







Medications to Treat Opioid Use Disorder (OUD)








Methadone, **buprenorphine**, and **naltrexone** are all approved by the U.S. Food and Drug Administration for the treatment of OUD. These medications reduce opioid cravings and create opioid blockade, thus preventing reward or euphoria from any opioids taken concurrently.


Which medication to recommend depends on many factors, including:

- Patient preference
- Practical access to care (e.g., availability of clinic or prescriber)
- Prior treatment experience (successes and challenges)
- Clinician’s assessment of the risks and benefits of each medication for the individual patient (e.g., medical comorbidities, overdose risk)

Here is an overview of the three medications:

	Methadone	Buprenorphine	Naltrexone
Mechanism of action	Full opioid agonist	Partial opioid agonist	Opioid antagonist
Classification	Schedule II opioid	Schedule III opioid	Nonopioid
Formulations and dosing frequency	 Liquid (most common), diskette, or tablet once daily, dispensed by a federally licensed opioid treatment program (OTP) with observed dosing, at least initially	 Transmucosal formulations (sublingual tablet or film; buccal film) once or twice daily Extended-release subcutaneous injection weekly or monthly 	 Pill once daily Extended-release intramuscular injection (with customized needle) monthly
Can this medication be prescribed legally in outpatient settings for OUD treatment?	<p>✗ No</p> <p>it must be ordered and dispensed by a federally licensed OTP in a separate system not involving primary care or pharmacies.</p>	<p>✓ Yes</p> <p>by any qualified clinician.</p> <p><i>Tablets and films</i> can be prescribed for up to one month’s supply at a time, with refills, and can be picked up at the pharmacy and self-administered.</p> <p><i>Injections</i> are available only through specialty pharmacies that send the medication to the prescriber’s office for administration.</p>	<p>✓ Yes</p> <p>by any qualified clinician.</p> <p><i>Pills</i> can be prescribed with refills and can be picked up at the pharmacy and self-administered.</p> <p><i>Injections</i> are available only through specialty pharmacies that send the medication to the prescriber’s office for administration.</p>

<p>Can it be used on the <i>inpatient</i> service or in the <i>emergency department</i>?</p>	<p>✓ Yes</p> <p>if it is on the hospital formulary, it can be ordered by any clinician with opioid-prescribing privileges and administered in the hospital.</p>	<p>✓ Yes</p> <p>if it is on the hospital formulary, it can be ordered by any clinician with opioid-prescribing privileges and administered in the hospital.</p>	<p>✓ Yes</p> <p>if it is on the hospital formulary, it can be ordered and administered in the hospital.</p>
<p>Practical considerations for patients</p>	<p>✓ Covered by Medicaid in most states</p> <p>Highly structured treatment with potential for onsite comprehensive addiction care</p> <p>Potential stigma and lack of privacy with OTP </p> <p>Patients may be eligible for take-home doses later in the treatment course depending on federal, state, and OTP regulations</p>	<p>✓ Covered by Medicaid in most states</p> <p></p>	<p>✓ Covered by Medicaid in most states</p> <p>Good for patients who do not want opioid agonist therapy</p> <p>Medical alert bracelet required, as patients who experience severe pain while taking naltrexone will not respond to usual doses of opioids</p> <p>Can treat OUD and alcohol use disorder simultaneously, as it is FDA-approved for the treatment of both </p>
<p>Ease of induction</p>	<p> Induction performed in OTPs over a period of months; relatively easy given absence of precipitated withdrawal first</p>	<p> More difficult induction than methadone, with risk of precipitated withdrawal</p>	<p> Very difficult induction, as the patient must be fully withdrawn from opioids for 7 to 10 days to prevent precipitated withdrawal</p>
<p>Evidence of benefit for OUD treatment</p>	<p>More than 50 years of use in OUD treatment</p> <p>Shown to reduce opioid use, improve treatment retention, decrease HIV and viral hepatitis seroconversion, and reduce all-cause and opioid-related mortality</p>	<p>Noninferior to methadone, although methadone may be associated with better treatment retention</p>	<p><i>When taken</i>, highly effective in reducing opioid use, but poor treatment retention is a problem</p> <p>Insufficient evidence of a reduction in all-cause or opioid-related mortality</p>
<p>Risk of overdose</p>	<p> Significant risk of severe respiratory depression (similar to other full opioid agonists); thus, initial dosing is low, and titration is slow</p> <p>Due to its long and variable half-life, methadone can accumulate in the body and increase the risk of overdose</p>	<p>Ceiling effect with less risk of respiratory depression and overdose than methadone</p>	<p>No risk of overdose by the drug itself, although if relapse occurs, the risk of overdose will be increased because of loss of tolerance to opioids</p>

Risk of misuse or diversion	Limited risk with observed dosing, although some patients may receive doses to take at home, which then increases the risk	 Some risk of misuse, but reduced with transmucosal formulations, which are typically prescribed in a combination product with naloxone, which acts as an opioid antagonist if injected High risk of diversion, mostly to individuals self-medicating to treat acute withdrawal or OUD	No risk
Other safety issues	Can prolong the corrected QT (QTc) interval and cause arrhythmias such as torsades de pointes	Can prolong the QTc interval, but lower risk than methadone	Not suitable for patients with severe liver disease

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