treatment of OUD

→ **MAJOR REVISION** – Patients’ psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment, based on their individual needs, in conjunction with any pharmacotherapy for the treatment of, or prevention of relapse to, OUD.

- However, a patient’s decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of OUD, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **Treatment planning should include collaboration with qualified behavioral healthcare 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.**

Table 4. Medication Formulations

Brand Name	Generic Name	Treatment of	Strengths / Formulations
Generic	Methadone	Opioid withdrawal and OUD	Tablet: 5mg, 10mg Dispersible tablet: 40mg Oral solution: 5mg/5mL, 10mg/5mL Oral concentrate solution: 10mg/mL
Generic	Buprenorphine (monoprodukt)		Sublingual tablet: 2mg, 8mg
Generic	Buprenorphine and naloxone		Sublingual tablet (bup/nal): 2mg/0.5mg, 8mg/2mg
Zubsolv			Sublingual tablet (bup/nal): 0.7mg/0.18mg, 1.4mg/0.36mg, 2.9mg/0.71mg, 5.7mg/1.4mg, 8.6mg/2.1mg, 11.4mg/2.9mg
Bunavail			Buccal film (bup/nal): 2.1mg/0.3mg, 4.2mg/0.7mg, 6.3mg/1mg
Suboxone			Sublingual film (or bucal) (bup/nal): 2mg/0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg
Cassipa			Sublingual film (bup/nal): 16mg/4mg

Common Dosing		Advantages	Disadvantages
	Range: 60mg–120mg (daily)	Strongest retention in treatment; improved social functioning associated with reductions in criminal activity, recidivism, and infectious disease acquisition and transmission	More frequent clinic visits; only SAMHSA-certified OTPs may provide methadone for addiction treatment; higher risk for respiratory depression due to long half-life and stacking effect (requires more monitoring)
	Range: 4mg–24mg (daily)	Ceiling effects on respiratory depression; more rapid induction to steady state dose; less potential for euphoria (compared to methadone); considered safe for office-based treatment; improved social functioning; associated with reductions in criminal activity, recidivism, and infectious disease acquisition and transmission	Requires X-Waiver to prescribe; risk for overdose when combined with alcohol, benzodiazepines, or other sedatives
	Range: 4mg/1mg to 24mg/6mg (daily)		
	Range: 2.9mg/0.71mg to 17.2mg/4.2mg (daily)		
	Range: 2.1mg/0.3mg to 12.6mg/2.1mg (daily)		
	Range: 4mg/1mg to 24mg/6mg (daily)		
	(daily)		

Table 4. Medication Formulations (*cont'd*)

Brand Name	Generic Name	Treatment of	Strengths / Formulations
<i>Sublocade</i>	Buprenorphine extended-release	Moderate to severe OUD in patients who have initiated treatment with transmucosal buprenorphine followed by dose adjustment for a minimum of 7 days	Subcutaneous injection: 100mg, 300mg
<i>Brixadi</i>		Moderate to severe OUD in patients who have initiated treatment with a single dose of transmucosal buprenorphine or who are already being treated with buprenorphine	Subcutaneous injection: Weekly: 8mg, 16mg, 24mg, 32mg Monthly: 64mg, 96mg, 128mg
<i>Probuphine</i>	Buprenorphine hydrochloride	Treatment of OUD in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine	Implants: 80mg/implant
<i>Revia</i>	Oral naltrexone ^a	Prevention of relapse to OUD following complete opioid withdrawal	Oral tablet: 50mg
<i>Vivitrol</i>	Extended-release naltrexone		Intramuscular injection: 380mg

^a Oral naltrexone is **NOT** recommended except under very limited circumstances (see Naltrexone section)

Common Dosing		Advantages	Disadvantages
	Range: 100mg to 300mg (monthly)	Ceiling effects on respiratory depression; more rapid induction to steady state dose; less potential for euphoria (compared to methadone); considered safe for office-based treatment; improved social functioning; associated with reductions in criminal activity, recidivism, and infectious disease acquisition and transmission	Requires X-Waiver to prescribe; risk for overdose when combined with alcohol, benzodiazepines, or other sedatives
	Range: 8mg–32mg (weekly) or Range 64–128mg (monthly)		
	4 implants for 6 months of treatment		
	Range: 25mg–50mg (daily)	No risk for misuse or physiological dependence; no special regulatory requirements; improved social functioning; associated with reductions in criminal activity and recidivism; and infectious disease acquisition and transmission	Patients must be fully withdrawn from opioids before beginning treatment, lower retention in treatment, high rates of medication non-adherence, has not been demonstrated to reduce mortality (and may increase mortality risk after medication discontinuation)
	Range: 380mg (monthly)		

Table 5. Bioequivalence Information and Charts^a

Suboxone or generic equivalent (sublingual tablet)	Suboxone or generic equivalent (sublingual film)	Zubsolv (sublingual tablet)	Bunavail (buccal film)
2mg bup/ 0.5mg nal tablet	2mg bup/ 0.5mg nal film	One 1.4mg bup/ 0.36mg nal tablet	
4mg bup/1mg nal (Taken as: two 2mg bup/0.5mg nal tablets)	4mg bup/ 1mg nal film	One 2.9mg bup/ 0.71mg nal tablet	One 2.1mg bup/ 0.3mg nal film
8mg bup/2mg nal tablet	8mg bup/ 2mg nal film	One 5.7mg bup/ 1.4mg nal tablet	One 4.2mg bup/ 0.7mg nal film
12mg bup/3mg nal (Taken as: One and a half 8mg bup/2mg nal tablets or one 8mg bup/2mg nal tablets plus two 2mg bup/2mg nal tablets)	12mg bup/ 3mg nal film	One 8.6mg bup/ 2.1mg nal tablet	One 6.3mg bup/ 1mg nal film
16mg bup/4mg nal (Taken as: Two 8mg bup/2mg nal tablets)	16mg bup/4mg nal (Taken as: Two 8mg bup/2mg nal films)	One 11.4mg bup/ 2.9mg nal tablet	Two 4.2mg bup/ 0.7mg nal films
24mg bup/6mg nal (Taken as: three 8mg bup/3mg nal tablets)	24mg bup/6mg nal (Taken as: Two 12mg bup/3mg nal films)	17.2mg bup/4.1mg nal (Taken as: Two 8.6mg bup/2.1mg nal tablets)	Two 6.3mg bup/ 1mg nal films

^a Table content was derived from FDA labels. Labels and label updates can be accessed at <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>

^b The recommended dose of SUBLOCADE following induction and dose adjustment with transmuscosal buprenorphine is 300mg monthly for the first two months followed by a maintenance dose of 100mg monthly. The maintenance dose may be increased to 300mg monthly for patients who tolerate the 100mg dose but do not demonstrate a satisfactory clinical response, as evidenced by self-reported illicit opioid use or urine drug screens positive for illicit opioid use.

^c In a pharmacokinetic study, the 16mg/4mg dose of CASSIPA showed comparable relative bioavailability of buprenorphine and naloxone compared with the same dose of buprenorphine/naloxone administered sublingually, as two 8mg/2mg sublingual films.

	Cassipa (sublingual film)	Generic equiv. of <i>Subutex</i> (sublingual tablet)	<i>Sublocade</i>^b (subcutaneous injection)	<i>Brixadi</i> (IM or deep SC injection)
		2mg bup tablet		
		Two 2mg bup tablets		
		One 8mg bup tablet	100mg	16mg SC bup weekly injection; or 64mg SC bup monthly injection
		12mg bup (Taken as: One and a half 8mg bup tablets or one 8mg bup tablets plus two 2mg bup tablets)		
	16mg bup/4mg nal ^c	16mg bup (Taken as: Two 8mg bup tablets)		24mg SC bup weekly injection; or 96mg SC bup monthly injection
		24mg bup (Taken as: Three 8mg bup tablets)	300mg	32mg SC bup weekly injection; or 128mg SC bup monthly injection

Figure 1. Evaluation and Treatment

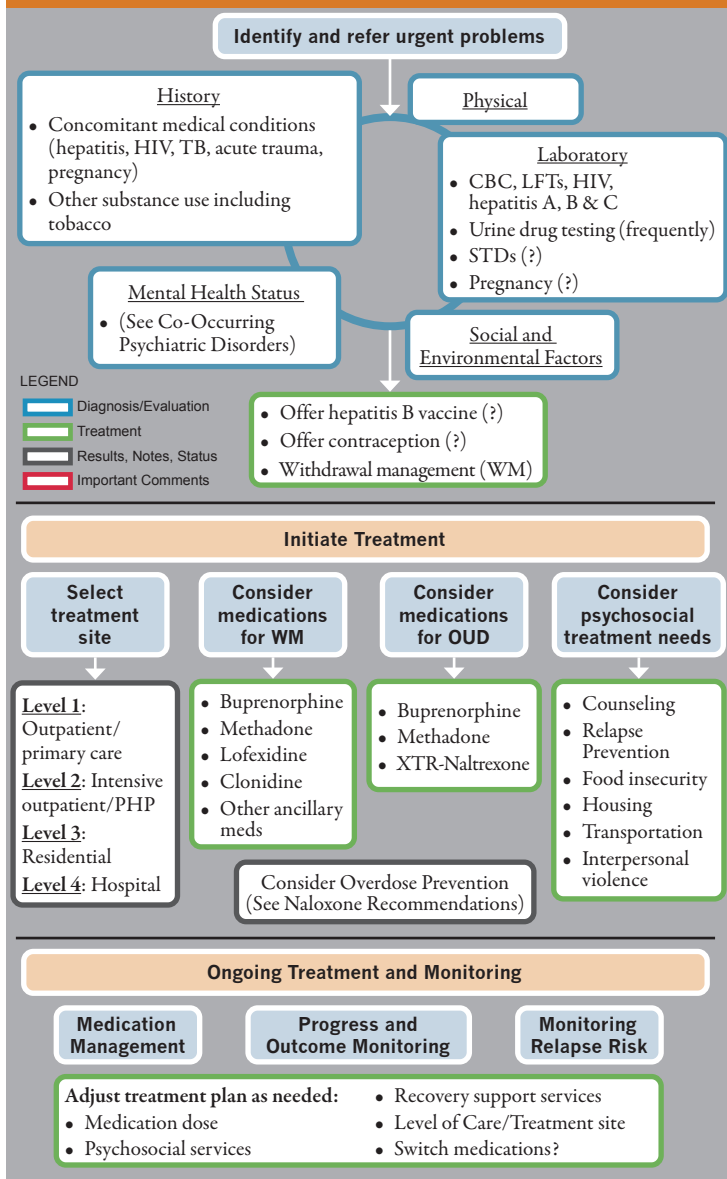
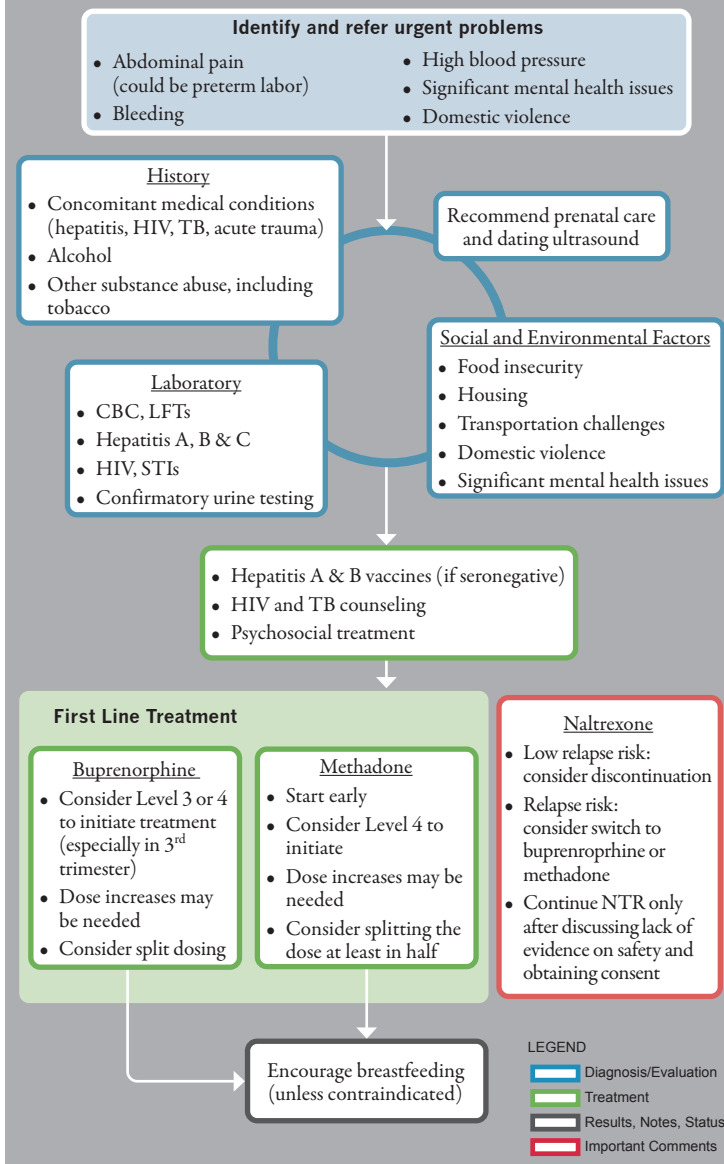


Figure 2. Pregnancy



↗ Special Populations

Pregnant Women

→ **NEW** – 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.

→ Treatment with methadone or buprenorphine is recommended and should be initiated as early as possible during pregnancy.

See the buprenorphine section for guidance on induction.

→ **MAJOR REVISION** – Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine rather than withdrawal management or psychosocial treatment alone.

→ **MAJOR REVISION** – A medical examination and psychosocial assessment are recommended when evaluating pregnant women for OUD.

- However, completion of all assessments should not delay or preclude initiating pharmacotherapy for OUD.
- If not completed before initiating treatment, assessments should be completed as soon as possible thereafter.

→ **Obstetricians, gynecologists, and other healthcare providers that care for pregnant women 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.

→ **MAJOR REVISION** – The psychosocial needs of pregnant women being treated for OUD should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs.

- A woman's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment, with appropriate medication management, during pregnancy.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **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.
- TB screening and testing, if appropriate.
- Hepatitis A and B vaccination is recommended for those whose hepatitis serology is negative.

→ **Drug and alcohol testing should be used to monitor patients for adherence to medication and for use of illicit and controlled substances.**

- This should be done with informed consent from the mother, realizing that there may be adverse legal and social consequences for substance use.
- State laws differ on reporting substance use during pregnancy. Laws that penalize women for substance use and for obtaining treatment serve to prevent women from obtaining prenatal care and worsen outcomes.
- For further clarity see *The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine*⁴ guidance document.

→ **Care for pregnant women with OUD should be comanaged by a clinician experienced in obstetrical care and a clinician experienced in the treatment of OUD.**

→ **Hospitalization during initiation of methadone or buprenorphine may be an option for those with co-morbid medical or psychosocial issues due to the potential for adverse events, especially in the third trimester.**

→ **MAJOR REVISION** – Methadone should be initiated at a dose range of 10–30mg. Incremental doses of 5–10mg is recommended every 3–6 hours, as needed, to treat withdrawal symptoms, to a maximum first day dose of 30–40mg.

→ **MAJOR REVISION** – After initiation, clinicians should increase the methadone dose by no more than 10mg approximately every 5 days. The goal is to maintain the lowest dose that controls withdrawal symptoms and minimizes the desire to use additional opioids.

→ **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 and/or split doses may be needed as pregnancy progresses.
- At least 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 OTP.
- After childbirth, doses will need to be adjusted (typically reduced) based on changes in weight and metabolism.

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

- A decision to remain on naltrexone during pregnancy should be carefully considered by the patient and her clinician and should include a discussion on the insufficiency of research on risks (if any) of continued use of naltrexone.
- If the patient chooses to discontinue treatment with naltrexone and is at risk for relapse, treatment with methadone or buprenorphine should be considered.

↗ Special Populations

- Use of naloxone challenge to test for opioid dependence and risk of precipitated withdrawal is **NOT** recommended for pregnant women with OUD.
- Unless otherwise contraindicated, mothers receiving methadone or buprenorphine for treatment of OUDs should be encouraged to breastfeed. And policies allowing for rooming in should be encouraged for hospitals taking care of infants at risk for neonatal withdrawal.

Individuals with Pain

- For all patients with pain, it is important that the correct diagnosis is made and that pain is addressed.
 - Alternative treatments including non-opioid medications with pain modulating properties, behavioral approaches, physical therapy, and procedural approaches (e.g., regional anesthesia) should be considered before prescribing opioid medications for pain.
- If pharmacological treatment is considered, non-opioid analgesics, such as acetaminophen and NSAIDs, and non-opioid medications with pain modulating properties should be tried first.
- For patients with pain who have an active OUD but are not in treatment, methadone or buprenorphine should be considered.
 - The patient's OUD and pain should be stabilized and managed concurrently.
- **MAJOR REVISION** – For patients taking methadone or buprenorphine for the treatment of OUD, temporarily increasing the dose or dosing frequency (i.e., split dosing to maximize the analgesic properties of these medications) may be effective for managing pain. (Titration of methadone should follow the guidance on pages 8–9 of this pocket guide.)
- **MAJOR REVISION** – For patients taking methadone for the treatment of OUD who have acute pain refractory to other treatments and require additional opioid-based analgesia, adding a short acting full agonist opioid to their regular dose of methadone can be considered to manage moderate to severe acute pain.
 - The dose of additional full agonist opioid analgesic prescribed is anticipated to be higher than the typical dose necessary to achieve adequate analgesia in opioid-naïve individuals.
- **NEW** – Patients receiving buprenorphine for OUD who have moderate to severe acute pain refractory to other treatments and require additional opioid-based analgesia may benefit from the addition of as-needed doses of buprenorphine.

→ **MAJOR REVISION** – The addition of a short-acting full agonist opioid to the patient's regular dose of buprenorphine can be effective for the management of severe acute pain in supervised settings, such as during hospitalization.

- The dose of additional full agonist opioid analgesic prescribed is anticipated to be higher than the typical dose necessary to achieve adequate analgesia in opioid-naïve individuals.
- Because of a lack of evidence, the committee was unable to come to consensus on whether this adjunct treatment can be safely prescribed in ambulatory care settings.

→ **MAJOR REVISION** – Discontinuation of methadone or buprenorphine before surgery is **NOT** required.

- Higher-potency intravenous full agonist opioids can be used perioperatively for analgesia.

→ **Decisions related to discontinuing or adjusting the dose of buprenorphine prior to a planned surgery should be made on an individual basis through consultation between the surgical and anesthesia teams and the addiction treatment provider when possible.**

→ **MAJOR REVISION** – If it is decided that buprenorphine or methadone should be discontinued before a planned surgery, this may occur the day before or the day of surgery, based on surgical and anesthesia team recommendations.

- Higher-potency intravenous full agonist opioids can be used perioperatively for analgesia.
- Methadone or buprenorphine can be resumed post-operatively when the need for full opioid agonist analgesia has resolved, with additional considerations for post-operative pain management as described for acute pain above.
- The initial dose and titration should typically be determined by the prescriber.
- In general, pre-surgery daily doses of these medications can be resumed if they were withheld for less than 2–3 days.

→ **Patients on naltrexone may not respond to opioid analgesics in the usual manner. Therefore, it is recommended that mild pain be treated with non-opioid analgesics, and moderate to severe pain be treated with higher potency NSAIDs (e.g., ketorolac) on a short-term basis.**

→ **Oral naltrexone should be discontinued 72 hours before surgery and extended-release injectable naltrexone should be discontinued 30 days before an anticipated surgery. (Reinitiation of naltrexone should follow the guidance on p. 12 of this pocket guide.)**

→ **NEW** – Naltrexone's blockade of the mu opioid receptor can often be overcome when necessary with high potency full agonist opioids.

- In these instances, patients should be closely monitored in an emergency department or hospital setting.

↗ Special Populations

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.**
 - Federal laws and FDA approvals should be considered when recommending pharmacotherapy for adolescent patients. Psychosocial treatment is recommended in the treatment of adolescents with OUD.
- **MAJOR REVISION – Psychosocial treatment is recommended in the treatment of adolescents with OUD.**
 - The risk benefit balance of pharmacological treatment without concurrent psychosocial treatment should be carefully considered and discussed with the patient and her or his parent or guardian as appropriate.
 - A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of OUD, with appropriate medication management.
 - Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.
- **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
 - 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 adherence for OUD and psychiatric disorder medications monitored more closely.

→ **Assessment for psychiatric disorder should occur at the onset of agonist or antagonist treatment.**

- However, completion of all assessments should not delay or preclude initiating pharmacotherapy for OUD.
- If not completed before initiating treatment, assessments should be completed as soon as possible thereafter.
- Reassessment using a detailed mental status examination should occur after stabilization with methadone, buprenorphine, or naltrexone.

→ **MAJOR REVISION – Pharmacotherapy in conjunction with psychosocial treatment should be offered to patients with OUD and a co-occurring psychiatric disorder.**

- A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of OUD, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **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

→ **NEW – All FDA-approved medications for the treatment of OUD should be available to individuals receiving healthcare within the criminal justice system.**

- The treatment plan, including choice of medication, should be based on the patient's individual clinical needs.

→ **Continuation of treatment after release results in a substantial reduction in all-cause and overdose mortality.**

- Treatment should be individualized, and patients should receive complete information to make informed decisions in consultation with a medical and treatment team.

→ **NEW – Individuals entering the criminal justice system should **NOT** be subject to forced opioid withdrawal.**

- Patients being treated for OUD at the time of entrance into the criminal justice system should continue their treatment.
- Patients with OUD who are not in treatment should be assessed and offered individualized pharmacotherapy and psychosocial treatment as appropriate.

↗ Special Populations

→ **MAJOR REVISION** – Initiation or maintenance of pharmacotherapy for the treatment of OUD is recommended for individuals within the criminal justice system (including both jails and prisons).

- Criminal justice staff should coordinate care and access to pharmacotherapy to avoid interruption in treatment.
- Patients should not be forced to transition from agonist (methadone or buprenorphine) to antagonist (naltrexone) treatment.

→ **MAJOR REVISION** – Individuals in the criminal justice system who have OUD or who are experiencing opioid withdrawal should be offered a combination of pharmacotherapy and psychosocial treatment (based on an assessment of their individual psychosocial needs).

- A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of OUD, with appropriate medication management.
- Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

→ **NEW** – If an OTP is not accessible, providers may need to transition individuals from methadone to buprenorphine.

- Effectively transitioning from methadone to buprenorphine can be challenging but can be achieved safely if managed by a provider experienced in the procedure.

→ **MAJOR REVISION** – Risk for relapse and overdose is particularly high in the weeks immediately following release from prison and jails.

- Patients being treated for OUD while in prison or jail should be stabilized on pharmacotherapy (methadone, buprenorphine or naltrexone) and continue in treatment after their release.
- Patient care on reentry to the community should be individualized and coordinated with treatment providers in the community.

→ **NEW** – Naloxone kits should be available within correctional facilities. Individuals with OUD should receive a naloxone kit prior to release, and individuals and families should be educated in how to administer naloxone.

Naloxone for the Treatment of Opioid Overdose

→ **MAJOR REVISION** – Naloxone should be given in case of opioid overdose.

→ Naloxone may be administered to pregnant women in cases of overdose to save the mother's life.

→ Patients who are being treated for OUD (as well as people with a history of OUD leaving incarceration) and their family members/significant others should be given naloxone kits or 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 carry and administer naloxone.

Abbreviations

AIDS, Acquired Immunodeficiency Syndrome; **ASAM**, American Society of Addiction Medicine; **BP**, blood pressure; **DSM-5**, Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; **FDA**, Food and Drug Administration; **HHS**, U.S. Department of Health & Human Services; **HIV**, Human Immunodeficiency Virus; **mL**, milliliter; **mg**, milligram; **NSAIDs**, Non-Steroidal Anti-Inflammatory Drugs; **OBOT**, Office-Based Opioid Treatment; **OTP**, Opioid treatment program; **ODU**, Opioid use disorder; **STI**, Sexually transmitted infection; **TB**, Tuberculosis; **UROD**, Ultra-Rapid Opioid Detoxification; **WM**, withdrawal management; **XR**, extended release

Resources

- ¹ The ASAM Criteria [<https://www.asam.org/asam-criteria>]
- ² The ASAM Standards
[<https://www.asam.org/resources/quality/standards-and-performance-measures>]
- ³ The ASAM Sample Diversion Control Policy
[<https://www.asam.org/docs/default-source/advocacy/sample-diversion-policy.pdf>]
- ⁴ The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine
[<https://www.asam.org/Quality-Science/quality/drug-testing>]
- ⁵ The Prescription Drug Monitoring Program
[<https://www.cdc.gov/drugoverdose/pdmp/providers.html>]
- ⁶ ASAM.GuidelineCentral.com for Calculators

Guideline Committee Members

Chinazo Cunningham, MD, MS, FASAM; Mark J. Edlund, MD, PhD; Marc Fishman, MD, DFASAM; Adam J. Gordon, MD, MPH, FACP, DFASAM; Hendrée E. Jones, PhD
Kyle Kampman, MD, FASAM, Chair; Daniel Langleben, MD; Marjorie Meyer, MD
Sandra Springer, MD, FASAM; George Woody, MD; Tricia E. Wright, MD, MS, FACOG, DFASAM; Stephen Wyatt, DO, FAOAAM, FASAM, Co-Chair

Source

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Disclaimer

This pocket guide 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 pocket guide 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. Neither IGC, the medical associations, nor the authors endorse any product or service associated with the distributor of this clinical reference tool.



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106 Commerce Street, Suite 105
Lake Mary, FL 32746
TEL: 407.878.7606 • FAX: 407.878.7611
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