HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VIVITROL® safely and effectively. See full prescribing information for VIVITROL.

VIVITROL® (naltrexone for extended-release injectable suspension)
Intramuscular
Initial U.S. Approval: 1984

RECENT MAJOR CHANGES

Dosage and Administration,
Directions for Use (2.4) 12/2015

INDICATIONS AND USAGE

- VIVITROL is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL. Patients should not be actively drinking at the time of initial VIVITROL administration (1.1).
- VIVITROL is indicated for the prevention of relapse to opioid dependence, following opioid detoxification (1.2).
- VIVITROL should be part of a comprehensive management program that includes psychosocial support (1).

DOSAGE AND ADMINISTRATION

The recommended dose of VIVITROL is 380 mg delivered intramuscularly every 4 weeks or once a month. The injection should be administered by a healthcare provider as an intramuscular (IM) gluteal injection, alternating buttocks for each subsequent injection, using the carton components provided (2 and 16.1).

Prior to initiating VIVITROL, an opioid-free duration of a minimum of 7–10 days is recommended for patients, to avoid precipitation of opioid withdrawal that may be severe enough to require hospitalization (5.3).

VIVITROL must not be administered intravenously or subcutaneously.
The entire dose pack should be stored in the refrigerator (2-8°C, 36-46°F) (2.3 and 16.1).
Do not expose the product to temperatures above 25°C (77°F). VIVITROL should not be frozen (2.4).

DOSAGE FORMS AND STRENGTHS

VIVITROL is an injectable suspension containing 380 mg of naltrexone in a microsphere formulation and 4 mL diluent (3).

CONTRAINDICATIONS

VIVITROL is contraindicated in:

- Patients receiving opioid analgesics (5.3).
- Patients with current physiologic opioid dependence (5.3).
- Patients in acute opioid withdrawal (5.3).
- Any individual who has failed the naloxone challenge test or has a positive urine screen for opioids (4).
- Patients who have previously exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent (4).

WARNINGS AND PRECAUTIONS

- **Vulnerability to Opioid Overdose:** Following VIVITROL treatment opioid tolerance is reduced from pretreatment baseline, and patients are vulnerable to potentially fatal overdose at the end of a dosing interval, after missing a dose, or after discontinuing VIVITROL treatment. Attempts to overcome blockade may also lead to fatal overdose (5.1).
- **Injection Site Reactions:** In some cases, injection site reactions may be very severe. Some cases of injection site reactions required surgical intervention (5.2).
- **Precipitation of Opioid Withdrawal:** Opioid-dependent and opioid-using patients, including those being treated for alcohol dependence, should be opioid-free before starting VIVITROL treatment, and should notify healthcare providers of any recent opioid use. An opioid-free duration of a minimum of 7-10 days is recommended for patients to avoid precipitation of opioid withdrawal that may be severe enough to require hospitalization. (5.3).
- **Hepatotoxicity:** Cases of hepatitis and clinically significant liver dysfunction were observed in association with VIVITROL treatment during the clinical development program and in the postmarketing period. Discontinue use of VIVITROL in the event of symptoms or signs of acute hepatitis (5.4).
- **Depression and Suicidality:** Monitor patients for the development of depression or suicidal thinking (5.5).
- **When Reversal of VIVITROL Blockade Is Required for Pain Management:** In an emergency situation in patients receiving VIVITROL, suggestions for pain management include regional analgesia or use of non-opioid analgesics (5.6).

ADVERSE REACTIONS

The adverse events seen most frequently in association with VIVITROL therapy for alcohol dependence (i.e, those occurring in ≥5% and at least twice as frequently with VIVITROL than placebo) include nausea, vomiting, injection site reactions (including induration, pruritus, nodules and swelling), muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders (6).

The adverse events seen most frequently in association with VIVITROL therapy in opioid-dependent patients (i.e., those occurring in ≥2% of patients treated with VIVITROL and at least twice as frequently with VIVITROL than placebo) were hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache (6).
To report SUSPECTED ADVERSE REACTIONS, contact Alkermes, Inc. at 1-800-VIVITROL (1-800-848-4876) and/or email: usmedinfo@alkermes.com or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

Naltrexone antagonizes the effects of opioid-containing medicines, such as cough and cold remedies, antidiarrheal preparations, and opioid analgesics (7).

USE IN SPECIFIC POPULATIONS

- VIVITROL pharmacokinetics have not been evaluated in subjects with severe hepatic impairment (8.7).
- Caution is recommended in administering VIVITROL to patients with moderate to severe renal impairment (8.6).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

Revised: 12/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.**

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support.

1.1 Alcohol Dependence

VIVITROL is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL. Patients should not be actively drinking at the time of initial VIVITROL administration.

1.2 Opioid Dependence

VIVITROL is indicated for the prevention of relapse to opioid dependence, following opioid detoxification.

2 DOSAGE AND ADMINISTRATION

VIVITROL must be prepared and administered by a healthcare provider.

Prior to initiating VIVITROL, an opioid-free duration of a minimum of 7–10 days is recommended for patients, to avoid precipitation of opioid withdrawal that may be severe enough to require hospitalization [*see Warnings and Precautions (5.3)]*.

The recommended dose of VIVITROL is 380 mg delivered intramuscularly every 4 weeks or once a month. The injection should be administered by a healthcare provider as an intramuscular (IM) gluteal injection, alternating buttocks for each subsequent injection, using the carton components provided *[see How Supplied/Storage and Handling (16)]*. The needles provided in the carton are customized needles. VIVITROL must not be injected using any other needle. The needle lengths (either 1 1/2 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 assure that needle length is adequate for intramuscular administration. For patients with a larger amount of subcutaneous tissue overlying the gluteal muscle, the administering healthcare provider may utilize the supplied 2-inch needle with needle protection device to help ensure that the injectate reaches the intramuscular mass. For very lean patients, the 1 1/2-inch needle may be appropriate to prevent the needle contacting the periosteum. Either needle may be used for patients with average body habitus. Healthcare providers should ensure that the VIVITROL 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.

VIVITROL must not be administered intravenously or subcutaneously.

If a patient misses a dose, he/she should be instructed to receive the next dose as soon as possible.

Pretreatment with oral naltrexone is not required before using VIVITROL.

2.1 Reinitiation of Treatment in Patients Previously Discontinued

There are no data to specifically address reinitiation of treatment. Patients reinitiating treatment with VIVITROL should be opioid-free at the time of dose administration *[see Indications and Usage (1), Contraindications (4), and Warnings and Precautions (5.3)]*.

2.2 Switching From Oral Naltrexone

There are no systematically collected data that specifically address the switch from oral naltrexone to VIVITROL.

2.3 Switching from Buprenorphine, Buprenorphine/Naloxone, or Methadone

There are no systematically collected data that specifically address the switch from buprenorphine or methadone to VIVITROL; however, review of postmarketing case reports have indicated that some patients may experience severe manifestations of precipitated withdrawal when being switched from opioid agonist therapy to opioid antagonist therapy *[see Warnings and Precautions (5.3)]*. Patients transitioning from buprenorphine or methadone may be vulnerable to precipitation of withdrawal symptoms for as long as 2 weeks. Healthcare providers should be prepared to manage withdrawal symptomatically with non-opioid medications.

2.4 Directions for Use

To ensure proper dosing, it is important that you follow the preparation and administration instructions outlined in this document.

VIVITROL 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 an administration needle with needle protection device are required for preparation and administration. Two thin-walled 1 1/2-inch needles with needle protection device and two 2-inch thin-walled needles with needle protection device have been provided to accommodate varying patient body habitus. For patients with a larger amount of subcutaneous tissue overlying the gluteal muscle, the administering healthcare provider may utilize the supplied 2-inch needle with needle protection device to help ensure that the injectate reaches the intramuscular mass. For very lean patients, the 1 1/2-inch needle may be appropriate to prevent the needle contacting the periosteum. Either needle may be used for patients with average body habitus. A spare administration needle of each size is provided in case of clogging *[see How Supplied/Storage and Handling (16)]*. Do not substitute any other components for the components of the carton.

Prior to preparation, allow drug to reach room temperature (approximately 45 minutes).

Parenteral products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit. A properly mixed suspension will be milky white, will not contain clumps, and will move freely down the wall of the vial *[see Directions for Use, illustration below]*.

Product to be prepared and administered by a healthcare provider.

Keep out of reach of children.

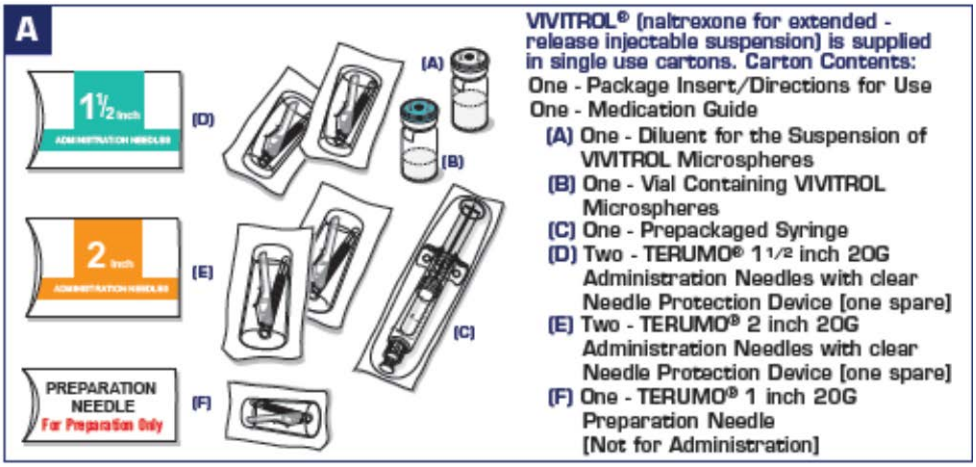
Prepare and administer the VIVITROL suspension using aseptic technique.

WARNING: To reduce the risk of a needlestick:

- Do not intentionally disengage the needle protection device.
- Discard bent or damaged needle into a sharps container and use the spare needle provided. Do not attempt to straighten the needle or engage needle protection device if the needle is bent or damaged.
- Do not mishandle the needle protection device in a way that could lead to protrusion of the needle.
- Do not use free hand to press sheath over needle.

THE CARTON SHOULD NOT BE EXPOSED TO TEMPERATURES EXCEEDING 25°C (77°F).

The entire carton should be stored in the refrigerator (2-8°C, 36-46°F). Unrefrigerated, VIVITROL 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). VIVITROL should not be frozen.



Parenteral products should be visually inspected for particulate matter and discoloration prior to administration.

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