

## **VIVITROL® (EXTENDED-RELEASE INJECTABLE NALTREXONE) MEDICAL PROTOCOL AND PROCEDURES**

### ***INTRODUCTION***

This is the protocol and procedures to administer VIVITROL® (extended-release naltrexone injection, or XR-NTX) in accordance with federal and state guidelines for medication-assisted treatment. Naltrexone is an FDA approved opioid antagonist, a medication that binds to and effectively blocks opioid receptors. It prevents receptors from being activated by agonist compounds, such as heroin or opioids and alcohol. VIVITROL (XR-NTX) is used along with counseling and social support to help people who are alcohol or opiate dependent to subsequently cease and/or decrease alcohol or opiate use. A benefit of using VIVITROL is a decrease in cravings for alcohol and/or opioids.

### ***INDICATIONS***

VIVITROL is indicated for use in adults (eighteen years or older) who meet the following criteria:

- 1) A primary diagnosis of alcohol dependence and/or opioid dependence disorder;
- 2) Intent and ability to abstain (in the clinician's judgment) from alcohol and all opioids immediately prior to receiving the VIVITROL dose and opioid-free (including Tramadol) at least 7-10 days before starting VIVITROL;
- 3) A baseline evaluation which includes a physical exam, and, where that indicates likelihood of hepatic disease or injury or diminished renal function, appropriate laboratory testing such as liver transaminase levels and bilirubin within normal limits, or creatinine clearance (estimated or measured) 50 ml/min or greater;
- 4) Negative results on urine beta-HCG (human chorionic gonadotropin) pregnancy test for females;
- 5) A urine drug screen negative for all opioids, a negative Naloxone/Narcan IV or IM challenge (for patients with opioid addiction) immediately prior to the first injection; and if the Naloxone challenge is negative, an oral Naltrexone Challenge (a half tab of 50 mg administered orally); with no opioid withdrawal present after 1 hour;
- 6) No signs or symptoms of opioid withdrawal.

## **CONTRAINDICATIONS AND PRECAUTIONS/WARNINGS**

Contraindications for VIVITROL administration include:

- 1) Patient receiving opioid analgesics;
- 2) Patient is expected to require opioid analgesics for pain management;
- 3) Patient with current physiologic opioid dependence;
- 4) Patient in acute opioid withdrawal;
- 5) Patient has positive urine screen for opioids;
- 6) Patient failed Naloxone Challenge or Naltrexone Challenge;
- 7) Patient has hypersensitivity to VIVITROL;
- 8) Hepatotoxicity (acute hepatitis and clinically significant liver dysfunction) are observed (i.e., transaminase levels >3 times normal and abnormal bilirubin);
- 9) Testing indicates severe renal failure or moderate to severe renal insufficiency;
- 10) Testing indicates pregnancy - Category C (The FDA-assigned pregnancy categories as used in the Drug Formulary - Category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks);

**Warning or precautions for VIVITROL administration (requiring clinical judgment) include:**

- 1) Precipitated withdrawal may result for as long as two weeks for patients transitioning from buprenorphine or methadone;
- 2) Stable chronic hepatitis, e.g., in Hepatitis C infection, may be treated with XR-NTX, based on clinical judgment and ongoing liver function test monitoring;
- 3) Intramuscular injections should be used with caution in patients with thrombocytopenia or coagulation disorders;
- 4) Depression and/or suicidality develop as a result of taking VIVITROL;

Pain management may be achieved during VIVITROL blockade with any anesthesia, local or regional nerve block, or with NSAIDs with or without concomitant anxiolytics/sedatives. When reversal of VIVITROL blockade is required for pain management, opioid doses should be carefully titrated by medical staff who are skilled in and equipped for life support management who are not themselves involved in any active medical or surgical procedures being conducted with the patient.

## **PATIENT COUNSELING AND INFORMATION**

Physicians should include the following issues in discussions with patients for whom they prescribe VIVITROL:

- 1) Advise patients that if they previously used opioids, the fact that they have completed detoxification means that in the future they will more sensitive to lower doses of opioids and at risk of accidental overdose should they use opioids when their next dose is due, if they miss a dose, or after VIVITROL treatment is discontinued. It is important that medical/nursing staff advise the rest of the treatment team of this, and for all care team members to remind patients of this and to have them inform family members and the people closest to the patient of this increased sensitivity to opioids and the risk of overdose.
- 2) Advise patients that because VIVITROL can block the effects of opioids, patients will not perceive any effect if they attempt to self-administer heroin or any other opioid drug in small doses while on VIVITROL. Further, emphasize that administration of large doses of heroin or any other opioid to try to bypass the blockade and get high while on VIVITROL may lead to serious injury, coma, or death.
- 3) Patients on VIVITROL may not experience the expected effects from opioid-containing analgesic, antidiarrheal, or antitussive medications.
- 4) Advise patients that a reaction at the site of VIVITROL injection may occur. Reactions include pain, tenderness, induration, swelling, erythema, bruising, or pruritus. Serious injection site reactions including necrosis may occur. Some of these injection site reactions have required surgery. Patients should receive their injection from a healthcare provider qualified to administer the injection. Patients should be advised to seek medical attention for worsening skin reactions.
- 5) Advise patients that they should be off all opioids, including opioid-containing medicines, for a minimum of 7 – 10 days before starting VIVITROL in order to avoid precipitation of opioid withdrawal. Patients transitioning from buprenorphine or methadone may be vulnerable to precipitation of withdrawal symptoms for as long as two weeks. Ensure that patients understand that withdrawal precipitated by administration of an opioid antagonist may be severe enough to require hospitalization if they have not been opioid-free for an adequate period of time, and is worse than the experience of spontaneous withdrawal that occurs with discontinuation of opioid in a dependent individual.

- 6) Advise patients that they absolutely must not take VIVITROL if they still have any symptoms of opioid withdrawal. Advise all patients, including those with alcohol dependence, that it is imperative to notify healthcare providers of any recent use of opioids or any history of opioid dependence before starting VIVITROL to avoid precipitation of opioid withdrawal.
- 7) Advise patients that VIVITROL may cause liver injury. Patients should immediately notify their physician if they develop symptoms and/or signs of liver disease, such as abdominal pain, or a yellowing in the skin or whites of the eyes.
- 8) Advise patients that they may experience depression while taking VIVITROL. It is important that patients inform family members and the people closest to the patient that they are taking VIVITROL and that they should call a doctor right away should they become depressed or experience symptoms of depression.
- 9) Advise patients to carry documentation to alert medical personnel to the fact that they are taking VIVITROL. This will help to ensure that patients obtain adequate medical treatment in an emergency.
- 10) Advise patients that VIVITROL may cause an allergic pneumonia. Patients should immediately notify their physician if they develop signs and symptoms of pneumonia, including dyspnea, coughing, or wheezing.
- 11) Advise patients that they should not take VIVITROL if they are allergic to VIVITROL or any of the microsphere or diluent components.
- 12) Advise patients that they may experience nausea following the initial injection of VIVITROL. These episodes of nausea tend to be mild and subside within a few days post-injection. Patients are less likely to experience nausea in subsequent injections. Patients should be advised that they may also experience tiredness, headache, vomiting, decreased appetite, painful joints, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders and muscle cramps.
- 13) Advise patients that because VIVITROL is an intramuscular injection and not an implanted device, once VIVITROL is injected, it is not possible to remove it from the body and the effects last for at least 30 days.
- 14) Advise patients that VIVITROL has been shown to treat alcohol and opioid dependence only when used as part of a treatment program that includes counseling and support.

- 15) Advise patients that dizziness may occur with VIVITROL treatment, and they should avoid driving or operating heavy machinery until they have determined how VIVITROL affects them.
- 16) Advise patients to notify their physician if they: become pregnant or intend to become pregnant during treatment with VIVITROL; are breast-feeding; experience respiratory symptoms such as dyspnea, coughing, or wheezing when taking VIVITROL; experience any allergic reactions when taking VIVITROL or experience other unusual or significant side effects while on VIVITROL therapy.

**Patients should be advised of any other risks and information based on the clinical judgment of their physician.**

### ***STORAGE OF VIVITROL***

VIVITROL is shipped and should be stored under specific temperature-controlled conditions to ensure proper delivery and patient safety. The following handling instructions must be used for VIVITROL before administering to patients:

- 1) VIVITROL should always be refrigerated at 2° to 8° C (36° to 46° F) and not frozen.
- 2) VIVITROL should be stored separately from food, in accordance with Occupational Safety and Health Administration Guidelines.
- 3) Unrefrigerated VIVITROL can be stored at temperatures not exceeding 25°C (77°F) for more than 7 days prior to administration.
- 4) Check the product expiration date printed on the carton.
- 5) VIVITROL product received from a specialty pharmacy is patient-specific.

### ***PREPARATION OF VIVITROL***

VIVITROL is supplied in single-use cartons containing one 380 mg vial of VIVITROL microspheres diluent for suspension, one 5-mL prepackaged syringe, and customized 1.5 and 2-inch administration (thin-walled) needles with needle protection devices.

- 1) Remove carton from refrigeration, open the box, and allow VIVITROL to reach room temperature (approximately 45 minutes) prior to injection.

- 2) Parenteral products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit.
- 3) VIVITROL must be suspended only in the diluent supplied and must be administered only with one of the needles supplied.
- 4) Select needle length based on assessment of patient's body habitus. Consider using the 2-inch needle with protection device for patients with a large amount of subcutaneous tissue overlying the gluteal muscle. Consider alternative treatment for patients whose body type precludes an intramuscular injection with one of the provided needles.
- 5) Warm the diluent vial to near body temperature by rolling in the hand until it no longer feels cool to the touch.
- 6) After preparation, a properly mixed suspension will be milky white, will not contain clumps, and will move freely down the walls of the vial.
- 7) VIVITROL **must not be administered intravenously, subcutaneously or into adipose** – it must be injected into the deep muscle to minimize the risk of adverse injection site reaction.

### ***MEDICAL PROCEDURES***

The physician or designee will obtain a thorough substance use-focused history and a baseline physical examination. Immediately prior to the first injection of VIVITROL, the physician or designee will conduct the following procedures:

- 1) Determine, based upon the patient's self-report and any other available information, that the patient is interested in remaining abstinent and ready to begin trying to do so.
- 2) Perform urine drug screen (UDS) for opiates (11 panel, on-site drug screen) for natural and synthetic opiates to detect all possible opioids patient may have used.
- 3) If any significant doubt remains about the assessment of the patient's opioid status or the veracity of patient self-reporting, the Naloxone Challenge should be administered for patients with opioid addiction because it minimizes the duration of severe withdrawal. In regions known to have significant prevalence of buprenorphine diversion, the Naltrexone Challenge should also be administered, following Naloxone Challenge, because naloxone does not displace buprenorphine whereas naltrexone does. The Naltrexone Challenge Test involves oral administration of 25 mg of

Naltrexone (i.e., half of a 50 mg tab), and is negative if no withdrawal signs or symptoms are apparent after 1 hour.

- 4) If any clinical concern is raised by history or physical exam of either hepatic or renal status, liver function tests/ with transaminase levels and bilirubin should be performed and results should be within normal limits and/or creatinine clearance (estimated or measured) 50 ml/min or greater.
- 5) Perform urine beta-HCG (human chorionic gonadotropin) pregnancy test for females.
- 6) The physician or designee will:
  - a. Explain to the client the benefits and risks/possible side effects as indicated in Patient Counseling and Information listed above.
  - b. Provide the client with written support information based on Patient Counseling and Information listed above.
  - c. Evaluate the client based on the above reference criteria and prescribe VIVITROL, as indicated.

VIVITROL will be administered by the appropriate medical personnel at the program, using aseptic techniques as follows:

- 1) The patient will recline, face down and the gluteal muscle must be relaxed prior to injection.
- 2) The injection will be given deep intramuscular (IM) using the 1 ½ inch or 2 inch 20 gauge needle provided in the VIVITROL kit into the upper, outer quadrant of the buttock.
- 3) Always first aspirate for blood prior to injection, and if blood is withdrawn, abort injection in that site and move to another site in same side buttock and quadrant.
- 4) Injection site will rotate monthly from right to left gluteal muscle.
- 5) The first injection will always be in the right gluteal muscle. In the event of the suspension viscosity thickening to the point of causing a needle jam, the needle should be withdrawn, replaced with the second needle provided in the kit, and injection reattempted at a different site on the same side buttock and quadrant.
- 6) Appropriate medical personnel will monitor the injection site for any problems (redness, infection, swelling and/or itching at the injection site that gets worse over time), observe the client for any adverse reactions, and monitor the client for medication effectiveness and side effects over time.
- 7) **Injection site side effects that develop and signs of allergic reaction must be reported immediately to the physician.**

- 8) If liver function tests were checked at baseline, these will be checked again at time intervals that are appropriate to the patient's underlying clinical condition(s).

### **STAFF RESPONSIBILITIES**

- 1) The nurse or appropriate designee at the program will store VIVITROL as per manufacturer guidelines, and maintain an accurate inventory.
- 2) The Medical Director will identify one person accountable for maintaining all state required documentation accurately and in a timely fashion.
- 3) All medical and nursing staff involved in prescribing and/or administering VIVITROL will receive approved training prior to using the medication.
- 4) VIVITROL is one aspect of medication management and behavioral health services. Clients taking VIVITROL will participate in counseling based upon assessed need and the administration of VIVITROL will be reflected in the client's treatment plan.
- 5) Prescribed VIVITROL frequency will be documented in the treatment plan, and doses received will be documented in the medication administration record by the healthcare provider who administered the injection.
- 6) The treatment plan will include education for clients, their families and the people closest to the patient that the patient may be more sensitive to lower doses of opioids and at risk of accidental overdose should they use opioids when their next dose is due or if they miss a VIVITROL dose, or after VIVITROL treatment is discontinued.

Authority: \_\_\_\_\_

\_\_\_\_\_, MD, Medical Director

Effective Date: \_\_\_\_\_