



# Identifying and Managing Opioid Use Disorder (OUD)

## Quick Reference Guide

**VA**



**U.S. Department of Veterans Affairs**

Veterans Health Administration  
*PBM Academic Detailing Service*

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## Changing the conversation<sup>1,2</sup>

	 <b>Instead of this:</b>	 <b>Consider saying this:</b>
<b>Use person-first language</b>	Mr. X is an <b>opioid addict</b> .	Mr. X is <b>diagnosed with opioid use disorder</b> .
	That Veteran has a <b>drug problem</b> .	That Veteran has <b>problems resulting from use of opioids</b> .
<b>Avoid judgmental terminology</b>	Your urine drug test was <b>clean</b> .	Your urine drug test was <b>negative</b> for illicit substances.
	Your urine drug test was <b>dirty</b> .	Your urine drug test result was <b>positive</b> for (insert drug/substance name).
	You have to <b>stop your habit</b> of using opioids.	I would like to offer you <b>treatment for opioid use disorder</b> .
<b>Be supportive</b>	There is <b>no cure</b> for your disease.	We have <b>very effective treatments</b> for opioid use disorder. <b>Recovery</b> is achievable.
	I can't help if you <b>choose</b> to keep using opioids.	We understand that <b>no one chooses to develop opioid use disorder</b> . It is a <b>medical disorder</b> that can be managed with treatment.

## Opioid withdrawal<sup>3</sup>

- Patients who regularly consume opioids (illicitly or as prescribed) will develop tolerance and withdrawal.
  - Opioid tolerance/withdrawal symptoms *in the absence of any other symptoms* do not indicate OUD (“addiction”), however they are signs of increased risk; please refer to ICD-10 features of opioid dependence or DSM-5 full criteria for OUD.
- The Clinical Opiate Withdrawal Scale (COWS) can be used to assess opioid withdrawal symptoms.

## Recognizing common signs of opioid intoxication and withdrawal\*<sup>3-7</sup>

### Common signs of intoxication

- Drooping eyelids
- Constricted pupils
- Decreased respiratory rate
- Scratching (due to histamine release)
- Drowsy but arousable
- Impaired memory or concentration
- Sleeping intermittently (“nodding off”)
- Slurred speech

### Common signs/symptoms of withdrawal\*\*

#### Objective (observable)

- Vomiting
- Elevated pulse
- Yawning
- Lacrimation or rhinorrhea
- Pupillary dilation
- Piloerection

#### Subjective (reported)

- GI distress/nausea
- Cravings
- Restlessness
- Insomnia
- Anxiety or irritability
- Dysphoria
- Muscle, bone, or joint aches/pains

GI = gastrointestinal. \*Signs/symptoms may vary based on various factors. \*\*Signs/symptoms of withdrawal cause clinically significant distress or impairment in social, occupational, or other important areas of functioning and are not attributable to another condition, disorder, or non-opioid substance. **Note: DSM-5 criteria for opioid withdrawal** require the presence of either cessation of (or reduction in) opioid use that has been heavy and prolonged (e.g., several weeks or longer) or administration of an opioid antagonist after a period of opioid use and three or more signs/symptoms developing within minutes to several days.

## Objective physical signs sometimes present in patients with substance use disorder<sup>3,5</sup>

System	Findings
<b>Dermatologic</b>	Abscesses, rashes, cellulitis, thrombosed veins, jaundice, spider angioma, palmer erythema, scars, track marks, pock marks from subcutaneous injection
<b>Ear, nose, throat, and eyes</b>	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
<b>Mouth</b>	Poor dentition, gum disease, abscesses
<b>Cardiovascular</b>	Murmurs, arrhythmias
<b>Respiratory</b>	Asthma, dyspnea, rales, chronic cough, hematemesis
<b>Musculoskeletal and extremities</b>	Pitting edema, broken bones, traumatic amputations, burns on fingers, gynecomastia
<b>Gastrointestinal</b>	Hepatomegaly, hernias

## Example components of a full assessment for patients with OUD<sup>5,6</sup>

System	Findings
<b>Medical history</b>	Medical effects of substance use (e.g., endocarditis, soft tissue infection, hepatitis B or C, HIV infection) that may need treatment, chronic pain issues, medical issues that may contraindicate or alter approaches for OUD pharmacotherapy
<b>Mental health history</b>	Co-morbid mental illness and current symptoms
<b>Substance use history</b>	Age at first use, routes of ingestion, history of withdrawal and overdose, drugs used, frequency, recency, intensity
<b>Substance use treatment history</b>	Treatment settings, use of support groups, previous responses to treatment
<b>Physical examination</b>	Signs of intoxication (e.g., head nodding, constricted pupils), withdrawal (e.g., restlessness, sweating, runny nose, dilated pupils, piloerection) and physical signs of substance use disorder
<b>Social history</b>	Transportation and child care needs, adequate/stable housing, employment status and quality of work environment, relationships, safety of home environment (including intimate partner violence), sexual orientation, criminal justice involvement (need for communication with parole/probation)

*Continued >*

## Example components of a full assessment for patients with OUD<sup>5,6</sup>

System	Findings
<b>Family history</b>	Substance use histories of parents, siblings, partners, and children
<b>Prescription drug monitoring program (PDMP)</b>	Check the PDMP prior to initiating therapy with controlled substances and at least annually (or per state requirements if more frequent) thereafter (Please see VHA Directive 1306 and your state laws for more detailed information). <b>Note:</b> Methadone from an Opioid Treatment Program (OTP) is not typically reported to the PDMP, but buprenorphine is reported.
<b>Laboratory tests</b>	Complete blood count, liver enzyme tests, drug screening test
<b>Infectious disease tests</b>	Tuberculosis, hepatitis B and C, HIV
<b>Pregnancy test</b>	For all women of childbearing potential; <b>Note:</b> Heavy drug use can cause amenorrhea; women may incorrectly assume that they are in menopause but experience a return to menstrual cycles/fertility once they stop using. Women should be given this information and counseled on contraception.

VHA = Veterans Health Administration

## Medical management\*<sup>8</sup>

### MONITOR

- Self-reported use, consequences, adherence, treatment response, adverse effects, and urine drug test
- Prescription drug monitoring program (PDMP)
- Consider using a measurement-based assessment tool (e.g., BAM-R)

### EDUCATE

Educate about OUD consequences and treatment options

### ENCOURAGE

- To abstain from non-prescribed opioids and other addictive substances
- To adhere to prescribed medications
- To engage in formal and/or informal treatment supports as needed
- To make lifestyle changes that support recovery

\*Session structure varies according to the patient's substance use status and treatment adherence.

BAM-R = brief addiction monitor-revised

## Expected results of urine drug tests<sup>6,9-11</sup>

Urine drug testing can generally only indicate whether an individual has used a substance one or more times within the window of detection. It cannot reveal whether there have been changes in amount, frequency, route of use, etc., nor whether these changes have had an impact on other areas of life. Therefore, it is important to incorporate patient report and clinical observations in addition to urine drug test results when assessing response to treatment.

### Normal characteristics of a urine sample<sup>9,12</sup>

- **Temperature within 4 minutes of voiding:**  
90°-100°F (cup will feel warm to the touch)
- **pH:** 4.5-8.0
- **Creatinine\*:**  $\geq 20$  mg/dL
- **Specific gravity\*:**  $> 1.002$
- **Volume\*:**  $\geq 30$  mL



### Urine drug testing specimen validity<sup>12,13</sup>

- Urine samples that are adulterated, substituted, or diluted may invalidate test results.
- Urine collected in the early morning is most concentrated and most reliable.
- Excessive water intake and diuretic use can lead to diluted urine samples (creatinine  $< 20$  mg/dL).

\*Abnormal creatinine, specific gravity, nitrates, or volume are not necessarily indicative of invalidity. These data should be discussed with the patient.

## Expected results of urine drug tests by drug or class<sup>6,9-11</sup>

Drug or class	Expected result	Considerations
<b>Opioids or opiates – Natural (from opium)</b>		
<b>Codeine</b>	Opiates Immunoassay – positive Confirmatory – codeine, possibly morphine and hydrocodone	<ul style="list-style-type: none"> <li>• Immunoassays for opiates are responsive to morphine and codeine but do not identify an individual substance.</li> <li>• Codeine is metabolized to morphine and small quantities of hydrocodone.</li> </ul>
<b>Morphine</b>	Opiates Immunoassay – positive Confirmatory – morphine, possibly hydromorphone	<ul style="list-style-type: none"> <li>• Immunoassays for opiates are responsive to morphine and codeine but do not identify an individual substance.</li> <li>• Morphine (&lt;10%) may be metabolized to hydromorphone.</li> </ul>
<b>Opioids – Semisynthetic (derived from opium)</b>		
<b>Buprenorphine</b>	Opiates Immunoassay – typically negative Confirmatory – buprenorphine, norbuprenorphine	<ul style="list-style-type: none"> <li>• Tramadol can cause false positives.</li> <li>• Negative result does not exclude use and confirmatory testing is required.</li> </ul>
<b>Heroin</b>	Opiates Immunoassay – positive Confirmatory – heroin (6-monoacetyl-morphine (MAM)), morphine, possibly codeine	<ul style="list-style-type: none"> <li>• 6-MAM is pathognomic for heroin use; detection windows may vary by lab.</li> </ul>

**Note:** Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details. **Continued >**

## Expected results of urine drug tests by drug or class<sup>6,9-11</sup>

Drug or class	Expected result	Considerations
<b>Opioids – Semisynthetic (derived from opium)</b>		
<b>Hydrocodone</b>	Opiates Immunoassay – may be negative* Confirmatory – hydrocodone, possibly hydromorphone	<ul style="list-style-type: none"> <li>• Both hydrocodone and hydromorphone may be detected in urine.</li> <li>• Negative immunoassay result does not exclude use; confirmatory testing is required.</li> </ul>
<b>Hydromorphone</b>	Opiates Immunoassay – may be negative* Confirmatory – hydromorphone	<ul style="list-style-type: none"> <li>• Hydrocodone would not be detected in urine from hydromorphone use alone.</li> <li>• Negative immunoassay result does not exclude use; confirmatory testing is required.</li> </ul>
<b>Oxycodone</b>	Opiates Immunoassay – typically negative Oxycodone Immunoassay – positive Confirmatory – oxycodone, possibly oxymorphone	<ul style="list-style-type: none"> <li>• Both oxycodone and oxymorphone may be detected in urine.</li> <li>• Negative immunoassay result does not exclude use; confirmatory testing is required.</li> </ul>
<b>Oxymorphone</b>	Opiates Immunoassay – positive Oxycodone Immunoassay – positive Confirmatory – oxymorphone	<ul style="list-style-type: none"> <li>• Oxycodone would not be detected in urine from oxymorphone use alone.</li> <li>• Negative immunoassay result does not exclude use; confirmatory testing is required.</li> </ul>

**Note:** Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

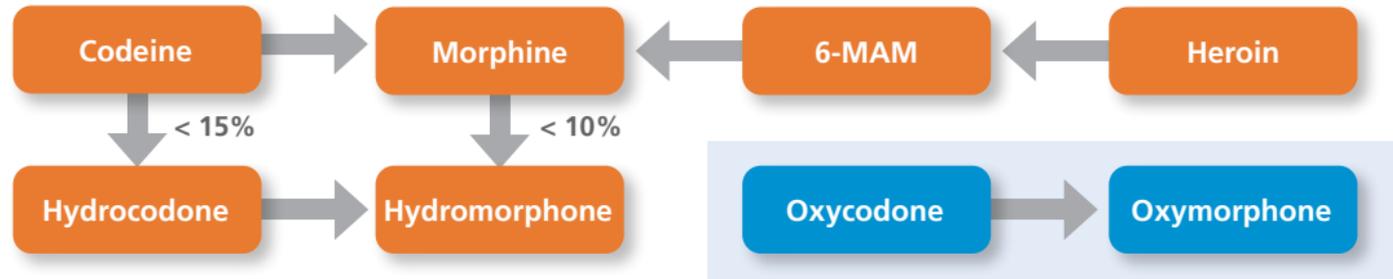
\*Low dose and/or infrequent use may result in negative immunoassay.

*Continued >*

## Expected results of urine drug tests by drug or class<sup>6,9-11</sup>

Drug or class	Expected result	Considerations
<b>Opioids – Synthetic (man-made)</b>		
<b>Fentanyl</b>	Opiates Immunoassay – negative Fentanyl Immunoassay – positive Confirmatory – fentanyl, norfentanyl	<ul style="list-style-type: none"> <li>• Current opiates immunoassays do not detect synthetic opioids.</li> <li>• Confirmatory testing is recommended.</li> <li>• Methadone urine assay will show positive if even a few drops of methadone are added to a urine sample. If there is doubt about urine tampering, consider obtaining a serum level.</li> <li>• For methadone, many commonly prescribed medications (e.g., buprenorphine, diphenhydramine, quetiapine, verapamil) may cause a false positive. Confirmatory testing may be required.</li> </ul>
<b>Meperidine</b>	Opiates Immunoassay – negative Confirmatory – normeperidine, possibly meperidine	
<b>Methadone</b>	Opiates Immunoassay – negative Methadone Immunoassay – positive Confirmatory – methadone, EDDP (2-ethylidene-1, 5-dimethyl-3, 3-diphenylpyrrolidine)	

### Opioid metabolic pathways<sup>10,11,14</sup>



## Expected results of urine drug tests by drug or class: other agents<sup>6,9</sup>

Drug or class	Expected result	Considerations
<b>Cocaine</b>	Immunoassay – benzoyllecgonine	Screening test is more sensitive and specific than other screening tests.
<b>Amphetamine; methamphetamine; 3,4-methylenedioxy-methamphetamine</b>	Immunoassay – amphetamine	Screening test is subject to many false-positives and should be interpreted with caution; false positives may be caused by bupropion, chlorpromazine, desipramine, fluoxetine, labetalol, promethazine, ranitidine, pseudoephedrine, trazodone, and other common medications. Confirm unexpected positive results with the laboratory. Methylphenidate is not detected by amphetamine immunoassay; it requires confirmatory testing. <sup>15,16</sup>
<b>Benzodiazepines</b>	Immunoassay – benzodiazepine	Immunoassays not sensitive to therapeutic doses, definitive testing may be required; many assays have low sensitivity for clonazepam or lorazepam. False positives may be caused by sertraline or oxaprozin.
<b>Cannabis; tetrahydrocannabinol (THC)</b>	Immunoassay – THC-9-carboxylic acid (THC-COOH)	For chronic cannabis users, cannabis tests may not reflect quit dates as clearance is slower after chronic use. False positives with efavirenz, ibuprofen, and pantoprazole.

## Buprenorphine product chart\*<sup>5,6</sup>

Generic name	Route/frequency	Brand names	For the treatment of	REMS**	Considerations
<b>Buprenorphine</b>	<ul style="list-style-type: none"> <li>• Sublingual tablets</li> <li>• Daily</li> </ul>	Generic versions available similar to Subutex <sup>®</sup>	Opioid withdrawal and OUD	Yes	OUD treatment guidelines generally recommend use of buprenorphine/naloxone over the monoproduct in most cases to prevent injection misuse
<b>Buprenorphine and naloxone</b>	<ul style="list-style-type: none"> <li>• Sublingual tablets, film</li> <li>• Daily</li> </ul>	Generic versions available in addition to Suboxone <sup>®</sup> , Zubsolv <sup>®</sup> , Bunavail <sup>®</sup>	Opioid withdrawal and OUD	Yes	Lower potential for misuse and diversion (compared to monoproduct); requires daily compliance

\*Products are listed based on evidenced based recommendations. Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: [www.pbm.va.gov/PBM/NationalFormulary.asp](http://www.pbm.va.gov/PBM/NationalFormulary.asp). \*\*REMS (risk evaluation and mitigation strategies) for all products can be found at [www.accessdata.fda.gov/scripts/cder/remis/index.cfm](http://www.accessdata.fda.gov/scripts/cder/remis/index.cfm).

*Continued >*

## Buprenorphine product chart\*<sup>5,6</sup>

Generic name	Route/frequency	Brand names	For the treatment of	REMS**	Considerations
<b>Buprenorphine extended-release</b>	<ul style="list-style-type: none"> <li>Abdominal subcutaneous injection</li> <li>Monthly</li> </ul>	Sublocade <sup>®</sup>	Moderate to severe OUD in patients who have initiated treatment with transmucosal buprenorphine followed by dose adjustment for at least 7 days <sup>17</sup>	Yes	No risk for patient diversion/misuse; requires patients to be on a stable dose of transmucosal buprenorphine for at least 7 days; monthly instead of daily medication compliance; less fluctuation in bup. levels compared to daily doses
<b>Buprenorphine hydrochloride</b>	<ul style="list-style-type: none"> <li>Subcutaneous implant</li> <li>Every 6 months</li> </ul>	Probuphine <sup>®</sup>	OUD in patients who have achieved and sustained prolonged clinical stability on doses of no more than 8 mg/day of transmucosal buprenorphine	Yes	No risk for patient diversion/misuse; training needed for insertion/removal; risks from improper insertion/removal; examine site 1 week after insertion; remove after 6 months; FDA approved for 1 year (1 insertion/arm); less fluctuation in bup. levels compared to daily doses

## Approximate buprenorphine equivalence chart\*<sup>5</sup>

Suboxone <sup>®</sup> or generic (SL tablet)	Suboxone <sup>®</sup> or generic (SL film)	Zubsolv <sup>®</sup> (SL tablet)	Bunavail <sup>®</sup> (buccal film)	Generic Subutex <sup>®</sup> (SL tablet)	Sublocade <sup>®**</sup> (injection)
2 mg bup / 0.5 mg nal	2 mg bup / 0.5 mg nal	1.4 mg bup / 0.36 mg nal		2 mg	
4 mg bup / 1 mg nal	4 mg bup / 1 mg nal	2.9 mg bup / 0.71 mg nal	2.1 mg bup / 0.3 mg nal	4 mg	
8 mg bup / 2 mg nal	8 mg bup / 2 mg nal	5.7 mg bup / 1.4 mg nal	4.2 mg bup / 0.7 mg nal	8 mg	100 mg
12 mg bup / 3 mg nal	12 mg bup / 3 mg nal	8.6 mg bup / 2.1 mg nal	6.3 mg bup / 1 mg nal	12 mg	
16 mg bup / 4 mg nal	16 mg bup / 4 mg nal	11.4 mg bup / 2.9 mg nal	8.4 mg bup / 1.4 mg nal	16 mg	
24 mg bup / 6 mg nal	24 mg bup / 6 mg nal	17.2 mg bup / 4.1 mg nal	12.6 mg bup / 2 mg nal	24 mg	300 mg

SL = sublingual tablet; nal = naloxone. This table is a guide for switching between buprenorphine products and should be used in conjunction with monitoring response to new product. \*Pharmacokinetic equivalence may vary depending on indicator used (e.g., C<sub>max</sub> vs. C<sub>avg</sub>).\*\*Recommended Sublocade dose is 300 mg for two months, then 100 mg monthly. The maintenance dose can be increased to 300 mg monthly for those who tolerate 100 mg but do not have a satisfactory clinical response.

## Example buprenorphine initiation follow-up schedules

**Buprenorphine initiation can occur in the office or at home.** Most clinical trials were conducted with office-based initiation; however, this can be a barrier to treatment initiation. Home initiation of buprenorphine is increasingly common and studies have shown that it is generally safe.<sup>6</sup>

**Note:** Home initiation may work best for patients who can describe and understand withdrawal, follow the dosing instructions, and maintain contact with the clinic or have prior experience with buprenorphine.

### Sample follow-up schedule for buprenorphine initiation and monitoring:<sup>18,19</sup>



Office-based initiation	Home-based initiation
Pre-initiation visit	Pre-initiation visit; phone contacts day of induction and subsequent days (use a validated tool to assess withdrawal, e.g., COWS)
Days 1, 2, and 3 post-initiation, then	3 to 7 days post-initiation, then
1-2 weeks post-initiation, then	2-3 weeks post-initiation, then
3-6 weeks post-initiation, then	4-7 weeks post-initiation, then
Monthly	Monthly

## Buprenorphine and buprenorphine/naloxone contraindications and cautions<sup>6,8,20</sup>

Contraindications/ Cautions	Recommendations
<b>Demonstrated allergy/hypersensitivity*</b>	<ul style="list-style-type: none"> <li>• Do not prescribe.</li> </ul>
<b>Compromised respiratory function</b> (e.g., COPD, decreased respiratory reserve, hypoxia, hypercapnia, preexisting respiratory depression)	<ul style="list-style-type: none"> <li>• Prescribe with caution; monitor closely.</li> <li>• Warn patients about the risk of using benzodiazepines, alcohol, or other depressants while taking buprenorphine.</li> </ul>
<p><b>Hepatic impairment</b> Moderate to severe liver impairment results in decreased clearance, increasing overall exposure to both medications. This results in higher risk of buprenorphine toxicity and precipitated withdrawal from naloxone.</p>	<ul style="list-style-type: none"> <li>• <b>Mild impairment</b> (Child-Pugh score of 5-6): No dose adjustment needed.</li> <li>• <b>Moderate impairment</b> (Child-Pugh score of 7-9):             <ul style="list-style-type: none"> <li>– Combination products not recommended for initiation as they may precipitate withdrawal.**</li> <li>– With careful monitoring, combination products may be used for maintenance treatment for those who have been initiated with mono-product.</li> </ul> </li> <li>• <b>Severe impairment</b> (Child-Pugh score of 10-15)             <ul style="list-style-type: none"> <li>– Use of the combination product is not recommended.<sup>20</sup></li> <li>– With a mono-product, reduce starting and titration doses by half; monitor for signs and symptoms of toxicity or overdose caused by increased levels of buprenorphine.</li> </ul> </li> </ul>

\*Many patients report negative experiences with taking illicit buprenorphine they call an “allergy” but could have been precipitated withdrawal. Obtain a detailed description of their symptoms and assess whether they are consistent with known allergic reactions. \*\*Moderate to severe hepatic impairment results in reduced clearance of naloxone. Versus subject with no/mild impairment, Nasser et al.<sup>21</sup> found moderate impairment led to 2-3 times the exposure for both naloxone and buprenorphine. In severe impairment, buprenorphine exposure was also 2-3 times higher, but naloxone exposure was  $\geq 10$  times higher.

## Methadone contraindications and cautions<sup>22,23</sup>

Contraindications/Cautions	Recommendations
<p><b>Demonstrated allergy/hypersensitivity*</b></p>	<ul style="list-style-type: none"> <li>• Do not prescribe.</li> </ul>
<p><b>Compromised respiratory function</b> (e.g., COPD, decreased respiratory reserve, hypoxia, hypercapnia, preexisting respiratory depression)</p>	<ul style="list-style-type: none"> <li>• Order and dispense with caution; monitor closely.</li> <li>• Warn patients about the risk of using benzodiazepines, alcohol, or other depressants while taking methadone.</li> </ul>
<p><b>Cardiac Prolonged QT interval</b>            QT interval prolongation and serious arrhythmia (torsades de pointes) have occurred during treatment with methadone</p> <p><b>Avoid use if QTc is &gt;500 ms</b>  <b>Caution if QTc 450–500 ms</b></p>	<ul style="list-style-type: none"> <li>• Closely monitor patients with:               <ul style="list-style-type: none"> <li>– Risk factors for prolonged QT interval (e.g., cardiac hypertrophy, concomitant diuretic use, hypokalemia, hypomagnesemia)</li> <li>– History of cardiac conduction abnormalities</li> <li>– Other medications affecting cardiac conduction</li> </ul> </li> <li>• QT prolongation has been reported with no prior cardiac history with high doses.</li> <li>• Evaluate patients developing QT prolongation on methadone for modifiable risk factors (e.g., concomitant medications with cardiac effects, drugs that cause electrolyte abnormalities, and drugs that inhibit methadone metabolism).</li> <li>• Use with already known prolonged QT interval has not been systematically studied.</li> </ul>

COPD = chronic obstructive pulmonary disease; \*Including red food coloring if the red liquid product is being used.

**Continued >**

## Methadone contraindications and cautions<sup>22,23</sup>

Contraindications/Cautions	Recommendations
<p><b>Hepatic impairment</b> Methadone is not hepatotoxic, but the liver has a key role in metabolism, clearance, drug storage</p>	<ul style="list-style-type: none"><li>• Methadone has not been extensively evaluated with hepatic insufficiency.</li><li>• Liver impairment may risk increased systemic exposure after multiple dosing.</li><li>• Start on lower doses, titrate slowly, and monitor for respiratory and CNS depression.</li></ul>
<p><b>Renal impairment</b> Up to 45% eliminated through feces, suggesting it may be used safely in renal disease</p>	<ul style="list-style-type: none"><li>• Recommend caution when dosing methadone in a low GFR population, and to start with lower doses titrating up. (GFR &lt;10, start with 50%-75% of original dosing.)</li></ul>
<p><b>Drug interactions</b></p> <ul style="list-style-type: none"><li>• Medications metabolized by CYP3A4, 2B6, 2C19 (and to a lesser extent by 2C9 and 2D6)</li><li>• Co-administered medications such as antiretrovirals, anticonvulsants, rifampin</li></ul>	<ul style="list-style-type: none"><li>• Consider methadone dose adjustments/increased monitoring if medication changes are made.</li></ul>

CNS = central nervous system; GFR = glomerular filtration rate

## Naltrexone XR contraindications and cautions<sup>8,24</sup>

Contraindications/ Cautions	Recommendations
<b>Demonstrated allergy/hypersensitivity</b>	<ul style="list-style-type: none"><li>• Do not prescribe.</li></ul>
<b>Vulnerability to opioid overdose</b>	<ul style="list-style-type: none"><li>• Counsel about opioid sensitivity if treatment is discontinued or nonadherence (overdose risk).</li><li>• Discuss the fact that naltrexone XR should not be thought of as a “one-time cure” shot but rather as a long-term maintenance strategy.</li><li>• Consider utilizing adjunctive psychosocial strategies to boost adherence (e.g., contingency management) in patients at risk of discontinuing treatment.</li></ul>
<b>Injection site reactions</b> <ul style="list-style-type: none"><li>• Pain, tenderness, induration, swelling, erythema</li><li>• Some reactions may be very severe</li></ul>	<ul style="list-style-type: none"><li>• Consider alternate treatment if body habitus precludes an IM gluteal injection.</li><li>• Monitor for injection site reactions; evaluate signs of abscess, cellulitis, necrosis, or extensive swelling; caution with patients with thrombocytopenia or coagulation disorders.</li></ul>

IM = intramuscular

*Continued >*

## Naltrexone XR contraindications and cautions<sup>8,24</sup>

Contraindications/ Cautions	Recommendations
<p><b>Precipitation of opioid withdrawal</b> May result in severe withdrawal/ hospitalization</p>	<ul style="list-style-type: none"> <li>• Patients should be opioid-free before starting treatment; consider challenge with naloxone</li> <li>• Opioid-free interval of 7–10 days if previously dependent on short-acting opioids</li> <li>• Transitioning from buprenorphine or methadone; risk of withdrawal for up to 2 weeks</li> <li>• If rapid transition from agonist to antagonist therapy is necessary, monitor closely in a medical setting to manage precipitated withdrawal</li> </ul>
<p><b>Hepatotoxicity</b> Undergoes extensive hepatic metabolism; may cause further hepatic injury in patients with liver dysfunction</p>	<ul style="list-style-type: none"> <li>• Warn of hepatic injury risk; advise to see provider if symptoms of acute hepatitis occur*</li> <li>• Discontinue naltrexone if symptoms and/or signs of acute hepatitis</li> <li>• No dose adjustment req. with mild or moderate liver dysfunction (Child-Pugh score A &amp; B)</li> <li>• Pharmacokinetics were not evaluated in subjects with severe hepatic impairment</li> </ul>
<p><b>Depression and suicidality</b></p>	<ul style="list-style-type: none"> <li>• Monitor for depression/suicidal thinking; inform caregivers of risk and report if present</li> <li>• Provide contact information for the Veterans Crisis Line (call, text, and online chat) and other resources as applicable: 800-273-8255</li> </ul>
<p><b>Renal Impairment</b> Urinary excretion primary route for metabolites</p>	<ul style="list-style-type: none"> <li>• No dosage adjustment required with mild renal dysfunction (CrCl 50-80 mL/min)</li> <li>• No data in patients with moderate to severe renal dysfunction (CrCl &lt; 50 mL/min)</li> </ul>

CrCl = creatinine clearance; \*Symptoms: fever, rash, itching, anorexia, nausea, vomiting, fatigue, malaise, right upper quadrant pain, dark urine, pale stools, and jaundice.

## Opioid use disorder and HIV/HCV<sup>3,25-28</sup>

Injection drug use problems	Management considerations
<p><b>HIV and HCV linked to injectable drug use</b></p> <ul style="list-style-type: none"><li>• Majority of injection drug users are addicted to heroin or other opioids</li><li>• 10% of new HIV cases are linked to injectable drug use</li><li>• 50% of new HCV cases are linked to injectable drug use</li><li>• Prevalence of HCV infection in patients with OUD range from 36%–95%</li></ul>	<ul style="list-style-type: none"><li>• <b>Treatment of OUD decreases the opportunity for HIV/HCV transmission</b> in people who inject drugs.</li><li>• <b>Pre-Exposure Prophylaxis (PrEP)</b> should be considered to prevent HIV infection secondary to IV drug use.<sup>29</sup></li><li>• <b>Routine HCV antibody testing</b><ul style="list-style-type: none"><li>– With HCV infection 3-5 times more common in the U.S. than HIV/AIDS, and more deadly, CDC recommends annual HCV antibody testing (screening) for all patients who currently or formerly injected drugs.<sup>30</sup></li></ul></li><li>• <b>Stigma/misinformation</b> about available HIV/HCV treatment and access to care is prevalent among this population.<ul style="list-style-type: none"><li>– <b>Please note:</b> Referring patients to the Infectious Disease/HCV/HIV clinics for testing and follow-up without clear and affirming psychoeducation about treatment options and a warm hand-off may result in poor patient follow through.</li></ul></li></ul>
<p><b>High risk practices of injectable drug use</b></p> <ul style="list-style-type: none"><li>• Sharing of needles and syringes</li><li>• Sharing of paraphernalia</li><li>• Sexual exposure</li></ul>	

HIV = human immunodeficiency virus; HCV = hepatitis C virus; AIDS = acquired immune deficiency syndrome; CDC = Centers for Disease Control and Prevention

## Pre-exposure prophylaxis in people who inject drugs

**What is PrEP?** Pre-exposure prophylaxis (PrEP) is the use of a single-tablet combination antiretroviral to prevent acquisition of HIV infection in conjunction with other prevention methods.

**What is the evidence for people who inject drugs (PWID)?** Tenofovir (TDF) reduces the risk of HIV by 74% in PWID.<sup>29,31</sup>

**What medications are used for PrEP?** Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC, Truvada®) is FDA approved to prevent HIV infection in cisgender and transgender men and women, PWID, and men who have sex with men (MSM). TDF alone is not FDA approved for PrEP. Tenofovir alafenamide/emtricitabine (TAF/FTC, Descovy®) is FDA approved for PrEP in cisgender men and transgender women who have sex with MSM. TAF/FTC has not been studied in individuals at risk from receptive vaginal sex or in PWID who are not at risk for sexually acquired HIV.

**When should PrEP be considered?** PrEP can be considered in individuals with substantial risk, such as having an HIV-infected injecting partner and sharing injection or drug preparation equipment. Other risk factors include inconsistent condom use, a high number of sex partners, a recent sexually transmitted infection, and engaging in commercial sex work.

Please see the **VA PrEP SharePoint** page for more information.

## What steps are needed to initiate PrEP?

- 1. Take a thorough history of recent sex and drug-use behaviors.**
- 2. Rule out HIV infection.** Assess for symptoms of acute HIV infection. Test for HIV.
- 3. Assess hepatitis B status.** If negative for evidence of infection or immunity – vaccinate. If positive, consult with HIV or HBV specialist before initiating PrEP.
- 4. Assess for renal impairment.** TDF/FTC should not be given if creatinine clearance is  $< 60$  mL/min. TAF/FTC should not be given if creatinine clearance is  $< 30$  mL/min.
- 5. Assess and refer for mental health or substance-use care,** if indicated.
- 6. Ask about pregnancy intention in women.** If the person plans to become pregnant, is pregnant, or is breastfeeding, consultation with an experienced PrEP clinician is recommended.
- 7. Educate patients about symptoms of acute infection,** instructing them to call immediately if these develop (e.g., fever, fatigue, myalgia, pharyngitis, headache, adenopathy, night sweats, arthralgia, diarrhea, rash).

**How should I prescribe PrEP?** TDF/FTC is one pill taken once a day. A 30-90 day supply, **without refills,** should be prescribed. **Note:** Counsel patients that it may take 2-3 weeks for TDF/FTC levels to be protective. Patients should return to clinic every 3 months for follow-up and laboratory monitoring, including HIV testing. A negative HIV test should be documented before renewing PrEP.

## Common symptomatic strategies for managing opioid withdrawal symptoms (e.g., prior to initiation of naltrexone XR or buprenorphine/naloxone)\*<sup>5,6</sup>

**Please note:** In patients with active OUD, follow opioid withdrawal management with medications for OUD. Do not provide withdrawal management alone due to high risk of relapse and overdose.<sup>6</sup>

Symptom	Medication examples
Nausea	Ondansetron, metoclopramide
Diarrhea	Loperamide
Anxiety, irritability, sweating	Clonidine*
Insomnia	Diphenhydramine, trazodone

\*Initiate clonidine at 0.1 mg by mouth every 6-8 hrs as needed for withdrawal symptoms. Max dose 1.2 mg per day.

## References

1. Boston Medical Center. Reducing stigma: why words about addiction matter. Grayken center for addiction. <https://www.bmc.org/addiction/reducing-stigma>. Published 2019. Accessed 28 October, 2019.
2. Livingston JD, et al. The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. *Addiction*. 2012;107(1):39-50.
3. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *J Addict Med*. 2015;9(5):358-367.
4. American Society of Addiction Medicine. ASAM National Practice Guideline Pocketguide. <https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-pocketguide.pdf?sfvrsn=0>. Accessed Dec 3, 2019.
5. American Society of Addiction Medicine. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. Rockville, MD: American Society of Addiction Medicine;2020.
6. Substance Abuse and Mental Health Services Administration. Medications for opioid use disorder. Treatment Improvement Protocol (TIP) Series 63, Full Document. Rockville, MD: Substance Abuse and Mental Health Services Administration;2020.
7. Handelsman L, et al. Two new rating scales for opiate withdrawal. *Am J Drug Alcohol Abuse*. 1987;13(3):293-308.
8. The Management of Substance Abuse Disorders Work Group. VA/DOD Clinical practice guideline for the management of substance use disorders. VA/DoD. 2015;Version 3.0(December 2015):1-169.
9. American Society of Addiction Medicine. Appropriate use of drug testing in clinical addiction medicine. Rockville, MD: American Society of Addiction Medicine;2017.
10. Kale N. Urine Drug Tests: Ordering and Interpreting Results. *Am Fam Physician*. 2019;99(1):33-39.
11. Agency Medical Directors' Group. Interagency guideline on prescribing opioids for pain. Olympia, WA: Washington State Agency Medical Directors' Group;2015.
12. Raouf M, et al. A Practical Guide to Urine Drug Monitoring. *Fed Pract*. 2018;35(4):38-44.
13. Moeller KE, et al. Urine drug screening: practical guide for clinicians. *Mayo Clin Proc*. 2008;83(1):66-76.
14. Gourlay DL, et al. Urine drug testing in clinical practice. The art and science of patient care. Edition 6. [https://www.remitigate.com/wp-content/uploads/2015/11/Urine-Drug-Testing-in-Clinical-Practice-Ed6\\_2015-08.pdf](https://www.remitigate.com/wp-content/uploads/2015/11/Urine-Drug-Testing-in-Clinical-Practice-Ed6_2015-08.pdf). Published August 31, 2015. Accessed May 12, 2020.
15. Breindahl T, Hindersson P. Methylphenidate is distinguished from amphetamine in drug-of-abuse testing. *J Anal Toxicol*. 2012;36(7):538-539.
16. von Mach MA, et al. Comparison of urinary on-site immunoassay screening and gas chromatography-mass spectrometry results of 111 patients with suspected poisoning presenting at an emergency department. *Ther Drug Monit*. 2007;29(1):27-39.
17. Sublocade (buprenorphine injection) [package insert]. North Chesterfield, VA: Indivior Inc.; 2019.
18. Rosen, MI, et al. A Manual for Prescribing Medications for Opioid Use Disorder (MOUD) for Veterans at CBOCs Using Telehealth. [https://vawww.portal.va.gov/sites/OMHS/SUD/SUDfiles/Telehealth/TeleMOUD%20Toolkit\\_with%20Covid19%20Updates.pdf](https://vawww.portal.va.gov/sites/OMHS/SUD/SUDfiles/Telehealth/TeleMOUD%20Toolkit_with%20Covid19%20Updates.pdf). Accessed 2020.
19. Integrating buprenorphine treatment for opioid use disorder in primary care. <https://ciswh.org/wp-content/uploads/2017/06/Buprenorphine-Implementation-Manual-for-Primary-Care-Settings-.pdf>. Published 2017. Accessed June 10, 2020.
20. Suboxone (buprenorphine/naloxone sublingual film) [package insert]. North Chesterfield, VA: Indivior Inc.; 2019.
21. Nasser AF, et al. Pharmacokinetics of Sublingual Buprenorphine and Naloxone in Subjects with Mild to Severe Hepatic Impairment (Child-Pugh Classes A, B, and C), in Hepatitis C Virus-Seropositive Subjects, and in Healthy Volunteers. *Clin Pharmacokinet*. 2015;54(8):837-849.
22. Methadose (methadone) [package insert]. Webster Groves, MO: Mallinckrodt Pharmaceuticals; 2019.
23. Gelot S. Opioid dosing in renal and hepatic impairment. *US Pharm*. 2014;39(8):34-38.
24. Vivitrol (naltrexone injection) [package insert]. Waltham, MA: Alkermes, Inc.; 2019.
25. Metzger DS, Zhang Y. Drug treatment as HIV prevention: expanding treatment options. *Curr HIV/AIDS Rep*. 2010;7(4):220-225.
26. Sullivan LE, Fiellin DA. Buprenorphine: its role in preventing HIV transmission and improving the care of HIV-infected patients with opioid dependence. *Clin Infect Dis*. 2005;41(6):891-896.
27. Centers for Disease Control and Prevention. Integrated prevention services for HIV infection, viral hepatitis, sexually transmitted diseases, and tuberculosis for persons who use drugs illicitly: summary guidance from CDC and the U.S. Department of Health and Human Services. *MMWR Recomm Rep*. 2012;61(RR-5):1-40.
28. Centers for Disease Control and Prevention. HIV. <https://www.cdc.gov/hiv/statistics/overview/index.html>. Published 2019. Accessed Dec 12, 2019.
29. Choopanya K, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2013;381(9883):2083-2090.
30. American Association for the Study of Liver Diseases, Infectious Diseases Society of America. HCV testing and linkage to care. <https://www.hcvguidelines.org/evaluate/testing-and-linkage>. Published Nov 6, 2019. Accessed July 9, 2020.
31. Centers for Disease Control and Prevention. PrEP. <https://www.cdc.gov/hiv/basics/prep.html>. Published June 4, 2020. Accessed July 9, 2020.

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This reference guide was created to be used as a tool for VA providers and is available from the Academic Detailing SharePoint. These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

### **VA PBM Academic Detailing Service Email Group:**

PharmacyAcademicDetailingProgram@va.gov

### **VA PBM Academic Detailing Service SharePoint Site:**

<https://vaww.portal2.va.gov/sites/ad>

### **VA PBM Academic Detailing Service Public Website:**

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