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SUMMIT: Procedures for Medication-Assisted Treatment of Alcohol or Opioid Dependence in Primary Care

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HEALTH

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Preface

Medical providers in primary care settings can play an important role in treating patients who have a substance use problem. FDA-approved medications are now available for primary care doctors in their offices to treat appropriate patients. The addition of these medications to a standard drug or alcohol counseling program or self-help program may improve outcomes over counseling or support alone. This guide provides an introduction to identifying and treating patients with substance use disorders in primary care settings. The tool is divided into three parts: Part I reviews the approach that primary care providers should take in discussing alcohol or opiate dependence with their patients. Part II is a step-by-step guide to treating alcohol-dependent patients with extended-release, injectable naltrexone in primary care settings. Part III is a reference guide for primary care practitioners administering buprenorphine/naloxone to patients with opioid dependence. Audiences that will be interested in this tool include primary care practitioners, as well as other medical providers who deliver medication-assisted treatment for alcohol or opioid use disorders in the outpatient setting.

Contents

Part I

Introduction to Medication-Assisted Treatment of Alcohol or Opioid Dependence in Primary Care

Medical providers in primary care settings can play an important role in treating patients who have a substance use problem. This document reviews the approach that primary care providers should take in discussing alcohol or opiate dependence with their patients.

Part II

Administering Extended-Release, Injectable Naltrexone for Patients with Alcohol Dependence: A Step-by-Step Guide for Primary Care Practitioners

This part is a step-by-step guide to treating alcohol-dependent patients with extended-release, injectable naltrexone (trade name: Vivitrol®) in primary care settings. In this guide, you will find procedures for: determining whether individuals are appropriate for treatment with extended-release, injectable naltrexone; initiating treatment; and assessing side effects and administering follow-up injections.

Part III

Administering Buprenorphine/Naloxone to Patients with Opioid Dependence: A Quick Reference Guide for Primary Care Practitioners

Buprenorphine is an opioid partial agonist/antagonist that is FDA approved for the treatment of opioid dependence by physicians in an office-based setting. It is a Schedule III controlled substance and requires that physicians obtain a DEA waiver ("X" waiver) to prescribe it for the office-based treatment of opioid dependence.

Part I

Introduction to Medication-Assisted Treatment of Alcohol or Opioid Dependence in Primary Care

Introduction

Medical providers in primary care settings can play an important role in treating patients who have a substance use problem. Medical providers who identify a patient with a drug or alcohol problem may refer the patient to a specialized drug or alcohol treatment program. These programs may include

Drug and alcohol problems are common among patients in primary care.

- counseling in an outpatient or inpatient setting
- self-help groups, such as Alcoholics or Narcotics Anonymous
- a methadone program for patients with opioid dependence.

However, many patients are unable to stop or reduce alcohol or other drug use with counseling and self-help alone, and some patients are not interested in going to a methadone or specialty treatment program—and therefore risk receiving no treatment at all.

FDA-approved medications, including extended-release, injectable naltrexone (Vivitrol®) for alcohol dependence and buprenorphine/naloxone (Suboxone®) for opioid dependence, are now available for primary care doctors in their offices to treat appropriate patients. The addition of these medications to a standard drug or alcohol counseling program or self-help program may improve outcomes over counseling or support alone.

Also, recent research has shown that patients who receive medication plus brief physician-delivered counseling and advice (medical-management counseling), without participation in formal treatment, can achieve similar outcomes to patients receiving specialized counseling.

Therefore, **medication plus brief physician counseling** is an option for patients who are not willing or able to participate in a specialized drug or alcohol treatment program or self-help program, such as Alcoholics Anonymous. This guide provides a brief overview on identifying potential patients and introducing them to the program, as well as an overview of the medical-management counseling process.

Talking to Patients About Alcohol or Opioid Dependence

Drug or alcohol use is often a sensitive subject for patients; when confronted, they may deny that they have a problem or minimize the extent of it. Even patients who are motivated to change their drug use or drinking behaviors often are ambivalent or apprehensive about beginning treatment because of past experiences with stigma or fear that they may fail.

As a result, it is critical that providers avoid saying anything that patients may construe as judgmental. It is also important for providers to use a motivational, nonconfrontational approach when discussing drug or alcohol use with patients. Providers should try to build rapport and an alliance with patients and use normalizing statements such as "many patients tell me they have trouble controlling their drinking/drug use."

Identifying Patients with Alcohol or Opioid Dependence

Patients for whom medication-assisted treatment is appropriate have alcohol or opioid dependence, characterized by signs and symptoms of **compulsive drug or alcohol use** or **loss of control** over drinking or drug use during the past 12 months.

To identify dependence, ask the patient:

- Do you feel like you need to use more of the drug/alcohol to get the same effect?
- Do you [feel ill (opioids)/have the "shakes" (alcohol)] when you don't use [opioids/alcohol]? (I.e., do you have withdrawal symptoms?)
- Do you feel like you can't just have one drink or end up using more opioids/ alcohol than you intended?
- Have you been unable to stop or reduce your drinking/opioid use when you have tried in the past?
- Are you spending more and more time getting opioids/alcohol, using opioids/alcohol, or recovering from opioids/alcohol use?
- Does your drinking/opioid use get in the way of you doing other things that don't involve alcohol/opioids, like work or family activities?
- Have any bad things happened as a result of your drinking/opioid use? Do you continue to drink/use opioids even though it causes these bad things to happen?

Patients with **three or more** "yes" responses in the past 12 months meet the criteria for alcohol or opioid dependence and are appropriate candidates for medication-assisted treatment. Note: *DSM-5* has replaced *DSM-IV* since the writing of this manual. The above *DSM-IV* criteria can still be used to assess appropriateness for injectable naltrexone, or moderate to severe use disorder would also suggest appropriateness for medication-assisted treatment if using *DSM-5*.

Patients with fewer than three "yes" responses may still be appropriate for treatment at the discretion of the treating physician.

Motivating Patients to Begin Treatment

After identifying an alcohol or opioid problem, the physician should discuss treatment options with the patient using a nonjudgmental, nonconfrontational, motivational approach.

Tell the patient:

- As your doctor, I am concerned about your drinking/opioid use.
- My assessment is that your drinking/opioid use is causing you/others harm.
- I recommend that you stop or cut down on your drinking/opioid use.
- But you are the only one who can change your behavior.
- I know you can do this, and I am happy to help.
- Is this something you are willing to try?

If the patient is NOT willing to change his or her drinking or opioid use:

- As I said, you are the only one who can change your behavior. I am ready to help you if you decide to make a change in the future.
- Could I see you in the future to discuss this again?

If the patient IS willing to change his or her drinking or opioid use:

- There is a medication I can prescribe that may help you to stop or reduce your drinking/opioid use. I can tell you more about this if you are interested.
- I can also give you information on counseling programs available at the clinic and elsewhere, as well as information on self-help groups, like Alcoholics Anonymous or SMART Recovery. Are you interested in this?

The physician should then discuss the specifics of the medication (see medication-specific information later).

Medical-Management Counseling

Patients who are being treated with extended-release, injectable naltrexone for alcohol dependence or buprenorphine/naloxone for opioid dependence should receive brief medical-management counseling from the physician during each clinic visit.

Important things to remember when counseling patients receiving treatment:

- Changing alcohol or opioid use is a process. Patients who have not quit alcohol or opioids but have made progress (e.g., cut down, attended counseling sessions or self-help meetings) should be praised and encouraged to continue to try hard to stop or reduce their alcohol or opioid use. Note that, in some studies, naltrexone had a greater effect on reducing heavy drinking than stopping alcohol use completely. Patients who have reduced, but not stopped, alcohol use should be encouraged to continue their treatment.
- Adherence to the medication is critical for success—especially for patients who are not participating in a specialized drug or alcohol program.
- Attendance at counseling or self-help programs should be encouraged but not mandated in patients who are having success with medication and physician-delivered medical-management counseling alone.
- Use a motivational approach and avoid confrontation, which is likely to elicit denial and resistance on the part of the patient.

At each visit:

- **<u>Assess alcohol or opioid use since the last visit</u>**
    - Say, "Tell me about your alcohol/opioid use since our last visit."
    - Congratulate patients who did not drink or use opioids.
    - For patients who did drink or use opioids, ask:
        - "Were you able to cut down some?"
        - "What were the circumstances that lead you to drink/use opioids?"

        - "Even though you did drink/use opioids, it is good that you are here, and I will continue to help you to change your drinking/opioid use."
        - Help patients to troubleshoot a plan to address their triggers for drinking or opioid use (e.g., deal with stress, avoid people, places, and things associated with alcohol or drugs).

- **Assess medication adherence and any medication side effects**
    - Ask, "Patients often tell me they sometimes miss their medication or forget to take it. Does this happen to you?"
    - Address any barriers to medication adherence or side effects.

- **Assess participation in counseling or self-help program**
    - Patients who are doing well with medication and medical-management counseling alone need not be mandated to attend specialized drug or alcohol counseling or self-help groups.
    - Patients who are struggling should be encouraged to increase participation in specialized drug or alcohol counseling or self-help groups. Encourage patients who are in Alcoholics Anonymous to have a sponsor.
    - **NOTE**: Some counselors or Alcoholics Anonymous members may discourage patients from taking medications. Advise patients that there is **no prohibition against medications** in any of the Alcoholics Anonymous fellowships or counseling programs and that taking medication will not conflict with participation in these groups. If necessary, patients should change to a different meeting or program.

Part II

Administering Extended-Release, Injectable Naltrexone for Patients with Alcohol Dependence

A Step-by-Step Guide for Primary Care Practitioners

Introduction

This part is a step-by-step guide to treating alcohol-dependent patients with extended-release, injectable naltrexone (trade name: Vivitrol) in primary care settings. In this guide, you will find procedures for

- determining whether individuals are appropriate for treatment with extended-release, injectable naltrexone
- initiating treatment
- assessing side effects and administering follow-up injections.

The first section of this guide provides an overview of the medication and its side effects, as well as quick-reference checklists. The remainder of the guide and the appendixes provide detailed recommendations and tools to facilitate treatment.

The contents of the guide are as follows:

- **Section 1: "Quick Guide for Administering Extended-Release, Injectable Naltrexone."** This section provides an overview of the medication, patient eligibility criteria, and side effects. It also contains three procedural checklists for initial and follow-up visits and for explaining the medication to patients.

- **Section 2: "Determining Patient Appropriateness for Treatment with Extended-Release, Injectable Naltrexone: Visit 1."** In this section, there are instructions for assessing patient appropriateness for the medication. This assessment will be conducted during the first visit, although some of the information may already be in the patient's chart from a previous visit or from the mental health therapist's assessment.

- **Section 3: "Administering Extended-Release, Injectable Naltrexone: Visit 1 or 2."** This section provides guidelines for administering the medication. If possible,

How Will an Initial Visit with a Naltrexone Candidate Differ from Most Regular Patient Visits?

- Assess alcohol dependence.
- Determine physical and mental appropriateness for treatment, including
  - level of alcohol withdrawal
  - use of opiates
  - motivation for treatment.
- Visits may take up to 30 minutes.

complete the necessary assessments to determine the appropriateness for injectable naltrexone and administer the first injection in the same visit.

- **Section 4: "Assessing Treatment Progress and Adverse Events and Administering Medication, If Appropriate: Follow-Up Visits."** This section provides guidelines for assessing progress, side effects, and whether the patient should continue the medication.

Section 1
Quick Guide for Administering Extended-Release, Injectable Naltrexone

This section provides an overview of essential information for clinicians treating alcohol dependence with extended-release, injectable naltrexone. Additional details can be found in the subsequent sections of this guide.

What is extended-release, injectable naltrexone?

Extended-release, injectable naltrexone (Vivitrol), which is FDA approved for the treatment of alcohol dependence, is an intra-gluteal injection of an opiate antagonist administered monthly, typically for three to six months. Studies have found similar outcomes for treatment with naltrexone and brief physician support as with specialty alcohol treatment without medication. As a result, participation in counseling or support services during naltrexone treatment is encouraged but NOT mandatory, and naltrexone and physician support is an option for patients not interested in specialty treatment or self-help approaches.

Who is appropriate for treatment with extended-release, injectable naltrexone?

Prior to administering the first naltrexone injection, confirm that the patient

- Is alcohol dependent
- Is motivated to reduce or stop alcohol use and is interested in a medication to treat alcohol dependence
- Has received information and/or referrals to counseling and self-help programs (Alcoholics Anonymous, SMART Recovery)
- Does **NOT** require inpatient alcohol detoxification
- Is **NOT** dependent on sedatives or benzodiazepines, which could require inpatient detoxification

- Is **NOT** currently using opioids (urine drug screen is negative) and is **NOT** expected to require opioid therapy in the next three months
- Does **NOT** have acute hepatitis (AST or ALT more than three times the upper limit of normal) or liver failure
- Does **NOT** have previous sensitivity or allergy to naltrexone or components of the diluent (e.g., polylactide-co-glycolide [PLG], carboxymethylcellulose)
- Does **NOT** have a condition that would impede safe intra-gluteal injection.

What are the most common side effects of extended-release, injectable naltrexone?

- Mild **nausea** (one-third of patients), which typically resolves within days of injection
- Headache
- Mild dizziness
- **Injection-site reactions,** ranging from mild tenderness to (rarely) cellulitis or abscess—in clinical trials, 3 percent of alcohol-dependent patients discontinued extended-release naltrexone because of injection-site pain or discomfort.

Rare side effects include

- Precipitation of **opioid withdrawal**: Patients should be abstinent from opioids prior to and during naltrexone treatment.
- **Hepatotoxicity:** Patients with severe acute hepatitis or liver failure should not receive treatment with naltrexone. Mild to moderate elevations in liver enzymes (less than three times the upper limit) typical in alcohol dependence or stable liver disease (e.g., chronic hepatitis C infection) are NOT a contraindication to naltrexone treatment. Note that successful naltrexone treatment leads to a reduction in liver enzymes as a result of lower alcohol use.
- **Depression:** Depression is a side effect in 5 percent of patients.

What assessments should be completed prior to initiating treatment with extended-release, injectable naltrexone?

- Recent history and physical exam
- Assessment for alcohol dependence and need for inpatient alcohol detoxification

- Assessment for drug use or dependence, especially opioids and benzodiazepine dependence
- Lab testing, including but not limited to
    - Urine drug screen for opioids, oxycodone, methadone, and other opioids, if indicated
    - Comprehensive metabolic panel, including blood urea nitrogen (BUN), creatinine, and hepatic enzymes
    - Pregnancy
- Consider the following tests if the patient shows signs of liver dysfunction:
    - Complete blood count, including platelet count
    - Prothrombin time (PT) and international normalized ratio (INR).

What should a physician assess prior to administering subsequent naltrexone injections?

- **Sufficient progress toward a goal of stopping or reducing alcohol use**. Assess recent alcohol use by asking the number of drinking days, number of drinks per day, and number of heavy drinking days (at least five drinks per day for men and at least four drinks for women). Signs of progress may include reductions in alcohol intake, participation in counseling or self-help programs, or increases in motivation to change drinking behavior.
- **Side effects, including**
    - Injection-site discomfort (injections should alternate between buttocks each month; proper intra-gluteal injection is critical to reduce risk of reactions)
    - Nausea
    - Acute hepatitis (consider a re-check of the hepatic panel if the patient shows signs or symptoms of acute hepatitis or has preexisting liver disease)
    - Anhedonia, depression, or suicidality.

How often should patients be seen during treatment with injectable naltrexone?

Patients should be seen at least monthly for each injection, or more often in the event of any possible side effects.

What if a patient misses a monthly injection?

The injection may be administered any time after the typical one-month interval, as long as the patient meets the criteria above for subsequent injections. In cases of missed injections, be careful to assess for intervening opioid use.

What if a patient requires opioid analgesia during naltrexone treatment?

High doses of potent opioids are required to achieve analgesia in patients with opioid blockade via naltrexone. Attempts to override naltrexone's opioid blockade by administering opioids may result in opioid overdose. As a result, **patients requiring opioid analgesics during treatment with injectable naltrexone should be treated by a specialist in a hospital setting**.

How should injection site reactions be managed?

Mild to moderate pain, redness, or swelling at the injection site may be managed with acetaminophen or NSAIDs, warm or cold compresses, and antibiotics if there are signs of infection. Abscesses, whether sterile or infectious, may require incision and drainage.

How should extended-release, injectable naltrexone be discontinued?

Injectable naltrexone cannot be removed once injected. Discontinuation of treatment is achieved by not administering the next monthly injection.

What if a patient does not participate in counseling or self-help programs?

Extended-release, injectable naltrexone with brief physician support may achieve similar outcomes as specialty alcohol treatment and self-help programs alone. Therefore, participation in counseling or self-help should be encouraged but not mandated.

What if a patient experiences alcohol withdrawal during naltrexone treatment?

Patients who reduce or stop alcohol use may experience alcohol withdrawal symptoms. Naltrexone does not treat alcohol withdrawal. Patients with severe alcohol withdrawal symptoms or previous episodes of severe alcohol withdrawal should be referred to an inpatient detoxification program or the emergency department if necessary. Patients with mild to moderate alcohol withdrawal who are medically and psychiatrically

stable, and have stable housing, may be treated as outpatients (e.g., chlordiazepoxide or off-label gabapentin) and given naltrexone concomitantly.

Pre-Injection Sample Checklist (Use Pullout Checklists in Appendix A)

IF YES TO ALL CRITERIA ABOVE, ADMINISTER FIRST INJECTION.

Yes	No	Criteria	Who Can Assess This?	More Info
☐	☐	Patient meets *DSM-IV* criteria for alcohol dependence. **Note**: *DSM-5* has replaced *DSM-IV* since the writing of this manual. The *DSM-IV* criteria can still be used to assess appropriateness for injectable naltrexone, or moderate to severe use disorder would also suggest appropriateness for injectable naltrexone if using *DSM-5*	Therapist or physician	Page 23
☐	☐	Patient does **NOT** require inpatient alcohol detoxification (no current signs of severe alcohol withdrawal; no past history of requiring hospitalization for severe alcohol withdrawal, seizures, or delirium tremens).	Physician	Page 27
☐	☐	Patient is motivated to reduce or stop alcohol use.	Therapist or physician	Page 31
☐	☐	Patient is **NOT** opioid dependent, is **NOT** currently using opioids, and is **NOT** exhibiting signs or symptoms of opioid intoxication or withdrawal (if any doubt, complete naloxone challenge prior to injection).	Physician	Page 32
☐	☐	All urine drug screens negative for opioids (if any doubt, complete naloxone challenge prior to injection).	Medical assistant, nurse, or physician	Page 32
☐	☐	Patient is **NOT** expected to require opioid therapy in the next three months.	Medical assistant, nurse, or physician	Page 32
☐	☐	Patient does **NOT** have signs or symptoms of acute hepatitis (AST or ALT > 3 times upper limit of normal) or liver failure.	Physician	Page 33
☐	☐	Patient does **NOT** have severe renal impairment (use caution if estimated glomerular filtration rate [GFR] < 50).	Physician	Page 33
☐	☐	Patient does **NOT** have severe thrombocytopenia (platelet count < 50,000) or coagulopathy (INR > 2).	Physician	Page 33
☐	☐	Patient does **NOT** have previous sensitivity or allergy to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent.	Physician	Page 33
☐	☐	Patient does **NOT** have an unstable or untreated serious medical (HIV, diabetes mellitus [DM], coronary artery disease) or psychiatric (schizophrenia, severe depression, bipolar disorder) condition. **Note**: Patients with serious conditions who are treated and stable may be appropriate for extended-release, injectable naltrexone treatment at the discretion of the treating physician.	Physician	Page 33
☐	☐	Patient does **NOT** have a body habitus or skin condition that would impede safe intra-gluteal injection.	Physician	Page 33

Sample Extended-Release, Injectable Naltrexone Patient Education Handout (Use Pullout Handouts in Appendix B)

What is extended-release, injectable naltrexone?
It is a monthly shot that may help you to stop or reduce your alcohol use, usually combined with counseling and support.

Important: Please tell your doctor before you start treatment if . . .

- You use drugs (for example, morphine, Vicodin, methadone, Suboxone, oxycodone, heroin)
    - Do NOT use drugs during treatment or for the first two to three weeks after stopping treatment; it may result in an overdose
- You are going to have surgery or medical treatment that may include pain medications
- You have any liver disease(s)
- You are pregnant, intend to get pregnant, or are breastfeeding
    - You should NOT get any treatment shots if you are pregnant or breastfeeding

Side effects and complications of extended-release, injectable naltrexone

- The most common side effect is mild nausea, which usually goes away within days after the shot
- You may experience a little pain at the location of the shot
    - You may use over-the-counter pain medications, such as Tylenol or Advil
- You may feel sad; if you have thoughts about hurting or killing yourself, notify your doctor RIGHT AWAY
- Some may experience an allergic reaction
- It may harm your liver or cause hepatitis in some individuals

Notify your doctor RIGHT AWAY, if . . .

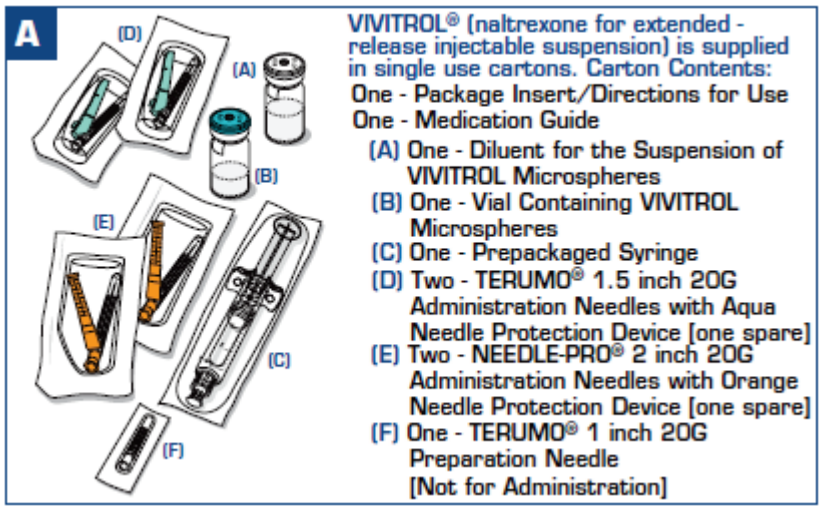
- you have bad pain at the site of the shot
- the location of the shot feels hard, there is a bump or blister, or is red
- there is an open cut at the site of the shot
- you have stomach pain lasting longer than a few days
- you have dark urine
- the area around your eyes is yellow
- you feel really tired
- you are having a hard time breathing
- you are coughing and it does not go away
- you have a skin rash
- swelling of your face, eyes, mouth, or tongue happens
- you feel chest pain
- you feel dizzy or weak

If you experience any side effects or complications, please contact your doctor immediately.

- [Insert clinic phone number here]

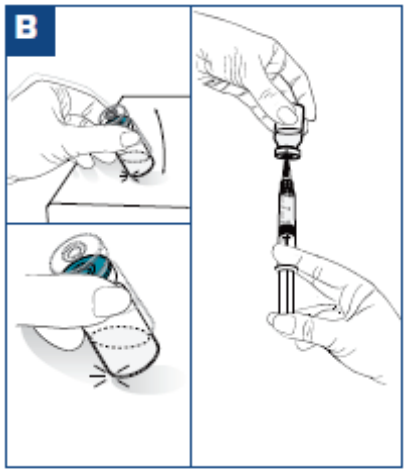
Instructions for Administering Extended-Release, Injectable Naltrexone (Also in Appendix C)

Injections should be administered by a physician or a nurse. Proper intra-gluteal injection is important to minimize the chance of injection-site reactions. Naltrexone must NOT be administered subcutaneously or intravenously. **Note:** These instructions and figures are from the Vivitrol package insert.

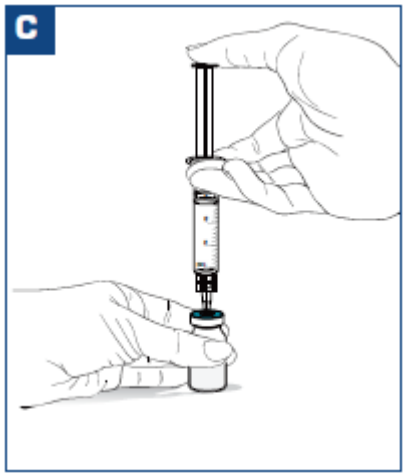


NEEDLE-PRO® and the color orange applied to the needle-protection device are trademarks of the Smiths Medical family of companies.

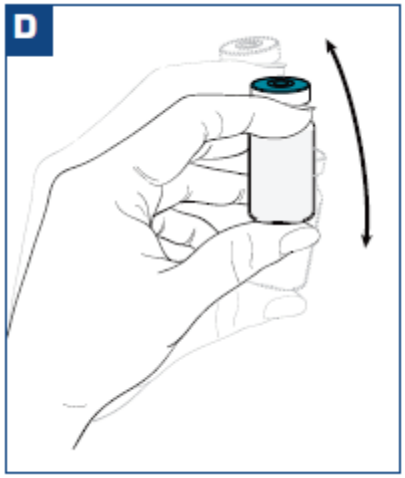
Parenteral products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit.



1. Remove the carton from refrigeration. Prior to preparation, allow drug to reach room temperature (approximately 45 minutes).
2. To ease mixing, firmly tap the VIVITROL Microspheres vial on a hard surface, ensuring the powder moves freely (see Figure B).
3. Remove flip-off caps from both vials. DO NOT USE IF FLIP-OFF CAPS ARE BROKEN OR MISSING.
4. Wipe the vial tops with an alcohol swab.
5. Place the 1-inch preparation needle on the syringe and withdraw 3.4 mL of the diluent from the diluent vial. Some diluent will remain in the diluent vial (see Figure B).

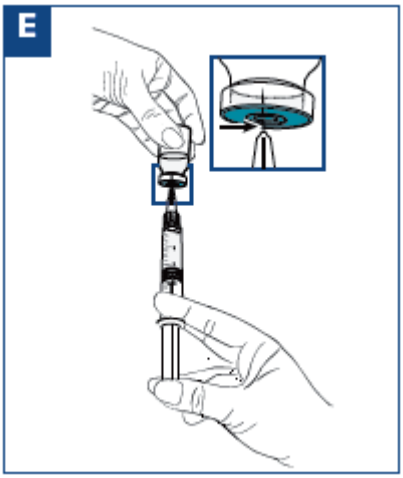


Inject the 3.4 mL of diluent into the VIVITROL Microsphere vial (see Figure C).

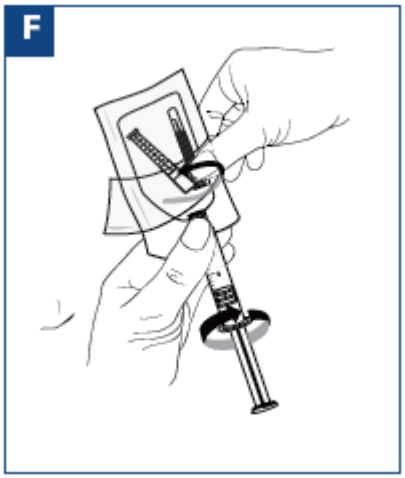


Mix the powder and diluent by vigorously shaking the vial for approximately 1 minute (see Figure D).
Ensure that the dose is thoroughly suspended prior to proceeding to Step E.

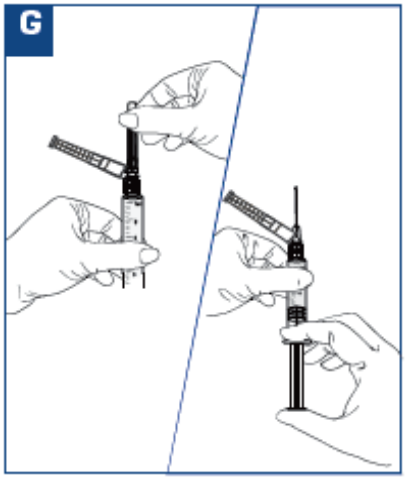
A PROPERLY MIXED SUSPENSION WILL BE MILKY WHITE, WILL NOT CONTAIN CLUMPS, AND WILL MOVE FREELY DOWN THE WALLS OF THE VIAL.



1. Immediately after suspension, withdraw 4.2 mL of the suspension into the syringe using the same preparation needle (see Figure E).
2. Select the appropriate needle for an intramuscular injection based on patient's body habitus:
   a. 1.5-inch TERUMO® Needle
   b. 2-inch NEEDLE-PRO® Needle

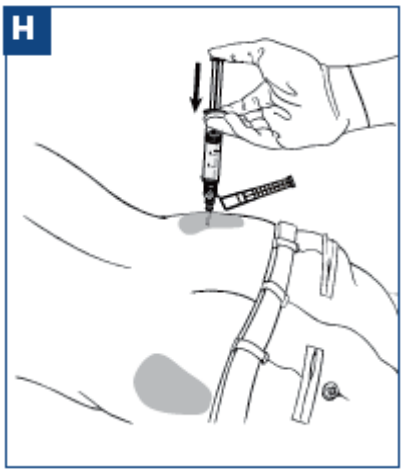


1. Remove the preparation needle and replace with appropriately selected administration needle for immediate use.
2. Peel the blister pouch of the selected administration needle open halfway. Grasp sheath using the plastic pouch. Attach the Luer connection to the syringe with an easy clockwise twisting motion (see Figure F).
3. Seat the needle firmly on the protection device with a push and clockwise twist.



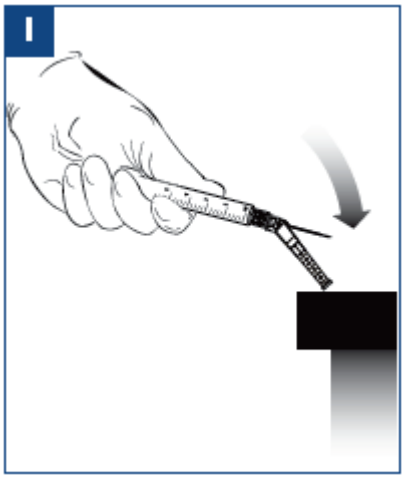
1. Pull the sheath away from the needle—do not twist the sheath because it could result in loosening the needle.
2. Prior to injecting, tap the syringe to release any air bubbles, then push gently on the plunger until 4 mL of the suspension remains in the syringe (see Figure G).

THE SUSPENSION IS NOW READY FOR IMMEDIATE ADMINISTRATION.

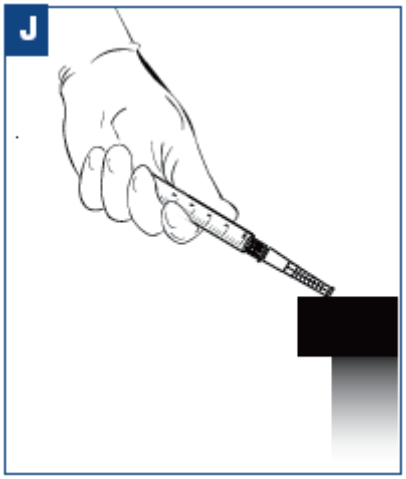


1. Administer the suspension by deep intramuscular (IM) injection into a gluteal muscle, alternating buttocks per monthly injection. Remember to aspirate for blood before injection (see Figure H).
2. If blood aspirates or the needle clogs, do not inject. Change to the spare needle provided in the carton and administer into an adjacent site in the same gluteal region, again aspirating for blood before injection.
3. Inject the suspension in a smooth and continuous motion.

VIVITROL must NOT be given intravenously or subcutaneously.



After the injection is administered, cover the needle by pressing the needle-protection device against a flat surface using a one-handed motion away from self and others (see Figure I).



Visually confirm needle is fully engaged into the needle-protection device (see Figure J).

DISPOSE OF USED AND UNUSED ITEMS IN PROPER WASTE CONTAINERS.

Sample Follow-Up Visit Checklist (Use Pullout Checklists in Appendix D)

Yes	No	Criteria	Who Can Assess This?	More Info
☐	☐	Patient is making sufficient progress toward goal of reducing or stopping alcohol use.	Therapist or physician	Page 40
☐	☐	Potential side effects have been assessed and managed—e.g., • Injection site reactions • Nausea • Acute hepatitis (consider re-check of hepatic panel if signs and symptoms of hepatitis) • Depression or suicidality • Eosinophilic pneumonia • Need for opioid analgesia	Physician	Page 41
☐	☐	There is no indication that treatment with opioid analgesics is likely in the next month.	Physician	Page 43

IF YES TO ALL CRITERIA ABOVE, ADMINISTER NEXT INJECTION.

Section 2

Determining Patient Appropriateness for Treatment with Extended-Release, Injectable Naltrexone: Visit 1

Visit Checklist:

- ☐ Step 1: Assess the Patient for Alcohol Dependence (Therapist or Physician)
- ☐ Step 2: Conduct an Exam to Assess the Patient for Appropriateness for Treatment with Extended-Release, Injectable Naltrexone (Physician)
- ☐ Step 3: Review the Patient Handout Concerning Potential Risks of Treatment

Note: Some of these steps may have already been completed in a previous visit or by the care coordinator or therapist; check the chart for relevant information.

Step 1: Assess the Patient for Alcohol Dependence (Use Pullout Checklists in Appendix E)

The first step in determining whether a patient is appropriate for treatment with extended-release, injectable naltrexone is to assess the patient for a diagnosis of alcohol dependence. **Note:** While patients with alcohol dependence typically drink far in excess of the recommended healthy limits for alcohol intake, the **quantity** of alcohol consumed is not by itself sufficient for establishing a diagnosis of alcohol dependence. Instead, the **extent** to which drinking has become compulsive, or out of the patient's control, is more important to consider in assessing patients for alcohol dependence. **Patients with alcohol dependence are unable to reduce or stop drinking on their own and therefore need treatment, which may include extended-release, injectable naltrexone.**

Diagnosis of Alcohol Dependence

Meets three or more *DSM-IV* criteria:

1. Tolerance
2. Withdrawal
3. Larger amounts or longer periods than intended
4. Desire or unsuccessful efforts to stop or control
5. A lot of time spent on obtaining, using, or recovering
6. Social or occupational consequences
7. Continued use despite physical or psychological problems

A diagnosis of current alcohol dependence is made when patients meet three or more of the *DSM-IV* criteria for alcohol dependence in the past 12 months. The *DSM-IV* diagnostic criteria for alcohol dependence, along with sample questions that physicians may use to assess each criterion, are below. Patients with past alcohol dependence and current risk of relapse may also be considered for treatment with naltrexone.

While assessing the patient, ***complete the* DSM-IV *alcohol dependence worksheet*** (Appendix E) and put the completed worksheet in the patient's chart. **(Note: The patient's therapist may already have done this step; check the patient's chart first.)** Note: *DSM-5* has replaced *DSM-IV* since the writing of this manual. The above *DSM-IV* criteria can still be used to assess appropriateness for medication-assisted treatment, or moderate to severe use disorder would also suggest appropriateness for medication-assisted treatment if using *DSM-5*.

Worksheet for *DSM-IV* Criteria for Diagnosis of ALCOHOL Dependence

Patient's name:			
Worksheet for *DSM-IV* criteria for diagnosis of ALCOHOL dependence			
Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the PAST 12 MONTHS)	**Meets criteria?** Yes	No	**Notes/supporting information**
(1) Tolerance, as defined by either of the following:			
(a) A need for markedly increased amounts of the substance to achieve intoxication of desired effect			
(b) Markedly diminished effect with continued use of the same amount of the substance			
Possible prompts: • *Do you feel like you have to drink more and more alcohol to feel the same effect?* • *Do you feel that over time you have become more used to drinking such that alcohol does not have as strong an effect on you as it did before?*			
(2) Withdrawal, as manifested by either of the following:			
(a) The characteristic withdrawal syndrome			
(b) The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms			
Possible prompt: • *Do you have symptoms, such as anxiety or "the shakes," when you don't drink?*			
(3) Too much, for too long: The substance is often taken in larger amounts or over a longer period of time than intended			
Possible prompts: • *Are you unable to have just one drink?* • *Can you stop when you want to?*			

Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the PAST 12 MONTHS)	**Meets criteria?** Yes	No	**Notes/supporting information**
(4) Can't stop using: There is a persistent desire or unsuccessful efforts to cut down or control substance use			
Possible prompt: • *Do you spend a great deal of your time drinking, getting alcohol, or recovering from drinking [hangovers]?*			
(5) Too much time spent on substance: A great deal of time is spent on activities necessary to obtain the substance, use the substance, or recover from its effects			
Possible prompt: • *Do you spend a great deal of your time drinking, getting alcohol, or recovering from drinking [hangovers]?*			
(6) Giving up activities: Important social, occupational, or recreational activities are given up or reduced because of substance use			
Possible prompt: • *Does your drinking get in the way of doing other things that don't involve alcohol? For example, do you miss work because of drinking or spend less time with family or friends who do not drink?*			
(7) Continue despite harm to self: The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance			
Possible prompts: • *Have any bad things happened as a result of your drinking—to you or other people?* • *Do you continue to drink even though your drinking is causing harm?*			

Current alcohol dependence (3 or more in the past 12 months) ☐ YES ☐ NO

Signature: **Date:**

For patients with problematic alcohol use who do not meet the criteria for *DSM-IV* alcohol dependence: The physician should advise these patients to cut down on their drinking, explain how their alcohol consumption may be affecting their health, and schedule a follow-up visit to ensure that they have reduced their alcohol intake.

Possible prompts (using a motivational interviewing style):

- *As your doctor, I am concerned about your drinking.*
- *My assessment is that you are drinking [too much/too often], which is more than is considered healthy for an adult.*
- *I advise that you cut down on your alcohol intake to less harmful amounts, such as fewer than [women: 1 drink per day on average; men: 2 drinks per day on average, or possibly less depending on condition], but only you can decide to change.*
- *I know you can do this, and I am happy to help.*
- *You are the only one who can change your behavior.*
- *Is this something you are willing to try?*

Occasionally, during a follow-up assessment or during visits with a mental health therapist, patients are identified as having alcohol dependence, and at that time they may be appropriate for treatment with extended-release, injectable naltrexone.

Step 2: Conduct an Exam to Assess Patient for Appropriateness for Treatment with Extended-Release, Injectable Naltrexone (See Pre-Injection Checklist, Appendix A)

The next step is to perform a physical exam to determine whether the patient is appropriate for treatment with extended-release, injectable naltrexone. In general, alcohol-dependent patients appropriate for treatment should meet the following criteria:

- does not currently require inpatient alcohol detoxification (i.e., no current signs of severe alcohol withdrawal) and does not have a history of hospitalization for severe alcohol withdrawal, seizures, or delirium tremens

Appropriateness for Treatment

- Does not require inpatient detox
- Is motivated
- Is stable medically, psychiatrically, and psychosocially
- Is not using and does not plan to use opioids
- Does not have severe liver disease
- Does not have a condition that precludes safe intra-gluteal injection

- is motivated to stop drinking and interested in treatment with extended-release, injectable naltrexone
- is not using opioids and is not expected to need treatment with opioids in the next several months (because naltrexone is an opioid antagonist)
- does not have severe liver disease
- does not have a condition that would preclude safe intra-gluteal injection.

Alcohol Withdrawal

Alcohol withdrawal may range in severity from mild symptoms that require little medical treatment to a severe and life-threating condition, such as delirium tremens that require aggressive treatment in an intensive care unit. Symptoms of alcohol withdrawal may occur within six to 12 hours after the patient's last drink but might not peak until three to five days of alcohol abstinence. Prior to recommending that a patient with alcohol dependence stop or reduce his or her alcohol consumption, the physician should assess the patient for current alcohol withdrawal symptoms, as well as the risk of developing severe alcohol withdrawal symptoms in the near future.

Assess the Need for Alcohol Detoxification

Patients who are in alcohol withdrawal or who have a history of hospitalization for severe alcohol withdrawal, seizures, or delirium tremens should be treated for their alcohol withdrawal and may receive therapy with naltrexone concurrent with this treatment.

1. Ask the patient about his or her history with alcohol withdrawal
2. Assess the level of alcohol withdrawal. If you are in doubt about alcohol withdrawal, use the **Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-Ar) (Appendix F)** to determine the level of withdrawal.

Assessing Alcohol Withdrawal with the CIWA-Ar

1. Complete the CIWA-Ar worksheet in Appendix F (sample is shown on next page). At the top of the worksheet, record the date and time of the patient's last drink. **Note**: Patients with recent alcohol intake may have minimal withdrawal symptoms but can develop symptoms later in the course of alcohol abstinence.
2. Add the scores for each question to obtain the total CIWA-Ar score for the patient and use it to assess the severity of current alcohol withdrawal symptoms according to the following:

Total CIWA-Ar Score	Severity	Treatment Setting
0 to 9 points	Very mild withdrawal	Ambulatory detoxification
10 to 15 points	Mild withdrawal	
16 to 20 points	Modest withdrawal	Inpatient detoxification
21 to 67 points	Severe withdrawal	

- **Patients with a CIWA-Ar score of > 15**: Should be referred for inpatient medical detoxification, including transport to the nearest emergency department, if appropriate. These patients may continue evaluation for possible treatment with extended-release, injectable naltrexone following completion of the inpatient alcohol detoxification.
- **Patients with a CIWA-Ar score of < 10:** May not need pharmacologic treatment for withdrawal but may need repeat assessment during the first 3 to 4 days of alcohol abstinence to monitor for the emergence of additional symptoms.
- **Patients with a CIWA-Ar score of 10 to 15:** Assess for potential ambulatory alcohol detoxification treatment (described below).

Patients who meet the following criteria may undergo ***ambulatory alcohol detoxification*** treatment:

- CIWA-Ar score of 10 to 15
- Able to take oral medications
- Have stable housing and a reliable family member or acquaintance who can monitor the patient for the first 3 to 4 days and get help if symptoms worsen
- No unstable psychiatric or medical condition
- Not pregnant
- No concurrent other substance abuse that might lead to withdrawal symptoms (e.g., narcotic or other sedative withdrawal)
- No history of previous severe alcohol withdrawal episodes (e.g., delirium tremens) or alcohol withdrawal seizures

Possible treatment for ambulatory alcohol detoxification:

- Prescribe benzodiazepines or off-label use of anti-convulsants, such as gabapentin
- Ask patient to return to clinic for reassessment and repeat CIWA-Ar on day 3 of alcohol abstinence, or sooner if symptoms worsen

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Last drink:
Date:
Time:

Patient:_____ **Date:** _____ **Time:** _____ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute:_____ **Blood pressure:**_____

NAUSEA AND VOMITING -- Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TACTILE DISTURBANCES -- Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

TREMOR -- Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

AUDITORY DISTURBANCES -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

PAROXYSMAL SWEATS -- Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

VISUAL DISTURBANCES -- Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

ANXIETY -- Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mild anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

HEADACHE, FULLNESS IN HEAD -- Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

AGITATION -- Observation.
0 normal activity
1 somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

ORIENTATION AND CLOUDING OF SENSORIUM -- Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place/or person

Total **CIWA-Ar** Score _____
Rater's Initials _____
Maximum Possible Score 67

---

*The **CIWA-Ar** is not* copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.

Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (**CIWA-Ar**). *British Journal of Addiction* 84:1353-1357, 1989.

Assess the Patient's Motivation and Willingness to Reduce Alcohol Use

Have a discussion with the patient about whether he or she is motivated to reduce or stop alcohol use.

This discussion with the patient should use a nonjudgmental, motivational approach. It should be frank and aimed at building rapport with the patient and eliciting a desire to change. **Accusing the patient or directing him or her to stop drinking too forcefully risks alienating the patient.** Suggested language for the discussion is below:

Possible prompts:

- *As a result of our assessments, I am able to make a diagnosis of alcohol dependence, or alcohol addiction.*
- *I recommend that you stop or cut down on your drinking.*
- *Only you can decide to change your drinking.*
- *If you are willing to try to change your drinking, I can help you.*
- *One of the ways I could help would be to treat you with a medication that may help you to reduce or stop your drinking. Is this something you might be interested in learning more about?*
- *In addition to taking this medication, you can get some support from a therapist. We have therapists here who can provide that support, or we can refer you to another place for counseling while you are on the medication. Are you interested in that?*
- *This medication involves getting an injection in your buttocks once a month. I will tell you more about it after I do an exam to see if you are physically able to take the medication. Would you be willing to come here once a month for an injection?*

Patients who are not interested in reducing or stopping their drinking should be asked to return in several weeks for additional encouragement to change.

Assess Current Opioid Use or Upcoming Need for Opiates

Because naltrexone is an opioid blocker, high doses of potent opioids delivered in a monitored setting are required to achieve analgesia in patients on naltrexone. In addition, patients who are currently taking opioids may experience immediate withdrawal effects after receiving an injection of extended-release naltrexone. To determine past, present, and potential future opioid use:

1. Take a thorough history. Ask whether the patient is planning any upcoming surgery that will require opioid use. Advise the patient that administering naltrexone to a patient on opioids would make him or her very sick (precipitated withdrawal) and therefore it is important that he or she tell his or her doctors about any and all opioid use.

2. Conduct a urinalysis. All patients should have a urine drug screen immediately prior to treatment with naltrexone. Urine drug screens should detect morphine and morphine derivatives (heroin and codeine), as well as synthetic or semi-synthetic opioids (methadone, oxycodone, buprenorphine, hydrocodone, hydromorphone, etc.). **Many standard drug screens sometimes do not test for these synthetic opiates—check to be sure you are testing for all opiates.**

3. If there is any remaining doubt that the patient is opioid-free, consider administering a ***naloxone challenge*** prior to injecting naltrexone.

Naloxone Challenge

- Administer naloxone 0.8 mg naloxone intramuscularly or subcutaneously.
- Observe for signs or symptoms of opioid withdrawal (chills, piloerection, pupil dilation, nausea, diarrhea, anxiety) for up to one hour.
- If there are no signs or symptoms of opioid withdrawal after one hour, proceed with naltrexone injection.
- If the patient shows any signs or symptoms of opioid withdrawal during the observation period, do not administer naltrexone.

Assess for Physical and Mental Conditions Contraindicated for Treatment with Extended-Release, Injectable Naltrexone

Prior to administering extended-release, injectable naltrexone, conduct a physical exam and lab tests to ensure that the patient does not have the following:

- acute hepatitis or hepatic impairment
- previous sensitivity or allergy to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent
- body habitus or a skin condition that would impede safe intra-gluteal injection
- for females, pregnancy.

Labs

Following completion of the assessment and potential management of alcohol withdrawal, order or review the results of the following **lab tests**:

- hepatic panel
- creatinine
- platelet count
- PT/INR
- pregnancy test (for females)

NOTE: Lab results may already be in the patient's file.

Interpretation of Lab Results

- **Hepatic panel.** Dose-related hepatocellular injury may occur with treatment with naltrexone, and therefore patients with severe liver disease or acute hepatitis should not be treated with naltrexone. Mild to moderate transaminitis (**AST/ALT ≤ 3 upper limit of normal**) is common in alcohol-dependent patients and in conditions often co-morbid with alcohol dependence, such as hepatitis C and HIV infections, and are NOT a contraindication to treatment with naltrexone.

- **Creatinine.** Use caution in patients with an estimated GFR of less than 50, as the safety of injectable naltrexone has not been established in this population.

- **Platelet count and PT/INR.** Extended-release, injectable naltrexone requires a deep intra-muscular injection, and therefore caution is recommended in patients with a severe coagulopathy (platelet count < 50,000 or INR > 2) or in patients treated with anti-coagulant medications (excepting aspirin or standard NSAID treatment).

- **Pregnancy test.** There are no studies assessing the safety and efficacy of naltrexone for alcohol dependence in pregnancy. Pregnant patients with alcohol dependence should be referred for specialty addiction treatment.

Step 3: Review the Patient Handout Concerning Potential Risks of Treatment (Use Pullout Version in Appendix B)

What is extended-release, injectable naltrexone?
It is a monthly shot that may help you to stop or reduce your alcohol use, usually combined with counseling and support.

Important: Please tell your doctor before you start treatment if . . .

- You use drugs (for example, morphine, Vicodin, methadone, Suboxone, oxycodone, heroin)
    - Do NOT use drugs during treatment or for the first two to three weeks after stopping treatment; it may result in an overdose
- You are going to have surgery or medical treatment that may include pain medications
- You have any liver disease(s)
- You are pregnant, intend to get pregnant, or are breastfeeding
    - You should NOT get any treatment shots if you are pregnant or breastfeeding

Side effects and complications of extended-release, injectable naltrexone

- The most common side effect is mild nausea, which usually goes away within days after the shot
- You may experience a little pain at the location of the shot
    - You may use over-the-counter pain medications, such as Tylenol or Advil
- You may feel sad; if you have thoughts about hurting or killing yourself, notify your doctor RIGHT AWAY
- Some may experience an allergic reaction
- It may harm your liver or cause hepatitis in some individuals

Notify your doctor RIGHT AWAY, if . . .

- you have bad pain at the site of the shot
- the location of the shot feels hard, there is a bump or blister, or is red
- there is an open cut at the site of the shot
- you have stomach pain lasting longer than a few days
- you have dark urine
- the area around your eyes is yellow
- you feel really tired
- you are having a hard time breathing
- you are coughing and it does not go away
- you have a skin rash
- swelling of your face, eyes, mouth, or tongue happens
- you feel chest pain
- you feel dizzy or weak

If you experience any side effects or complications, please contact your doctor immediately at

- Venice Family Clinic: (310) 392-8636
- The call center is open Monday through Thursday, 8:00 a.m. to 5:00 p.m. and Friday 8:00 a.m. to 4:00 p.m.

Section 3

Administering Extended-Release, Injectable Naltrexone: Visit 1 or 2

Visit Checklist:

- ☐ Step 1: Administer the First Injection of Extended-Release, Injectable Naltrexone
- ☐ Step 2: Monitor the Patient, Schedule the Next Visit, and Provide Counseling and Support Referrals

Step 1: Administer the First Injection of Extended-Release, Injectable Naltrexone (See Steps in Appendix C)

If the patient is appropriate for the medication, a licensed health care professional should prepare and administer the injection. (See Appendix C for step-by-step instructions.)

To ensure proper dosing, it is important to follow these preparation and administration instructions:

- **Dose:** The recommended dose is 380 mg, delivered intramuscularly every four weeks or once a month.

- **Injection:** The injection should be administered by a health care professional as an **intramuscular gluteal injection**, alternating buttocks for each subsequent injection, using the carton components provided (details below). **Extended-release, injectable naltrexone must not be administered intravenously or subcutaneously.**

- **Needles and suspension:** The needles provided in the carton are customized needles. **Extended-release, injectable naltrexone must not be injected using any other needle**.

    - Two thin-walled, 1.5-inch needles with needle protection device are provided in the clinical drug cartons for intramuscular administration.

    - In addition, longer (2-inch) thin-walled needles with needle-protection devices have been provided as ancillary supplies. For patients with a larger amount of subcutaneous tissue overlying the gluteal muscle, the administering health care professional may utilize the supplied 2-inch needle with needle-protection device to ensure that the injectate reaches the intramuscular mass.

    - Both 1.5- and 2-inch administration needles are provided to accommodate varying body habitus. A spare administration needle of each size is provided in case of clogging. **Do not substitute any other components for the components of the carton.**

- The needle lengths (either 1.5 or 2 inches) may not be adequate in every patient because of body habitus. Body habitus should be assessed prior to each injection for each patient to ensure that needle length is adequate for intramuscular administration. Health care professionals should ensure that the extended-release, injectable naltrexone injection is given correctly and should consider alternate treatment for those patients whose body habitus precludes an intramuscular gluteal injection with one of the provided needles.

- Extended-release, injectable naltrexone must be suspended only in the diluent supplied in the carton and must be administered only with one of the administration needles supplied in the carton. The microspheres, diluent, preparation needle, and administration needle with needle-protection device are required for preparation and administration.

- **Preparing the injection.** Prior to preparation, allow the drug to reach room temperature (approximately 45 minutes). Parenteral products should be visually inspected for particulate matter and discoloration prior to administration. A properly mixed suspension will be milky white, will not contain clumps, and will move freely down the wall of the vial. Prepare and administer the extended-release, injectable naltrexone suspension using aseptic technique.

Pretreatment with oral naltrexone is not required before administering extended-release, injectable naltrexone.

Proper Storage of Extended-Release, Injectable Naltrexone

The entire carton should be stored in the refrigerator (2–8 °C, 36–46 °F). Unrefrigerated, extended-release, injectable naltrexone microspheres can be stored at temperatures not exceeding 25 °C (77 °F) for no more than 7 days prior to administration. Do not expose unrefrigerated product to temperatures above 25 °C (77 °F). Extended-release, injectable naltrexone should not be frozen.

Detailed, step-by-step ***instructions for the preparation and injection*** of extended-release, injectable naltrexone are provided in Appendix C.

Step 2: Monitor the Patient, Schedule the Next Visit, and Provide Counseling and Support Referrals

After receiving an injection, the following steps should be taken:

1. Give the patient a wallet card (Appendix G) with notification and warning to health care providers that the patient is under opioid blockade, on one side, and information for the patient regarding who to contact in case of questions regarding side effects, on the other.
2. Schedule the patient to return to the clinic in four weeks for the next injection.
3. Provide local counseling and support resources (Appendix H).

Section 4

Assessing Treatment Progress and Adverse Events and Administering Medication, If Appropriate: Follow-Up Visits

Follow-Up Visit Checklist:

- ☐ Step 1: Assess Patient's Drinking Since the Last Visit (Therapist or Physician)
- ☐ Step 2: Assess the Patient's Involvement in Counseling and Support Services (Therapist or Physician)
- ☐ Step 3: Assess and Manage Any Potential Medication Side Effects (Physician)
- ☐ Step 4: Assess and Manage Any Interruptions in Therapy or Opioid Use (Physician)
- ☐ Step 5: If Appropriate, Administer Next Injection of Extended-Release, Injectable Naltrexone (Physician or Nurse)

A typical course of treatment with extended-release, injectable naltrexone for alcohol dependence involves three to six monthly injections. Reasons to discontinue extended-release, injectable naltrexone include intolerable side effects, clinical deterioration, or patient preference.

Because the optimal duration of therapy with extended-release, injectable naltrexone has not been definitively established, a reasonable approach is to plan for an initial course of three monthly injections, with the decision to continue beyond three months made by the physician and patient on a case-by-case basis.

Step 1: Assess the Patient's Drinking Since the Last Visit

(Adapted from Pettinati, H. M., Weiss, R. D., Miller, W. R., Donovan, D., Ernst, D. B., and Rounsaville, B. J., *COMBINE Medical Management Treatment Manual*, COMBINE Monograph Series, Vol. 2, *Medical Management Treatment Manual: A Clinical Research Guide for Medically Trained Clinicians Providing Pharmacotherapy as Part of the Treatment for Alcohol Dependence*, DHHS Publication No. [NIH] 04–5289, Bethesda, MD: *National Institute on Alcohol Abuse and Alcoholism*, 2004.)

Ask the patient about his or her drinking status since the last visit, as well as about any opioid use or other drug use and attendance at mutual-support groups (e.g., Alcoholics Anonymous, SMART Recovery). Allow for some open-ended discussion of the patient's current concerns about drinking or his or her treatment with extended-release, injectable naltrexone. Reward any positive steps the patient has made toward reducing or stopping alcohol use. Do not gloss over any problems, but attempt to stay positive and provide the patient with optimism that he or she can recover. The patient is more likely to respond to a motivational approach than a confrontational one.

Possible Prompts

- *How have you been since the last visit?*
- *How well were you able to reduce or stop your drinking?*
- *What was difficult? What went well?*

For patients who did drink:

- *What were the circumstances when you drank? Remember, this is hard; change happens through small steps. It's a good sign that you are here at your visit and still trying hard at this. Keep trying and don't get too discouraged!*
- *How strong was your desire to drink? Did you have strong cravings or urges?*

If patient did drink but has experienced fewer cravings since starting treatment:

- *Reductions in your cravings are a sign that the treatment is working and that you are beginning the process of change!*

If the patient's desire to drink was strong but he or she didn't drink:

- *Congratulations on choosing not to drink when you really wanted to. You have taken an important step toward your recovery!*

If the patient did not drink:

- *Congratulations for staying abstinent. You are demonstrating your determination to change. You are making great progress toward your recovery!*

Step 2: Assess the Patient's Involvement in Counseling and Support Services

If the patient attended any counseling or self-help or support meetings, provide him or her with positive feedback and encourage continued attendance. For patients who are not attending these services, ask if there are any practical problems, such as coordinating the schedule of visits or transportation, so the patient can attend both treatments. If this is a problem, work with the patient to ensure that he or she can continue to attend both types of treatment.

Step 3: Assess and Manage Any Potential Medication Side Effects

Injection-Site Reactions

Ask the patient about pain, redness, swelling, or irritation at the previous injection site. Mild to moderate pain and tenderness for the first several days after the injection can be treated conservatively with NSAIDs or acetaminophen, as well as ice. ***Patients with signs or symptoms of cellulitis (fever, chills, warmth, erythema) should receive a course of treatment with antibiotics.*** Rarely, patients develop an abscess that may require incision and drainage. Patients with mild injection-site reactions who respond to conservative treatment may continue to receive extended-release, injectable naltrexone injections.

Hepatitis

Routine repeat liver-function tests (LFTs) are not required unless the patient presents with any signs or symptoms suggestive of hepatitis (e.g., jaundice, dark urine, right upper-quadrant abdominal pain) or the patient's initial medical history suggests that further monitoring is required (e.g., chronic hepatitis C infection). Patients who develop severe hepatitis while on naltrexone should discontinue naltrexone (injectable and oral).

Depression and Suicidality

Mild to moderate depressed mood during treatment for alcohol dependence is common. Mood will improve during the first two to three weeks of alcohol abstinence for most patients. These patients may be managed by explaining that their mood will likely improve and providing additional support in the meantime. For patients whose mood does not improve during initial alcohol abstinence or are troubled by the symptoms, prescription of an antidepressant would be appropriate.

Patients with severe depressive symptoms or serious suicidal ideation or behavior should be referred through usual care procedures to a mental health therapist. Extended-release, injectable naltrexone should generally be discontinued in these patients if the depression seems related to the patient's treatment with extended-release, injectable naltrexone.

Eosinophilic Pneumonia

Eosinophilic pneumonia is a rare complication but should be considered in patients who develop progressive dyspnea and hypoxemia during treatment.

Step 4: Assess and Manage Any Interruptions in Treatment and Opioid Use

The greatest concern for precipitating opioid withdrawal among patients receiving ongoing treatment with extended-release, injectable naltrexone involves patients whose treatment has been interrupted (more than four weeks since the last injection). **Prior to any naltrexone injection, patients should be assessed for opioid use and should be** reminded that the administration of naltrexone to someone who is using opioids may precipitate severe opioid withdrawal symptoms. Patients who have used opioids while under continuous naltrexone blockade are unlikely to experience precipitated opioid withdrawal.

Patients Requiring Opioid Analgesia

In an emergency situation requiring pain control among patients receiving extended-release, injectable naltrexone, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required as part of anesthesia or analgesia, patients should be continuously monitored in an anesthesia care setting by qualified medical personnel. The opioid therapy must be provided by individuals specifically trained in the use of anesthetic drugs and the management of the respiratory effects of potent opioids, specifically the establishment and maintenance of a patent airway and assisted ventilation. Irrespective of the drug chosen to reverse naltrexone opioid blockade, the patient should be monitored closely by appropriately trained personnel in a hospital emergency or intensive care setting equipped and staffed for cardiopulmonary resuscitation.

Step 5: If Appropriate, Administer the Next Injection of Extended-Release, Injectable Naltrexone

Patients who have not experienced a serious side effect, are not at risk for precipitated opioid withdrawal, and are making progress in reducing or stopping alcohol use should receive the next injection of extended-release, injectable naltrexone.

If, after several months of treatment, patients are not making progress toward stopping or reducing their alcohol use, they should be encouraged to enter a treatment setting where a higher intensity of treatment can be provided (e.g., specialty outpatient or inpatient alcohol treatment program).

I**t is important to note that reductions in alcohol use short of complete alcohol abstinence may be reasonable signs of progress, especially early in the treatment course and among patients who are otherwise motivated and engaged in the treatment process. In clinical trials, naltrexone significantly reduced heavy drinking days (at least five drinks per day for men and at least four drinks per day for women). Patients reducing heavy drinking days without achieving abstinence will also experience reductions in the negative health and social consequences of heavy drinking.**

There are no special procedures for discontinuing extended-release, injectable naltrexone; simply do not administer any further injections.

Appendix A: Pre-Injection Checklist for Appropriateness for Extended-Release, Injectable Naltrexone

Pre-injection Checklist for Appropriateness for Extended-Release, Injectable Naltrexone

Patient name: _____

Date: _____

YES	NO	Criteria
☐	☐	Patient meets *DSM-IV* criteria for alcohol dependence
☐	☐	Patient does **NOT** require inpatient alcohol detoxification (no current signs of severe alcohol withdrawal; no past history of requiring hospitalization for severe alcohol withdrawal, seizures, or delirium tremens).
☐	☐	Patient is motivated to reduce or stop alcohol use
☐	☐	Patient is **NOT** opioid dependent, is **NOT** currently using opioids, and is **NOT** exhibiting signs or symptoms of opioid withdrawal
☐	☐	All urine drug screens negative for opioids
☐	☐	Patient is **NOT** expected to require opioid therapy in the next three months
☐	☐	Patient does **NOT** have signs or symptoms of acute hepatitis or liver failure
☐	☐	Patient does **NOT** have severe renal impairment (use caution if estimated GFR < 50)
☐	☐	Patient does **NOT** have severe thrombocytopenia (platelet count < 50,000) or coagulopathy (INR > 2)
☐	☐	Patient does **NOT** have previous sensitivity or allergy to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent
☐	☐	Patient does **NOT** have an unstable or untreated serious medical (HIV, diabetes mellitus [DM], coronary artery disease) or psychiatric (schizophrenia, severe depression, bipolar disorder) condition **Note**: Patients with serious conditions who are treated and stable may be appropriate for extended-release, injectable naltrexone treatment at the discretion of the treating physician
☐	☐	Patient does **NOT** have a body habitus or skin condition that would impede safe intra-gluteal injection

IF YES TO ALL CRITERIA ABOVE, ADMINISTER FIRST INJECTION

Completed by: _____

MD name: _____

MD signature: _____

Date: _____

Appendix B: Introduction to the Risks of Extended-Release, Injectable Naltrexone Worksheet

Extended-Release, Injectable Naltrexone Patient Handout

What is extended-release, injectable naltrexone?
It is a monthly shot that may help you to stop or reduce your alcohol use, usually combined with counseling and support.

Important: Please tell your doctor before you start treatment if . . .

- You use drugs (for example, morphine, Vicodin, methadone, Suboxone, oxycodone, heroin)
    - Do NOT use drugs during treatment or for the first two to three weeks after stopping treatment; it may result in an overdose
- You are going to have surgery or medical treatment that may include pain medications
- You have any liver disease(s)
- You are pregnant, intend to get pregnant, or are breastfeeding
    - You should NOT get any treatment shots if you are pregnant or breastfeeding

Side effects and complications of extended-release, injectable naltrexone

- The most common side effect is mild nausea, which usually goes away within days after the shot
- You may experience a little pain at the location of the shot
    - You may use over-the-counter pain medications, such as Tylenol or Advil
- You may feel sad; if you have thoughts about hurting or killing yourself, notify your doctor RIGHT AWAY
- Some may experience an allergic reaction
- It may harm your liver or cause hepatitis in some individuals

Notify your doctor RIGHT AWAY, if . . .

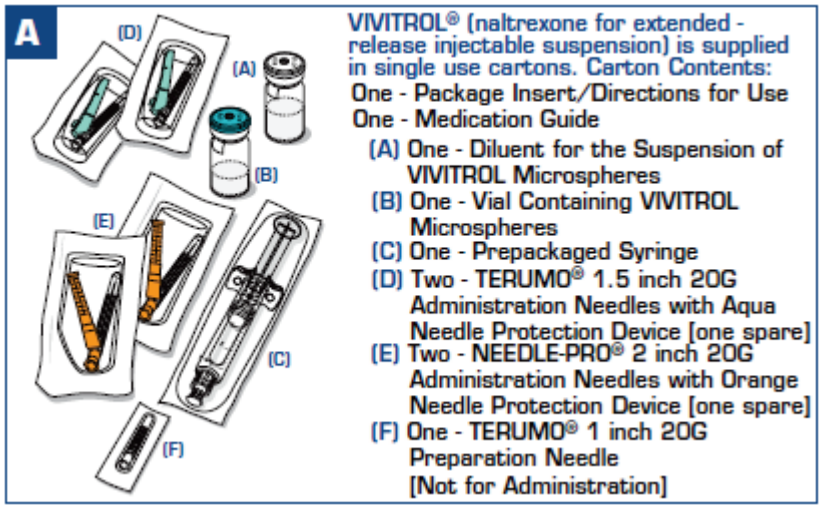
- you have bad pain at the site of the shot
- the location of the shot feels hard, there is a bump or blister, or is red
- there is an open cut at the site of the shot
- you have stomach pain lasting longer than a few days
- you have dark urine
- the area around your eyes is yellow
- you feel really tired
- you are having a hard time breathing
- you are coughing and it does not go away
- you have a skin rash
- swelling of your face, eyes, mouth, or tongue happens
- you feel chest pain
- you feel dizzy or weak

If you experience any side effects or complications, please contact your doctor immediately at

- Venice Family Clinic: (310) 392-8636
- The call center is open Monday through Thursday, 8:00 a.m. to 5:00 p.m. and Friday 8:00 a.m. to 4:00 p.m.

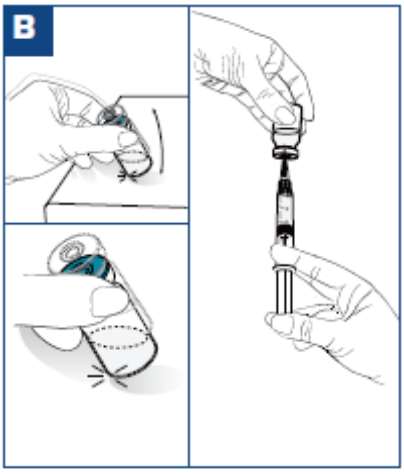
Appendix C: Step-by-Step Instructions for the Preparation and Injection of Extended-Release, Injectable Naltrexone

Injections should be administered by a physician or a nurse. Proper intra-gluteal injection is important to minimize the chance of injection-site reactions. Naltrexone must NOT be administered subcutaneously or intravenously. Note: These instructions and figures are from the Vivitrol package insert.

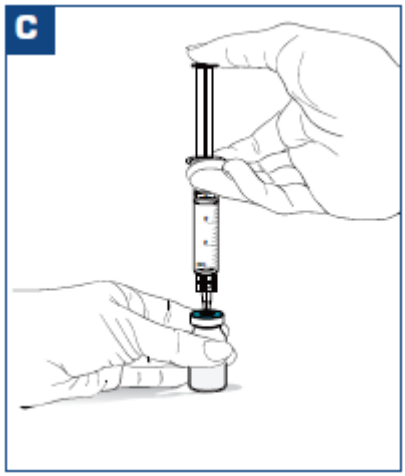


NEEDLE-PRO® and the color orange applied to the needle-protection device are trademarks of the Smiths Medical family of companies.

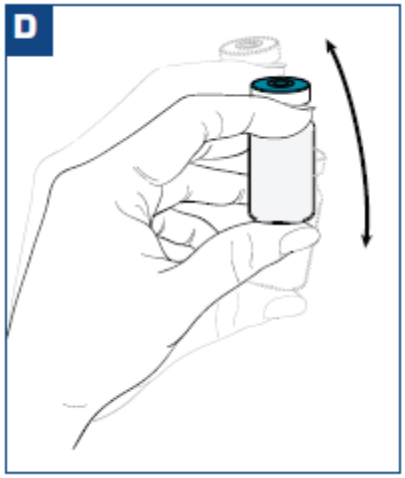
Parenteral products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit.



1. Remove the carton from refrigeration. Prior to preparation, allow drug to reach room temperature (approximately 45 minutes).
2. To ease mixing, firmly tap the VIVITROL Microspheres vial on a hard surface, ensuring the powder moves freely (see Figure B).
3. Remove flip-off caps from both vials. DO NOT USE IF FLIP-OFF CAPS ARE BROKEN OR MISSING.
4. Wipe the vial tops with an alcohol swab.
5. Place the 1-inch preparation needle on the syringe and withdraw 3.4 mL of the diluent from the diluent vial. Some diluent will remain in the diluent vial (see Figure B).

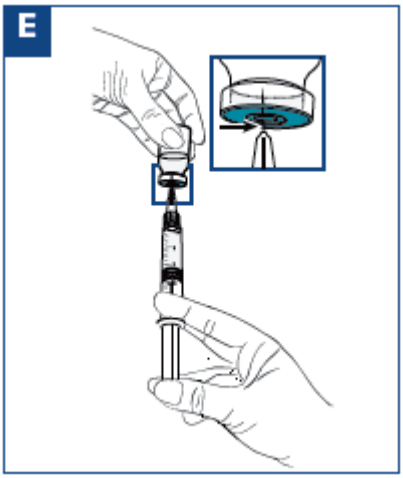


Inject the 3.4 mL of diluent into the VIVITROL Microsphere vial (see Figure C).

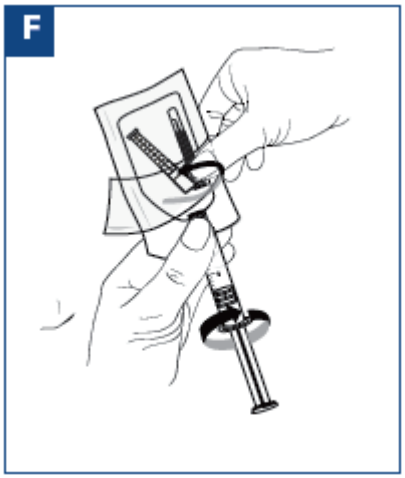


Mix the powder and diluent by vigorously shaking the vial for approximately 1 minute (see Figure D).
Ensure that the dose is thoroughly suspended prior to proceeding to Step E.

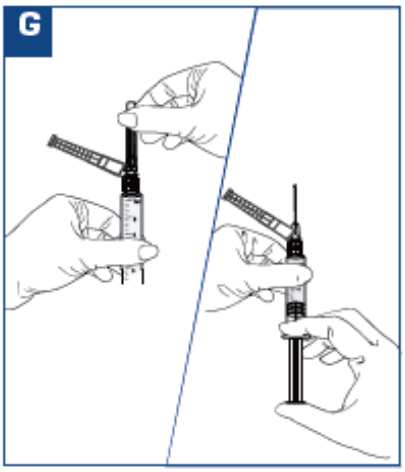
A PROPERLY MIXED SUSPENSION WILL BE MILKY WHITE, WILL NOT CONTAIN CLUMPS, AND WILL MOVE FREELY DOWN THE WALLS OF THE VIAL.



1. Immediately after suspension, withdraw 4.2 mL of the suspension into the syringe using the same preparation needle (see Figure E).
2. Select the appropriate needle for an intramuscular injection based on patient's body habitus:
   a. 1.5-inch TERUMO® Needle
   b. 2-inch NEEDLE-PRO® Needle

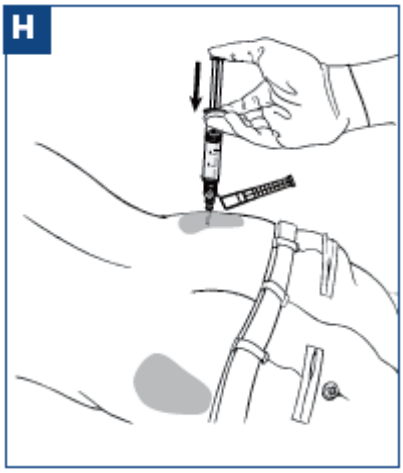


1. Remove the preparation needle and replace with appropriately selected administration needle for immediate use.
2. Peel the blister pouch of the selected administration needle open halfway. Grasp sheath using the plastic pouch. Attach the Luer connection to the syringe with an easy clockwise twisting motion (see Figure F).
3. Seat the needle firmly on the protection device with a push and clockwise twist.



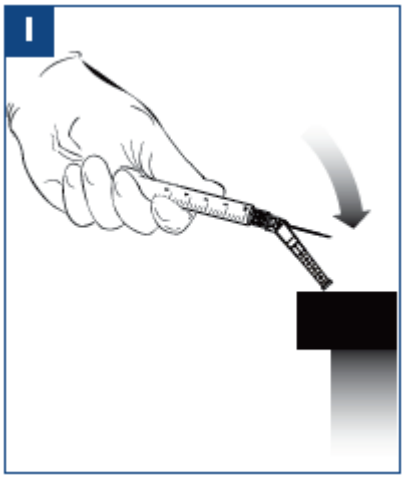
1. Pull the sheath away from the needle—do not twist the sheath because it could result in loosening the needle.
2. Prior to injecting, tap the syringe to release any air bubbles, then push gently on the plunger until 4 mL of the suspension remains in the syringe (see Figure G).

THE SUSPENSION IS NOW READY FOR IMMEDIATE ADMINISTRATION.

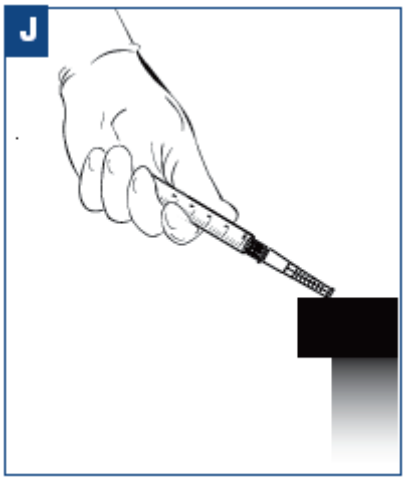


1. Administer the suspension by deep intramuscular (IM) injection into a gluteal muscle, alternating buttocks per monthly injection. Remember to aspirate for blood before injection (see Figure H).
2. If blood aspirates or the needle clogs, do not inject. Change to the spare needle provided in the carton and administer into an adjacent site in the same gluteal region, again aspirating for blood before injection.
3. Inject the suspension in a smooth and continuous motion.

VIVITROL must NOT be given intravenously or subcutaneously.



After the injection is administered, cover the needle by pressing the needle-protection device against a flat surface using a one-handed motion away from self and others (see Figure I).



Visually confirm needle is fully engaged into the needle-protection device (see Figure J).

DISPOSE OF USED AND UNUSED ITEMS IN PROPER WASTE CONTAINERS.

Appendix D: Follow-Up Visit Pre-Injection Checklists

Extended-Release, Injectable Naltrexone Follow-Up Visit Pre-Injection Checklist

Patient name:
Date:

Yes	No	Criteria
☐	☐	Patient is making sufficient progress toward goal of alcohol abstinence
☐	☐	Potential side effects have been assessed and managed—e.g., • Injection site reactions • Nausea • Acute hepatitis (consider re-check of hepatic panel if there are signs and symptoms of hepatitis) • Depression or suicidality • Eosinophilic pneumonia • Need for opioid analgesia
☐	☐	Interruptions of naltrexone opioid blockade and any intervening opioid use have been assessed.
☐	☐	There is no indication that treatment with opioid analgesics is likely in the next month.

IF YES TO ALL CRITERIA ABOVE, ADMINISTER NEXT INJECTION

Completed by: _____
MD name: _____
MD signature: _____
Date: _____

Appendix E: *DSM-IV* Alcohol Dependence Diagnosis Worksheet

Patient's name:			
Worksheet for *DSM-IV* criteria for diagnosis of ALCOHOL dependence			
Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the PAST 12 MONTHS)	**Meets criteria?** Yes	No	**Notes/supporting information**
(1) Tolerance, as defined by either of the following:			
(a) A need for markedly increased amounts of the substance to achieve intoxication of desired effect			
(b) Markedly diminished effect with continued use of the same amount of the substance			
Possible prompts: • *Do you feel like you have to drink more and more alcohol to feel the same effect?* • *Do you feel that over time you have become more used to drinking such that alcohol does not have as strong an effect on you as it did before?*			
(2) Withdrawal, as manifested by either of the following:			
(a) The characteristic withdrawal syndrome			
(b) The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms			
Possible prompt: • *Do you have symptoms, such as anxiety or "the shakes," when you don't drink?*			
(3) Too much, for too long: The substance is often taken in larger amounts or over a longer period of time than intended			
Possible prompts: • *Are you unable to have just one drink?* • *Can you stop when you want to?*			

Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the PAST 12 MONTHS)	**Meets criteria?** Yes	No	**Notes/supporting information**
(4) Can't stop using: There is a persistent desire or unsuccessful efforts to cut down or control substance use			
Possible prompt: • *Do you spend a great deal of your time drinking, getting alcohol, or recovering from drinking [hangovers]?*			
(5) Too much time spent on substance: A great deal of time is spent on activities necessary to obtain the substance, use the substance, or recover from its effects			
Possible prompt: • *Do you spend a great deal of your time drinking, getting alcohol, or recovering from drinking [hangovers]?*			
(6) Giving up activities: Important social, occupational, or recreational activities are given up or reduced because of substance use			
Possible prompt: • *Does your drinking get in the way of doing other things that don't involve alcohol? For example, do you miss work because of drinking or spend less time with family or friends who do not drink?*			
(7) Continue despite harm to self: The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance			
Possible prompts: • *Have any bad things happened as a result of your drinking—to you or other people?* • *Do you continue to drink even though your drinking is causing harm?*			

Current alcohol dependence (3 or more in the past 12 months) ☐ YES ☐ NO

Signature: **Date:**

Appendix F: CIWA-Ar Worksheet

Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar)

Last drink:
Date:
Time:

Patient:_____ **Date:** _____ **Time:** _____ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute:_____ **Blood pressure:**_____

NAUSEA AND VOMITING -- Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TACTILE DISTURBANCES -- Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

TREMOR -- Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

AUDITORY DISTURBANCES -- Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

PAROXYSMAL SWEATS -- Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

VISUAL DISTURBANCES -- Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

ANXIETY -- Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mild anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

HEADACHE, FULLNESS IN HEAD -- Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

AGITATION -- Observation.
0 normal activity
1 somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

ORIENTATION AND CLOUDING OF SENSORIUM -- Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place/or person

Total **CIWA-Ar** Score _____
Rater's Initials _____
Maximum Possible Score 67

---

*The **CIWA-Ar** is not* copyrighted and may be reproduced freely. This assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.

Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (**CIWA-Ar**). *British Journal of Addiction* 84:1353-1357, 1989.

Appendix G: Wallet Cards

Important Information For Emergency Pain Management

I am currently taking **naltrexone extended-release injectable suspension**, an opioid antagonist. Please see the back of this card for important information about pain management.

My name: ____

Emergency contact name:__________________________

My doctor: Venice Family Clinic

My doctor's number: (310) 392-8636

Call 1-888-835-8008

For Full Prescribing Information, including boxed warning visit www.ntx-xrmedinfo.com

SUMMIT

Substance Use, Motivation and Medication Integrated Treatment

Important Information For Emergency Pain Management

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Call 1-888-835-8008

For Full Prescribing Information, including boxed warning visit www.ntx-xrmedinfo.com

SUMMIT

Substance Use, Motivation and Medication Integrated Treatment

To Medical Personnel Treating me in An Emergency

In an emergency situation in patients receiving naltrexone, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required as part of anesthesia or analgesia, patients should be continuously monitored in an anesthesia care setting by persons not involved in the conduct of the surgical or diagnostic procedure. The opioid therapy must be provided by individuals specifically trained in the use of anesthetic drugs and the management of the respiratory effects of potent opioids, specifically the establishment and maintenance of a patent airway and assisted ventilation. Irrespective of the drug chosen to reverse naltrexone blockade, the patient should be monitored closely by appropriately trained personnel in a setting equipped and staffed for cardiopulmonary resuscitation.

Call 1-888-835-8008

SUMMIT
Substance Use, Motivation and Medication Integrated Treatment

For Full Prescribing Information, including boxed warning, visit www.ntx-xrmedinfo.com

To Medical Personnel Treating me in An Emergency

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Call 1-888-835-8008

SUMMIT
Substance Use, Motivation and Medication Integrated Treatment

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Appendix H: Local Referral Resources

SUBSTANCE USE AND MENTAL HEALTH REFERRALS / USO DE SUSTANCIAS Y REFERENCIAS DE SALUD MENTAL

SUBSTANCE ABUSE/ ABUSO DE SUSTANCIAS	CONTACT/CONTACTO	$ AND SPANISH/ESPANOL
Venice Family Clinic 604 Rose Ave., Venice, CA 90291 2509 Pico Blvd., Santa Monica, CA 90405	310-392-8636	Venice Family Clinic patients only
CLARE Foundation (detox) 909 Pico Blvd., Santa Monica, CA 90404	310-314-6200	MediCal, SSI, GR, free for low income
Redgate Hospital (medical detox) 1775 Chestnut Ave., Long Beach, CA 90813	562-599-8444 (may call collect)	Call every morning at 8 a.m.
Alcoholics Anonymous Hundreds of locations	Eng: 800-923-8722 Esp: 323-735-2089	Free 12-step groups
Al-Anon (for family members) Many locations	Eng: 323-936-4343 Esp: 562-948-2190	Free 12-step groups
Narcotics Anonymous Many locations	310-390-0279	Free 12-step groups
Cocaine Anonymous Many locations	310-216-4444	Free 12-step groups
CRISIS		
Suicide Prevention Hotline	Eng: 310-391-1253 Eng/Esp: 877-727-4747	Free
L.A. Rape & Battering Hotline	310-392-8381	Free
Exodus Mental Health Urgent Care 3828 Delmas Terrace, Culver City, CA 90231	310-253-9494	Free—psychiatric emergencies

PSYCHIATRIC MEDICATION/MEDICAMENTOS PSIQUITRICOS		
Edelman Westside Mental Health Center 11080 Olympic Blvd., Los Angeles, CA 90064	310-966-6500 Walk-in M–Th 8 a.m.	All MediCal, HMOs, Medicare, no insurance
Didi Hirsch Mental Health Services Many locations	310-390-6612	MediCal (adults/child), Medi-Medi (adults), Medicare, Healthy families (child)

DOMESTIC VIOLENCE & SEXUAL ASSAULT/ DOMÉSTICA & ASALTO SEXUAL		
Venice Family Clinic	310-392-8636	Venice Family Clinic patients only
Sojourn Services	310-264-6646	Free
Chicana Service Action Center	323-262-9847	Free
Center for Pacific Asian Families	323-653-4045	Free

COUNSELING / CONSEJERIA		
Didi Hirsch Community MH Ctr.	310-390-6612 M–F: 8:30 a.m.–5 p.m.	Free crisis counseling, only for event that happened within last 2 months Free for victims of child abuse MediCal/Medicare for most services Español
Family Service of Santa Monica 1533 Euclid St., Santa Monica 90404	310-451-9747	Sliding scale Bilingual staff/interns (español) Bill any insurance, Medical for 18 years and younger (no adults), sliding scale, victims of crime, government aid

Airport Marina Counseling Ctr. 7891 La Tijera Blvd., Los Angeles, CA 90045	310-670-1410	Sliding scale Bilingual interns (español) PPO (private), no HMO
Antioch University Counseling Center 400 Corporate Pointe, Culver City, CA 90230	310-574-2813 x366	Sliding scale
WISE Center for Healthy Aging (55+) 1527 4th St. #200, Santa Monica, CA 90401	310-394-9871	Medi-medi, MediCal, Medicare, sliding scale, Private, HMO Sliding scale or free for very low income Español
Chicago School of Professional Psychology 1145 Gayley, #322, Los Angeles, CA 90024	310-208-3120	Sliding scale Español, Farsi
Open Path Counseling Center 5731 W Slauson Ave #175, Culver City, CA 90230	310-258-9677 M–F: 8 a.m.–9 p.m. Sat: 9 a.m.–5 p.m.	Sliding scale Español
Pepperdine Psychology Clinic 400 Corporate Pointe #458, Culver City, CA 90230	310-568-5752	Sliding scale
Southern California Counseling Center 5615 W. Pico Blvd., Los Angeles, CA 90019	323-937-1344 M-Th: 6pm–8pm Sat: 9am–2pm	Español Walk-in for intake
South Bay Center for Counseling 360 N. Sepulveda Blvd. # 2075, El Segundo, CA 90245	310-414-2090 M–Th: 8am–9pm F: 8am–5pm Sat: 9am–2pm	Sliding scale—ask for intake line Bilingual interns
Kedren Community Health Center 4211 Avalon Blvd., Los Angeles, CA 90011	323-233-0425 323-233-0344 (TDD) M–F: 8:30 a.m.–5 p.m.	Walk-in, sliding scale, Medicare, MediCal All types of MediCal (adult/child)
LA Gay and Lesbian Center 1625 N. Schrader Blvd., Los Angeles, CA 90028	323-993-7669 M–F: 9 a.m.–9 p.m. Walk-in intake: 1–4 p.m./call	Sliding scale Español Straight MediCal, straight Medicare as long as assigned as their medical home (adult/child) Private

CHILDREN'S COUNSELING / CONSEJERIA PARA NIÑOS		
St. John's Child and Family Development Center 1339 20th Street, Santa Monica, CA 90404	310-829-8921	MediCal, Healthy Families
Didi Hirsch 4760 S. Sepulveda Blvd., Culver City, CA 90230	310-390-8896	MediCal, SSI, Medicare, free for child abuse (Child Alert)
Venice Family Clinic 604 Rose Ave., Venice 90291 2509 Pico Blvd., Santa Monica, 90405	310-392-8636	Venice Family Clinic patient only
Family Services of Santa Monica 1533 Euclid St., Santa Monica 90404	310-451-9747	Sliding scale, some MediCal, cheaper for Santa Monica residents

ABUSE HOTLINES/ LÍNEAS DE ABUSO		
Child Abuse Hotline	800-540-4000	24 hour
Elder Abuse Hotline	213-351-5401	24 hour
L.A. Rape & Battering Hotline	310-932-8331	24 hour
Sojourn Services for Battered Women	310-264-6644	24 hour

Part III

Administering Buprenorphine/Naloxone to Patients with Opioid Dependence

A Quick Reference Guide for Primary Care Practitioners

Overview

Buprenorphine is an opioid partial agonist/antagonist that is FDA approved for the treatment of opioid dependence by physicians in an office-based setting. It is a Schedule III controlled substance and requires that physicians obtain a DEA waiver ("X" waiver) to prescribe it for office-based treatment of opioid dependence.

Like methadone, buprenorphine treatment involves substituting buprenorphine for the opioid of abuse. But while methadone is a full opioid agonist, buprenorphine is a partial opioid agonist/antagonist with minimal additional opioid effects at doses above the maximum recommended dose (32 mg—known as a "ceiling effect"). As a result, buprenorphine is safer than methadone. Risk of overdose from buprenorphine is relatively low, **except** when buprenorphine is combined with other sedatives, such as alcohol or benzodiazepines. As a result, patients abusing alcohol or sedatives are not good candidates for office-based buprenorphine treatment, and patients on buprenorphine should be monitored for alcohol and sedative abuse.

Naloxone, an opioid antagonist, is added to buprenorphine (buprenorphine/naloxone) to prevent intravenous abuse of buprenorphine. Injection of buprenorphine/naloxone will precipitate opioid withdrawal in an opioid-dependent person.

Buprenorphine/naloxone must be taken sublingually.

Available formulations are:

- **Sublingual film (Suboxone)***
  - Buprenorphine 2 mg and naloxone 0.5 mg (2 mg/0.5 mg)
  - Buprenorphine 4 mg and naloxone 1 mg (4 mg/1 mg)
  - Buprenorphine 8 mg and naloxone 2 mg (8 mg/2 mg)
  - Buprenorphine 12 mg and naloxone 3 mg (12 mg/3 mg)

- **Sublingual tablets (generic)**
  - Buprenorphine 2 mg and naloxone 0.5 mg (2 mg/0.5 mg)
  - Buprenorphine 8 mg and naloxone 2 mg (8 mg/2 mg)

*Note: Materials in this manual refer to the sublingual film in 4- and 8-mg strips; 4-mg strips may not be readily available in all locations, in which case, 2- and 8-mg strips may be used. Patient dosing instructions must be adjusted accordingly.

The buprenorphine-only formulation (Subutex®) should generally not be used except in unusual cases (e.g., pregnancy), as this formulation has a higher risk of intravenous abuse and diversion than the buprenorphine/naloxone formulations.

Typical side effects of buprenorphine/naloxone include the following:

- Constipation is the most common side effect. Patients should be instructed to use a bowel regimen, including stool softeners, fiber, plenty of liquids, regular physical activity, and laxatives, as necessary, to prevent severe constipation.
- Sedation, headache, or nausea may result when doses of buprenorphine are too high.
- Hepatitis is rare; studies have found buprenorphine/naloxone to be safe in patients with chronic hepatitis C, but use caution in patients with acute hepatitis or severe cirrhosis.
- Opioid-dependent patients will experience mild to moderate opioid withdrawal when buprenorphine/naloxone is discontinued, which may be minimized by a slow taper.

Warning: Overdose from buprenorphine alone is very rare, but buprenorphine combined with other sedatives (for example, benzodiazepines, alcohol) may result in fatal overdose.

Appropriate patients for treatment with buprenorphine/naloxone in primary care are

- Opioid dependent
- Motivated to stop or reduce opioid use
- Able to adhere to medication instructions and attend outpatient clinic visits
- Relatively stable medically and psychiatrically

Patients who are not appropriate for treatment with buprenorphine/naloxone in a primary care setting include the following:

- Pregnant patients
- Patients with co-morbid benzodiazepine or alcohol dependence (risk of overdose)
- Patients with severe, unstable psychiatric conditions
- Patients with acute or severe liver disease

These patients may be more appropriate for treatment in a specialty (i.e., inpatient or methadone) program.

Patients who have failed multiple previous treatments for opioid dependence, while eligible to receive buprenorphine /naloxone, may have difficulty.

Liver enzymes should be checked prior to initiating buprenorphine treatment. Use caution in prescribing buprenorphine to patients with liver enzyme elevations greater than three times normal; patients with liver enzyme elevations greater than five times normal should be referred to an addiction specialist for care. In patients with normal baseline liver enzymes, rechecking in three months and then annually while on buprenorphine is recommended. Patients with pretreatment liver enzyme elevations should have liver enzymes monitored more frequently.

Using Buprenorphine/Naloxone for Patients with Chronic Pain

Buprenorphine has analgesic effects but is a weaker analgesic than full opioid agonists. Chronic pain is not a contraindication to buprenorphine treatment in a patient with opioid dependence, and some patients may achieve adequate analgesia from buprenorphine, especially when available non-opioid and non-pharmacologic pain treatments have been maximized. Splitting the daily buprenorphine dose may increase the duration of analgesia. Patients who cannot achieve adequate analgesia with buprenorphine and non-opioid pain-management approaches may be best managed by pain management and addiction medicine specialists collaboratively.

Buprenorphine induction from methadone doses of more than 40 mg per day is complicated and should generally only be undertaken by clinicians experienced in the use of buprenorphine. Transfer of these patients to buprenorphine/naloxone in a primary care setting should only be done by an experienced clinician.

Treatment with buprenorphine/naloxone can be divided into the following stages:

- Assessment
- Induction (transition from other opioid[s] to buprenorphine/naloxone)
- Stabilization
- Maintenance.

The optimal length of treatment with buprenorphine/naloxone has not been established, but research studies strongly support better outcomes with maintenance treatment. Many successful patients are treated with buprenorphine/naloxone indefinitely to prevent relapse to opioid use.

Assessment

Prior to starting buprenorphine/naloxone:

- ☐ Complete a history and physical exam (or review if previously completed).
- ☐ Confirm that the patient is opioid dependent (see the opiate dependence worksheet in Appendix I).
- ☐ Carefully review all opioids that the patient is using, with attention to long-acting (methadone, Oxycontin, etc.) versus short-acting opioids (heroin, Vicodin, etc.).
- ☐ Confirm that the patient is not dependent on sedatives (for example, alcohol, benzodiazepines).
- ☐ Confirm that the patient is not pregnant (negative pregnancy test).
- ☐ Perform a urine drug screen (expect positive for opioid[s] but be cautious if positive for benzodiazepines).
- ☐ Check a hepatic panel and HIV and hepatitis serologies if indicated (for example, IV drug use) (use caution if LFTs are more than five times the upper limit of normal).
- ☐ Consider checking a Prescription Drug Monitoring Program report (controlled-substance prescriptions).
- ☐ Fill out the Suboxone patient enrollment form and patient consent (Appendix J).

Induction

Because buprenorphine is a partial opioid agonist/antagonist, buprenorphine will precipitate opioid withdrawal in patients with recent opioid use. Therefore, patients must stop opioid use and be experiencing at least moderate opioid withdrawal symptoms prior to starting buprenorphine.

The amount of time patients should wait after their last opioid use before starting buprenorphine/naloxone varies, depending on whether they are using short-acting (shorter wait) or long-acting opioids (longer wait):

- short-acting opioids (for example, heroin, Vicodin, Norco, immediate-release oxycodone): at least 12 hours without opioids

- intermediate-acting opioids (for example, OxyContin, MS Contin): at least 24 hours without opioids

- long-acting opioids (for example, methadone): at least 72 hours without opioids.

In addition, because buprenorphine is a relatively weak partial agonist, patients on high doses of opioids (for example, more than 40 mg of methadone per day) might not be successful in buprenorphine induction, and tapering to lower opioid doses prior to induction is recommended.

Buprenorphine induction may be initiated under physician observation with the patient in the office, or at home for patients deemed likely to be adherent to instructions for home induction. In a busy primary care setting, home induction may be preferable.

Regardless of whether induction is supervised in the office or done at home, the following is an overview of the induction process followed by additional information specific to at-home and in-office inductions.

Day 1

- **The patient must WAIT** until he or she is experiencing at least moderate physical withdrawal symptoms (at least 12 hours after last opioid use for short-acting opioids, 24 hours for intermediate-acting opioids, and 72 hours for long-acting opioids) prior to taking the first dose of buprenorphine. For office inductions, the clinician can use the Clinical Opiate Withdrawal Scale (COWS) (Appendix K) to assess withdrawal symptoms and determine the timing of the first buprenorphine dose (details below).
- Once withdrawal has reached at least moderate intensity, the patient should put one Suboxone 4-mg strip under the tongue and let it dissolve.
- **WAIT** at least one hour after the first Suboxone strip:
    - If the patient's withdrawal symptoms are the same or worse, then he or she should take a second Suboxone 4-mg strip under the tongue and allow it to dissolve (total of 8 mg).
    - If the patient's withdrawal is better, then wait. The patient can take the second Suboxone 4-mg strip later if the withdrawal symptoms start to get worse again.
- The target dose for day 1 is 8 mg (two strips).
- If withdrawal continues to be bad even six hours after having taken 8 mg (two strips), the patient may take additional 4-mg strips, up to a maximum of 16 mg (four strips) in the first 24 hours.
- Rarely, patients may require more than 16 mg on day 1 for severe withdrawal symptoms, but never administer more than 32 mg in a 24-hour period.

Day 2

- If the patient has minimal or no withdrawal symptoms in the morning of day 2, then the patient should take the same dose (same number of Suboxone 4-mg strips) in the morning as the patient took in total all of day 1.
- If the patient feels withdrawal in the morning of day 2, then he or she should take the same dose as day 1 **PLUS** an additional 4 mg (one more of the Suboxone 4-mg strips than the patient took on day 1).
- If withdrawal begins to get worse later in the day, the patient should take an additional 4-mg strip.
- The target dose on day 2 is 12 mg (three strips).
- If the patient continues to experience withdrawal after taking the day 1 dose plus an additional 4-mg strip, the patient may take one additional 4-mg strip, up to a maximum of 16 mg (four strips) on day 2.

- Rarely, patients may require more than 16 mg on day 2 for severe withdrawal symptoms, but never administer more than 32 mg in a 24-hour period.

Day 3

- If the patient has minimal or no withdrawal symptoms in the morning of day 3, then he or she should take the same dose (same number of Suboxone 4-mg strips) in the morning as he or she took in total all of day 2.
- If the patient feels withdrawal in the morning of day 3, then he or she should take the same dose as day 2 PLUS an additional 4 mg (one more of the Suboxone 4-mg strips than the patient took on day 2).
- If withdrawal begins to get worse later in the day, he or she should take an additional 4-mg strip.
- The target dose on day 3 is 16 mg (four strips).
- If the patient continues to experience withdrawal after taking the day-2 dose plus an additional 4-mg strip, the patient may take additional 4-mg strips, up to a maximum of 16 mg (four strips) on day 3.
- Rarely, patients may require more than 16 mg on day 3 for severe withdrawal symptoms, but never administer more than 32 mg in a 24-hour period.

Day 4 and Onward

By day 4, the patient should be stabilized on a dose of Suboxone most likely between 8 mg and 16 mg per day. Rarely, patients may require doses higher than 16 mg per day in order to fully relieve opioid withdrawal symptoms or reduce opioid cravings, but patients should never take more than 32 mg per day, because higher doses are less safe and no more effective.

In summary, recommended Suboxone dosing during induction is as follows:

Day	Target Dose (mg per day)	Maximum Dose (mg per day)
1	**8 (occasionally up to 16)**	32
2	**12 (occasionally up to 16)**	32
3	**16**	32
4	**16**	32

Note: Doses above 16 mg may be required in patients with withdrawal symptoms on 16 mg, but more than 32 mg should never be administered in a 24-hour period.

Additional Information for Home Induction

Review the written home-induction instruction sheet with the patient and answer any questions.

- Advise the patient to obtain the Suboxone, pick a day to start the induction, follow the home-induction instruction sheet (Appendix L), and call the clinic or come in if there are any problems.

- Prescribe a sufficient supply of Suboxone 4 mg/1 mg strips for the patient to take up to 16 mg (four strips) per day until his or her return appointment, which should be within the next three to seven days.

- An initial supply of 30 Suboxone 4 mg/1 mg strips would ensure that the patient could take up to 16 mg (four strips) per day for the first week, but smaller amounts with closer follow-up may be necessary for some patients.

- Consider calling the patient to check in on his or her progress with the induction and answer any questions about Suboxone dosing, especially during the first three or four days.

- Discuss the availability of comfort medications to alleviate symptoms as needed (discussed below).

Additional Information for In-Office Induction

In-office induction follows the outline above, but Suboxone is administered in the office under physician supervision. (In-office induction may not be realistic in a busy primary care setting; nevertheless, it is always an option if home induction is not possible.)

- Advise the patient to arrive at the office in early opioid withdrawal (no opioid use for 12 hours for short-acting opioids, 24 hours for intermediate-acting opioids, and 72 hours for long-acting opioids).

- Confirm that the patient is experiencing at least moderate opioid withdrawal symptoms (score of 12 to 16 on the Clinical Opiate Withdrawal Scale [COWS]; see Appendix K) prior to the patient taking the first dose of Suboxone.

- Once moderate withdrawal is confirmed, observe the patient taking one Suboxone 4 mg/1 mg strip under the tongue.

- Observe the patient for reductions in withdrawal symptoms within 30 to 60 minutes after the first dose. If the patient is still experiencing withdrawal symptoms (e.g., COWS > 12) one hour after the first dose, administer an additional buprenorphine/naloxone 4 mg/1 mg sublingually.

- If initial doses of buprenorphine precipitate opioid withdrawal (withdrawal symptoms are worsening instead of improving), administer "comfort" medications (detailed below) as needed, and proceed cautiously with the induction.

- Patients who improve after the initial dose of buprenorphine may leave with instructions and buprenorphine/naloxone to administer at home.

- Patients may return to the clinic daily for observation of Suboxone administration and adjustment of Suboxone dosing.

    - For these patients, review the written instructions for at-home induction and advise the patient to follow the written instruction sheet and call the clinic or come in if there are any problems.
    - Prescribe a sufficient supply of Suboxone 4 mg/1 mg strips for the patient to take up to 16 mg (four strips) per day until his or her return appointment, which should be within the next three to seven days.
    - An initial supply of 30 Suboxone 4 mg/1 mg strips would ensure that the patient could take up to 16 mg (four strips) per day for the first week, but smaller amounts with closer follow-up may be necessary for some patients.
    - Consider calling the patient to check in on his or her progress with the induction and answer any questions about Suboxone dosing, especially during the first three or four days.

Comfort Medications

The following "comfort" medications may be used as needed for opioid withdrawal symptoms during buprenorphine induction:

- anti-emetics p.r.n. nausea and vomiting
- acetaminophen or NSAIDs p.r.n. musculoskeletal pain
- hydroxyzine, 25–50 mg, every six hours p.r.n. anxiety or insomnia
- Ambien 5–10 mg QHS p.r.n. insomnia
- Imodium p.r.n. diarrhea
- cautious use of benzodiazepines for severe anxiety (provide only a one- to two-day supply).

Stabilization

During buprenorphine stabilization (approximately the first week following completion of induction), patients will stabilize on a daily dose of buprenorphine (an average of 16 mg per day), depending on their level of opioid withdrawal and cravings.

Patients continuing to experience opioid withdrawal and cravings require higher doses. Sedation, headaches, and nausea not accompanied by other opioid withdrawal symptoms indicate that the dose may be too high and may abate following dose reduction.

Once stabilized, the patient should begin to feel well. This is an optimal time to begin to assist the patient in arranging a program of counseling or behavioral support to address his or her opioid dependence. Patients who are unable to achieve stabilization on buprenorphine (continued opioid use) should be referred to a specialty addiction program.

Consider switching the patient at this point to Suboxone 8 mg/2 mg film and advising the patient to administer the appropriate number of film for the daily dose.

Patients may administer the total daily dose once daily or split the dose during the day, according to their preferences.

Maintenance

During maintenance, the following tasks should be performed during follow-up visits:

- ☐ Ask about support patients have received (if no support, discuss options).
- ☐ Ask about adherence to buprenorphine/naloxone.
- ☐ Ask about any opioid use in addition to buprenorphine/naloxone and discuss triggers for ongoing use.
- ☐ Ask about use of sedatives or alcohol.
- ☐ Conduct urine drug screen to test for presence of buprenorphine/naloxone and absence of other opioids and benzodiazepines.
- ☐ Determine whether changes in dose are needed or whether buprenorphine/naloxone should be discontinued.
- ☐ Determine whether patient will remain on maintenance or begin to taper.
- ☐ Ask whether the patient is attending psychosocial or counseling sessions. Encourage attendance and provide referrals or assistance in accessing counseling if needed.

Following stabilization (on a stable dose, opioid withdrawal and cravings manageable, and opioid abstinent), patients enter the buprenorphine maintenance phase. Research studies have not identified the optimal duration of treatment with buprenorphine/naloxone, but studies strongly support much better outcomes with longer treatment. A rule of thumb is that patients should be optimally stable in their opioid abstinence with established support for continued abstinence prior to considering discontinuing buprenorphine. For most patients, this will mean treatment with buprenorphine for several months, during which time they will work to establish these supports. Once stable, patients may be seen once a month or less frequently for assessment, a urine drug screen, and additional medication, if needed.

Troubleshooting and FAQs

How should patients be tapered off of buprenorphine/naloxone?

Patients who choose to discontinue buprenorphine/naloxone should taper slowly to minimize withdrawal symptoms. Taper buprenorphine slowly, to 2 mg buprenorphine per day or lower, prior to discontinuing. A variety of tapering schedules have been proposed, but the most important aspect of the taper is that it is slow in order to minimize the development of opioid withdrawal symptoms or cravings, which could precipitate relapse. The "comfort" medication used during induction may also be used

during tapering, as needed. Reducing the buprenorphine dose by 2 mg every week or two is usually comfortable for the patient. Faster tapers are safe but risk precipitating relapse if the patient is too uncomfortable.

What if a patient relapses to opioid use during treatment?
Patients who relapse to opioid use during office-based treatment with buprenorphine/naloxone may respond to an increase in buprenorphine dose and/or an increase in frequency or intensity of counseling or behavioral support. Also assess the patient for side effects, abuse, and diversion. Patients who do not tolerate buprenorphine/naloxone or who may be abusing or diverting buprenorphine/naloxone should be referred to a specialty addiction treatment program. Patients who are making overall progress in treatment may experience intermittent lapses and should not be discontinued from treatment if they can reestablish opioid abstinence following a lapse.

What if patients are abusing sedatives or alcohol during treatment?
Patients who are abusing sedatives or alcohol during treatment with buprenorphine/naloxone are at risk of overdose and should be transferred to a specialty addiction program. Prescription of benzodiazepines for an appropriate indication under supervision of a physician is not a contraindication to buprenorphine/naloxone treatment but warrants very close monitoring.

What if a patient needs analgesics while on buprenorphine/naloxone?
Buprenorphine-treated patients who require analgesics for acute pain should be treated with non-opioid analgesics, if possible. Patients requiring temporary use of opioid analgesics (minor surgery or dental procedure) may continue buprenorphine/naloxone while receiving a short course of opioid analgesics. Buprenorphine may block the analgesic effect of the opioid to some degree, but continuing the buprenorphine to avoid the development of opioid withdrawal is usually preferable in these cases. Patients requiring major analgesia (major surgery or major trauma) should be referred to an addiction or pain-management specialist.

What if a patient becomes pregnant?
Buprenorphine should *not* be abruptly discontinued if a patient becomes pregnant. Opioid withdrawal may be dangerous to the fetus, and treatment with buprenorphine during pregnancy is likely to be less dangerous than opioid relapse. Therefore, continue buprenorphine in a woman who becomes pregnant and arrange for consultation with an addiction specialist and high-risk pregnancy obstetrics. Naloxone is not known to be safe during pregnancy, and therefore it is recommended that pregnant women be switched from buprenorphine/naloxone to the buprenorphine-only formulation (a.k.a. Subutex) at the same buprenorphine dose.

What if a patient has elevated LFTs?
Patients who develop severe elevations in liver enzymes (more than five times the upper limit of normal) while on buprenorphine should be transferred to the care of an addiction specialist and may require switching to methadone treatment at a licensed methadone program.

What if a patient requests a refill before the next visit or misses a visit?
Patients who request an early refill of buprenorphine should be assessed for possible diversion (a urine drug screen negative for buprenorphine would suggest diversion). If there is no sign of diversion, the patient's dose should be assessed. Patients experiencing opioid withdrawal symptoms or opioid cravings while on buprenorphine may need a dose increase but should be advised to not increase the dose without discussing with their doctor first. Patients who run out of buprenorphine because of missed visits should be counseled on the importance of adherence to visits. Patients who regularly miss visits may not be appropriate for buprenorphine treatment in a primary care setting.

Appendix I: Opiate Dependence Worksheet

Worksheet for *DSM-IV* Criteria for Diagnosis of OPIATE Dependence

Patient's name:			
Worksheet for *DSM-IV* criteria for diagnosis of OPIATE dependence			
Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the PAST 12 MONTHS)	**Meets criteria?** Yes	No	**Notes/supporting information**
(1) Tolerance, as defined by either of the following:			
(a) A need for markedly increased amounts of the substance to achieve intoxication or desired effect			
(b) Markedly diminished effect with continued use of the same amount of the substance			
Possible prompts: • *Do you feel like you have to use more and more [PILLS/HEROIN] to feel the same effect?* • *Do you feel that over time you have become more used to using [PILLS/HEROIN], such that the effect on you is not as strong as before?*			
(2) Withdrawal, as manifested by either of the following:			
(a) The characteristic withdrawal syndrome			
(b) The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms			
Possible prompt: • *Do you have symptoms, such as muscle aches, restlessness, anxiety, runny nose, sweating, frequent yawning, when you don't use [PILLS/HEROIN]?*			
(3) Too much, for too long: The substance is often taken in larger amounts or over a longer period of time than intended.			

Worksheet for *DSM-IV* Criteria for Diagnosis of OPIATE Dependence

Patient's name:			
Worksheet for *DSM-IV* criteria for diagnosis of OPIATE dependence			
Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the <u>PAST 12 MONTHS</u>)	**Meets criteria?** Yes	No	**Notes/supporting information**
Possible prompts: • *Have you take pills for longer than the doctor prescribed?*			
(4) <u>Can't stop using:</u> There is a persistent desire or unsuccessful efforts to cut down or control substance use.			
Possible prompt • *Have you tried to stop using [PILLS/HEROIN] before?*			
(5) <u>Too much time spent on substance</u>: A great deal of time is spent on activities necessary to obtain the substance, use the substance, or recover from its effects.			
Possible prompt: • *Do you spend a great deal of your time taking or using [PILLS/HEROIN], thinking about getting or getting [PILLS/HEROIN], or trying to avoid withdrawal from [PILLS/HEROIN]?*			
(6) <u>Giving up activities:</u> Important social, occupational, or recreational activities are given up or reduced because of substance use.			
Possible prompt: • *Does your use of [PILLS/HEROIN] get in the way of doing other things that don't involve the drug? For example, do you miss work or spend less time with family or friends?*			
(7) <u>Continue despite harm to self:</u> The substance use is continued despite knowledge of having a persistent or recurrent <u>physical or psychological</u> problem that is likely to have been caused or exacerbated by the substance.			

Worksheet for *DSM-IV* Criteria for Diagnosis of OPIATE Dependence

Patient's name:		
Worksheet for *DSM-IV* criteria for diagnosis of OPIATE dependence		
Diagnostic criteria* (Current dependence requires meeting 3 or more criteria in the <u>PAST 12 MONTHS</u>)	**Meets criteria?** Yes No	**Notes/supporting information**
Possible prompts: • *Have any bad things happened as a result of your use of [PILLS/HEROIN]—to you or other people?* • *Do you continue to use [PILLS/HEROIN] even though your use is causing harm?*		

Current opiate dependence (3 or more in the past 12 months)

☐ **YES** ☐ **NO**

Appendix J: Suboxone Enrollment Form and Patient Consent

Suboxone® Sublingual (buprenorphine and naloxone) Film

Here to Help®

Enrollment Form for Here to Help® Patient Assistance Program

Please complete the enrollment form and fax to **1-888-407-9788**. Both the physician and patient signature must be included for services to be performed. If your patient may be a candidate for the Here to Help® Patient Assistance Program, please include proof of income. Please call the Here to Help® Patient Assistance Program at **1-888-898-4818** if you have any questions.

Patient Information

Patient Name:_____

Date of Birth: _____Phone: _____Gender: _____

Mailing Address: _____

City: _____State: _____Zip: _____

Patient Financial Information

1. Are you a US resident? ☐YES ☐NO 2. Number of persons in household: _____

3. What is your households total yearly GROSS INCOME (including Social Security, Disability, Veterans, Wages, pension benefits, etc.)? $_____

4. Do you file a Federal Income Tax Return? ☐ YES ☐ NO If yes, attach proof of income: 1040, 1040EZ, or Social Security Statement)

IMPORTANT - Required to Process Application

***Patient Authorization and Consent to Share and Disclose Health Information with the Here to Help® Patient Assistance Program* form MUST be reviewed and signed by patient or authorized representative**

Physician Information

Treating Physician: _____ DEA #:_____

Primary Contact: _____*DEA "X" #*: _____

Facility Name: _____

Phone: _____Fax: _____

Street Address: _____

City: _____ State: _____ ZIP: _____

Insurance Information

1. Is the patient enrolled in Medicare / Medicare Part D? ☐YES ☐NO
2. Is the patient enrolled in Medicaid? ☐YES ☐NO
3. Does the patient have prescription drug coverage? ☐YES ☐NO

Medical Information -

Patient Diagnosis: _____include applicable ICD 9 code(s)

The program only covers doses of SUBOXONE Film that are within the recommended dosing range of buprenorphine as described in the product information. Eligibility for the program is limited to one year from the date of acceptance.

Physician Declaration - Required to Process Application

My signature below certifies that the person named in this form is my patient and medications received from RBP Patient Help for patient assistance are only for use of the patient named on this form. These medications will not be offered for sale, trade, or barter. Additionally, no claim for reimbursement will be submitted concerning these medications to Medicare, Medicaid, or any third party, or returned for credit. By signing, I also agree that RBP Patient Help has the right to contact my patient directly to confirm receipt of medications, perform program quality reviews and revise, change, or terminate the program at any time. To the best of my knowledge, my patient meets the criteria for this Patient Assistance Program.

Physician Signature: _____Date: _____

The DEA 'X' number is assigned to each specific physician that has been authorized to prescribe Suboxone.

Suboxone® Sublingual (buprenorphine and naloxone) C Film

Here to Help

Patient Authorization and Consent to Share and Disclose Health Information with the Here to Help® Patient Assistance Program

Provider Instructions: Patient must read and sign this form before he or she can participate in the Here to Help® Patient Assistance Program (the "Program").

I, _____, acknowledge and agree that all the information I provide in connection with my application to the Here to Help® Patient Assistance Program will be used to decide if I am eligible to participate in the Program. By signing below, I verify that the information on my application, including a signed copy of my prior year's tax return/supporting documentation, is complete and accurate. I attest that I have no prescription insurance coverage, including Medicaid, Medicare or other public or private program, and I have insufficient financial resources to pay for the prescribed product. I further acknowledge that any changes to my financial, prescription drug coverage, or insurance information may affect my continued eligibility in the Program. Accordingly, I agree to contact the Program to inform them of any changes to my financial, prescription drug coverage, or insurance information.

I hereby allow my doctor(s), my pharmacy(ies), any other health care providers, and my health plan or insurers to give medical information relating to my use or need for products provided under the Program to The Lash Group, Inc. The Lash Group runs the Program for RBP Patient Help. My medical information can include spoken or written facts about my health and payment benefits. It can include copies of records from my health provider, my pharmacy, or my health plan about my health or health care.

I verify that I have no other coverage for prescription medications, including Medicaid, Medicare, or any public or private assistance programs or any other prescription insurance.

I also agree that The Lash Group and RBP Patient Help have the right to verify my eligibility and to evaluate any financial documentation, insurance information, and medical records submitted to the Program to determine if I qualify for the Program and to operate the Program. People who work for The Lash Group and RBP Patient Help may also see my information, but they may use it only to help me get assistance receiving Suboxone®, to determine my eligibility for the Program, to operate the Program, or as otherwise required or permitted by law. I understand that The Lash Group and RBP Patient Help have the right to contact me directly to confirm receipt of medications [or to obtain my feedback about the Program] and that RBP Patient Help can revise, change, or terminate the Program at any time.

I acknowledge that this authorization and consent is subject to revocation by me at any time, except to the extent that the Program has already taken action in reliance on it. If not previously revoked, this authorization and consent will last until I am no longer participating in the Program. If I change my mind before that time, I can tell my health care provider, my pharmacy, and my insurer in writing that I do not want them to share any more information with The Lash Group and RBP Patient Help, but it will not change any actions they took before I told them and it will terminate my participation in the Program. I know that I have a right to see or copy the information my health care providers, my pharmacy, or insurers have given to The Lash Group and RBP Patient Help.

I KNOW THAT I MAY REFUSE TO SIGN THIS FORM. My choice about whether to sign this form will not change the way my health care providers, pharmacies, or insurers treat me. If I refuse to sign this form, I know that this means I will not be eligible to participate in the Program.

Patient Signature: _____ Date: _____

Patient Name: _____

If the patient cannot sign, the patient's legal representative must sign below:

Representative Name: _____

Signature: _____

Describe relationship to patient and authority to make medical decisions for patient:_____

Fax with Here to Help Patient Assistance Program Enrollment Application to 1-888-407-9788.

Appendix K: Clinical Opiate Withdrawal Scale

Clinical Opiate Withdrawal Scale (COWS)

For each item, write in the number that best describes the patient's signs or symptoms. Rate just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Patient's Name: _____ Date: _____ **Buprenorphine induction: _____** **Enter scores at time 0, 30 minutes after first dose, 2 hours after first dose, etc.** **Times: _____ _____ _____ _____**				
<u>Resting pulse rate</u>: (record beats per minute) *Measured after patient is sitting or lying for one minute* **0** pulse rate 80 or below **1** pulse rate 81–100 **2** pulse rate 101–120 **4** pulse rate greater than 120				
<u>Sweating:</u> *Over past half-hour, not accounting for room temperature or patient activity.* **0** no report of chills or flushing **1** subjective report of chills or flushing **2** flushed or observable moistness on face **3** beads of sweat on brow or face **4** sweat streaming off face				
<u>Restlessness:</u> *Observation during assessment* **0** able to sit still **1** reports difficulty sitting still, but is able to do so **3** frequent shifting or extraneous movements of legs/arms **5** Unable to sit still for more than a few seconds				

Pupil size: **0** pupils pinned or normal size for room light **1** pupils possibly larger than normal for room light **2** pupils moderately dilated **5** pupils so dilated that only the rim of the iris is visible				
Bone or joint aches: *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* **0** not present **1** mild diffuse discomfort **2** patient reports severe diffuse aching of joints/ muscles **4** patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: *Not accounted for by cold symptoms or allergies* **0** not present **1** nasal stuffiness or unusually moist eyes **2** nose running or tearing **4** nose constantly running or tears streaming down cheeks				
GI upset: *over last half-hour* **0** no GI symptoms **1** stomach cramps **2** nausea or loose stool **3** vomiting or diarrhea **5** multiple episodes of diarrhea or vomiting				
Tremor: *observation of outstretched hands* **0** No tremor **1** tremor can be felt, but not observed **2** slight tremor observable **4** gross tremor or muscle twitching				

<u>Yawning:</u> *Observation during assessment* **0** no yawning **1** yawning once or twice during assessment **2** yawning three or more times during assessment **4** yawning several times per minute				
<u>Anxiety or irritability:</u> **0** none **1** patient reports increasing irritability or anxiousness **2** patient obviously irritable or anxious **4** patient so irritable or anxious that participation in the assessment is difficult				
<u>Gooseflesh skin:</u> **0** skin is smooth **3** piloerection of skin can be felt or hairs standing up on arms **5** prominent piloerection				
Total score 5–12 = Mild 13–24 = Moderate 25–36 = Moderately severe More than 36 = Severe withdrawal **with observer's initials:**				

Appendix L: Home-Induction Patient Handout

SUMMIT

Substance Use, Motivation and Medication Integrated Treatment

Buprenorphine

Beginning Treatment

Day 1

Before taking Buprenorphine, you want to feel lousy from your withdrawal symptoms.
Very lousy.

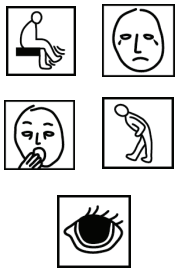
CHECK-IN

It should be **at least 12 hours since you used heroin or pain pills** (e.g., short-acting acting Oxycodone, Morphine, Vicodin, Codeine, Hydromorphone, Oxymorphone, Hydrocodone) and **at least 24 hours since you used methadone or other longer-acting drugs** (e.g., long-acting Oxcycodone (OxyContin), Morphine, Oxymorphone, and Fentanyl).

Wait it out as long as you can. The worse you feel when you begin the medication, the better it will make you feel and the more satisfied you will be with the whole experience.

Before you take Buprenorphine, you should have **at least 3** of the following feelings:

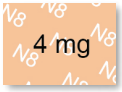
- Twitching, tremors, or shaking
- Joint and bone aches
- Bad chills or sweating
- Anxious or irritable
- Goose pimples



- Very restless, can't sit still
- Heavy yawning
- Enlarged pupils
- Runny nose, tears in eyes
- Stomach cramps, nausea, vomiting, or diarrhea

FIRST DOSE

4 mg of Buprenorphine under the tongue. (You will start with 4-mg films; later your doctor may change to 8-mg films.)



1. Put the film under your tongue. Keep it there. If you swallow, Buprenorphine film it will not work. The medicine is best absorbed through the thin skin on the bottom of your tongue.

   It takes 20-45 minutes for the medication to be absorbed and have an effect. Feel better? Good, the medicine is working. Still feel lousy after 45 minutes? Don't worry, you just need more medication.

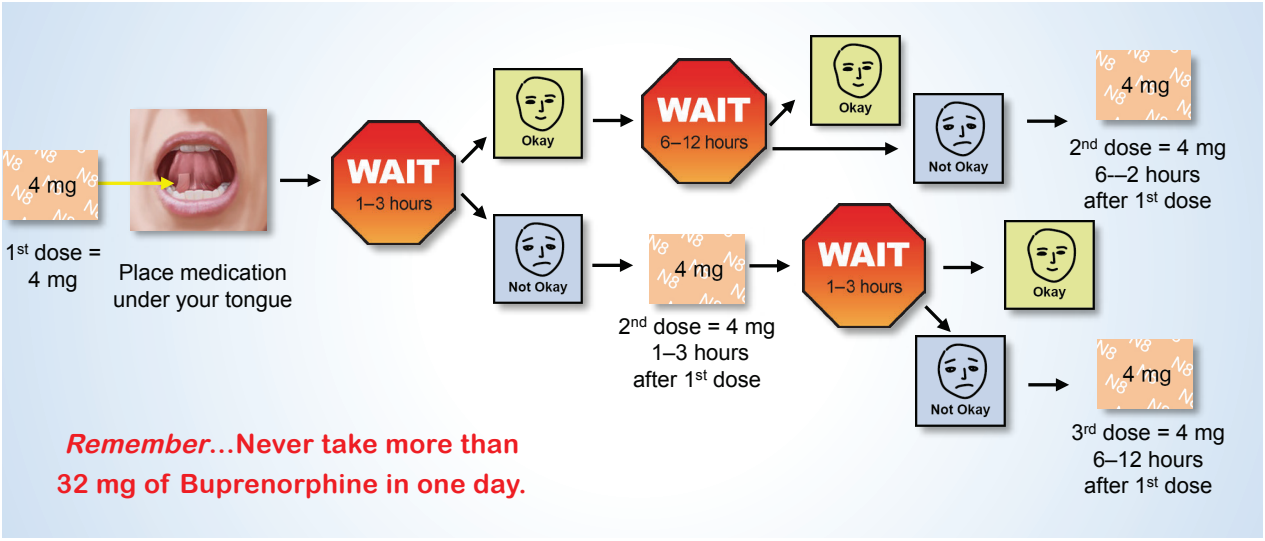
2. At 1–3 hours (60–180 minutes) after your first dose, see how you feel. If you feel fine after the first 4 mg, don't take any more; this may be all you need. If you have withdrawal feelings, take another 4-mg dose under your tongue.

3. Later in the day (6–12 hours after the first dose), see how you feel again. If you feel fine, don't take any more. If you have withdrawal feelings, take another 4-mg dose under your tongue.

It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 1 Summary

1. 4 mg under your tongue
2. Wait 1–3 hours
3. If still feel sick, take 4 mg again
4. Wait 1–3 hours
5. If still feel sick, take 4 mg again



***Remember*...Never take more than 32 mg of Buprenorphine in one day.**

Track Your Doses On Day 1

Use this table to track how much medication you take today.

	Time	Amount
1st dose		**4 mg**
2nd dose, if needed		
3rd dose, if needed		
Total mg taken on Day 1 =		

How Are You Feeling?

How's it going?

Still feel really bad?

Call your doctor at:

( ) -

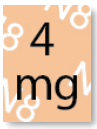
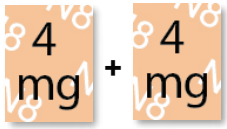
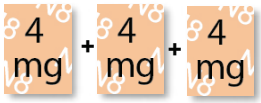
It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 2

The right dose for you on Day 2 depends on how you felt on Day 1.

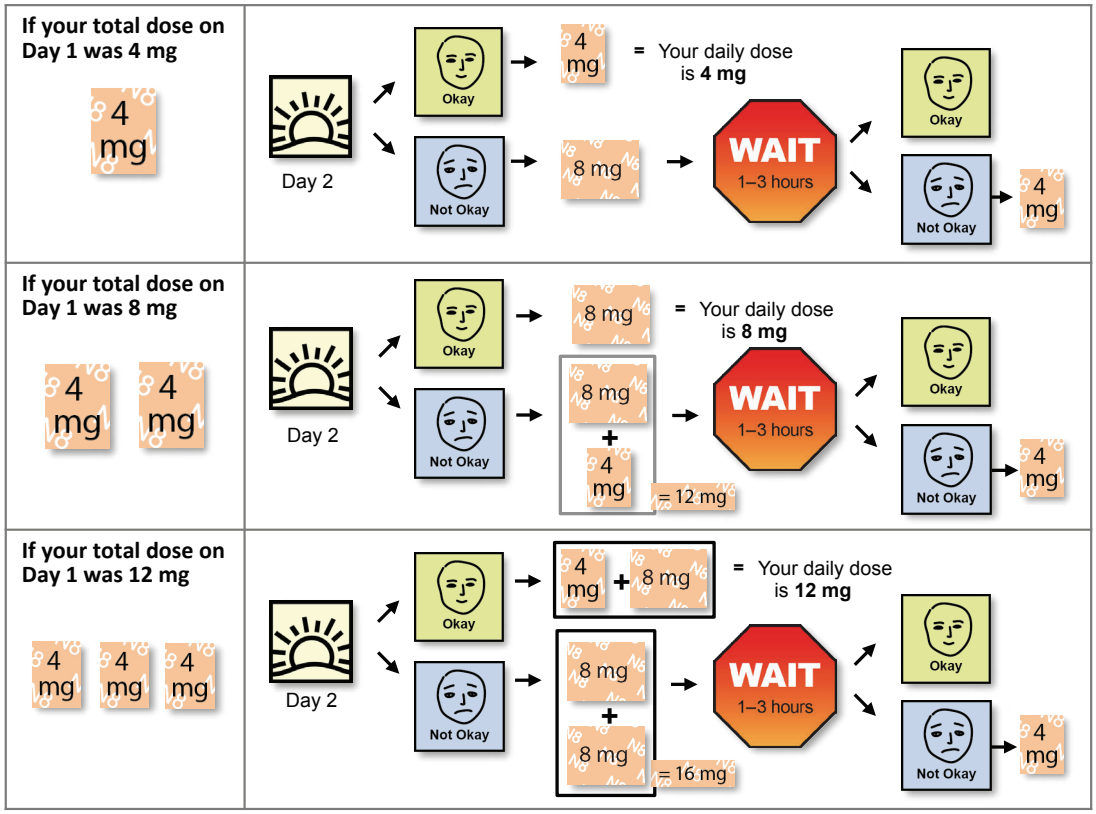
CHECK-IN

Use the table below to determine what the right dose for Day 2 should be. Make sure you remember the dose you took on Day 1.

If your total dose on Day 1 was 4 mg 	 If you took **4 mg total on Day 1 and feel fine the next morning**, take 4 mg again on Day 2. This will be your new daily dose.  If you took **4 mg total on Day 1 and feel some withdrawal the next morning**, try starting with 8 mg on the morning of Day 2. Later in the day on Day 2, see how you feel. If you feel fine, there is no need to take more. If you still feel withdrawal, you can try taking another 4-mg dose.
If your total dose on Day 1 was 8 mg 	 If you took **8 mg total on Day 1 and feel fine the next morning**, take 8 mg again on Day 2. This will be your new daily dose.  If you took **8 mg total on Day 1 and feel some withdrawal the next morning**, try starting with 12 mg on the morning of Day 2. Later in the day on Day 2, see how you feel. If you feel fine, there is no need to take more. If you still feel withdrawal, you can try taking another 4 mg dose.
If your total dose on Day 1 was 12 mg 	 If you took **12 mg total on Day 1 and feel fine the next morning**, take 12 mg again on Day 2. This will be your new daily dose.  If you took 12 mg total on Day 1 and feel some withdrawal the next morning, try starting with 16 mg on the morning of Day 2.

It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 2 Summary



Track Your Doses On Day 2

Use this table to track how much medication you take today.

	Time	Amount
1st dose		
2nd dose, if needed		
3rd dose, if needed		
Total mg taken on Day 2 =		

Enter the total mg you took on Day 2

(Never take more than 32 mg of Buprenorphine in one day.)

How Are You Feeling?

How's it going?

Still feel really bad?

Call your doctor at: ( ) -

It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 3

The right dose for you on Day 3 depends on how you felt on Day 2.

CHECK-IN

By the evening or night of Day 2, did you still feel unwell, like you were in some withdrawal? Or did you feel like the medication was too strong, leaving you too groggy? Different people need different doses of Buprenorphine; some feel fine on just 4 mg per day, and others can need up to 32 mg per day to feel comfortable.

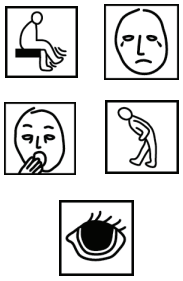
If you felt good at the end of Day 2, repeat the dose you took on Day 2. This is your new daily dose.

If you felt too tired or groggy on Day 2, try taking a lower dose on Day 3. Take 4 mg less on Day 3 than you took on Day 2.

If you still felt some withdrawal at the end of Day 2, start Day 3 by taking the same total dose you took on Day 2. If you still have withdrawal symptoms later on Day 3, take another 4 mg later in the day.

Here are some things you still might be feeling if you're having withdrawals:

- Twitching, tremors, or shaking
- Joint and bone aches
- Bad chills or sweating
- Anxious or irritable
- Goose pimples



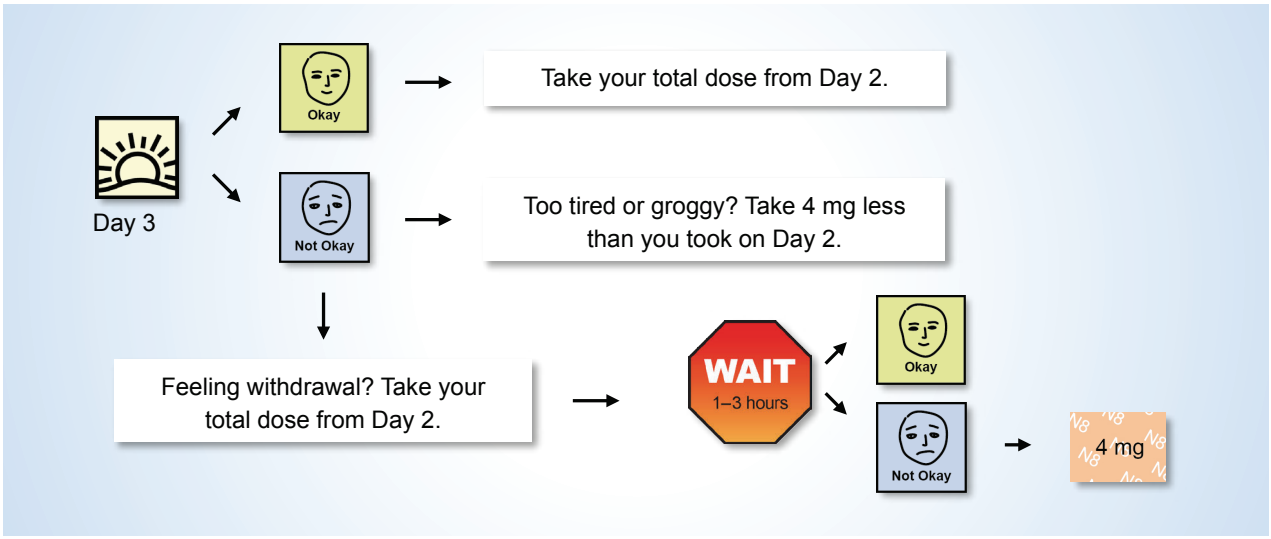
- Very restless, can't sit still
- Heavy yawning
- Enlarged pupils
- Runny nose, tears in eyes
- Stomach cramps, nausea, vomiting, or diarrhea

It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 3 Summary

Take the total dose you took on Day 2 under your tongue in the morning.

You can try a little less if the Day 2 dose felt too strong and you can take an extra 4 mg dose if you still feel withdrawal.



Track Your Doses On Day 3

Use this table to track how much medication you take today.

	Time	Amount
1st dose		
2nd dose, if needed		
Total mg taken on Day 3 =		

This is your new daily dose.

Remember . . .
Never take more than 32 mg of Buprenorphine in one day.

How Are You Feeling?

How's it going?
Still feel really bad?
Call your doctor at:

( ) -

It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.

Day 4 and beyond

CHECK-IN

On Day 4 and beyond, take the dose you used on Day 3. This is now your daily dose. You can take more or less depending on how you feel overall, whether or not you still have cravings or are still using, etc.

You should discuss any dose adjustments after this point with your doctor. If you do need to increase your dose, you should not change it by more than 4 mg per day.

Remember:

- **Never take more than 32 mg of Buprenorphine in one day.**
- **It is dangerous to mix Buprenorphine with alcohol, sleeping pills, or other sedatives.**
- **Come back to your next clinic appointment.**

My appointment is on: _____ at _____ AM PM.

SUMMIT
Substance Use, Motivation and Medication Integrated Treatment

Adapted from: Lee JD, Grossman E, DiRocco D, Gourevitch MN. Home buprenorphine/naloxone induction in primary care. *Journal of General Internal Medicine, 24*(2):226-32. doi:10.1007/s11606-008-0866-8. Epub 2008 Dec 17. PubMed Central PMCID: PMC2628995.

Appendix M: Training and Resources

Physician Training

The Drug Addiction Treatment Act of 2000 (DATA 2000) expands the clinical context of medication-assisted opioid addiction treatment by allowing qualified physicians to dispense or prescribe specifically approved Schedule III, IV, and V narcotic medications for the treatment of opioid addiction in treatment settings other than the traditional opioid treatment program (i.e., methadone clinic).

According to DATA 2000, licensed physicians (doctors of medicine [MDs] and doctors of osteopathic medicine [DOs]) are considered qualified to prescribe SUBOXONE if at least one of the following criteria has been met:

- completion of not less than eight hours of authorized training on the treatment or management of opioid-dependent patients (see http://www.buppractice.com/buprenorphine)
- holds an addiction psychiatry subspecialty board certification from the American Board of Medical Specialties
- holds an addiction medicine certification from the American Society of Addiction Medicine (ASAM)
- holds an addiction medicine subspecialty board certification from the American Osteopathic Association (AOA)
- participation as an investigator in one or more clinical trials leading to the approval of a narcotic drug in Schedule III, IV, or V for maintenance or detoxification treatment
- training or other such experience as determined by the physician's state medical licensing board
- training or other such experience as determined by the U.S. Secretary of Health and Human Services.

In addition, physicians must satisfy <u>ALL</u> of the following criteria:

- have the capacity to provide or to refer patients for necessary ancillary services, such as psychosocial therapy
- agree to treat no more than 30 patients at any one time in an individual or group practice during the first year following certification; after treating patients for one year and sending in a second notice of intent and need to Substance Abuse and Mental Health Services Administration (SAMHSA), agree to treat no more than 100 patients at any given time.

All of the above, including certification qualifications and training criteria, is described in more detail in the full text of DATA 2000.

Buprenorphine/Naloxone Resources

Suboxone website
www.Suboxone.com
This portal was developed and is currently maintained by Reckitt-Benister, the pharmaceutical company that produces Suboxone. It contains extensive information regarding opioid dependence and the mechanism of action of the drug, and it links to technical resources for clinicians and to information leaflets and videos for patients. The resource section of the site refers to several other knowledge depositories around the web (National Institute on Drug Abuse, Center for Substance Abuse Treatment, DrugFree.org, Physician Clinical Support System, and SAMHSA).

The website does not offer peer-to-peer assistance or mentoring, nor does it connect providers, though providers have an option to enroll in the Here to Help program.

SAMHSA- Sponsored Buprenorphine Physician Clinical Support System (PCSS)
http://pcssmat.org/about/goals-objectives/
The SAMHSA-funded PCSS is a national network of trained physician mentors with expertise in buprenorphine treatment and skilled in clinical education designed to assist practicing physicians in incorporating into their practices the treatment of prescription opioid and heroin dependent patients using buprenorphine.

Although it focuses on buprenorphine treatment specifically (not necessarily Suboxone), the website has a good knowledge base for providers, coupled with reference and patient materials. The portal contains links to register for available waiver eligibility training based on schedule availability, which requires basic information, as well as a national provider identifier. The network also offers a series of clinical guides and tools, coupled with a large number of webinars covering any and all topics related to buprenorphine-centric treatment.

The PCSS also offers a mentor/mentee program, as well as educational and training resources and an FAQ section. It offers links to specific legislation and policy resources for physicians to keep abreast of any changes that may impact their medication-assisted treatment procedures. There is no required registration other than for waiver eligibility trainings.

The Center for Substance Abuse Treatment (CSAT)
http://buprenorphine.samhsa.gov/
The CSAT buprenorphine website contains extensive up-to-date information on the use and distribution of buprenorphine. The website contains several resources, ranging

from waiver applications, to FAQs, to journal articles and government reports concerning buprenorphine-based medication-assisted treatments. Though somewhat difficult to navigate, providers have access to both a calendar of buprenorphine summits and meetings and the clinical discussion WebBoard. To use the decision support services and access the provider network, physicians must already have completed the DATA waiver. Only then will they be allowed to access these materials following an e-mail based registration.

Although the portal contains extensive written information regarding all aspects of buprenorphine-based medication-assisted treatment, including government-sponsored manuals and an extensive FAQ section, there is very little in the way of interactive content. There are no provider seminars or instructional or educational videos available for streaming or download.

National Institute on Drug Abuse (NIDA) Prescription Drugs Portal
http://www.drugabuse.gov/drugs-abuse/prescription-drugs

NIDA has a section of its website dedicated to prescription drug abuse (and heroin abuse). Although fairly sparse, the website does contain an FAQ section, as well as information related to statistics and trends regarding prescription drug abuse. The portal also offers links to NIDA's publication series, as well as its e-tool continuing medical education courses. The e-courses deal specifically with safe prescription practices for pain, as well as pain management for those abusing prescription drugs.

The National Alliance of Advocates for Buprenorphine Treatment
http://www.naabt.org/tl/Buprenorphine-Suboxone-treatment.cfm
This physician-led website offers a series of links to waiver eligibility websites, clinical studies concerning the use of buprenorphine, educational materials, and online support communities (which links directly to www.addictionsurvivors.org, a series of forums that require email registration). The "Information for Treatment Providers" section breaks the educational materials down by profession (physicians, counselors, nurses, pharmacists) and contains links to both SAMHSA and a database of relevant literature. The portal offers "most popular" downloadable items for physicians, ranging from clinical tools (such as "intent to treat" forms), to Treatment Improvement Protocol guides related to buprenorphine, to DEA regulatory information. The site also has an FAQ section, which is more limited than those found in other resources mentioned above.

UCLA SARx
http://www.uclasarx.org/
UCLA SARX is a group of world-class clinical researchers and providers in Los Angeles who specialize in office-based treatment for addiction to opioids, stimulants, tobacco,

alcohol, and marijuana. They are a part of the UCLA Center for Behavioral and Addiction Medicine. The website has direct links to physician specialists (along with contact information), as well as several links to research publications and FAQs.

BupPractice
http://www.buppractice.com/
Although primarily focused on physician training for buprenorphine administration, BupPractice has several other resources throughout its website. These range from specific how-to guides to extensive resource links, including topical overviews, clinical tools, patient handouts, and both patient and provider informational and educational materials.

The portal provides a holistic set of information for buprenorphine-driven medication-assisted treatment, with information ranging from billing assistance to guides for external referrals. The site does not have a peer-to-peer support component and does not include any interactive materials or aspects.