Chapter 69: Opioid Use Disorder

INTRODUCTION

- *Opioid use disorder* (OUD) consists of intoxication and withdrawal from the substance for which there is no cure. Since 1999, the number of overdose deaths contributed to OUD has more than tripled. These deaths have involved opioid substances including prescription opioids (ie, natural opioids, semisynthetic opioids, and methadone), as well as heroin and synthetic opioids (ie, illicitly manufactured fentanyl).

PATHOPHYSIOLOGY

- The true etiology behind substance use disorders (SUD) is unknown. In general, it is felt that there needs to be a triad of the right patient, with the right genetic risk factors, being exposed to the right medication or substance in order for a SUD to occur.

CLINICAL PRESENTATION

- Signs and symptoms of opioid intoxication include euphoria, dysphoria, slurred speech, miosis, apathy, sedation, and attention impairment. Signs and symptoms of withdrawal include lacrimation, mydriasis, piloerection, diaphoresis, diarrhea, yawning, muscle aches, and insomnia. Pinpoint pupils, decreased breathing, pulmonary edema, loss of consciousness, and death may occur with opioid intoxication.
- The onset of withdrawal ranges from a few hours after stopping heroin to 3–5 days after stopping methadone. Duration of withdrawal ranges from 3–14 days. Occurrence of delirium suggests withdrawal from another drug (eg, alcohol).
- Symptoms can be scored on the Clinical Opiate Withdrawal Symptoms (COWS) assessment tool to assess severity of opioid withdrawal.
- Laboratory tests to obtain include a comprehensive metabolic panel to monitor serum electrolyte concentrations in the setting of significant vomiting or diarrhea; check liver function tests if using buprenorphine. Arterial blood gases, pulse oximetry, and capnography are useful to assess respiratory depression in opioid intoxication.

DIAGNOSIS

- The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (*DSM-5*) defines SUD as "problematic pattern of substance use leading to clinically significant impairment or distress as manifested by at least two of eleven criteria occurring in the preceding 12-month period."
- These behaviors fall into the categories of: (1) impaired control, (2) social impairment, (3) risky use, and (4) pharmacological criteria, including tolerance and withdrawal, and are outlined in **Table 69-1**.
- SUDs occur in a broad range of severity from mild (2–3 symptoms) to moderate (4–5 symptoms) to severe (6 or more symptoms).
- *DSM-5* does not separate the diagnoses of substance abuse and substance dependence. Criteria are provided for SUD, accompanied by criteria for intoxication, withdrawal, substance-induced disorders, and unspecified substance-related disorders in some cases.
- *Addiction:* A primary chronic neurobiologic disease characterized by the inability to consistently abstain, impairment in behavioral control, craving, dysfunctional emotional response, and diminished recognition of significant problems with behaviors and interpersonal relationships.
- *Intoxication:* Development of a substance-specific syndrome after recent ingestion and presence in the body of a substance; it is associated with maladaptive behavior during the waking state caused by effects of the substance on the central nervous system (CNS).

- *Physical dependence:* A state of adaptation manifested by a drug-class–specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.
- *Substance dependence:* The continued use of the substance despite adverse substance-related problems.
- *Tolerance:* A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.
- *Withdrawal:* A substance-specific syndrome occurring after cessation of or reduction in intake of a substance that was used regularly.

TABLE 69-1

Eleven Criteria for Substance Use Disorder as Defined by *DSM-5*

Specific Category	Specific Behavior
Impaired Control	1. Substance is often taken in larger amounts or over a longer period of time than intended
Impaired Control	2. Persistent desire or continued unsuccessful efforts to cut down or control substance use
Impaired Control	3. Considerable amount of time is spent obtaining substance, using substance, or recovering from use of substance
Impaired Control	4. Craving or strong desire to use substance
Social Impairment	5. Recurrent use of substance is resulting in failure to fulfill major obligations at work, home, or school
Social Impairment	6. Continue to use substance despite persistent social or interpersonal problems
Social Impairment	7. Reducing or missing social, occupation, or recreational events due to substance use
Risky Use	8. Recurrent substance use in situations with increasing risk of physical harm
Risky Use	9. Continued use of substance despite knowledge of persistent or recurrent physical or psychological harm that was caused or worsened by the substance
Pharmacological Indicators	10. Tolerance as experienced by either: a. Need for increased amounts of the substance to achieve intoxication or desired result, or b. A noticeably decreased effect with continued use of the same amount of substance
Pharmacological Indicators	11. Withdrawal as experienced by either: a. Standard symptoms of withdrawal as defined by specific substance, or b. Use of a substance or a similar substance to relieve or avoid withdrawal symptoms

Opioids

- Deaths from prescription opioids have reached epidemic levels.
- **Heroin** can be snorted, smoked, and given IV. Complications of heroin use include overdoses, anaphylactic reactions to impurities, nephrotic syndrome, septicemia, endocarditis, and acquired immunodeficiency.

- **Hydrocodone** is the most widely abused pharmaceutical controlled substance in the United States.
- **Fentanyl** is a synthetic short-acting opioid which is 50–100 times more potent than morphine and approved for management of acute or chronic pain associated with advanced cancer. Most fentanyl-related morbidity and mortality have been linked to illicitly manufactured fentanyl and fentanyl analogs. It is often mixed with heroin or cocaine, with or without the user's knowledge. Several states have reported spikes in overdose deaths due to fentanyl and its analogs (eg, carfentanil).
- Opioids are commonly combined with stimulants (eg, cocaine [speedball]) or lcohol.
- **Methadone** has caused an increased number of deaths in recent years. Converting to methadone from other opioid agonists can be tricky, and lethal when done improperly. Peak respiratory depressant effects occur later and last longer than peak analgesic effects.
- **Dextromethorphan** and **loperamide** are over-the-counter drugs that cause depressant and mild hallucinogenic effects in high doses and significant hallucinations and CNS depression in excessive doses. Loperamide is sometimes taken with medications or foods that enhance its ability to cross the blood-brain barrier (ie, verapamil, methadone, cimetidine or grapefruit juice) to obtain CNS effects.

  ✔ Loperamide side effects associated with supratherapeutic doses include possible cardiac arrhythmias including QTc interval prolongation, torsades de pointes, ventricular dysrhythmias, syncope, and cardiac arrest.

  ✔ Acute overdoses of dextromethorphan can be treated with naloxone.

TREATMENT

- Goals of Treatment: Cessation of use of the drug, termination of drug-seeking behaviors, and return to normal functioning. The goals of treatment of withdrawal include prevention of progression to life-threatening severity, thus enabling comfort and functionality conducive to participation in a treatment program. OUD is a chronic disorder, and providing long-term medication decreases the risk of an accidental overdose or full relapse into opioid use.

Nonpharmacologic Therapy

- The treatment of OUD may also include behavioral therapy, but participation in this should not be required for receiving medications. Behavioral therapy should be introduced if and when the patient is ready.

Pharmacologic Therapy

- Naloxone is a key strategy in reducing opioid-related deaths because it may revive unconscious patients with respiratory depression. Naloxone is a competitive mu-opioid receptor antagonist that can be used in the reversal of an opioid overdose, but it may precipitate physical withdrawal in dependent patients. **Table 69-2** outlines the naloxone delivery options.
- Patients and their caregivers should be educated on the availability of naloxone and the proper use of this agent. The World Health Organization (WHO) recommends that anyone who might witness an overdose should have access to naloxone and proper training. Many states have simplified the process to obtain naloxone to prevent opioid-related overdoses.

TABLE 69-2

Naloxone Delivery Options

	Intramuscular Injection	Auto-Injector (Evzio)	Nasal Spray (Narcan)	Intranasal Spray (Atomizer)
Description of device or what is provided to patient	Two single-use 0.4 mg/mL naloxone vials Two single-use 3 mL syringes, 23–25 gauge, 1–1.5 inch needles	One box of 2 mg/0.4 mL prefilled auto injectors that includes 2 devices and a trainer device	One box of two 4 mg/0.1 mL intranasal devices	2 mg/2 mL prefilled naloxone needleless syringe Two mucosal atomizer devices
Directions for use	Inject 1 mL intramuscularly in shoulder or thigh upon signs of opioid overdose. Call 911 immediately. May repeat once in 2–3 minutes if no response or patient is showing minimal response	Use one auto-injector by injecting in outer thigh by depressing and holding for 5 seconds. Voice automation will direct the patient. Call 911. May repeat ×1 in 2–3 minutes if no response or patient shows minimal response	Use full contents of spray in one nostril upon signs of opioid overdose. Call 911. May repeat ×1 in 2–3 minutes if no response or patient shows minimal response, using the other nostril	Spray one-half of contents of syringe into each nostril upon signs of opioid overdose. Call 911. May repeat ×1 in 2–3 minutes if no response or patient shows minimal response

Naloxone pearls

- Naloxone has not been shown to cause severe effects or side effects if administered to patients who are currently not taking opioids.
- Naloxone should be given if the patient is intoxicated by a combination of products since the naloxone will still work for the opioid but not for other products such as benzodiazepines or alcohol.

Naloxone counseling topics

- Overdose recognition, response, prevention
- Importance of seeking emergency medical care
- Proper device use and counseling of family members and caregivers
- Proper storage, shelf life. Periodically check expiration date
- Potential side effects associated with naloxone
- Availability of drug treatment program

General opioid safety counseling

- Take medication only prescribed for you, only take prescribed doses
- Do not mix opioids with alcohol or sleeping pills
- Always store all medications in a locked and secure place
- Dispose of unused medications appropriately
- Do not use opioids/drugs alone. Never buy opioids/drugs from unknown source
- Do not restart opioid at same dose if there is a period of abstinence. Overdose is possible due to lower tolerance

Withdrawal

- A variety of treatment regimens are used for patients during the acute opioid withdrawal phase and are summarized in **Tables 69-3** and **69-4**.
- Avoid unnecessary detoxification with drugs if possible (eg, if symptoms are tolerable), and provide patient-specific supportive care measures, such as fluids, until the patient stabilizes.

- The three FDA-approved medications used in OUD include **methadone**, **buprenorphine**, and **naltrexone**, all of which work by blocking the effects of the opioids and reducing or eliminating the cravings.

TABLE 69-3

Differences Between Medication-Assisted Therapy (MAT) Products

	Methadone	Extended-Release Injectable Naltrexone (XR-NTX)	Buprenorphine
Pharmacology in OUD	Full opioid agonist at mu-opioid receptor with long half-life to allow for once-daily dosing for OUD	Antagonist at mu-opioid receptor (*note: does not provide analgesia and is not addictive*)	Partial agonist at mu-opioid receptor with long half-life (up to 36 hours via sublingual administration); blocks intoxicating effects of other opioids
Phase of treatment in OUD; effect	Medically supervised withdrawal, maintenance; reduces or eliminates withdrawal symptoms and cravings to use opioids, blocks or blunts the effects of illicit opioids	Prevention of relapse to opioid dependence following medically supervised withdrawal; reduces or eliminates cravings to use opioids and blunts or blocks the effects of illicit opioids	Medically supervised withdrawal, maintenance; reduces or eliminates withdrawal symptoms and cravings to use opioids and blocks or blunts the effects of illicit opioids
Route of administration used in MAT	Provided orally once daily: commonly given as liquid concentrate in OTPs but current guidelines also allow solid oral-dosage forms as well	IM extended-release (depot naltrexone)	Sublingual, buccal tablet, buccal film
		(*note: oral not as effective and use is not common in the treatment of OUD due to insufficient evidence of efficacy and poor medication adherence*)	Other routes of administration available after meeting specific criteria: subdermal implant, subcutaneous extended-release injection
Restrictions for prescribing each product	CII; patient must meet Federal Opioid-Treatment Program standards; can be used in hospital settings for OUD treatment	Not a controlled substance but requires a prescription. All naltrexone products can be prescribed by general practitioners and in OUD treatment	CIII; requires waiver to prescribe outside of OTPs. Prescribers will receive separate DEA number with a "X" upon meeting requirements of DATA 2000. To confirm practitioner verification: https//www.samhsa.gov/bupe/lookup-form
			Implant: prescribers must be certified in Probuphine REMS program to insert/remove implants
			Subcutaneous: healthcare settings and pharmacies must be certified in the Sublocade REMS program and only dispense the medication directly to a provider for administration
Patients that are commonly considered for this type of therapy	Patients with OUD; physiologically dependent on opioids and meet federal OTP admission criteria	Patients with OUD; patients who are abstinent from short-acting opioids for 7–10 days and long-acting opioids 10–14 days	Patients with OUD; physiologically dependent on opioids
Major side	Constipation, vomiting, dizziness,	Injection site pain and tenderness,	Constipation, vomiting, dizziness, sedation, insomnia,

effects	sedation, QTc prolongation, respiratory depression (risk is highest during initiation of methadone or dose titration and concurrent use of benzodiazepines or alcohol)	risk of injection site induration, toothache, LFT elevation, insomnia, nasopharyngitis	blurred vision, respiratory depression (highest risk with concurrent use of CNS depressants including benzodiazepines); sublingual buprenorphine/naloxone sublingual and buccal film: oral hypoesthesia, oral mucosal erythema, glossodynia

CII, Schedule II prescription; CIII, Schedule III prescription; IM, intramuscular; LFT, liver function test; OTP, Opioid Treatment Program; OUD, opioid use disorder; REMS, Risk Evaluation and Mitigation Strategy.

TABLE 69-4

Extended-Release Products Approved by FDA for Opioid Use Disorder

Drug	Trade Name	Dose	Comments
Naltrexone tablets	Revia	Following a 7–10 day opioidfree period for short-acting opioids or a 10–14 day opioid-free period for long-acting opioids: begin with dose of 25 mg daily with food. If no signs of withdrawal, increase dose to 50 mg po daily	Should be part of a comprehensive treatment plan that includes psychosocial support Although specific dosage adjustments are not available for patient with hepatic dysfunction, reports of elevated LFTs have been reported; use with caution Use with caution in patients with renal impairment, although data are limited, naltrexone and active metabolite are renally excreted
Naltrexone XR injection	Vivitrol	Following a 7–10 day opioid-free period for short-acting opioids or a 10–14 day opioid-free period for long-acting opioids: 380 mg IM in gluteal area alternating buttocks; every 4 weeks or once a month	Must be administered by a healthcare provider Must use manufacturer provided needle and assess body size of patient at each visit so proper needle size is used Monitor injection site closely for any signs of abnormal pain and contact healthcare provider immediately if this occurs Dose adjustment is required in mild or moderate hepatic impairment. No data available in severe hepatic impairment No dose adjustments in mild renal impairment; use caution in patients with moderate-to-severe renal impairment, naltrexone and active metabolite are renally excreted
Buprenorphine	Probuphine	Four implants are inserted subdermally in the inner side of the upper arm and should remain in place for 6 months	Patients must meet specific criteria for use of Probuphine: a. Only indicated for patients who are opioid tolerant b. Demonstrates clinical stability on transmucosal buprenorphine with Subutex or Suboxone 8 mg/day or less (or transmucosal equivalent) for 3 months or longer without requiring supplemental dose adjustments Probuphine must be inserted or removed within a facility and by a certified provider who has completed the required live training

			It is recommended to not prescribe as-needed transmucosal buprenorphine products. If patient is requesting these products, reassessment is indicated Moderate-to-severe hepatic impairment: use not recommended Limited data in renal impairment, currently no dosage adjustments listed
Buprenorphine	Sublocade	For patients who have achieved clinical stability on equivalent of 8–24 mg of a transmucosal buprenorphine product daily *Available in two extended-release solutions:* *100 mg/0.5 mL* *300 mg/1.5 mL* Directions: inject 300 mg subcutaneously once a month in abdominal area for 2 months, then decrease dose to 100 mg once monthly in abdominal area	Must be administered by a healthcare provider Steady state occurs after 4–6 months; after discontinuation detectable buprenorphine levels could occur 12 months or longer; urine and plasma concentration correlations are not known Injections must occur at least 26 days apart. Follow all manufacturer directions for preparation and injection Do not give the injection at the belt or waistband area where pressure will occur Counsel the patient that there will be a small bump at the injection site that will decrease in size over the next several weeks. Do not rub or massage this area If needed, the most recently injected depot can be removed within the 14 days of injection under local anesthesia Doses can be adjusted back to 300 mg monthly for patients in whom benefits exceed risks Examine injection site each month for evidence of tampering Moderate-to-severe hepatic impairment: use not recommended Limited data in renal impairment, currently no dosage adjustments listed

IM, intramuscularly; LFTs, liver function tests; mg, milligram; mL, milliliters.

Methadone

- Methadone is a mu-opioid agonist that suppresses withdrawal symptoms and controls cravings for maintenance therapy.
- Once-daily dosing can range from 10 to 30 mg, depending on the patient's use pattern. This dose should be reduced to 10–20 mg for those over the age of 60, or if drug–drug interactions are identified.
- Dose adjustments of 5–10 mg should occur gradually, no sooner than every 4–7 days based on clinical response. Maintenance doses range between 60 and 120 mg/day.
- Adverse effects seen with methadone use include sedation and respiratory depression.
- Methadone has many cytochrome P450 drug interactions, and concomitant use of alcohol or benzodiazepines can lead to overdose and use should be assessed.
- Methadone carries a risk of QT prolongation, which is increased when given with other drugs that also prolong the QT interval.

- The use of methadone for OUD treatment is only approved through the Opioid Treatment Program (OTP), controlled by the Drug Enforcement Agency (DEA) and Substance Abuse and Mental Health Services Administration (SAMHSA). Methadone for the treatment of OUD may be provided to patients during a hospital admission for treatment of other health conditions.

Buprenorphine

- Buprenorphine is a partial mu-receptor agonist that is available as buprenorphine alone or buprenorphine/naloxone formulations. **Table 69-5** outlines the products used in the treatment of OUD. Due to its partial agonist activity, buprenorphine does provide some intrinsic pain control and has a ceiling effect for respiratory depression. Buprenorphine can be abused.
- Initiation in the emergency room for patients who present with opioid withdrawal symptoms is a treatment option, and federal guidelines state that buprenorphine should be offered to patients with OUD who are appropriate candidates.
- Buprenorphine is a Schedule III controlled substance with specific prescribing restrictions. Refer to the DEA webpage for the most up-to-date regulations regarding buprenorphine prescribing. Sedation or intoxication is the main adverse effect seen with use.
- It is recommended that treatment starts with a COWS score of 12 or higher for the first dose, based on buprenorphine Risk Evaluation and Mitigation Strategy (REMS).
- Medically supervised withdrawal with buprenorphine consists of an induction phase and a dose reduction phase followed by maintenance. SAMHSA provides evidence-based recommendations for use of buprenorphine for opioid addiction through various Treatment Improvement Protocols (TIPs). The same buprenorphine preparation is commonly used for induction, stabilization, and maintenance for most patients.
- Induction helps patients switch from the opioid of abuse to buprenorphine, and the goal is to find the minimum dose of buprenorphine at which the patient discontinues or markedly diminishes use of the opioid of abuse and experiences no withdrawal symptoms, minimal or no side effects, and no craving. The initial induction doses should be administered as observed treatment.
- The stabilization phase starts when the patient is experiencing no withdrawal symptoms, is having minimal or no side effects, and no longer has uncontrollable cravings.
- The maintenance phase may be indefinite and should focus on psychosocial and family issues. Attention must be focused on psychosocial and family issues identified during the course of treatment that contribute to a patient's OUD.
- Patient education is important (**Table 69-6**).

TABLE 69-5

Oral Buprenorphine Products Used for Treating Opioid Use Disorder

	Buprenorphine SL Tablet	Suboxone SL Tablet	Zubsolv SL Tablet	Suboxone SL or Buccal Film	Bunavail Buccal Film
Strengths of products commercially available/Routes of administration	2 mg 8 mg	Buprenorphine/Naloxone 2 mg/0.5 mg 8 mg/2 mg	Buprenorphine/Naloxone 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	Buprenorphine/Naloxone 2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg	Buprenorphine/Naloxone 2.1 mg/0.3 mg 4.2 mg/0.7 mg 6.3 mg/1 mg
Recommended once-daily target maintenance dose and dosing ranges	Target maintenance dose 16 mg **Dosing range** 4–24 mg[a]	Target maintenance dose 16 mg/4 mg **Dosing range** 4 mg/1 mg to 24 mg/6 mg[b]	Target maintenance dose 11.4 mg/2.9 mg **Dosing range** 2.9 mg/0.71 mg to 17.2 mg/4.2 mg[a]	Target maintenance dose 16 mg/4 mg **Dosing range** 4 mg/1 mg to 24 mg/6 mg[a]	Target maintenance dose 8.4 mg/1.4 mg **Dosing range** 2.1 mg/0.3 mg to 12.6 mg/2.1 mg

[a]Doses higher than 24 mg/6 mg have not been shown to offer any further benefit.

[b]Doses higher than 17.2 mg/4.2 mg have not been shown to offer any added benefit.

SL, sublingual.

Note: Refer to individual product dosing information when switching formulations due to possible bioequivalence variability. Monitoring is recommended following a switch in products due to possible variation in response to different formulations.

TABLE 69-6

Patient Education Points for Buprenorphine Treatment

Prior to Starting Buprenorphine Therapy and Repeat Education at Induction:

- **Communication with prescriber:** Tell your doctors all medications including over-thecounter, herbal, creams, injections, inhalants, street medications, etc. that you are currently taking. This is important so your doctor is aware of what is in your body and if there are any chances of a dangerous drug interaction. Additionally, tell all of your doctors you are taking buprenorphine. If you are being treated for pain, it is very important to tell your doctor you are taking buprenorphine.
- **Goals of therapy:** The goal of your first week of treatment is to improve the symptoms of withdrawal without causing any oversedation (making you too tired or feeling over medicated). Notify your doctor/prescriber if you are feeling overly tired/sedated or euphoric within 1–4 hours of your dose. Dose adjustments might occur initially and it will take a little time for the buprenorphine to become stable in your system. The goals of therapy include finding the right dose to eliminate withdrawal, decrease or even eliminate cravings for opioids, and block the effects of other opioids without severe side effects.
- **Product use:**
  - Buprenorphine products (tablets, sublingual film, and buccal film) are not equivalent. If you have to transition to a new buprenorphine product, a dose adjustment might be required.
  - Take your dose at regular intervals and only as prescribed.
  - If you miss a dose, take the dose as soon as possible. If it is almost time for the next dose, do not double your dose, take only the dose that is

prescribed.
- Leave medication in packaging until you are ready to use.
- Do not swallow sublingual tablets or film. This can reduce the effect of buprenorphine and lead to withdrawal symptoms.
- Sublingual tablets
  i. Place tablets under your tongue and allow the tablet to fully dissolve, which can take several minutes.
  ii. If your dose requires multiple tablets, all tablets can be placed under the tongue at one time. If this is uncomfortable, only place two tablets under the tongue at a time.
- Sublingual film
  i. Drink water prior to placing the film to help the film dissolve easily.
  ii. Place film under the tongue, to the left or right of the center of the tongue, and allow to completely dissolve.
  iii. If you are prescribed 2 films at a time, place the second film on the opposite side of the tongue. Do not allow the films to touch.
  iv. If you are prescribed more than 2 films at a time, wait until previous films have dissolved and repeat the process.
- Buccal film
  i. Wet the inside of your cheek with your tongue or rinse with water prior to placing film.
  ii. Hold the film by the edges with two fingers and place on inside of cheek until fully dissolved, which can take up to 30 minutes.
  iii. If you are prescribed 2 films, place the second film inside the opposite cheek.
  iv. Do not adjust the film placement or touch the film, do not chew or swallow the film
  v. Do not drink or eat until the film has completely dissolved.
- **Common side effects:** Some side effects can occur when taking buprenorphine. These do not happen all of the time and do not happen to everyone. If you are experiencing any of these side effects please tell your doctor immediately. Do not stop taking buprenorphine without first speaking to your doctor. The most common side effects include headache, nausea, constipation, abdominal pain, insomnia, sweating, and a possible feeling of weakness or lack of energy.

- **Precautions and warnings**
  - Using alcohol while taking buprenorphine is very dangerous and can lead to increased risk of overdose and possibly death.
  - There is a risk of overdose and possibly death if taking buprenorphine with benzodiazepines or alcohol.
  - Using tobacco products prior to using buprenorphine decreases the absorption of buprenorphine, thereby decreasing its effectiveness.
  - Long-term buprenorphine maintenance is recommended in many cases. If you stop buprenorphine, there is a high risk of overdose if you return to illicit opioid use.
  - Buprenorphine is an opioid that can cause physical dependence. Do not stop taking buprenorphine without consulting your doctor. If you stop buprenorphine abruptly, you could experience withdrawal symptoms.
  - All medications, including buprenorphine, should be stored in a secure area, preferably in a locked cabinet or safe. It is important to keep medication away from children.
  - It is recommended that you do not drive, operate heavy machinery, or perform any dangerous activities until you are fully aware of how this medication affects you.
  - If you feel you have taken too much buprenorphine, you will need emergency medical attention immediately. Some possible signs include dizziness, confusion, unsteady or faint, slowed reflexes, or breathing slower.
  - Do not inject these products. Serious life-threatening infections could occur. Additionally, serious withdrawal reactions can also occur upon injecting many of these buprenorphine products.
- **Pregnancy:** It is very important to inform your doctors if you become pregnant.
- **Counseling options:** Recovery resources and counseling resources are available for you and your family. We can give you further information on this when you are ready.

Maintenance:

- **Adherence assessment:** If any discrepancies arise, initiate discussion to identify reasons for discrepancies
  - Complete pill/film count
  - Review PDMP
  - Confirm current buprenorphine dose
  - Review results of urine drug screen

- **Treatment assessment and counseling**
  - Review treatment goals and assess progress
  - Review and assess benefits and risks of continuing buprenorphine treatment
  - Discuss participation in counseling or encourage counseling if not receiving counseling

Naltrexone

- Naltrexone is a mu-opioid antagonist that is available for OUD in both an oral tablet and an extended-release injectable formulation.
- After confirming patients have been opioid free for 7–10 days, the initial dose is 25 mg given once daily, which can be increased to 50 mg/daily. Extended-release injectable naltrexone (Vivitrol®) is FDA-approved for use following opioid detoxification to help prevent relapse.
- The main adverse effects include swelling, bruising, and pruritus at the injection site. Elevations in liver function tests may occur with oral use.

Alpha-2 Agonists

- **Clonidine** or **lofexidine** may be used to attenuate withdrawal symptoms such as anxiety, tachycardia, hypertension, chills, and piloerection.
- Adverse effects include hypotension, dizziness, and sedation.

EVALUATION OF THERAPEUTIC OUTCOMES

- OUD is a chronic disorder that requires pharmacological treatment and psychosocial and educational support. Consistent monitoring for efficacy and appropriateness through treatment is critical.
- Monitoring for withdrawal reactions utilizing proper assessment scales (ie, COWS) can aid in evaluating the patient appropriately.
- Medication safety has to be considered based on unique side-effect profiles and drug-interaction concerns for the selected treatment regimen.
- Data from urine drug screens and profiles from the Prescription Drug Monitoring Program (PDMP) can provide critical information on the full clinical picture for each patient.
- Continual patient education must occur to ensure proper medication administration and safety as the therapy continues.

See Chapter 82, Substance-Related Disorders I: Overview and Depressants, Stimulants, and Hallucinogens, authored by Robin Moorman Li, Patrick Leffers, and Paul L. Doering, for a more detailed discussion of the topic.