# Buprenorphine Protocol: Induction

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References used in this module:
BUPRENORPHINE PROTOCOL: INDUCTION

Goal:
To train providers to initiate patients on buprenorphine safely and effectively.

After completing this module participants will be able to:
• Prepare patients to get ready to start taking buprenorphine successfully
• Demonstrate a thorough understanding of dosing guidelines to start patients on buprenorphine treatment
• Titrate buprenorphine dose to address the individual patient’s needs
• Recognize, anticipate, and treat complications of buprenorphine use in your patients during induction

Professional Practice Gaps
The Substance Abuse and Mental Health Services Administration (SAMHSA), based on National Survey on the 2013 Drug Use and Health survey, found the following evidence of a continuing opioid epidemic and need for additional treatment among Americans age 12 and over:\(^1\):

• Current use:
  • 289,000 or 0.1 percent current users of heroin (similar to 2008 to 2012)
  • 4.5 million or 1.7% current users of non-medical use of pain relievers (similar to 2011 and 2012).
• New use:
  • 169,000 new initiates to heroin (similar to estimates from 2007 to 2012)
  • 1.5 million new initiates to nonmedical use of pain relievers (lower than 2002 to 2012, which was 1.9 million to 2.5 million).
• Receiving treatment: Only a small fraction of users needing treatment for an opioid use disorder receive it, especially for prescription pain relievers, but the numbers increased in 2013:
  • Past year receipt of treatment for heroin users rose from 277,000 persons in 2002 to 526,000 persons in 2013
  • Past year receipt of treatment for nonmedical users of prescription pain relievers increased from 360,000 in 2002 to 746,000 in 2013.

Buprenorphine is a safe and effective treatment for opioid use disorder that offers patients a more widely available, accessible, convenient treatment option as compared to traditional opioid treatment programs (OTP)\(^2-4\). The Drug Addiction Treatment Act (DATA) of 2000—an amendment to the Controlled Substances Act — allowed physicians who are not part of an OTP to prescribe buprenorphine with additional training and a waiver to the Controlled Substances Act. The Comprehensive Addiction and Recovery Act of 2016 (CARA) added nurse practitioners and physician assistants to the list of providers who can train to prescribe buprenorphine and become waivered.

The law requires physicians to complete an 8-hour buprenorphine training conducted by an approved organization in order to prescribe it; the required training for nurse practitioners and physician
assistants is 24 hours. While buprenorphine is relatively safe, there are risks of overdose and death due to buprenorphine and there is a risk of diversion\textsuperscript{5}, which, in addition to skills needed to prescribe the medication effectively for each individual, are among the reasons for the mandatory training. This buprenorphine training activity prepares providers to prescribe buprenorphine safely and effectively to address needs of the millions of Americans with opioid use problems. The activity has been developed to meet the DATA 2000 training guidelines as defined in Public Law 106-310-106th Congress as well as the Comprehensive Addiction and Recovery Act of 2016 (S 524, Title III, Section 303-114th Congress) and is endorsed by the American Society of Addiction Medicine, one of the approved training organizations named in DATA 2000. The activity content was initially based upon SAMHSA's 2004 publication Treatment Improvement Protocol (TIP) #40: Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction and follow the Model Policy on DATA 2000 and Treatment of Opioid Addiction in the Medical Office\textsuperscript{5}. It has been edited to SAMHSA's \textit{Sublingual and Transmucosal Buprenorphine for Opioid Use Disorder - Review and Update} (2016), ASAM's \textit{National Practice Guideline For the Use of Medication in the Treatment of Addiction Involving Opioid Use} (2015), and the CDC's guidelines on opioid treatment\textsuperscript{6} as well as CARA 2016. The courses are regularly reviewed and updated by ASAM members who are experts in the field of addiction medicine and buprenorphine treatment.

Specific Gap in Training:
Providers need to be able to prepare patients to start buprenorphine therapy, titrate the dose, and establish a final dose. Chapter 4 of TIP 40\textsuperscript{4}, more recent guidelines\textsuperscript{7}, and the FSMB Model policy\textsuperscript{5} describe this process in detail.

\section*{MODULE INTRODUCTION}
Starting buprenorphine treatment is called "induction." This module discusses appropriate preparation of the patient for induction, dosing principles, and how to respond to complications that may present during induction.

\section*{Case Illustrations}
The following cases will be used to illustrate the application of the induction protocol as well as common variations that might be encountered.

\textbf{MR. ROSSMAN}
Mr. Rossman has developed moderate opioid use disorder. How would you address his need to taper?
MS. COLLIER
Ms. Collier arrives for induction with only some of the expected withdrawal symptoms.
How can you determine if she is in sufficient withdrawal for induction?

MR. ALLEN
Mr. Allen has come in for his first day of induction.
What dosage should be used to start and what are the appropriate increments for increasing the dose?

MS. SANchez
After having surgery for an ovarian cyst 3 years ago, Ms. Sanchez has had trouble getting off a low dose of Vicodin®.
How would you modify induction given her low regular dose of opioids?

Source
This content was originally adapted from the Substance Abuse and Mental Health Services Administration's (SAMHSA's) Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction (TIP 40) (2004). Because it is the basis for the content, we do not cite the TIP 40 source in the text.

The content has been updated, as noted by citations, according to SAMHSA's (2016) Sublingual and Transmucosal Buprenorphine for Opioid Use Disorder - Review and Update, expert review, and other subsequent literature including The ASAM National Practice Guideline For the Use of Medication in the Treatment of Addiction Involving Opioid Use (2015).

BupPractice was created using NO pharmaceutical or other industry support.

PHASES OF BUPRENORPHINE TREATMENT

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The 3 Phases of Buprenorphine Treatment

Induction is the first of three phases of buprenorphine treatment. The three phases are the following:

1. Induction
2. Stabilization
3. Maintenance

1. Induction

During induction, buprenorphine is started. Many providers conduct induction in-office, because it requires a higher degree of attention and monitoring than later treatment.

**Goal of induction:**
To start buprenorphine treatment when the patient is in an appropriate state of withdrawal and to find your patient's ideal daily dose of buprenorphine

The patient should be in withdrawal as they take the first dose. This will avoid triggering severe withdrawal and also allow the titration of dose to an effective level for abstinence. The ideal daily dose minimizes both side effects and drug craving.

For most of your patients with opioid use disorder:

- The daily dose is 12 to 16 mg* buprenorphine/day
- Use the combination naloxone plus buprenorphine film or tablet
- Induction usually takes 2 to 4 days to complete

*Doses were established with the original Suboxone® sublingual tablets. Adjust dosage for the formulation you are prescribing.

2. Stabilization

The stabilization period begins after induction and continues until your patient is no longer experiencing withdrawal symptoms or intense cravings. This typically occurs at about 6-8 weeks following induction. Side effects should be minimal or none.

**Goal of Stabilization:** Eliminate opioid use other than the partial agonist buprenorphine, as noted by patient reports and confirmed by urine drug testing

During this phase:

- Monitor patients weekly
- Adjust dosing if needed
- Recommend starting psychosocial therapies along with medication assisted therapy

3. Maintenance

Because of a high relapse rate if buprenorphine is discontinued, many patients need to be maintained on buprenorphine indefinitely.

**Goal of maintenance:** Continue daily dose of buprenorphine to prevent relapse

For patients requiring maintenance:
• Patients should be maintained at a comfortable dose and feel minimal cravings and side effects.
• Some patients can taper off of buprenorphine after a year or two.
  • Many need to continue taking it for years\(^9\).
• Clinic visits should still occur during this time but may be less frequent.
• Recommend that patients continue psychosocial therapies. Medication should not be stopped, however, because of non-adherence to counseling. Checking in with the provider or trained staff may also be an effective way to support maintenance.

Induction is the focus of this module. The brief stage of treatment, Stabilization, will also be discussed briefly. Maintenance, the final and usually ongoing stage of treatment is covered in more detail in its own module.

**PRACTICE TIP**
The FDA has produced an Appropriate Use checklist to follow for each patient that helps you make sure you follow the REMS guidelines for the medication with each patient. Items in the checklist are explained in this module on Induction and the module on Maintenance.

**MEDICAL EVALUATION BEFORE INDUCTION**

After determining that your patient is appropriate for OBOT, complete the following before starting induction\(^10\):

- History & physical
- Verification of patient list of medications
- Screening for use of illicit drugs, misuse of prescription drugs, and alcohol use
- Brief psychosocial assessment
- Lab testing:
  - Liver function tests – patients with elevated liver function 3 to 5 times above normal should not be considered for buprenorphine
  - Urine toxicology – Screen for naturally occurring opioids (heroin is detected as morphine), synthetic and semisynthetic opioids (methadone, oxycodone), and other commonly abused drugs such as cocaine, amphetamines, and benzodiazepines
  - Pregnancy test
  - HIV and viral hepatitis serologies

**PRACTICE TIP**
While conducting the pre-induction interview, it can be useful to have the patient describe their withdrawal symptoms in the order of typical appearance to use for comparison during induction. This information can be used later, on the day of induction, to predict when the patient will be ready, that is, in sufficient withdrawal, to receive their first dose of buprenorphine.
PREPARE FOR INDUCTION

Patient Interaction Steps Before Induction
1. Consent forms and treatment agreements
2. Determine when and where to start induction (clinic vs. home induction)
3. Provide patient education about the induction, stabilization, and maintenance processes

Patient Education Part 1: Preparing for Induction
Review patient education in detail before induction day and repeat the key points on induction day. Follow a checklist to assure that all patient education points are reviewed with all of your patients. (See: Appropriate Use Checklist, under Resources)

The following patient education points are important to emphasize before induction and again on induction day:

1. **Be in withdrawal at induction**: Advise your patients not to use opioids for the appropriate amount of time to be in withdrawal at induction in order to prevent precipitated withdrawal. This may be 12 to 24 hours for many opioids and potentially longer for long-acting opioids. Patients often know the timing from experiences with running out of the drug they take.
2. **Come with a driver**: Recommend your patient get a friend/family member to drive them home when doing clinic-based induction.
3. **Review medication guide**: Provide your patients with a written Medication Guide that is specific for the buprenorphine formulation you will prescribe.

PATIENT EDUCATION ABOUT INDUCTION AND ONGOING TREATMENT

Patient Education Part 2
**Medication Instructions**: Instruct your patients to follow directions exactly, including:
- When to begin dosing
- How to take the medication properly
- Frequency of subsequent doses

**Sedating Effects**: Sedation effects are most obvious in early stages of treatment (induction, titration of dose). Use caution with psychomotor activities (e.g., driving a car).

Instructions to avoid other sedating medications and alcohol are particularly important in this phase.

SAFE MEDICATION STORAGE AND DISPOSAL
A guideline by the AMA (2017) recommends that providers:

1. Talk to their patients about opioid misuse, letting them know that 70% of misused opioids come from family and friends.

Proper storage of medications should start from the beginning and be revisited periodically throughout the module of treatment. This is to safeguard against potentially dangerous use by others:
- Any visitor can steal from a medicine cabinet and so it is not a good storage place.
• Individuals not tolerant of opioids can overdose on a relatively low dose.
• Risks to children should be emphasized; "Even very brief exposure to buprenorphine formulations can result in sedation, respiratory depression, cerebral anoxia, and death". Following exposure of even a few seconds, children should receive immediate medical attention and observation for 24 hours.
• Proper disposal of medications should also be part of patient education.
• Document these discussions in the patient record.

QUIZ: INFORMED CONSENT

An informed consent document discussed with and signed by the patient is a good way to reinforce practice policies and establish ground rules. Obtaining your patient's informed consent includes the following key steps:

1. Providing sufficient information
2. Your patient being able to process the information
3. Your patient's consent being freely granted

What are some areas of informed consent that are unique to buprenorphine?
Choose all that apply

1. The success rates with weaning off the medication at a future date
   • Feedback: Correct! It is important to inform patients that success rates of weaning off buprenorphine at a later date are low.
2. The anticipated duration of treatment
   • Feedback: Correct. The anticipated duration of treatment is a component of informed consent, and the typically indefinite duration for buprenorphine maintenance is unique to buprenorphine treatment.
3. The withdrawal that will be experienced if the medication is discontinued
   • Feedback: Correct! Patients will experience withdrawal symptoms if they discontinue buprenorphine treatment and the sharing of this information is a component of informed consent in this instance. They must understand that they will be physically dependent on buprenorphine.

INFORMED CONSENT

Topics to Cover In Consent
Written and reviewed informed consent, signed by the provider and patient, should include the following elements:

Treatment:
• Purpose of the treatment
• Alternative treatment options, including other medication-assisted treatment (e.g., methadone, naltrexone) and no medication assistance, and their relative risk for relapse
• Anticipated duration of treatment
• The success rates of buprenorphine maintenance and of weaning off buprenorphine at a future date
• The importance of seeking support from counseling and of a social support system

Medication:
• Name of medication and what it does
• The mechanism by which buprenorphine treats opioid addiction: That one opioid dependence and addiction is basically being replaced by another dependence, buprenorphine, but not addiction. As part of explaining this topic, many of your patients will need an explanation of the difference between addiction, dependence, and the diagnosis of opioid use disorder.
• Risks and benefits:
  • Dependence on buprenorphine that will develop and withdrawal that would be experienced if it is stopped
  • The likelihood of relapse if treatment is discontinued
  • Contraindications, warnings, adverse reactions, side effects, and drug interactions

Confidentiality
• Your patient's wishes regarding privacy (i.e., who can be told about treatment) 5,7

PRACTICE TIP
1. Document the informed consent in the patient's medical record.
2. Recommend that the patient be accompanied by someone who can help them recall instructions. This is a lot of information for patients to remember.

WITHDRAWAL AT INDUCTION

Objectively Assessing Withdrawal
Patient education prior to induction includes describing the target state of withdrawal that is needed before taking the first dose of buprenorphine. The target level of withdrawal is mild to moderate.

Immediately before induction, use an objective measure - like the Clinical Opioid Withdrawal Scale (COWS) – to evaluate your patient's withdrawal symptoms. An objective measure is important, for example, because patients may exaggerate their symptoms to avoid discomfort. When patients have a mild to moderate COWS score of 12 to 16 11, they are ready for the first dose. Some providers go as low as 5 or as high as 24 on the COWS scale, but ideally > 10. Other withdrawal scales, such as the Subjective Opiate Withdrawal Scale (SOWS) and the Objective Opiate Withdrawal Scale (OOWS), may also be used.

Scale Components
The COWS measures withdrawal symptoms with observations of the following:
  • Resting Pulse Rate
  • Sweating
• Restlessness
• Pupil Size
• Bone or Joint Aches
• Running Nose or Tearing
• GI Upset
• Tremors
• Yawning
• Anxiety or Irritability
• Goose-flesh Skin

PRACTICE TIP
Be sure to look for objective signs of withdrawal to help confirm reports of subjective symptoms.

EFFECT OF OPIOID TYPE ON INDUCTION
Determine the formulation your patient has been taking, short-acting vs. long acting/extended release, because it can affect induction in several ways. Note that some opioids, including fentanyl, oxycodone, and morphine are available in both formulations.

Short acting opioids
• Buprenorphine treatment of dependence on short-acting opioids differs from treatment of dependence on long-acting opioids in a few ways. Most patients who present for buprenorphine treatment are dependent on short-acting opioids. Heroin and many abused prescription narcotics are short-acting opioids.
• Abstinence timing for short-acting is 12-16 hours; for intermediate-acting is 17-24 hours

Long acting opioids
• Due to their longer action, patients on long-acting opioids must start abstaining from their medication for longer before their induction appointment to evoke withdrawal.
• Patients may need more "comfort" medicine (e.g., non-opioid analgesics, anxiolytic used sparingly and very carefully, antidiarrheal agents, antiemetics, antispasmodics) to help with remaining withdrawal after the first day until a stable daily dose is established.
• Differences in the activity of these two types of opioids at the mu opioid receptors make precipitated withdrawal much more likely for long-acting opioids than for short-acting opioids, so treat induction for long-acting opioids with care.
• Methadone is a long-acting opioid. Transferring from methadone requires some additional details and will be covered separately in another module in the section on special patients in this training activity.
• Abstinence timing for methadone is 30-48 hours
**Meet Your Patient**

**Name:** Mr. Rossman  
**Age:** 35 years old  
**Reason for visit:** Mr. Rossman began taking immediate release oxycodone 20 mg for his back and developed moderate opioid use disorder. For the past year he has been taking 30 mg extended-release oxycodone, but 6 months ago, his provider tapered the dose and stopped prescribing it. His back has not been a problem for over a year, but he continues to take oxycodone ER daily getting it wherever he can. When he considered using heroin because of the difficulty maintaining a supply of oxycodone, he got scared of becoming a heroin addict and decided it was time to seek treatment. He came to you for help.

**NEXT STEP**

During his pre-induction office visit, you describe the level of withdrawal you would want him to be in at his induction visit.

**Question:** Which of the following is true regarding Mr. Rossman’s preparation for induction? Choose all that apply:

1. He will need to take his last extended-release oxycodone at least an hour before induction so that his opioid blood levels are high enough at the time of induction.  
   - Feedback: Incorrect. This choice is inappropriate. Opioids should be cleared from his blood, not "high enough." To start buprenorphine treatment, ie., induction, the patient needs to be in a state of moderate withdrawal. This will avoid triggering severe withdrawal and also allow the titration of dose to an effective level for abstinence. Because Mr. Rossman is taking an extended-release opioid, he must start abstaining from his medication for longer before his induction appointment to evoke withdrawal, in comparison to a patient who is taking an immediate-release opioid. One hour will not be sufficient. The time needed is likely to be around 24 hours or more.

2. A medical evaluation should include a history and physical; verification of his medications, alcohol use, and use of illicit drugs; a brief psychosocial assessment; and laboratory testing if there is a history of liver disease, alcohol, or illicit substance use.  
   - Feedback: Incorrect. While the first items in this list are all a part of medical evaluation prior to induction, laboratory testing should be completed for all patients starting buprenorphine. Lab tests for all patient should include liver function tests, urine toxicology, pregnancy test for women, and viral serologies for HIV and viral hepatitis.

3. Prior to induction, Mr. Rossman should be given a written medication guide for the formulation of buprenorphine that he will be prescribed.  
   - Feedback: Correct. Mr. Rossman should be given a written medication guide that is specific for the formulation of buprenorphine that he will be prescribed, as part of his education prior to induction. Patient education prior to induction also includes the
importance of being in withdrawal at induction, warning about sedating effects and recommending that he have someone with him to drive him home if induction will be in the clinic, all the usual components of informed consent including an understanding of the phases of treatment, alternative treatments, and anticipated duration of treatment, and ideally a written doctor-patient treatment agreement.

Medical evaluations are important for all buprenorphine patients, including, history and physical; verification of his medications, alcohol use, and use of illicit drugs; a brief psychosocial assessment and laboratory testing are all a part of medical evaluation prior to induction. Laboratory testing should include liver function tests, urine toxicology, pregnancy test, and viral serologies for HIV and viral hepatitis.

**QUIZ: DOSE DAY 1**

Buprenorphine induction should be gradual. The patient's dose should be increased slowly over the course of a few days.

**Question:** What is the recommended first day total dose (Suboxone or generic – Day 1 of induction)?

Choose one

1. 2 mg/day
   - Feedback: Incorrect. The recommended first day TOTAL dose is 8 mg buprenorphine (Generic or Suboxone, a little lower for other formulations) but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

2. 4 mg/day
   - Feedback: Incorrect. 4 mg is the recommended INITIAL dose (Suboxone or generic, a little lower for other formulations). The recommended first day TOTAL dose is 8 mg buprenorphine, but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

3. 8 mg/day
   - Feedback: Correct. The recommended first day total dose is 8 mg buprenorphine (Generic or Suboxone, a little lower for other formulations), but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

4. 16 mg/day
   - Feedback: Incorrect. 16 mg (generic or Suboxone, a little lower for other formulations) is the recommended total daily dose of buprenorphine AT THE END OF INDUCTION, not day 1. The recommended FIRST DAY TOTAL dose is 8 mg buprenorphine. Many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.
INDUCTION: DAY

Abstinence Period Before First Dose
When presenting for their first dose, your patients should be in mild/moderate withdrawal, which is a COWS score (12-16).11

- **Short-acting opioids.** Patients who are dependent on short-acting opioids (includes heroin) should abstain from opioids for at least 12-16 hours before beginning induction, according to SAMHSA recommended PCSS-MAT guidelines11. Specific formulation prescribing instructions may differ, for example, SuboxoneTM prescribing instructions recommend only “not less than 6 hours” since last short-acting opioid use, but recommend moderate withdrawal12. Guidelines suggest that withdrawal symptoms are the more important indicator than a specific number of hours of abstinence11. For intermediate-acting opioids 17-24 hours of abstinence is needed11.

- **Long acting opioids.** The abstinence period is longer for long-acting opioids, 30-48 hours for methadone11.

Confirming and documenting that your patient is in mild/moderate withdrawal before beginning induction will minimize the risk of precipitated withdrawal. Be honest with your patients about these withdrawal symptoms, explain that this is an important step in the induction process, and encourage them to wait it out. Having prepared the patient by going over the symptoms of mild to moderate withdrawal during the induction appointment, minimizes problems at this step.

**PRACTICE TIP**
Patients being inducted in the office can stop at the pharmacy on the way to the appointment to pick up the first day’s doses.

**FYI**
Remember: Formulations vary. Unless otherwise stated, dosages in this activity refer to the dosages and pharmacodynamics of generic buprenorphine or buprenorphine / naloxone combinations.

**FIRST DOSES**

**Giving the First Dose**
Start with a first dose of 4 mg* of the combination film or tablet. You may also start induction using the monotherapy tablets and then switch to the combination film or tablets after a few days. A lower starting dose of 2 mg* may be used if the patient is not currently physically dependent or uses methadone.
*Doses described were established for the original Suboxone or generic sublingual tablets; use equivalent doses for other formulations

**After the First Dose**
The current recommendation for observation is to:

- Keep your patients in the office after the first dose
- Re-dose in 1-2 hour intervals (Gunderson 1+, Individior 2) with another 2 or 4 mg* buprenorphine if withdrawal symptoms persist or recur\(^{12,13}\).

[This is a shift from a previous recommendation that in-office induction requires a half-day of observation.]

After giving the second 4 mg dose, you can:

1. Observe your patients in the office for another 1+ hour and then re-dose if necessary
2. Have patients call in from home an hour later to report withdrawal symptoms
3. Allow patients to use their judgment to determine if they need an additional 4 mg buprenorphine

**Maximum first day dose is now 16 mg**\(^{11}\)/ previously it was 8 mg\(^{4}\). Some patients do well on a lower dose and some formulations will require a lower dose, so individualized treatment is important. You should not exceed 16 mg buprenorphine on day one.

*Doses described were established for the original Suboxone or generic sublingual tablets; use equivalent doses for other formulations

**FYI**
Remember: Formulations vary. Unless otherwise stated, dosages in this program refer to the buprenorphine or buprenorphine / naloxone formulation in Suboxone.

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**INDUCTION: DAY 1 (CONTINUED)**

**Evaluating Dosing**
When the patient is not exhibiting withdrawal symptoms and does not feel cravings for opioids, you may have established the daily dose – let your patient go overnight without additional doses. The next day, evaluate whether your patient was overmedicated, undermedicated, or medicated appropriately. Examination prior to the daily dose is important to identify medication status. According to updated PCSS-MAT guidelines recommended by SAMHSA (2016), this next day evaluation can happen via phone and the next in-office visit is recommended in 3-4 days\(^{11}\).

- When your patients are **undermedicated**, they will experience craving or withdrawal between doses.
- When your patients are **overmedicated**, they will experience buprenorphine side effects.
- When your patients are **properly medicated**, they will have neither side effects nor craving or withdrawal between doses.

**Managing Precipitated Withdrawal**
Precipitated withdrawal (withdrawal from not having gone long enough without the opioid of dependence before starting buprenorphine) can be managed in two ways\(^{10}\):
1. Continue induction with additional doses of buprenorphine until withdrawal abates, up to the recommended target dose of the formulation you are using.

2. Or stop induction and treat withdrawal symptomatically as above (especially clonidine, antidiarrheals, nonsteroidal anti-inflammatory drugs). Have your patient continue abstinence from the opioid of dependence and re-induce on buprenorphine the next day.

You may be able to determine if it is precipitated withdrawal from severity of symptoms or by re-asking your patient about their abstinence schedule, reassuring them you just need the information to help them.

PATIENT INSTRUCTION ON HOW TO TAKE BUPRENORPHINE

Review Key Patient Education Points
Remind patients of key points relevant to successful induction covered the day of *induction*. These include:

- The possibility of taking recommended comfort medications for residual withdrawal symptoms or requesting additional comfort medications as needed
- Taking doses as directed; not taking a dose on their own unless this has been carefully explained and authorized by you
- Reminders of the importance to abstain from the opioid they were using and other substances

Tips for Taking Buprenorphine Sublingually
There is a specific approach to sublingual administration that will improve absorption of buprenorphine.

Below are some tips you can provide to your patients when taking sublingual buprenorphine. Advise patients that:

- Each buprenorphine tablet or film will take some time to dissolve under their tongues, but the film dissolves more quickly than generic tablets.
  - The mean time for generic tablets is 7 to 12.4 minutes; the mean time for Suboxone® film is 5 to 6.6 minutes; the relatively newer, smaller, sublingual tablet, Zubsolv® and the buccal film, Bunavail™, dissolve faster
  - Note that with the buccal film formulation, two films can be applied in their mouths simultaneously, one inside each cheek.
- They should grasp the film by the edges and place under their tongues at the base, just to the side of the center.
- While the medication is dissolving, they should not talk, drink, or swallow.
- While the tablet is dissolving, they will salivate a lot, so they will need to tilt their heads forward to avoid swallowing the saliva.
- Suggest rinsing their mouths or eating a mint prior to taking buprenorphine to help with the taste.
- Patients with higher buprenorphine doses might find it more comfortable to take their pills sequentially rather than all at once.
• For instance, a film can be placed on the left and right base of tongue; but if a third film is needed, it should be taken after the first two films have dissolved.
• Your patients should not try to take more than two tablets at one time.

*We are using brand names since there is a difference in the product that is not reflected in the generic name. We are not advocating one brand or the other.

PRACTICE TIP
Some patients crush the tablets and pour them under their tongue to speed absorption. This approach is not listed as a method of administering buprenorphine, but it has become popular in inpatient settings due to easier monitoring and assuring that patients take their medication.  

WAITING BETWEEN DOSES AND BEFORE GOING HOME
Buprenorphine induction is often uncomfortable for patients because they have to enter into withdrawal before taking their first dose.

When patients come into the office and are in withdrawal, assess them right away and provide a dose of buprenorphine so as to keep them from being uncomfortable any longer than necessary. You may also want to have them get their initial buprenorphine doses from the pharmacy before the induction appointment so there is no wait time for the medication.

Conducting induction in your office
• Symptom relief generally occurs in a little over an hour to two hours
• Keep patients in a private room between doses if possible.
• You can provide books, magazines, videos, patient education materials, etc. to help them pass the time.

If a separate room is not possible, patients can wait in the general waiting room and should be told to inform staff immediately if their withdrawal symptoms worsen or return.

Monitor patients for 1+ hours to assess their response to treatment before sending them home. Some programs dismiss the patient when the COWS score goes below 4. Consider following with a phone call later.

Combining office and home induction
Another option for induction is to have your patients come to the office for evaluation of withdrawal symptoms and to take the initial buprenorphine dose. Then they can leave the office and return home where they can have some privacy and comfort. You can then ask the patient to come back to the office 1-2 hours later for re-evaluation of withdrawal symptoms and another dose of medication. Trustworthy patients could be instructed to remain home and call into the office if withdrawal symptoms return. If needed, the additional dose can be approved over the phone.

Note: The "Appropriate Use" checklist published by the FDA includes "Provided induction doses under appropriate supervision." If you do home induction, be sure to consider the patient and the circumstances to assure that this guideline is fulfilled.
QUIZ: MR. ROSSMAN INDUCTION: DAY 1

Mr. Rossman
Age: 35 years old

Summary to Date: Mr. Rossman presents for day 1 of buprenorphine induction. He has moderate opioid use disorder and is dependent on extended release oxycodone. He presented for his induction appointment with mild withdrawal and when symptoms were mild to moderate, was given an initial dose of buprenorphine.

Next Step

Mr. Rossman has been given an initial dose of 4 mg and remained the in office. After one hour, you re-evaluate him and he feels better, but is still experiencing some withdrawal symptoms.

Question: What is the correct next dose (still on day 1 of induction) to give Mr. Rossman in order to reduce his withdrawal symptoms?

Choose one

1. 2 mg
   • Feedback: This is a little low. While gradual increase is advisable, subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

2. 4 mg
   • Feedback: Correct. should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

3. 6 mg
   • Feedback: This is a little high. Gradual increase is advisable; subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

4. 8 mg
   • Feedback: Incorrect. Gradual increase is advisable. Subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

MEDICAL MANAGEMENT OF REMAINING WITHDRAWAL SYMPTOMS

After day 1 dosing, a single dose of buprenorphine can be sent home with the patient for remaining spontaneous withdrawal (withdrawal from stopping the opioid of dependence) symptoms. Remaining symptoms can also be managed medically with non-opioid medications, however, most of the time it is not necessary. Sometimes called "comfort meds", they are most often needed by patients transferring from long-acting opioids and include:

• Anxiolytics (use very carefully and in limited quantities)
• Non-opioid pain relievers (NSAIDs or acetaminophen)
Buprenorphine Training Activity v5.0 For Physicians

- Antidiarrheal agents
- Antiemetics
- Antispasmodics

**BUPRENORPHINE FORMULATIONS COMPARISON**

<table>
<thead>
<tr>
<th>Product</th>
<th>How Supplied (Buprenorphine / Naloxone mg)</th>
<th>Induction Dosage</th>
<th>Recommended Target Dose for Maintenance</th>
<th>Instructions for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suboxone®</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sublingual Film</td>
<td>2 mg bup./0.5 mg nal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reckitt Benckiser</td>
<td>4 mg bup./1 mg nal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 mg bup./2 mg nal.</td>
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<tr>
<td></td>
<td>12 mg bup./3 mg nal.</td>
<td></td>
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<tr>
<td><strong>Zubsolv®</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sublingual Tablet</td>
<td>1.4 mg bup./0.36 mg nal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orexo</td>
<td>Dissolves more rapidly, menthol flavor, and smaller tablet.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Increments/ decrements of 2 mg bup./0.5 mg nal. or 4 mg bup./1 mg nal. up to 8 mg bup./2 mg nal. day 1 (in divided doses at around 2 hour intervals)
Day 2, administer up to 16 mg bup./4 mg nal. of sublingual film single daily dose.

Target Dose: 16 mg bup./4 mg nal. single daily dose (Range: 4 mg bup./1 mg nal. to 24 mg bup./6 mg nal. per day)
Place film under the tongue, close to the base on the left or right side. Must be kept under tongue until completely dissolved.

Increments/ decrements of 1.4 mg bup./0.36 mg nal. or 2.8 mg bup./0.72 mg nal.

Target Dose: 11.4 mg bup./2.8 mg nal. single daily dose (Range: 2.8 mg bup./0.72 mg nal. to 17.1 mg bup./4.2 mg nal. per day)
Conversion Information: One ZUBSOLV 5.7 mg Tablet should be placed under the tongue until dissolved. Do not cut, chew, or swallow tablets.
<table>
<thead>
<tr>
<th>Product</th>
<th>How Supplied (Buprenorphine / Naloxone mg)</th>
<th>Induction Dosage Increments (until opioid withdrawal signs and symptoms are suppressed)</th>
<th>Recommended Target Dose for Maintenance</th>
<th>Instructions for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunavail™ Buccal Film</td>
<td>2.1 mg bup./0.3 mg nal.</td>
<td>bup./1.4 mg nal. sublingual tablet equivalent to one SUBOXONE 8 mg bup./2 mg nal.</td>
<td>Wet the inside of the cheek. Hold the film with the text (BN2, BN4, or BN6) facing up and place that side with the text against the inside of the cheek. Press and hold the film in place for 5 seconds.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.2 mg bup./0.7 mg nal.</td>
<td>12.6 mg bup./2.1 mg nal. per day.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.3 mg bup./1 mg nal.</td>
<td>Increments/decrements of 2.1 mg bup./0.3 mg nal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BioDelivery Sciences International</td>
<td>Half a normal dose can achieve same result as other products, due to twice the bioavailability.</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Conversion information: BUNAVAIL 4.2 mg bup./0.7 mg nal. buccal film equivalent to a SUBOXONE 8 mg bup./2 mg nal. sublingual tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Target Dose: 8.4 mg bup./1.4 mg nal. per day single daily dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic Buprenorphine HCl &amp; Naloxone HCl Dihydrate</td>
<td>2 mg bup./0.5 mg nal.</td>
<td>Target Dose: 16 mg bup./4 mg nal. single daily dose</td>
<td>Tablet should be placed under the tongue until it is dissolved.</td>
<td></td>
</tr>
<tr>
<td>Sublingual Tablets</td>
<td>8 mg bup./2 mg nal.</td>
<td>(Range: 4 mg bup./1 mg nal. to 24 mg bup./6 mg nal. per day).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actavis Elizabeth LLC</td>
<td></td>
<td>Increment/decrements of 2 mg bup./0.5 mg nal. or 4 mg bup./1 mg nal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine (Without Naloxone)</td>
<td>2 mg bup.</td>
<td>Target Dose: 16 mg bup. single daily dose</td>
<td>Put the tablet(s) under your tongue. Let</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 mg bup.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>How Supplied (Buprenorphine / Naloxone mg)</td>
<td>Induction Dosage Increments (until opioid withdrawal signs and symptoms are suppressed)</td>
<td>Recommended Target Dose for Maintenance</td>
<td>Instructions for Use</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>---------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>HCI Sublingual Tablet</td>
<td>Up to 8 mg bup. on Day 1 and 16 mg bup. on Day 2. (Range: 4 mg bup. to 24 mg bup. per day).</td>
<td>Not used for induction. For use in patients already stable on a low to moderate dose of 8 mg buprenorphine or less per day. Placed surgically. Replaced at 6 months.</td>
<td>Target dose is 8 mg or less per day</td>
<td>Up to 8 mg bup. on Day 1 and 16 mg bup. on Day 2. (Range: 4 mg bup. to 24 mg bup. per day).</td>
</tr>
<tr>
<td>Probuphine® Subdermal Implant</td>
<td>One inch long rods containing buprenorphine</td>
<td>Target Dose: 300 mg monthly for two months, then 100 mg monthly but may be increased up to 300 mg if needed. See product information for details.</td>
<td>Implant is typically placed inside the upper arm, under the skin, for 6 months. Requires specific REMS training and certification for the physician to insert and remove.</td>
<td></td>
</tr>
<tr>
<td>Sublocade™ Injectable Invidior</td>
<td>Comes pre-filled syringes with a 19 gauge 5/8-inch needle. In 100mg and 300 mg doses. Prescribe for individual patient and have it sent from a certified pharmacy or become a</td>
<td>Not used for induction. For use after patient is stabilized for at least one week on transmucosal buprenorphine.</td>
<td>Once monthly subcutaneous injection by a qualified health care provider after dose stabilized at least one week on submucosal buprenorphine. Forms visible</td>
<td></td>
</tr>
</tbody>
</table>

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Buprenorphine Protocol: Induction
**Induction Dosage Increments** (until opioid withdrawal signs and symptoms are suppressed)

<table>
<thead>
<tr>
<th>Product</th>
<th>How Supplied (Buprenorphine / Naloxone mg)</th>
<th>Recommended Target Dose for Maintenance</th>
<th>Instructions for Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMS-certified clinic. Not dispensed to the patient.</td>
<td></td>
<td></td>
<td>depot under the skin from which medication is slowly released over time.</td>
</tr>
</tbody>
</table>

**SCHEDULING OFFICE VISITS**

**Induction Day 1**
It is helpful to allow a 2-4 hour window on the first day of induction. After the initial dose of buprenorphine, you should monitor the patient for 1-2 hours and give an additional dose if withdrawal symptoms return. Consider follow-up with a phone call after the patient goes home. As you get more comfortable with the medication, the observation period will become more abbreviated.

**Induction Day 2**
On the second day, many patients will need a higher dose and will wake up in withdrawal, which is a reason to plan for 2nd day induction dosing first thing in the morning. The second day of induction may take several hours as you increase the dose again and wait to see if withdrawal symptoms appear. Updated PCSS_MAT guidelines say that **day two monitoring and advising may happen by phone**¹¹, however, consider that some patients may benefit from in-person structure and guidance.

**Stabilization**
Ideally, there would be another appointment in 3-4 days¹¹.

**Maintenance**
After a maintenance dose is established, you should see patients weekly during the first month of treatment to monitor their toleration of the medication, their medication adherence, psychosocial stability, drug use, and adherence to counseling or recovery group involvement. Consider seeing them more frequently at first if they are high risk for relapse (many episodes of previous relapse, poor social support, mental health problems, etc.), have cognitive problems, have an atypical response, or have a particularly strong physical dependence. You should emphasize that treatment for opioid dependence involves more than just taking a pill.
INDUCTION: DAY 2+

Evaluating your Patient on Day 2
On the second day, evaluate your patient's response to the first day's dose.

- If your patient was over-medicated at the end of the first day, decrease the dose.
- If your patient experienced withdrawal symptoms or opioid cravings after leaving the office on the first day, increase the dose.

In most cases, you can do patient monitoring over the phone on day 2. When your patient leaves the office at the end of day 1, schedule a time to talk to your patient first thing the following morning.

Then ask a series of questions to gauge how your patient is feeling and to determine if the dose needs to be adjusted:

- How are you feeling now?
- How do you feel physically?
- What did you have for dinner last night? (having a good dinner is indicative of how they felt all day)
- How did you sleep?
- Did you eat breakfast yet? If not, why not? (if patient has upset stomach then patient may be going back to withdrawal – in which case may need dose increase)
- Have you had any cravings?

Dosing on Day 2
If your patient reports feeling unwell, then evaluate for withdrawal again and increase the dose by another 4 mg. So a patient who took a total of 8 mg (two 4 mg doses) on day 1 and who requires a dose increase, would start day 2 with a 12 mg dose. If symptoms persist after an hour, you can increase the dose by another 4 mg buprenorphine.

The maintenance dose for most patients is generally in the range of 4 mg to 24 mg buprenorphine. Clinical advantage has "not been demonstrated" for doses higher than 24 mg. The required dosage varies; patients who were dependent on higher doses of opioids may require a higher daily dose.

Next few days: Many of your patients will be stabilized by day 2, and almost all will be stabilized by day 3.

PRACTICE TIP
On day 2 be sure to emphasize that, although you are not requiring an office visit, your patients should not adjust the dose on their own.

Day 3 and Beyond
Repeat the same protocol for dosing on day 3.

- Start the day with a phone appointment
- Evaluate cravings and withdrawal
- Then determine if a dose increase is needed
You can safely prescribe up to 32 mg/day, but there is a ceiling effect around 16 mg and higher doses will do little to decrease cravings. Patients who insist on a high dose should be re-evaluated at the time of induction and/or monitored throughout treatment for diversion.

**CASE EXAMPLE – MR. ALLEN**

**Prior to Induction Day**
You are preparing to treat Mr. Allen for dependence on heroin (a short-acting opioid). After consultation, you decided that he is a suitable candidate for buprenorphine treatment.

You meet with Mr. Allen the day before you plan to begin induction. You impress upon him that he needs to be in mild/moderate opioid withdrawal before beginning buprenorphine treatment (COWS score of around 12 to 16) and therefore, should abstain from heroin for around 12 to 16 hours before beginning treatment. You also explain that there is a risk of greater discomfort and the treatment not working properly if he comes to the first induction appointment and is not in withdrawal.

**Induction, Day 1**
Mr. Allen shows up on time for his appointment the following day. He affirms that he has not taken heroin in 12 hours. Your patient's behavior and physical signs are consistent with someone in mild/moderate opioid withdrawal (COWS = 12).

- You go ahead and give Mr. Allen his first 4 mg dose of medication, sublingual Suboxone® film. You advise him not to talk or swallow until the medication is all gone. You check under his tongue to make sure it is completely gone and ask him to remain in the office for monitoring for an hour or so.
- After 30 minutes, Mr. Allen reports that he is beginning to feel relief from withdrawal, but he still reports (and shows signs of) being under-medicated. His COWS is reduced to 9.
- After 60 minutes, it is clear that while Mr. Allen has responded further to the buprenorphine, he is still under-medicated. He continues to show signs of withdrawal (a little flushing and slightly elevated pulse). Upon questioning, he confirms that he feels calmer but still feels some mild flu-like pain and stomach cramps of withdrawal (COWS=5). Accordingly, you give him an additional 4 mg dose. Following this dose, Mr. Allen leaves the office.
- Mr. Allen calls an hour later and reports that all symptoms are resolved except some mild generalized pain (COWS=1) so you do not recommend an additional 1st day dose. You recommend he take acetaminophen (500 mg) if needed and call your office in the morning.

**QUIZ: MR. ALLEN INDUCTION DAY 2**
After induction on Day 1 with a dose of 8 mg, Mr. Allen calls the office for dosing at the scheduled time on the morning of Day 2. His withdrawal symptoms have increased a little from the previous evening. The physician assistant confirmed that Mr. Allen did not take any heroin and other opioids overnight and reminded him of the importance of being candid. Your evaluation confirms he still has some minor withdrawal symptoms (COWS is 3-4).
Question: What dose changes, if any, would you make at this time?
Choose one

1. No additional buprenorphine needed. Have him take his day 1 dose of 8 mg and call in 1-2 hours.
   - Feedback: Incorrect. Mr. Allen needs additional buprenorphine from his day 1 dose of 8 mg. Leaving the patient with withdrawal symptoms is likely to lead to relapse.

2. Add 4 mg for a total dose of 12 mg and ask him to call back in 1-2 hours
   - Feedback: Correct. Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine. Increments of 4 mg are recommended.

3. Add 8 mg for a total dose of 16 mg and ask him to call back in 1-2 hours
   - Feedback: Incorrect. Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine from his day 1 dose of 8 mg. The goal is to titrate him to the lowest dose needed to prevent symptoms and return to opioid use.

4. Add 12 mg for a total dose of 20 mg and ask him to call back in 1-2 hours
   - Feedback: Incorrect. Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine. However, increments of 4 mg are recommended. The goal is to titrate him to the lowest dose needed to prevent symptoms and return to opioid use.

MR. ALLEN – DAYS 2 AND 3

Induction, Day 2 (continued)
As described in the previous quiz, on Day 2, Mr. Allen called the office with some increase in withdrawal symptoms, from the previous night, a COWS score of 3-4. He had not had any other opioids since before starting induction. After evaluating him and confirming some withdrawal symptoms, you prescribed Mr. Allen a 12 mg dose (8 mg dose established on Day 1, plus an increase of 4 mg) and ask him to call in around an hour.

   - A short time later, Mr. Allen felt much calmer and most signs of withdrawal appeared to have abated or disappeared. Mr. Allen called after an hour saying he does not feel like he’s about to go into withdrawal anymore. It appears that you may have found Mr. Allen’s daily dose. You tell him to call again after two hours to report how he is doing, which he does and reports no problems.

Induction, Day 3
The next morning (induction day 3) you re-evaluate Mr. Allen via phone. He reports no problems with withdrawal symptoms and that he is not aware of drug craving. He says that he "feels good". He also reports that he went to a support group the night before and that it went "really well." It appears that you have found a therapeutic daily dose for him. You prescribe him a week’s worth of buprenorphine at a 12 mg/day dose. He makes an appointment to meet with you again in 3-4 days for his first follow-up appointment.
QUIZ: CASE – MS. COLLIER

Meet Your Patient

Name: Yolanda Collier
Age: 47 years old
Reason for visit: Now that she has grandchildren, Ms. Collier would like to "stop using illegal drugs." She would like to try buprenorphine.

Medical History: She is currently heroin-dependent. Ms. Collier has a 20-year history of opioid (heroin) dependence. She also has a history of asymptomatic hepatitis C; her liver function tests from a year ago showed only mild abnormalities.

Treatment History: She had tried methadone treatment for almost a year, five years ago, but could not maintain it due to her work and family commitments.

Next Step

During her visit, you learn that Ms. Collier is mentally stable and complete blood tests and learn that her liver function is unchanged. Otherwise she is apparently healthy and has a good understanding of buprenorphine treatment and its benefits. The day before induction, you complete patient education and the written, signed patient-provider treatment agreement.

Question: What is the best next step for Ms. Collier?

Choose one

1. Refer her to a hepatologist for a thorough hepatitis C evaluation
   - Feedback: This is not the best answer. Ms. Collier's hepatic function test is unchanged. It is a good idea, however, to get Ms. Collier's consent to allow you to discuss her opioid treatment with her hepatologist.

2. Refer her to an opioid treatment program since she has had a period of success with methadone maintenance in the past.
   - Feedback: This is not the best answer. Ms. Collier was maintained on methadone successfully for awhile, but ultimately this treatment approach failed, for a variety of reasons. In some cases a patient's treatment history makes them an unlikely candidate for success with buprenorphine treatment, but this does not appear to be the situation in Ms. Collier's case.

3. Induct her onto buprenorphine
   - Feedback: Correct! If her blood and urine results come back as expected, Ms. Collier seems to be an appropriate candidate for buprenorphine induction.

QUIZ: MS. COLLIER – INDUCTION

Prior to Induction: Ms. Collier wants to try buprenorphine and agrees to the terms of your treatment agreement. She seems committed to getting clean and has a better support system around her than she has in past years. Together, you decide to induct her onto buprenorphine.
Ms. Collier expresses concern about going into withdrawal, she says she always gets severely nauseated. To treat this you prescribe an antiemetic, dolasetron (commonly used, serotonin (5-HT3) antagonist), to start taking an hour before she anticipates withdrawal symptoms would start.

**Induction Day:** On induction day, Ms. Collier arrives at your office at 9:00 am. She reports that her last heroin use was 14 hours ago. She reports chills, nasal stuffiness, and having some difficulty sitting still, although she appears able to do so. She denies pain or gastrointestinal complaints. She says she is anxious, slightly irritable, and feels a tremor in her hands, although it is not visible to others. Her vitals are stable (BP 120/70, P 77), pupils are normal, and she is without diaphoresis, flushing, yawning, rhinorrhea, lacrimation, or piloerection.

**Question:** How would you characterize her degree of withdrawal? What is her score on the Clinical Opioid Withdrawal Scale? (Link opens a PDF copy of the COWS scale, provided by NAABT)

Choose one

1. COWS 2 points: Little to no withdrawal
   - Feedback: Incorrect. In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

2. COWS 5 points: Mild withdrawal
   - Feedback: Correct. In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

3. COWS 14 points: Moderate withdrawal
   - Feedback: Incorrect. In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

4. COWS 28 points: Moderately severe withdrawal
   - Feedback: Incorrect. In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

**Discussion:** Mild/moderate withdrawal or a COWS score of 12 to 16 is recommended before starting induction (PCSS-MAT guidelines -11). Ms. Collier should be in at least this level of withdrawal in order to prevent precipitated withdrawal. Also, it would be better to observe some objective evidence of withdrawal (e.g., diaphoresis, dilated pupils), rather than rely only subjective symptoms as reported by the patient.
**Case:** At this point you express concern to Ms. Collier that her degree of withdrawal is not sufficient and explain the risk of precipitated withdrawal. You offer her a quiet room in which to wait, but she says she has things to do. You ask her to return to your office in a couple of hours for induction.

When she returns 2 hours later, Ms. Collier is still experiencing chills, nasal congestion, and mild tremor and now reports escalating restlessness and anxiety. She also is having mild, diffuse pain and is nauseated. On exam, she appears more anxious but does not appear to be fidgety. Her pulse is 90 and she is flushed. Her pupils are moderately dilated. Her exam and symptoms are otherwise unchanged.

**QUIZ: MS. COLLIER**  
**Question:** Would you start buprenorphine induction now?

Choose one

1. Yes, her withdrawal is adequate to begin the induction.
   - **Feedback:** This is the best option. Currently, Ms. Collier appears in adequate withdrawal to initiate induction. Her score on the COWS would be a 12, indicating mild to moderate withdrawal:
     - Pulse: 90 (1)
     - Sweating: flushed (2)
     - Restlessness: subjective restlessness but still (1)
     - Pupils: moderately dilated (2)
     - Bone/Joint Aches (1)
     - Runny nose or tearing (1)
     - GI Upset: nausea (2)
     - Tremor: still mild, subjective tremor (1)
     - Yawning: none
     - Anxiety: observable (2)
     - Gooseflesh: none
   - **TOTAL:** 13 Mild/moderate withdrawal

2. No, withdrawal is not adequate to begin induction.
   - **Feedback:** No, this is not the best option. Currently, Ms. Collier appears in adequate withdrawal to initiate induction. Her score on the COWS would be a 12, indicating mild withdrawal. Her COWS score would determined as follows:
     - Pulse: 90 (1)
     - Sweating: flushed (2)
     - Restlessness: subjective restlessness but still (1)
     - Pupils: moderately dilated (2)
     - Bone/Joint Aches (1)
     - Runny nose or tearing (1)
     - GI Upset: nausea (2)
     - Tremor: still mild, subjective tremor (1)
Yawning: none  
Anxiety: observable (2)  
Gooseflesh: none  
TOTAL: 13 (Mild/moderate withdrawal)

MS. COLLIER – CONTINUE INDUCTION

Initiating Treatment and Assessing via Phone
Day One

- You initiate treatment with a 2.8 mg dose of the Zubsolv® formulation of buprenorphine/naloxone (two 1.4 mg tablets). You chose Zubsolve because you are concerned about her ability to be patient enough for a more slowly dissolving formulation. This is similar to starting her with 4 mg of Suboxone.
- One hour later, Ms. Collier reports that she no longer is nauseated or having chills. She is much less anxious and her pain is almost gone. Her vitals are BP 116/78, P 76, and she is no longer flushed. Her cravings have decreased but are still present slightly.
- You give her an additional 2.8 mg dose prior to leaving the clinic (equivalent to adding 4 mg Suboxone).
- Later in the afternoon you speak on the phone, and Ms. Collier reports that she is feeling well, without withdrawal or cravings. Her total first day dose was 5.7 mg Zubsolv, the equivalent to 8 mg Suboxone.

Day Two

The next morning you assess Ms. Collier via phone. She is having some cravings and slight withdrawal symptoms. You increase her dose of buprenorphine to 8.5 mg (equivalent to 12 mg Suboxone). She reports feeling good for the rest of the day. She does not need another dose increase.

Day Three

She awakes on Day 3 feeling good. She calls the office reporting no cravings or withdrawal symptoms, so you have established her daily dose of buprenorphine (Zubsolv® formulation) at 8.5 mg. Note that medication information states that the typical target dose is 11.4 mg and range is 2.8 to 17.1 mg)

Orexo, 2013

HOME INDUCTION

Many clinicians now complete induction for a substantial portion of their buprenorphine patients at home. At-home buprenorphine induction is a safe and convenient option for some patients. Several studies found at-home induction to be as effective as office-based induction16,17. Patients who have been on buprenorphine previously may be comfortable with home re-induction. Note, however, that in an expert consensus opinion,
ASAM recommends home induction be offered only by a provider who is experienced with buprenorphine treatment. Note: The "Appropriate Use" checklist published by the FDA states that the following should be completed for each patient starting buprenorphine induction: "Provided induction doses under appropriate supervision." Providers should consider their availability to provide "appropriate supervision" as needed for a patient, for example, by talking to them on the phone.

**PREPARING FOR AT-HOME INDUCTION**

Before deciding upon at-home induction, your patients must come into the office for an initial consultation, assessment, physical exam, lab work, etc. In other words, the process leading up to induction is the same. You should provide patients who are going to be inducted at home with thorough patient education about the process. Here are some more specific guidelines:

- Confirm that your patients do not have any complicating medical or psychiatric problems
- Verify that your patients have support from family and friends and that someone can be at home with them on induction day
- Instructions need to be reviewed with the patient, asking them questions to confirm their understanding and giving them the opportunity to ask questions
  - Educate your patients on how to recognize signs and symptoms of withdrawal and how to rate it so that they have sufficient withdrawal
  - Educate your patients about precipitated withdrawal
  - Educate your patients about correct administration of buprenorphine formulation prescribed
  - Send instructional materials home with your patients and ensure that they understand procedures
- Prescribe only a limited supply of buprenorphine to start until the dose is established
- Put dose amount and timing in writing.

**PROTOCOL FOR HOME DOSING**

**Assuring Adequate Withdrawal in Home Induction**

With at-home dosing, your patients are responsible for:

- Assessing their own symptoms
- Taking their first dose when they are in mild/moderate withdrawal

You can refer them to the COWS scale if needed to objectively assess their withdrawal symptoms. Recommend that your patients have a friend or relative assist them, because withdrawal is uncomfortable, and your patients might be tempted to take their first dose prematurely.

**Dosing Guidelines for at Home Induction**

Dosing protocols for at-home induction follow a similar protocol as office induction:

- Start with a 4 mg* (sublingual tablets or equivalent of other formulations) buprenorphine dose.

After the first dose, patients should continue to monitor their withdrawal symptoms and take 1 or 2 more 4 mg doses as needed on Day 1.
• Check on process via phone and document in patient record.
• Maximum dose of 8 mg day one; allow up to 16 mg total dose first day if approved by phone. Follow the same dosing protocols as would be used for patients who are inducted in the office.
• Day 2: Maximum of 16 mg, but allow up to 24 mg if approved by phone.
• Day 3: Same as for in-office induction.

Schedule a follow-up office visit for 3-7 days.

**Monitoring and Follow-up for at Home Induction**

Your comfort level and that of your patient will determine how much monitoring is needed during the at-home induction process. If you are a newer prescriber, you might want to have your patient call-in to the office and have their withdrawal symptoms assessed over the phone before taking the first dose or subsequent doses. Or, patients who are concerned about precipitated withdrawal may feel more comfortable checking in with a nurse before taking the first dose. Each clinician should set practice guidelines accordingly.

• Follow-up visit is recommended; between 3 and 7 days has been recommended.

**PRACTICE TIP**

Having another individual, who reviews the guidelines, observe the home induction process, may improve the outcome.

**POLL: AFTER READING ABOUT HOME VS. OFFICE-VISIT INDUCTIONS, DO YOU PLAN TO DO ANY HOME INDUCTIONS?**

Choices

1. Yes
   • 12% (519 votes)
2. No
   • 28% (1206 votes)
3. Unsure
   • 16% (683 votes)
4. Later, after I have more experience
   • 40% (1734 votes)
5. Does not apply to me
COMPLICATIONS DURING INDUCTION

Having a Mentor to Consult
Before starting your buprenorphine practice, you may want to establish a relationship with another buprenorphine provider in your area as a mentor. Alternatively, you could choose a Physician Clinical Support System-Medication Assisted Treatment (PCSS-MAT) mentor (see sidebar) to consult if questions or problems arise.

Patients Presenting without Withdrawal
One of the most common problems in buprenorphine inductions is that patients present for their first dose without being in withdrawal\textsuperscript{13}. Many addicted patients have a fear of going into withdrawal.

In this situation, you must decide if your patient is going to be in withdrawal soon or if the induction needs to be rescheduled.

It is also appropriate to question your patient further about their:

• Commitment to seeking treatment.
• Recent opioid use. Note that some patients may not know what medications are included in opioids. Patients sometimes do not understand that you meant for them to stop all opioids, even those in combination with other medications, like Vicodin®.

COMPLICATIONS DURING INDUCTION CONTINUED

Dealing with Precipitated Withdrawal
If withdrawal symptoms get worse instead of better after you give the first dose, it is possible that precipitated withdrawal has occurred. Taking a problem-solving approach, try to identify if the patient inadvertently swallowed the buprenorphine rather than letting it be slowly absorbed. Another possibility is that they may have taken an opioid, intentionally or not, while they were trying to abstain.

Patients should be warned in advance about the possibility of precipitated withdrawal if they take an opioid while going into withdrawal for induction.

Even if you proceed slowly with induction, precipitated withdrawal may still occur, but infrequently.

There are two alternatives in this situation:

1. Stop induction and treat symptoms
2. Or continue induction and treat symptoms

There is no formal clinical guideline, but expert consensus supports continuing induction\textsuperscript{13}. Precipitated withdrawal will not get worse by continuing and the withdrawal symptoms may be alleviated by additional buprenorphine. Further, your patient will have fewer opioid receptors available for illicit opioids. This will present less of a risk for overdose if they take drugs to treat withdrawal symptoms\textsuperscript{13}. 
Treating Precipitated Withdrawal
Continue buprenorphine but decrease the dose. Use the COWS or other withdrawal screening tool sequentially as a guide.

Infrequently, symptomatic management may also be needed:\(^4,19\):
- Clonidine (keep dose low to prevent hypotension)
- Antiemetics to treat nausea
- Anti-anxiety medication if needed (avoid benzodiazepines)
- NSAIDs for headache or joint and muscle pain, while considering risks vs. benefits

Dealing with Other Adverse Reactions
Headache and sweating are commonly experienced.

Severe adverse reactions to buprenorphine during induction are exceedingly rare. Complications can arise when patients are taking medications that interact with buprenorphine. Take a thorough history and conduct urinalysis prior to induction to reduce the likelihood of such problems occurring.

**KEY POINTS**
Precipitated withdrawal can be treated by lowering the buprenorphine dose and with several other supportive therapies.

**STABILIZATION**

You can determine your patients' ideal daily dose within the first few days of induction.

Guidelines for dose adjustments:\(^5\):
- Increments of 2 mg/day generally
- Allow 5 days between adjustments, due to long plasma half-life and longer duration of action

Most of your patients will stabilize at a dose of between 8 and 24 mg per day\(^10\). Rarely, a dose of 32 mg may be needed for high opioid tolerance.

The next few weeks are a stabilization period, during which patients should be maintained at their established dose. Continue monitoring patients to see how treatment is incorporated into their lives and whether use of other opioids is controlled. Further dose adjustments are considered minor 'tweaks', but usually not a big part of stabilization. At an ideal daily dose, your patient should experience no withdrawal symptoms. They should have no cravings, no other opioid use, and the best possible functional status.

Key elements of the stabilization phase include:
- Regular and frequent clinic visits until the patient stabilizes medically and psychosocially.
- Weekly or more frequent for the first month, adjusting for the patient's behavior:
  - Adherence to the treatment plan
• Being responsible with their medication supply
• No high risk behaviors/diversion risks
  • Patient education about and starting psychosocial treatment
  • Limit medication supply until the next appointment time with no early prescriptions
  • Require that patients attend clinic visits to get next prescription

It may take up to 6-8 weeks following induction until the patient is no longer experiencing any withdrawal symptoms or intense cravings.

Following stabilization, visits can be less often, usually monthly, and larger supplies of medication can be provided.

**PRACTICE TIP**
Your patients who are maintained on high doses of buprenorphine can take their doses sequentially, taking no more than 16 mg at one time.

During stabilization, observe your patients for possible complications of buprenorphine use and counsel patients to be aware of potential complications.

**FYI**
Remember: Formulations vary. Unless otherwise stated, dosages in this program refer to film or generic tablet formulations.

**FOLLOW-UP TIMETABLE**
The following timetable can be used as a guideline, assuming adherence to treatment, no treatment complications, and no opioid use:

• Weekly follow-up or more often if needed, for around the first 4 to 6 weeks post-induction
• Every other week follow-up for around the next 6 to 8 weeks
• Monthly follow-up indefinitely
• Quarterly follow-up for very stable, long-term patients

One possible guide for when to change from weekly to monthly visits is to change when the patient has three negative random urine drug tests in a row. If the patient de-stabilizes, resume weekly visits.

**Protocol at Follow Ups**
During follow-up sessions, you should:

• Assess any medical complaints your patient may have.
• Adjust your patient's daily dose if he or she appears to be over- or undermedicated
• Direct your patient toward psychosocial services and thereafter assess whether the patient is using these services.
• Monitor for signs of buprenorphine misuse or diversion.
• Conduct random urine drug screens (weekly during the first 2 months) to monitor for continued abuse of other opioids and other drugs and for proper use of buprenorphine (if concerned).
PRACTICE TIP
Some providers, rather than seeing the patient weekly themselves, have the patient go to counseling weekly. The provider checks with the psychosocial provider regularly but sees the patient in person less often.

QUIZ: LOOKING AHEAD TO MAINTENANCE

Question: Which of the following are recommendations for providers during the maintenance phase of buprenorphine therapy?

Choose all that apply:

1. Adjust patients’ daily dose if they are either over- or undermedicated
   • Feedback: Correct. Providers are encouraged to adjust patients' buprenorphine doses as appropriate.

2. Assess patients for readiness to discontinue buprenorphine use, and discontinue most patients
   • Feedback: Incorrect. Most patients should be encouraged to continue buprenorphine use indefinitely, given the very high relapse rate for patients who discontinue pharmacotherapy.

3. Remain vigilant for signs of resumed opioid abuse
   • Feedback: Correct. Providers are encouraged to monitor for resumed opioid abuse.

4. Assess the patients' medical complaints
   • Feedback: Correct. Providers are encouraged to assess patients' medical complaints.

QUIZ: CASE – MS. SANCHEZ

Meet Your Patient
Name: Andrea Sanchez
Age: 32 years old
Reason for visit: Ms. Sanchez is having trouble getting off Vicodin®. She saw your name on the SAMHSA locator list of providers who prescribe buprenorphine in her area.

Present History: Currently takes Vicodin daily. She had surgery for an ovarian cyst three years ago, and had trouble controlling pain in the weeks after the surgery. She ended up using 10 to 12 Vicodin tablets per day, always ran out too soon, and started looking forward to taking them. She is a schoolteacher and mother of two.

Question: What additional information would help you decide whether buprenorphine treatment is indicated for Ms. Sanchez? (Check all that apply.)

Choose all that apply

1. More information about signs of her physical dependence on opioids
• Feedback: Correct. These items and more are among the information to obtain prior to initiating buprenorphine treatment

2. More information about any current pain
• Feedback: Correct. These items and more are among the information to obtain prior to initiating buprenorphine treatment

3. Her state of mind
• Feedback: Correct. These items and more are among the information to obtain prior to initiating buprenorphine treatment

4. What she expects from buprenorphine treatment
• Feedback: Correct. These items and more are among the information to obtain prior to initiating buprenorphine treatment

**MS. SANCHEZ – FURTHER EVALUATION**

**About: Opioid Use Disorder**
To discover if she meets criteria for opioid use disorder, you ask Ms. Sanchez whether she has experienced any withdrawal symptoms and if she feels she is giving up significant work or family time to use or to obtain hydrocodone/acetaminophen.

**Ms. Sanchez:** I'm not a junkie, I don't get sick if I stop taking Vicodin®. I do notice that I'm crabby and I'm sluggish at work if I don't take it. I just can't stand how I feel, so I take one. Then I take more to keep going. My husband is very supportive and put up with a lot while I was cutting my dose down, but I haven't told him I'm still using.

**About: Pain**
To learn more information about her pain, you ask Ms. Sanchez whether her pain recurs when she reduces her dosage, if her pain interferes with her work or family activities, or if she has chronic intractable pain.

**Ms. Sanchez:** I don't have pain anymore, although my hips ache a little after my morning run. I do some stretches and the achiness goes away.

**About: State of Mind**
To screen for depression, you ask Ms. Sanchez whether she has been or is currently depressed, if she has experienced loss of energy, or has feelings of hopelessness. You also ask what it means when she says she can't get through the day.

**Ms. Sanchez:** I just love my family and my life. I was in therapy for years, but I don't need therapy. Of course I get tired since I have kids and a busy job. Yes, I do notice that when I take Vicodin I feel more energy and I'm nicer. Don't worry, I'm not depressed and I'm certainly not suicidal or anything.

**About: Treatment Expectations**
To learn what she expects from buprenorphine treatment, you ask Ms. Sanchez if she would be able to participate in the counseling and monitoring necessary to treat addiction. It is crucial to determine whether her request for buprenorphine is actually for treatment of her opioid use disorder, or whether it is really part of drug-seeking behavior (i.e., just another way to get a legitimate opioid), whether she expects that buprenorphine will magically dissolve her addiction.
Ms. Sanchez: I just want to get rid of this addiction. When I was drinking, I just decided to stop, and I did. I've been in AA ever since. I thought quitting Vicodin would be like that, but it wasn't as simple. I heard that buprenorphine will help you get off opiates. I don't need any more therapy, since I was in therapy for years. Do I really need a urine test? I'm not a junkie. I told you what I'm taking.

MS. SANCHEZ - ADDITIONAL CONCERNS

Ms. Sanchez seems to meet the criteria for buprenorphine treatment. However, her case should be examined a bit more closely first.

Before prescribing buprenorphine, it is important to examine the reasons why Ms. Sanchez may be having trouble stopping her use of hydrocodone/acetaminophen. Also, it is important to examine her motivation and pre-conceptions about addiction treatment. On the surface she appears to be addiction-savvy, having gone to AA. However, on closer inspection, she is resisting counseling and testing. She has superficial expectations about buprenorphine, considering it a way to simply eliminate her opioid use problem.

She does not have chronic pain currently and does meet DSM 5 criteria for opioid use disorder*. She may or may not have underlying depression. It would certainly be something to evaluate further if she continues to use hydrocodone/acetaminophen or other opioid even when the addiction is properly addressed.

In spite of flowery statements about family and work, she is not finding her husband fully supportive at this point. These "wonderful" parts of her life may actually be stressful and triggers to use. It could be helpful to have her name individuals who will be her support system when she stops using.

*Review of the diagnosis, opioid use disorder: The DSM 5 diagnosis, opioid use disorder, requires a minimum of two criteria for a diagnosis. A patient who meets 2-3 criteria has a mild case, 4-5 moderate, and 6-7 severe.

QUIZ: MS. SANCHEZ – INDUCTION DOSE

Preparing for Induction

You review the treatment options with Ms. Sanchez, including psychosocial components of addiction treatment. You explain that at such a low dose of hydrocodone/acetaminophen, she may be able to discontinue opioids with few physical problems, but she needs some support to carry this out. You discuss the requirements of your office-based buprenorphine treatment with Ms. Sanchez, which includes at least one counseling session with a physician assistant. Together you decide to try to first stabilize her medically on buprenorphine, so she can stop her Vicodin® use. She reluctantly agrees to the counseling session and a urine drug screen.

You go over patient education with Ms. Sanchez and review the patient-provider treatment agreement for her to sign.

You perform a urine drug test and upon receiving the results instruct her on correct usage of the Suboxone® film (e.g., holding the edges).
Ms. Sanchez will start home induction the next day.

**Question:** What should be Ms. Sanchez's initial buprenorphine dose, considering that she is dependent on a relatively low dose of opioids?

Choose all that apply

1. 2 mg
   - Feedback:
     This is one possible option. Most prescribers start with a 4 mg dose on Day 1, however a low level of physical dependence is an indication for starting with 2 mg. If started with 4 mg, Ms. Sanchez may not need another dose increase on Day 2. Most likely she will be maintained on at least 8 mg. Because she is dependent on such a low dose of hydrocodone/acetaminophen, her physical withdrawal symptoms may be minimal. For home induction, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose.

2. 4 mg
   - Feedback:
     This is the usual recommended first dose for Day 1. Ms. Sanchez may not need another dose increase on Day 2, but most likely she will be maintained on at least 8 mg. Because she is dependent on such a low dose of hydrocodone/acetaminophen, her physical withdrawal symptoms may be minimal. For home induction, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose.

3. 8 mg
   - Feedback:
     Incorrect; start with a 4 mg dose on Day 1. 2 mg also may work as an initial dose with increments of 2 mg. With 4 mg starting dose, she may or may not need a dose increase on Day 2. Most likely she will be maintained on at least 8 mg. Because she is dependent on such a low dose of hydrocodone/acetaminophen, her physical withdrawal symptoms may be minimal. Instead, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose.

4. See if she can get through Day 1 without buprenorphine; she may not really need it
   - Feedback:
     This is not the best option. She shows signs of being physically dependent and has struggled in past attempts to cut back without buprenorphine. For home induction, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose. It isn't clear whether 2 mg or 4 mg dose increments are best. A total dose of around 8 mg buprenorphine is likely to be needed.
MS. SANCHEZ – STABILIZATION & MAINTENANCE

Stabilization
Ms. Sanchez took two 4 mg doses on day 1, as guided, and did not experience any physical or psychological cravings in subsequent days. She was stabilized on an 8 mg dose.

Maintenance Phase
Ms. Sanchez continued at 8 mg for three months with no side effects and no cravings. We will pick up her case again in the Maintenance module.

DOSAGE GUIDELINES IN EACH TREATMENT PHASE

GUIDELINES FOR BUPRENORPHINE TREATMENT

In Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders, produced by expert panel process, the guidelines recommended most often on administering appropriate doses of buprenorphine of different stages of treatment are the following:

Administer appropriate doses of buprenorphine during induction, stabilization, and maintenance phases.

- Induction: Make sure the patient is experiencing objective signs of withdrawal.
- Induction: The maximum dose for day two, based on this consensus meeting was described as being between 8-16 mg. Other guidelines put 16 mg as the maximum dose for day 1 and suggest that going beyond 24 mg on day two and beyond gains little clinical effectiveness.
- Induction after methadone: Should be managed by experienced physicians.
- Induction after methadone: Monitor for withdrawal symptoms. If none are present within 24+ hours of last methadone treatment, wait prior to initiation.
- Stabilization: Adjust the dose in no more than 2-4 mg per week.
- Stabilization: Daily dose is established when patient is not longer using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings.
- Maintenance: Research shows that 16 mg or greater or the equivalent is effective at suppressing illicit opioid use. The dose range for effectiveness is usually 4 to 24 mg buprenorphine.

Note that these are the guidelines for which there was strong consensus by expert review and not a complete protocol.

MEDICALLY SUPERVISED WITHDRAWAL

Requesting Medically Supervised Withdrawal (Detoxification)
Detoxification, or medically supervised withdrawal (MSW), involves using a medication such as buprenorphine to take a patient from an opioid-dependent to an opioid-free medication-free and drug-
Patients who want to stop using opioids but do not want to be maintained on buprenorphine may request MSW.

Research has shown buprenorphine to be an effective medication in helping patients detoxify from other opioids, superior to clonidine alone, and relatively equal to methadone in relieving withdrawal symptoms\(^{23-25}\). Buprenorphine is relatively equal to methadone in relieving signs and symptoms of withdrawal.

**Risks of Medically Supervised Withdrawal**

Relapse is a significant concern when conducting MSW. It is extremely common and, in some cases, can lead to overdose. The implications of relapse and possible risk of overdose should be carefully explained to patients who are requesting MSW. Also, the benefits of maintenance therapy should be discussed. Detoxification-based treatments have a low likelihood of long-term success as compared to medication maintenance treatments\(^{26}\), which is not surprising given our understanding of addiction as a chronic relapsing disease.

**Inpatient Detoxification with Office-Based Maintenance**

Hospitals, typically do not admit a person specifically to transfer them from methadone to buprenorphine. However, some patients who already are hospitalized for other reasons might be able to do so. Advantages include that they can be monitored and treated symptomatically in a safe and secure setting\(^{14}\). Patients can be inducted at an inpatient detox center and then, upon discharge, can make a seamless transfer to the outpatient setting, if they were evaluated prior to admission.

**DETOXIFICATION PROTOCOL**

**Patients Should be Closely Monitored for Medically Supervised Withdrawal**

If patients in detoxification become unstable, they should be:

- Carefully monitored
- Offered appropriate psychosocial support
- Offered medication maintenance treatment, such as buprenorphine

Detoxification is often conducted in an inpatient setting.

**Clinical Guidelines**

There is no absolute standard for how fast or slowly to detoxify a patient using buprenorphine. The general guideline is to detoxify as gradually as possible to minimize symptoms of withdrawal.

Conducting medically supervised withdrawal involves inducting the patient onto buprenorphine and then tapering the patient back off of buprenorphine. The buprenorphine/naloxone combination formulation should be used in most cases.

**Dosing Schedule for Medically Supervised Withdrawal**

In some instances the medically supervised withdrawal process can be completed in a week:

1. Induction on days 1 to 3
2. Tapering on days 4 to 7
In all instances, you should work closely with your patient to determine a realistic time frame for conducting medically supervised withdrawal.

**Further Guidance**
Detailed information about rapid detoxification is beyond the scope of this module. However, should you wish to learn more about protocols or how to implement such programs in your practice, refer to the articles that are included below. Or, you may wish to seek advice from a more experienced buprenorphine provider; you can find a waivered mentor through the *Physician Clinical Support System-MAT*.

**SUMMARY AND KEY POINTS**

**Indicated Use of Buprenorphine**
- Buprenorphine treatment phases are:
  - Induction
  - Stabilization
  - Maintenance

**Formulations**
- Buprenorphine is available as buprenorphine/naloxone combination therapy; the form that should be prescribed for most patients, and buprenorphine monotherapy
- Sublingual film, buccal film, or sublingual tablet are available currently

**General Induction Guidelines**
- Induction can be conducted in the office or at home. Consider that the "Appropriate Use" checklist published by the FDA includes "Provided induction doses under appropriate supervision" and that some patients may need the guidance and monitoring of an in-office visit.
- Patients should be in mild/moderate withdrawal (COWS score of 12-16), typically achieved by 12 to 16 hours of abstinence if dependent on short-acting opioids, 17-24 hours for intermediate acting, and 30-48 hours for methadone and other long acting opioids.
- Initial dose is 2 mg to 4 mg buprenorphine, typically with the corresponding dose of naloxone.
- Monitor the patient for around 1+ hour for response to dose should occur at induction, followed by increments of 2 to 4 mg, followed by another 1 + monitoring.
- Maximum dose day 1 is 16 mg
- Follow-up by phone that day and for each day of induction until the maintenance dose is established
- Recommended maintenance daily dose is 4 to 24 mg. Most commonly, the maintenance dose is 12 to 16 mg (Suboxone, generic, or equivalent doses for Zubsolv or Bunavail), which is as effective as 60 mg of methadone.
- After maintenance dose is established, have an office visit in 3-4 days
- Dose adjustments potentially occur during all 3 phases of treatment, but are far less common after induction.
Standard Induction Protocol

- First day maximum dose can range from 8-16 mg (Suboxone or equivalent doses for Zubsolv or Bunavail), given in 4 mg increments.
- After day 1, dose can be increased a maximum of 8 mg per day, to a ceiling dose of 32 mg.
- Daily dose is established when the patient is neither undermedicated nor overmedicated. Average daily dose is 16 mg.
- During induction, treat withdrawal symptomatically.

Stabilization

- The stabilization period lasts several weeks following induction. Patients should receive a limited supply of medication during stabilization and return for regular follow-up, weekly for the first month.

Medically Supervised Withdrawal

Buprenorphine can be used to ease acute symptoms of withdrawal for patients who want complete detoxification followed by taking no medication assisted treatment or opioids. It generally has poorer success rates than continued medication-assisted treatment.

RESOURCES AVAILABLE THROUGH THIS MODULE:

- AMA Guide: Promote safe storage and disposal of opioids and all medications
  AMA Task Force to Reduce Opioid Abuse produced a brief flier with 3 steps providers should take to promote safe storage and disposal of opioids and all medications with links to resources for patients.
- Appropriate Use Checklist
  Reminder of the safe use conditions and monitoring requirements for prescribing buprenorphine-containing transmucosal products for opioid dependence.
- Buprenorphine Product Formulations Comparison
  Describes the different formulations of buprenorphine for treatment of opioid use disorder. Includes Brand Names, How Supplied, Dosage, Maintenance Target Dose, and Instructions for Use.
- Buprenorphine Product Formulations Comparison
  Compares the different formulations of buprenorphine products made by different drug companies.
- Clinical Opioid Withdrawal Scale (COWS)
  This PDF Document contains the Clinical Opioid Withdrawal Scale (COWS), a common instrument used to assess a patient's opioid withdrawal severity.
- Home Buprenorphine / Naloxone Induction in Primary Care
  This abstract discusses a study done on the feasibility of an unobserved buprenorphine induction protocol. The study involved 103 patients who were heroin users and prescription opioid misusers, and discusses safety and rates of complications from induction through follow-up.
- Información sobre la Buprenorfina (The Facts about Buprenorphine for Treatment of Opioid Addiction (en Español))
Ofrece información a los pacientes sobre la buprenorfina y los tratamientos con ayuda de medicamentos para tratar la adicción a los opioides, y también describe la adicción y los síntomas del síndrome de abstinencia. Además, explica cómo funciona la buprenorfina, su uso apropiado, sus efectos secundarios y cómo se la utiliza en conjunto con la consejería en el proceso de recuperación.

- **Models of Buprenorphine Induction**
  A learning activity that includes the different clinical models of buprenorphine induction, the associated evidence, and the pros and cons of each.

- **Objective Opiate Withdrawal Scale (OOWS)**
  The Objective Opiate Withdrawal Scale (OOWS) contains 13 physically observable signs, rated present or absent, based on a timed period of observation of the patient by a rater.

- **Patient Handout: The Facts about Buprenorphine for Treatment of Opioid Addiction**
  This patient booklet is free to download from the Substance Abuse and Mental Health Services Administration (SAMHSA). It gives patients information on buprenorphine and medication-assisted treatment for opioid addiction. Describes addiction and withdrawal, how buprenorphine works, its proper use, its side effects, and how it fits with counseling in the recovery process.

- **Patient Rights: Confidentiality and Consent**
  This is a patient handout to inform patients about their rights when undergoing office-based buprenorphine treatment.

- **Physician Clinical Support System – Clinical Coaching**
  This website is designed to provide coaching for providers in treating chronic pain, and substance use disorders including opioid use disorder.

- **Sample Consent Form**
  This is a sample of a consent form that can be used when initiating buprenorphine treatment for a new patient.

- **Side Effect Management**
  This form provides a list of possible symptoms that a patient may have during buprenorphine treatment, possible causes, and recommended management of the symptoms.

- **Subjective Opiate Withdrawal Scale (SOWS)**
  Annex of opioid withdrawal scales for downloading includes the Subjective Opiate Withdrawal Scale (SOWS). The SOWS contains 16 symptoms whose intensity the patient rates on a scale of 0 (not at all) to 4 (extremely).

- **TIP 40 Chapter 4: Treatment Protocols**
  Discusses protocols for office-based buprenorphine treatment, including the administering of the drug itself, devising a treatment plan, and choosing an appropriate frequency for visits.

- **Withdrawal Versus Precipitated Withdrawal**
  Two types of withdrawal are associated with mu opioid agonist dependence: withdrawal and precipitated withdrawal.

**REFERENCES USED IN THIS MODULE:**


