Initial REMS Approved: March 2010

Most Recent Modification: July 2013

NDA 21-897 VIVITROL® (naltrexone for extended-release injectable suspension)

Opioid Antagonist

Alkermes, Inc.

852 Winter Street

Waltham, MA 02451

1-800-848-4876

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goals of this REMS are:

- To inform patients and healthcare providers about severe injection site reactions associated with the use of VIVITROL.
- To inform healthcare providers about the importance of counseling their patients about severe injection site reactions associated with the use of VIVITROL.

II. REMS Elements

A. Medication Guide

A Medication Guide will be included with each VIVITROL package in accordance with 21 CFR 208.24.

The Medication Guide is part of the REMS and is appended.

B. Communication Plan A Communication Plan will be implemented for those healthcare providers who are likely to prescribe and/or inject VIVITROL. This Communication Plan will consist of the following components:

1. **Dear Healthcare Provider Letter**

Within 60 days of the modified REMS approval date, a *Dear Healthcare Provider (DHCP) Letter* will be distributed to all healthcare providers who are likely to prescribe and/or inject VIVITROL as ascertained through the Touchpoints database, specialty pharmacy data, and third party data. Annually, for 3 years following approval of the modified VIVITROL REMS, Alkermes will identify new prescribers of VIVITROL who were not previously sent the *DHCP Letter* and will distribute *DHCP Letter* to these prescribers.

The *DHCP Letter* will be distributed electronically (via email) or by the US Postal Service. The *DHCP Letter* will inform healthcare providers of the serious risks associated

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with VIVITROL, especially the continued occurrence of serious injection site reactions. It will also reinforce the importance of healthcare providers discussing the risks of VIVITROL with their patients and providing their patients with a copy of the Medication Guide. The full VIVITROL Prescribing Information, Medication Guide, *Key Techniques to Reduce Severe Injection Site Reactions* Poster and VIVITROL Patient Counseling Tool will accompany the *DHCP Letter*.

In addition, the field sales force will provide a copy of the *DHCP Letter* to each healthcare provider upon whom they call and it will be available on the VIVITROL REMS website (www.vivitrolrems.com) for 3 years following approval of the modified VIVITROL REMS.

The *DHCP Letter* is appended.

2. **Prescriber tool to facilitate counseling/educating patients (VIVITROL Patient Counseling Tool)**

Alkermes will provide healthcare providers with the VIVITROL *Patient Counseling Tool* that will be in the form of a two-page document highlighting important risks associated with VIVITROL use.

This tool will be distributed beginning within 60 days after the modified REMS approval date with the *DHCP Letter*. It will be distributed by the sales force to each healthcare provider upon whom they call and it will be available on the VIVITROL REMS website (www.vivitrolrems.com) for 3 years following approval of the modified VIVITROL REMS.

The VIVITROL *Patient Counseling Tool* is appended.

3. **Visual aid reinforcing proper VIVITROL injection technique (***Key Techniques to Reduce Severe Injection Site Reactions* poster**)**

Alkermes will provide healthcare providers with a *Key Techniques to Reduce Severe Injection Site Reactions* poster reinforcing proper intramuscular injection procedure for VIVITROL. Alkermes will request that healthcare providers hang this poster in the area in which VIVITROL injections are administered.

This *Key Techniques to Reduce Severe Injection Site Reactions* poster will be distributed beginning within 60 days of the modified REMS approval date with the *DHCP Letter*. It will be distributed by the sales force to each healthcare provider upon whom they call and it will be available on the VIVITROL REMS website (www.vivitrolrems.com) for 3 years following approval of the modified VIVITROL REMS.

The *Key Techniques to Reduce Severe Injection Site Reactions* poster is appended.

4. **VIVITROL REMS Website**

Within 30 days of the modified REMS approval, Alkermes will post information for healthcare providers and patients on the new VIVITROL REMS website (www.vivitrolrems.com). This information will be available on the website for 3 years following approval of the modified VIVITROL REMS.

The content of the web-based material will include the following:

- Goals of the REMS

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- Medication Guide for VIVITROL
- Prescribing Information for VIVITROL
- *Dear Healthcare Provider (DHCP) Letter*
- *VIVITROL Patient Counseling Tool*
- *Key Techniques to Reduce Severe Injection Site Reactions* poster

The web-based material is appended.

C. Timetable for Submission of Assessments

Alkermes will submit REMS Assessments to FDA 2 years, 4 years and 7 years from the date of the approval of the modified REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment.

Alkermes will submit each assessment so it will be received by the FDA on or before the due date.

Reference ID: 3348450

852 Winter Street
Waltham
Massachusetts
02451-1420
USA

Telephone
781-609-6000
Facsimile
617-812-2417
www.alkermes.com

Alkermes

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IMPORTANT DRUG WARNING

Subject: VIVITROL® (naltrexone for extended release injectable suspension)
- **Risk of Severe Injection Site Reactions**
- **New Patient Counseling Tool and Safety Poster**

Dear Healthcare Provider:

The purpose of this letter is to inform you of important new safety information for VIVITROL (naltrexone for extended-release injectable suspension). VIVITROL is a prescription injectable medicine used to treat alcohol dependence and for the prevention of relapse to opioid dependence following opioid detoxification.

Severe injection site reactions continue to occur. In addition, a recent assessment demonstrated that patients are not fully aware of the serious risks associated with the use of VIVITROL. Therefore, the FDA has modified the VIVITROL Risk Evaluation and Mitigation Strategy (REMS) to highlight the potential risk of severe injection site reactions and to emphasize the importance of healthcare providers counseling their patients about the serious risks associated with VIVITROL.

The REMS program now includes the following:

Patient Counseling Tool

A patient counseling tool has been created for prescribers to use when counseling their patients about the serious risks associated with the use of VIVITROL. Prescribers should remember to counsel their patients about the serious risks, including any relevant signs and symptoms, associated with the use of VIVITROL, including the following:

- risk of opioid overdose
- serious risk of severe injection site reactions
- risk of precipitated opioid withdrawal (new Warning: see enclosed Prescribing Information)
- risk of hepatotoxicity, including hepatitis
- possibility that patients may not feel the therapeutic effects of opioid-containing medicines for pain, cough, and diarrhea while taking VIVITROL.

Poster: Key Techniques to Reduce Severe Injection Site Reactions

Severe injection site reactions have been reported in the postmarketing period with the following features: induration, cellulitis, hematoma, abscess, sterile abscess, and necrosis. Some cases have required hospitalization and surgical intervention, including debridement of necrotic tissue, and have resulted in significant scarring.

The *Directions for Use* section in the Prescribing Information has been revised to include additional detail regarding how to inject VIVITROL. The following three recommendations may help decrease the risk of severe injection site reactions for VIVITROL:

1. **Proper needle selection**
   Select the 2-inch NEEDLE-Pro Needle for patients with more subcutaneous adipose tissue. Select the 1.5 inch TERUMO Needle for patients with less subcutaneous adipose tissue. Use either needle for patients of average body habitus. The correct needle-length is required to ensure VIVITROL is injected into the gluteal muscle.

2. **Proper aseptic technique**
   Ensure you are using proper aseptic injection technique when administering VIVITROL as described in the *Directions for Use* section in the Prescribing Information.

3. **Proper Intramuscular (IM) injection**
   Administer VIVITROL intramuscularly into the gluteal muscle of the buttock. VIVITROL must NOT be administered intravenously or subcutaneously.

A VIVITROL visual aid poster is available to emphasize the importance of proper administration of VIVITROL. The poster, titled *Key Techniques to Reduce Severe Injection Site Reactions*, **includes proper needle selection, proper aseptic technique, and proper intramuscular injection technique**. This poster should be displayed in your office in the area where VIVITROL injections are administered.

VIVITROL REMS website

You can find more information and materials at the VIVITROL REMS website at ***www.vivitrolrems.com***

Medication Guide

The Medication Guide contains information to support patient education regarding the risks and benefits of treatment with VIVITROL. **The VIVITROL Medication Guide must be provided to patients before each administration of VIVITROL.**

How do I Order Free Copies of Materials?

For copies of the Patient Counseling Tool, *Key Techniques to Reduce Severe Injection Site Reactions* Poster, and/or Medication Guide please contact Alkermes at www.vivitrolrems.com or by calling 1-800-848-4876, Option #1.

Reporting Adverse Reactions

To report any adverse events with the use of VIVITROL contact:

- Alkermes at 1-800-848-4876 (option#1) or by email at usmedinfo@alkermes.com, or
- FDA's MedWatch Reporting System by phone at 1-800-332-1088, or online at www.fda.gov/medwatch/report.htm.

This letter is not a comprehensive description of the risks and benefits associated with the use of VIVITROL. **Healthcare Providers must read the accompanying Prescribing Information, for a complete description of VIVITROL.**

For additional information, please call Alkermes at 1-800-848-4876 (option #1) or visit usmedinfo@alkermes.com.

Thank you,

Bernard L. Silverman, M.D.
Vice President, Clinical Sciences
Alkermes, Inc.

Enclosures: VIVITROL Prescribing Information
VIVITROL Medication Guide
VIVITROL Patient Counseling Tool
VIVITROL *Key Techniques To Reduce Severe Injection Site Reactions* Poster

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Patient Counseling Tool

VIVITROL® (naltrexone for extended-release injectable suspension)

Risk of sudden opioid withdrawal during initiation and re-initiation of VIVITROL

Using any type of opioid including street drugs, prescription pain medicines, cough, cold or diarrhea medicines that contain opioids, or opioid dependence treatments buprenorphine or methadone, in the 7 to 14 days before starting VIVITROL may cause severe and potentially dangerous sudden opioid withdrawal.

Risk of opioid overdose

Patients may be more sensitive to the effects of lower amounts of opioids:

- After stopping opioids (detoxification)
- When the next VIVITROL dose is due
- If a dose of VIVITROL is missed
- After VIVITROL treatment stops

Patients should tell their family and people close to them about the increased sensitivity to opioids and the risk of overdose even when using lower doses of opioids or amounts that they used before treatment. Using large amounts of opioids, such as prescription pain pills or heroin, to overcome effects of VIVITROL can lead to serious injury, coma, and death.

Risk of severe reactions at the injection site

Remind patients of these **possible** symptoms at the **injection site:**

- Intense pain
- The area feels hard
- Large areas of swelling
- Lumps
- Blisters
- Open wound
- Dark scab

Some of these injection site reactions have required surgery.
Tell your patients to contact a healthcare provider if they have any reactions at the injection site.

Risk of liver injury, including liver damage or hepatitis

Remind patients of the possible symptoms of liver damage or hepatitis.

- Stomach area pain lasting more than a few days
- Dark urine
- Yellowing of the whites of eyes
- Tiredness

Patients may not feel the therapeutic effects of opioid-containing medicines for pain, cough or cold, or diarrhea while taking VIVITROL.

Patients should carry written information with them at all times to alert healthcare providers that they are taking VIVITROL, so they can be treated properly in an emergency.

A Patient Wallet Card or Medical Alert Bracelet can be ordered from: 1-800-848-4876, Option #1.

PLEASE SEE PRESCRIBING INFORMATION AND MEDICATION GUIDE.

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Vivitrol®
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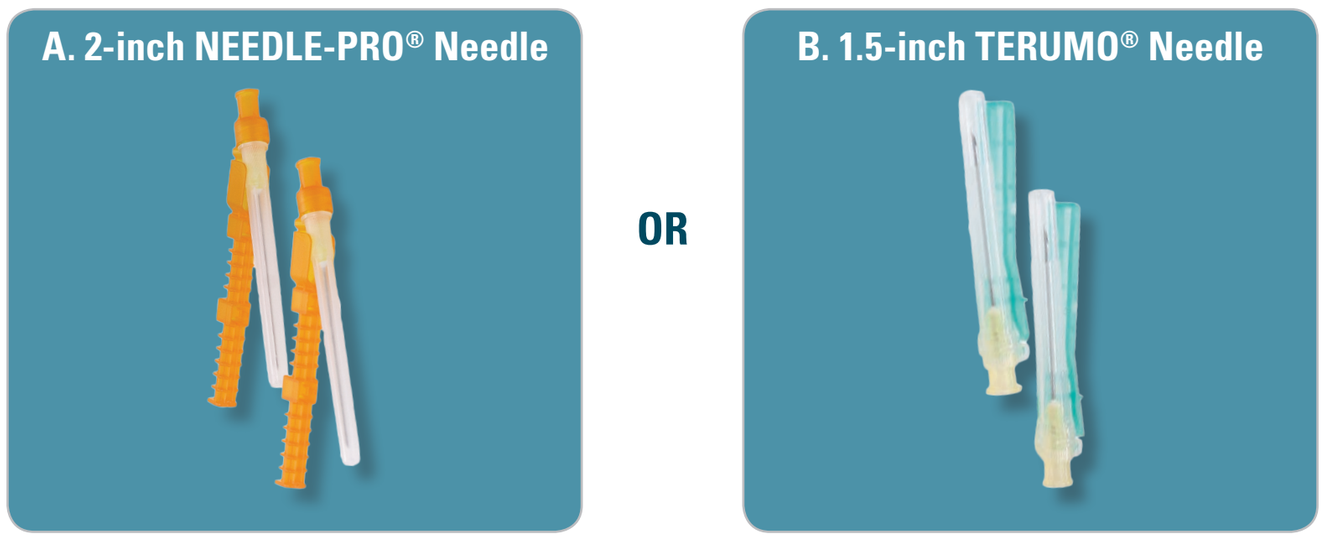
Key Techniques to Reduce Severe Injection Site Reactions VIVITROL® (naltrexone for extended-release injectable suspension) Intramuscular Injection

- **Use appropriate VIVITROL needle to ensure the injection reaches the gluteal muscle**

  Select the **2-inch needle** for patients with **more subcutaneous** adipose tissue. Select the **1.5-inch** needle for patients with **less subcutaneous** adipose tissue. Use either needle for patients of average body habitus.



- **Use aseptic technique when administering VIVITROL intramuscularly**

  Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting. Do not touch this area again before giving the injection.

- **Use proper deep intramuscular injection technique into gluteal muscle**

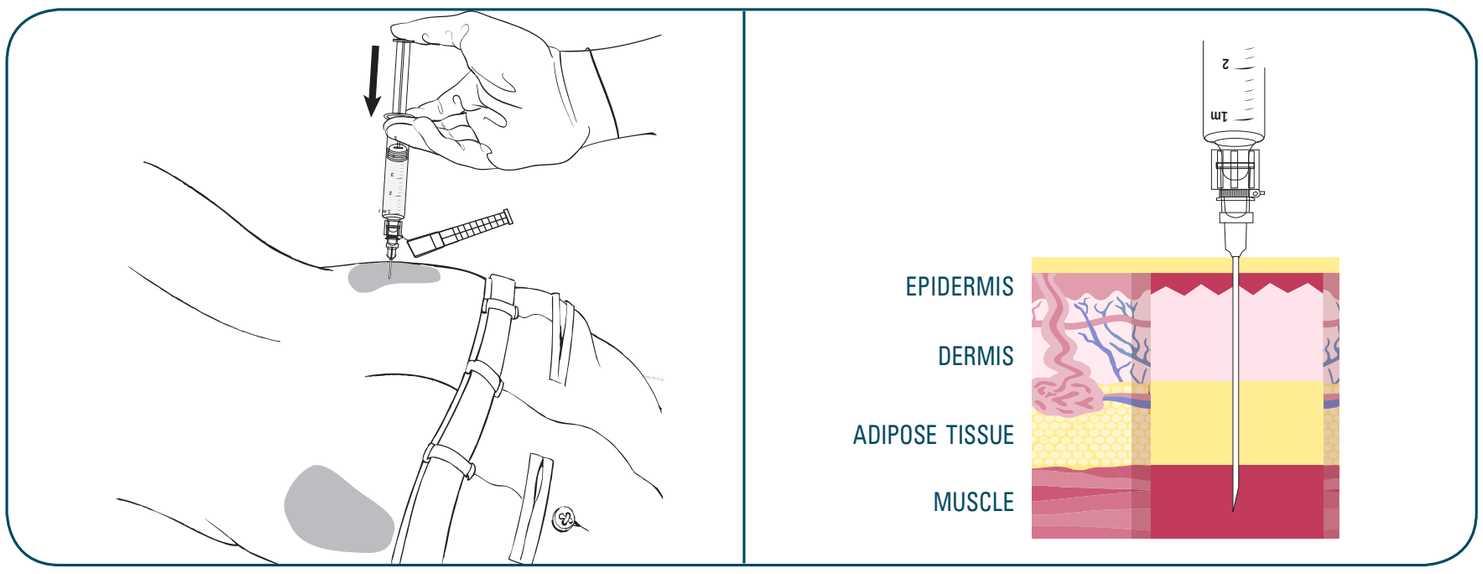
  VIVITROL must NOT be given intravenously, subcutaneously, or into adipose tissue.

  Inadvertent subcutaneous injection of VIVITROL may increase the likelihood of severe injection site reactions.

1. Administer the suspension by deep intramuscular injection into the upper, outer quadrant of a gluteal muscle, alternating buttocks per monthly injection. **Remember to aspirate for blood before injection.**

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.



Gluteal Intramuscular Injection of VIVITROL (Figure not to scale)

A Patient Counseling Tool is available to counsel your patients prior to administration about the serious risks associated with VIVITROL.*

The above information is a selection of key Safety Information relating to the VIVITROL injection. Please refer to the Directions for Use and Prescribing Information for the complete Safety Information.*

*The Prescribing Information and Patient Counseling Tool are available from www.vivitrolrems.com or by calling 1-800-VIVITROL, Option #1. The Prescribing Information is also included in the VIVITROL Kit.

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INFORMATION FOR HEALTHCARE PROFESSIONALS

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

VIVITROL, when used as part of a comprehensive management program, is indicated for the following:

- Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL
- Prevention of relapse to opioid dependence, following opioid detoxification

Providers and patients should be aware of the following risks of VIVITROL:

- Risk of opioid overdose
- Severe injection site reactions
- Precipitation of opioid withdrawal during initiation and re-initiation of VIVITROL
- Hepatotoxicity
- Patients may not feel the therapeutic effects of opioid-containing medicines for pain, cough or cold, or diarrhea while taking VIVITROL

Materials for Healthcare Providers

Dear Healthcare Provider Letter ▶

Patient Counseling Tool for Providers ▶

Important Injection Safety Information Poster ▶

To order any of the healthcare provider materials, call:

1-800-848-4876

- Dear Healthcare Provider Letter
- Patient Counseling Tool for Providers
- Important Injection Safety Information Poster
- Patient Wallet Card
- Patient Safety Bracelet

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/s/

JUDITH A RACOOSIN
07/29/2013