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March 2023 ~ Resource #390303

Management of Opioid Use Disorder

modified February 2025

Opioid use disorder (OUD) is "a problematic pattern of opioid use leading to clinically significant impairment or distress."[2] Medications to treat OUD prevent withdrawal (methadone, buprenorphine), decrease illicit opioid use, reduce criminal activity, improve social functioning, increase treatment retention, and reduce risk of overdose death.[4,9] The chart below covers common clinical questions about approved medications for OUD, with a focus on buprenorphine/naloxone. COVID-related considerations are included. Advise having naloxone or nalmefene (US) on hand; US labeling now advises discussion of an opioid reversal agent with patients being treated with medications for OUD.[12]

Question	Answer/Pertinent Information
How can I **identify patients with opioid use disorder**?	• Diagnostic criteria (DSM-V) for OUD includes a problematic opioid use leading to clinically significant impairment or distress, manifested as at least two of the following within 12 months:[2] o opioid is taken in larger quantity or longer duration than originally planned. o continuing desire to cut back, or failed efforts to cut back. o significant time is spent obtaining or using the opioid or recovering from its effects. o craving, strong desire, or urge to use. o use interferes with obligations. o use continues despite persistent or recurrent social or interpersonal problems caused or worsened by opioid. o use continues despite knowledge of having a persistent or recurrent physical or psychological problem likely caused or worsened by the opioid. o important social, work, or recreational activities are abandoned or reduced due to opioid use. o opioids are used in situations where use is physically hazardous. o tolerance (need for markedly increased amounts to achieve intoxication or desired effect, or markedly diminished effect with continued use of same amount). (Note: this criterion is not considered to be met for patients taking opioids solely under appropriate medical supervision.) o withdrawal (three or more of the following, developing within minutes to several days after cessation or reduction in heavy and prolonged [several weeks] use, or after administration of an opioid antagonist: dysphoria; nausea or vomiting; diarrhea; muscle aches; lacrimation or rhinorrhea; pupil dilation, goosebumps, or sweating; yawning; fever; insomnia). (Note: this criterion is not considered to be met for patients taking opioids solely under appropriate medical supervision.) • Validated screening tools can help to identify opioid misuse **in patients taking opioids for chronic pain**. For example, the COMM (Current Opioid Misuse Measure) is available at https://www.mdcalc.com/calc/10428/current-opioid-misuse-measure-comm.

Question	Answer/Pertinent Information
What approved **pharmacologic treatment options** are available for opioid use disorder?	• Opioid agonists: methadone, hydromorphone injection (*Hydromorphone HP* [Canada]). *Kadian* (morphine slow-release) is recommended by Canadian guidelines, although this is an off-label use.[36] Diacetylmorphine (heroin) is available to Canadians through Special Access.[24] • Opioid partial agonists: buprenorphine, buprenorphine/naloxone (products listed below). • Opioid antagonists: naltrexone (*Revia* [Canada], generics; depot naltrexone *Vivitrol* [US]).
How does pharmacotherapy work in the treatment of opioid use disorder?	**Buprenorphine and Buprenorphine/Naloxone** • Buprenorphine is a partial mu opioid receptor agonist.[4] Buprenorphine at sublingual doses as low as 4 mg daily can produce enough agonist effect to allow opioid-dependent individuals to discontinue the misuse of opioids without experiencing withdrawal symptoms or cravings.[3,4] • At daily sublingual doses as low as 16 mg, buprenorphine can block the reinforcing and subjective effects of usual doses of abused opioids.[3] • Sublingual naloxone has low bioavailability.[3] So when buprenorphine/naloxone is taken in sublingual form, naloxone does not precipitate severe, prolonged withdrawal in the opioid-dependent user.[3] However, if buprenorphine/naloxone is misused by injection, naloxone may block the effects of buprenorphine, or precipitate opioid withdrawal in an opioid dependent person.[3,8] However, blockade may be moderate and brief relative to the duration of action of buprenorphine.[8] **Pure mu opioid agonists** (e.g., methadone, morphine slow-release [*Kadian*]) • Stimulates mu opioid receptors to suppress withdrawal and craving.[4,36-38] • With appropriately titrated, stable dosing, should not cause intoxication or oversedation, allowing the patient to function in society.[17,36-38] **Naltrexone** • Binds tightly to mu opioid receptors. Displaces mu agonists from their receptors, blocking their effects.[4] • Can precipitate withdrawal in patients who have not been abstinent from short-acting opioids for at least seven to ten days, and at least ten to 14 days from long-acting opioids (e.g., methadone).[4]
How do I **identify patients who may be candidates for medications to treat opioid use disorder**?	• Pharmacotherapy is an option for all patients with OUD.[4] Opioid pharmacotherapy should be reserved for those with moderate-to-severe OUD (i.e., meeting ≥4 of the DSM-5 criteria) and physical dependence.[4]

Question	Answer/Pertinent Information	
What are the **pros and cons of the pharmacotherapy options** for opioid use disorder?	**Pros**	**Cons**
	Buprenorphine/naloxone	
	• Safer than methadone.[3,4] • In US, more accessible than methadone. • At sufficient doses, as effective as methadone and superior to oral naltrexone.[1,16] • Easier to discontinue than methadone.[29] • May require less frequent dosing than methadone.[29] • Fewer drug interactions than methadone.[4] • If misused by injection, naloxone in the combo product may blunt the effects of buprenorphine or precipitate opioid withdrawal if opioid dependent.[4]	• Moderate abuse potential.[4] Opioid side effects (e.g., constipation, sedation [not common], respiratory depression [rare]).[4] • Potential for interaction with CYP3A4 inhibitors/inducers, serotonergic drugs (rare), and QT-prolonging drugs.[3,4] • Limited safety data in pregnancy; concern that naloxone component of combo product may cause withdrawal in fetus.[4] (**Single-ingredient** buprenorphine product can be used.[4,18,33]) • Can precipitate withdrawal if started too soon after use of other opioid; patients should be in withdrawal to receive their first dose (see "How is sublingual buprenorphine generally dosed?" section below for details).[4]
	Methadone	
	• Option after buprenorphine failure.[13] • No risk of precipitating withdrawal.[4] • First-line option for pregnant patients.[4]	• More respiratory depression, sedation, and QT prolongation than buprenorphine.[3,4] • Serious drug interactions.[4] • In US, available only through a certified OTP facility.[4] (Note: daily dosing/supervision at an OTP facility could be a "pro.")[4] • Difficult switch to buprenorphine/naloxone.[4] • Abuse potential. Opioid side effects.[4]
	Naltrexone	
	• Not limited to certain clinics or prescribers like methadone in the US.[4] • Not abusable.[4] No opioid side effects.[4] • Extended-release (*Vivitrol*) as effective as buprenorphine/naloxone.[1] • *Vivitrol* administered monthly.[4] • May carry less of a stigma because it is not an opioid.[19] • Good choice for highly motivated patients and patients who have already been detoxified (e.g., persons leaving prison or rehab).[4,19] • Cheapest option in US (oral tablets).	• Adherence is an issue with oral product.[4] • Can precipitate withdrawal in patients who have not been abstinent from short-acting opioids for at least 7 days, and abstinent from long-acting opioids for at least 10 days (perhaps 14 days from methadone or buprenorphine).[20,25] Patients may relapse before naltrexone can be started.[15] • Carries risk of liver toxicity.[4] • Due to mu receptor up-regulation, naltrexone patients are more sensitive to the effects of opioids and are therefore at risk of fatal opioid overdose if they take an opioid.[19] • Not a good choice for patients who may require opioids for pain.[20] • Serious injection site reactions with *Vivitrol*.[25] • *Vivitrol* most expensive option (~$1,600/month[a] [US]).

Continued…

Question	Answer/Pertinent Information	
What are the **pros and cons of the pharmacotherapy options** for opioid use disorder, continued	**Pros**	**Cons**
	Buprenorphine implant (*Probuphine* [Canada])	
	• Lasts six months.[23] • Unique formulation may address problems with diversion, nonmedical use, and adherence.[31] • Fewer drug interactions than methadone.[4]	• Only for patients who have achieved clinical stability on the equivalent of not more than 8 mg per day of sublingual buprenorphine (for at least 90 days in the pivotal clinical trial), with counseling and psychosocial support.[23] • System consists of four subdermal rods implanted in the inside of the upper arm.[23] • Abuse potential.[23] • May not be appropriate during pregnancy because dose cannot be titrated.[23] • Consider alternative for patients with ongoing need for occasional supplemental doses of transmucosal buprenorphine.[23] • After two six-month treatment periods, new implants can be inserted into a previously unused area of the opposite arm after considering benefit of ongoing treatment vs risk of additional insertion/removal procedures for a total of four six-month treatment periods (i.e., 24 months).[23] • About one more patient will avoid illicit drug use for every 10 switched to the implant vs remaining on buprenorphine/naloxone.[23] • Potential for interaction with CYP3A4 inhibitors/inducers, serotonergic drugs, and QT-prolonging drugs.[23]
	Long-acting buprenorphine injection (*Brixadi* [US])	
	• Lasts a week or a month (two different formulations.[35] • Fewer interactions than methadone.[4] • Can use in patients who are buprenorphine-naive (after a test dose of transmucosal buprenorphine), or in patients requiring up to 24 mg/day of buprenorphine.[35]	• Abuse potential; injection site could be tampered with.[35] • Forms a gel after injection that would be difficult to surgically remove in the event of adverse effects.[35] • Available only through certified prescribers in a controlled distribution system.[35] • Potential for interaction with CYP3A4 inhibitors/inducers, serotonergic drugs, and QT-prolonging drugs.[35]
Continued…		

<table>
<tr><th>Question</th><th colspan="2">Answer/Pertinent Information</th></tr>
<tr><td rowspan="8">What are the pros and cons of the pharmacotherapy options for opioid use disorder, continued</td><td>Pros</td><td>Cons</td></tr>
<tr><td colspan="2">Long-acting buprenorphine injection (Sublocade)</td></tr>
<tr><td>• Lasts a month or longer (minimum of 26 days between doses).[28,32]
• Fewer drug interactions than methadone.[4]
• Can use in patients requiring up to 24 mg/day of buprenorphine.[28,32]</td><td>• Only for patients clinically stable on transmucosal buprenorphine (8 to 24 mg daily for at least seven days).[28,32]
• Abuse potential; injection site could be tampered with.[28,32]
• In event of an adverse reaction, depot must be surgically removed.[28,32]
• Available only through certified prescribers in a controlled distribution system.[28,32]
• Potential for interaction with CYP3A4 inhibitors/inducers, serotonergic drugs, and QT-prolonging drugs.[28,32]</td></tr>
<tr><td colspan="2">Morphine slow release (Kadian [Canada])</td></tr>
<tr><td>• May be comparable to methadone for reducing high-risk opioid use, with less craving and side effects (e.g., nausea, anxiety).[36]
• No QT prolongation.[36] Few drug interactions.[36]
• May work for patients who find buprenorphine or methadone inadequate.[36]</td><td>• Once-daily supervised dosing at a pharmacy could be a “pro” or “con.”
• Potential for misuse with take-home doses.[36] Pellets can be crushed, dissolved, and injected.[36]
• Patients may need 600 to 1,200 mg/day (2,000 mg/day reported), but largest capsule strength is 100 mg.[36] Capsules can be opened and pellets sprinkled into water, or on applesauce. This could be time-consuming for the pharmacist, and pellets could stick to the container.[36]</td></tr>
<tr><td colspan="2">Hydromorphone injection (Hydromorphone HP)</td></tr>
<tr><td>• Option for those with severe, long-term injection opioid dependence who fail oral opioid maintenance.[22]
• May reduce use of street heroin and other opioids.[22]
• Program has safeguards to prevent diversion.[21]</td><td>• High doses (max 200 mg) self-injected up to three times daily (max 500 mg/day) in a supervised clinic setting.[21,22]
• May require co-prescription of methadone, sustained-release morphine, or hydromorphone (e.g., bridging to next dose; travel).[21]</td></tr>
<tr><td>Is there any reason to use sublingual buprenorphine monotherapy vs a buprenorphine/ naloxone product?</td><td colspan="2">• Experts recommend that the buprenorphine/naloxone combination be used for most patients.[4]
• Some experts recommend sublingual buprenorphine monotherapy for pregnant women due to concerns that naloxone may cause withdrawal in the woman and fetus.[4,18,33] However, combination products are often used, and other experts feel it is safe and effective when used as directed because naloxone is minimally absorbed.[13] Use will likely increase with additional safety data.[33]
• Experts suggest closer monitoring for drug abuse in patients using sublingual buprenorphine monotherapy vs buprenorphine/naloxone.[27] Quantities dispensed should be smaller compared to treatment with the buprenorphine/naloxone combination formulation.[27]</td></tr>
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<table>
<tr><th>Question</th><th colspan="3">Answer/Pertinent Information</th></tr>
<tr><td rowspan="6">What buprenorphine products are available in the US for treatment of opioid use disorder?</td><td>Product</td><td colspan="2">Available Dosage Strengths</td></tr>
<tr><td>Sublocade (buprenorphine) depot injection</td><td colspan="2">300 mg or 100 mg injection</td></tr>
<tr><td>Brixadi (buprenorphine) depot injection</td><td colspan="2">weekly: 8 mg, 16 mg, 24 mg, 32 mg
monthly: 64 mg, 96 mg, 128 mg</td></tr>
<tr><td>Suboxone (buprenorphine/naloxone) sublingual film, generics</td><td colspan="2">2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg</td></tr>
<tr><td>Suboxone (buprenorphine/naloxone) sublingual tablet, (generic only; brand no longer available)</td><td colspan="2">2 mg/0.5 mg; 8 mg/2 mg</td></tr>
<tr><td>Subutex (buprenorphine sublingual tablets) (generic only; brand no longer available)</td><td colspan="2">2 mg; 8 mg</td></tr>
<tr><td></td><td>Zubsolv (buprenorphine/naloxone) sublingual tablets</td><td colspan="2">0.7 mg/0.18 mg; 1.4 mg/0.36 mg; 2.9 mg/0.71 mg;
5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg</td></tr>
<tr><td>Are there differences among the available transmucosal US buprenorphine products?</td><td colspan="3">• There are differences in dose-equivalencies among the products:
o One Zubsolv 1.4 mg/0.36 mg tab provides the same amount of buprenorphine as one generic 2 mg/0.5 mg sublingual tab. One Zubsolv 5.7 mg/1.4 mg tab provides the same amount of buprenorphine as one generic 8 mg/2 mg sublingual tab.[5]
• There is no evidence that one product is more effective than another.
• Generic transmucosal products cost about $390 per month[a] (i.e., WAC, 16 mg/day buprenorphine).
• The tablets may be abused by crushing and snorting (faster “high” than sublingual despite some naloxone absorption).[30] Both tablets and film can be abused intranasally or by injection.[7]</td></tr>
<tr><td rowspan="5">What buprenorphine products are available in Canada for treatment of opioid use disorder?</td><td>Product</td><td colspan="2">Available Dosage Strengths and Cost (wholesale)</td></tr>
<tr><td>Suboxone (buprenorphine/naloxone) sublingual tablet, generic</td><td colspan="2">2 mg/0.5 mg: $43.25 for 30 tabs (generic)
8 mg/2 mg: $76.63 for 30 tabs (generic)
12 mg/3 mg: $234.71 for 30 tabs (brand)
16 mg/4 mg: $312.94 for 30 tabs (brand)</td></tr>
<tr><td>Suboxone (buprenorphine/naloxone) film</td><td colspan="2">2 mg/0.5 mg: $86.51 for 30
4 mg/1 mg: $119.53 for 30
8 mg/2 mg: $153.25 for 30
12 mg/3 mg: $229.88 for 30</td></tr>
<tr><td>Sublocade (buprenorphine) extended-release injection</td><td colspan="2">300 mg or 100 mg injection</td></tr>
<tr><td>Probuphine (buprenorphine) implant</td><td colspan="2">320 mg total in four implantable rods</td></tr>
<tr><td colspan="3">For women who are pregnant, single-ingredient buprenorphine (Subutex) is available through Health Canada’s Special Access Programme.[18]</td></tr>
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Question	Answer/Pertinent Information
How is sublingual buprenorphine generally dosed for opioid use disorder?	Dosing presented here may differ from product labeling. Induction protocols vary. Dosing should be individualized.[4] • Patients **currently physically dependent on opioids**: Induction can happen in the office, hospital, or at home for appropriate patients.[4] Patients should be exhibiting withdrawal symptoms before starting, to prevent precipitating withdrawal.[4] This will require a washout of at least six to 24 hours after the last dose of short-acting opioid, or up to 36 hours after the last dose of long-acting opioid.[4,26] Patients switching from methadone should first taper to a dose of 30 to 40 mg/day for at least a week before stopping.[4] (Based on limited evidence, some prescribers are using microdosing [also called the Bernese method] to start buprenorphine when opioids are still on board.[10]) • Patients **not currently using opioids** are usually started with just 1 mg (or equivalent) of buprenorphine once daily, increasing slowly (e.g., 1 mg/day weekly to 4 mg/day, then 2 mg/day weekly to 8 mg/day). It is recommended that these patients take their first dose in the clinic so that they can be observed for sedation.[4] • A dose of ≥16 mg (or equivalent) of buprenorphine once daily may be more effective than lower doses for cessation of illicit opioid use.[13] Daily doses >24 mg (e.g., 32 mg) may be appropriate for some patients.[40,41] Some patients can be maintained on a dose every other day or three times weekly (e.g., 16 mg every other day instead of 8 mg once daily, or 16 mg on Monday and Wednesday, and 24 mg on Friday).[4,26] • See our *Buprenorphine Quick Start Guide,* below, for more practical tips on prescribing buprenorphine.
Is there a **limit** as to how long a patient can use buprenorphine for opioid use disorder?	• There is no known duration of buprenorphine use after which patients can stop and be certain not to return to illicit opioid use. The longer patients stay on it, the lower their risk of illicit use. Patients can take buprenorphine as long as they benefit (i.e., are meeting their individualized treatment goals) and wish to continue.[4] • Continue to address psychosocial and family issues that may contribute to opioid abuse.[4] • An "appropriate use checklist" to help ensure safe use and appropriate monitoring is available at https://btodrems.com/files/Appropriate_Use_Checklist_May2022.pdf. • If the patient wishes to discontinue buprenorphine, it is generally tapered over several months with psychosocial support and clonidine or other medications to address withdrawal symptoms, if they occur. See our FAQ, *Opioid Tapering: Tips for Success*, for more information.[4]
What **adjunctive nonpharmacologic treatmen**t should be considered? *Continued…*	• Address the patient's need for mental health services.[4] • Refer to a support group (in-person or virtual).[4,13] (Before making a referral, be aware that some patient support groups will not accept patients taking methadone or buprenorphine.[4]) o A list of virtual recovery resources is available at https://www.samhsa.gov/sites/default/files/virtual-recovery-resources.pdf. • Motivational enhancement/interviewing or cognitive-behavioral therapy may help change behaviors and drug use, respectively.[4]

Question	Answer/Pertinent Information
Adjuncts, continued	• Case management can help people get food, shelter, financial support, legal aid, transportation, and vocational services to stabilize their life situation.[4] • Family therapy (especially for adolescents) can address conduct disorder and conflict, and educate families about treatment to get buy-in.[4] • Note that adjunctive counseling **is not necessary** for buprenorphine success.[4]
How can I **identify patients who may be misusing their** buprenorphine or methadone, or taking nonprescribed substances?	• Look for potential signs of misuse such as requests for early refills. Also look for **late** refills; some patients will use heroin on the weekends and buprenorphine/naloxone during the week to temper withdrawal. • Interestingly, people who misuse and divert buprenorphine have some advice for prescribers: prescribe smaller quantities, and look for it in urine drug screens. Keep in mind that buprenorphine and methadone don't show up on **routine** urine drugs screens; if you are looking for it, let the lab know so that they can use the appropriate test. • Look for non-prescribed opioids on urine drug tests, and monitor opioid use with your state prescription drug monitoring program (US) or your provincial prescription or narcotic monitoring system if available (Canada).
Who can prescribe buprenorphine for opioid use disorder **in the US**?	• All prescribers who have a current DEA registration that includes Schedule III authority may now prescribe buprenorphine for OUD in their practice if permitted by state law, with no cap on the number of patients the prescriber can treat.[6,34] • *Sublocade*: US prescribers, and health systems and pharmacies that order and dispense *Sublocade*, must be certified in the *Sublocade* REMS program. • *Brixadi*: US prescribers, and health systems and pharmacies that order and dispense *Brixadi*, must be certified in the *Brixadi* REMS program (https://brixadirems.com/).
Who can prescribe buprenorphine for opioid use disorder **in Canada**?	• *Suboxone***:** in Canada, physicians generally must have experience in opioid substitution treatment, and complete the *Suboxone* Training Program (877-782-6966).[26] However, some provinces/territories have different requirements, so check with your provincial licensing body. • *Probuphine*: Canadian prescribers can call 844-483-5636 to get information on the live training program.[23] • *Sublocade*: In **Canada**, *Sublocade* is only available through a controlled distribution process.[32] See http://www.sublocadecertification.ca/Login.aspx?dest=/default.aspx.
What are some practical considerations for opioid use disorder **patients admitted to the hospital**? *Continued…*	• See our chart, *Treatment of Opioid Withdrawal*, which includes information on opioid substitution pertinent to the inpatient setting. • In the US, patients prescribed methadone can be continued on it in the hospital setting.[4] • In the US, an opioid can be administered in a hospital to maintain or detoxify a patient as an adjunct to treatment of medical or surgical conditions.[43] • In the US, in the hospital, an opioid can be administered (but not prescribed) for up to 72 hours for the purpose of relieving the patient's withdrawal symptoms while arranging for referral to a treatment program.[14]

Question	Answer/Pertinent Information
Considerations for hospitalized patients, continued	• Consider setting up a program in the emergency department to screen for opioid dependence, provide a brief intervention, and refer for (or even initiate) buprenorphine/naloxone.[11] • In Canada, check with your provincial licensing body.
How should acute pain be treated in patients with opioid use disorder?	• Our chart, *Treatment of Acute Pain in Opioid Use Disorder*, addresses common clinical scenarios, such as treatment of pain in patients taking buprenorphine or methadone for treatment of OUD, analgesia for patients with a history of OUD, and treatment of pain in patients actively abusing opioids.

a. Wholesale acquisition cost: US medication pricing by Elsevier, accessed September 2023.

--Continue to the next section for a Buprenorphine Quick Start Guide—

Buprenorphine Quick Start Guide

Use this stepwise approach to identify candidates for buprenorphine treatment of OUD and get them started quickly and safely. This guide is based on our FAQ, *Management of Opioid Use Disorder* (above), and SAMHSA's *Treatment Improvement Protocol*, *Medications for Opioid Use Disorder* (https://store.samhsa.gov/sites/default/files/pep21-02-01-002.pdf), which you can consult for additional information (e.g., buprenorphine products available, drug interactions, use in special populations).

1. **Identify** buprenorphine candidates. Candidates are people with moderate-to-severe OUD and physical dependence (withdrawal symptoms when trying to quit). A validated screening tool that can help to identify opioid misuse **in patients taking opioids for chronic pain** is the COMM (Current Opioid Misuse Measure) available at: https://www.mdcalc.com/calc/10428/current-opioid-misuse-measure-comm.
2. **Educate the patient** about buprenorphine. Explain that:
   - buprenorphine is not trading one addiction for another; it is a tool to help regain function.
   - OUD is a chronic condition. Buprenorphine may reduce risk of relapse and can be continued as long as they benefit.
   - stopping buprenorphine to use opioids poses a risk of overdose, as does using buprenorphine with alcohol or sedatives (e.g., benzodiazepines).
3. **Initiate** buprenorphine/naloxone in the office, hospital, or at home (for reliable patients):
   - **Prepare the practice site**. Have naloxone or nalmefene (US) on-hand and a policy for handling allergic reactions or precipitating withdrawal. Educate staff about buprenorphine to get buy-in to ensure a supportive environment. Engage billing professionals.
   - **Prescribe** (for outpatient induction) a sublingual buprenorphine/naloxone product. Example Rx: Buprenorphine/naloxone 2 mg/0.5 mg. Dispense #XX (enough for a few days, or #4 for in-office induction). No refills. Fill on [date]. Also prescribe naloxone or nalmefene (US) for home use.
   - **Discontinue opioids** when no longer needed for pain and the patient is stable enough to tolerate withdrawal. Usual intervals between opioid discontinuation and onset of withdrawal are provided above in the FAQ, *Management of Opioid Use Disorder*.
   - **Start** induction when the patient is experiencing clear signs of withdrawal. If naloxone has been given (e.g., in the emergency department), generally wait two hours to assess withdrawal (nalmefene [US] lasts longer than naloxone,[39] but no specific guidance is available in the context of starting buprenorphine).
   - **Target** a buprenorphine dose that improves withdrawal without causing sedation or euphoria.
     - **Outpatient clinic dosing example**: Allow several hours for up-titration. Target a dose that improves withdrawal without causing sedation or euphoria (usual first-day total = 8 mg).
     - **Hospital/emergency department dosing example**: Consider starting with 4 mg for Clinical Opiate Withdrawal Scale (COWS) ≥8, or 8 mg for COWS ≥13, with an additional 4 to 8 mg in 45 to 60 minutes, to a usual first-day total of 16 mg (range 12 to 24 mg).
     - Patients not yet in withdrawal can be educated on initiating at home when they are in withdrawal. See: https://medicine.yale.edu/edbup/.
   - **Educate** on withdrawal symptoms and proper sublingual use.
4. **Prescribe** buprenorphine/naloxone and **rescue naloxone or nalmefene** (US) for home use after initiation.
   - **After outpatient/clinic induction**, one **suggested approach** from SAMHSA is:
     - The next day, the patient will take the same total dose they took on day 1, in one dose. After two hours, if they are experiencing withdrawal, they can take an additional 2 mg/0.5 mg tablet (or equivalent), repeated once in another two hours if needed.
     - On days #3 and #4, they will take the same total dose they took the previous day, in one dose, with the potential for 2 additional doses, as above.

    - Patients should call the prescriber if they reach a total daily dose of 16 mg/4 mg, or if they feel sleepy after their dose.
- **After hospital/emergency department induction**:
    - Example discharge prescription: Buprenorphine/naloxone 8 mg/2 mg tabs or film. One sublingually twice daily. Dispense XX (enough to last until outpatient appointment).
    - Patients should call the prescriber if they feel sleepy after their dose, or if the prescribed dose feels inadequate.

5. **Follow up** at least weekly (initially).
    - Hospitals/emergency departments can maintain a list of local buprenorphine prescribers who will see new patients promptly, and pharmacies that carry buprenorphine/naloxone. Discharge the patient to a specific buprenorphine prescriber for stabilization and maintenance. Send discharge information (e.g., treatment course, medications administered, medications prescribed).
    - At follow-up, check for misuse (e.g., check Prescription Drug Monitoring Program [PDMP], urine drug screen, pill count), side effects (e.g., sedation), and progress toward predetermined goals (First week goal might be symptom improvement without oversedation.).

Abbreviations: COWS = Clinical Opioid Withdrawal Scale; OTP = opioid treatment program; OUD = opioid use disorder; SAMHSA = Substance Abuse and Mental Health Services Administration

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Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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