



Meeting the Need

Doing more to help address the crisis of opioid and alcohol dependence

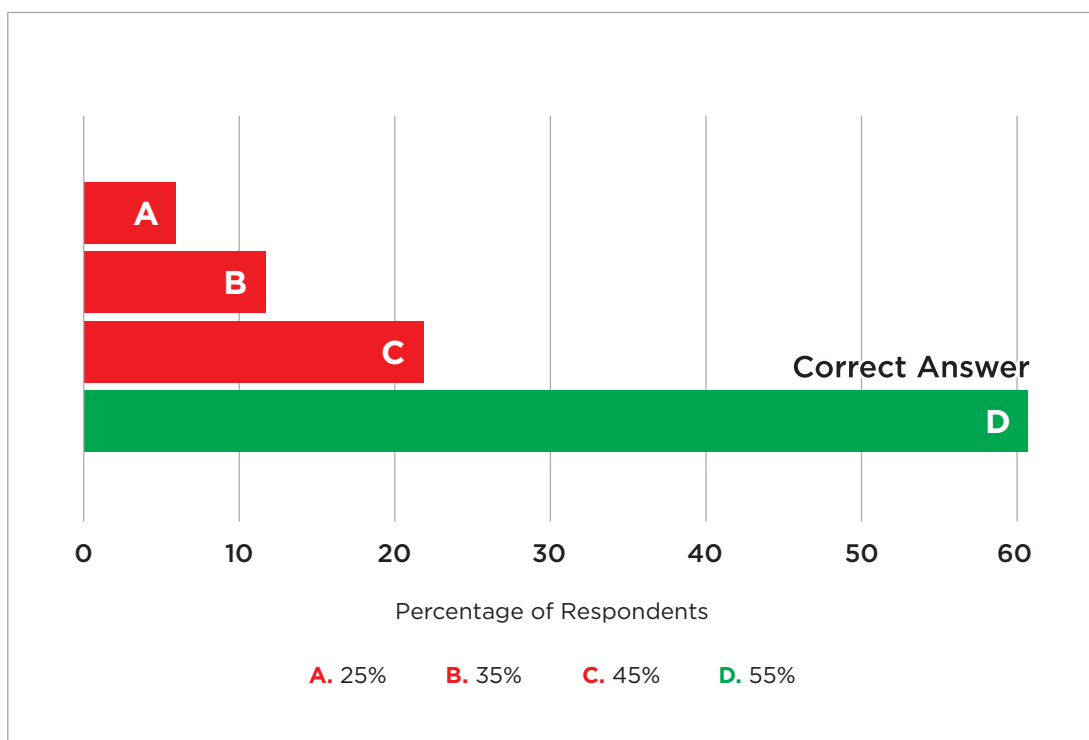
Quiz Results

Understanding Opioid Dependence: Important Considerations

Note: A total of 1064 completed quizzes were received as of the date of this report (January 22, 2018).

Question 1 of 5: Of about 78,000 deaths due to illicit drug use disorders globally in 2010, what percentage was attributable to opioid dependence?

Finding: Nearly 40% of respondents underestimated the contribution of opioid dependence to total deaths due to illicit drug use disorders.



Explanation

A systematic review of the epidemiology of drug dependence was conducted to assess the global and regional prevalence and burden of amphetamine, cannabis, cocaine, and opioid dependence. The highest estimated global burden was attributable to opioid dependence, with 9.2 million disability-adjusted life years. Of about 78,000 deaths due to illicit drug use disorders in 2010, more than half (55%, 43,000 deaths) were attributable to opioid dependence.

For complete information, see:

Degenhardt L, Whiteford HA, Ferrari AJ, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010. *Lancet*. 2013;382(9904):1564-1574.

Please see [Prescribing Information](#) and [Medication Guide](#). Review the [Medication Guide](#) with your patients.

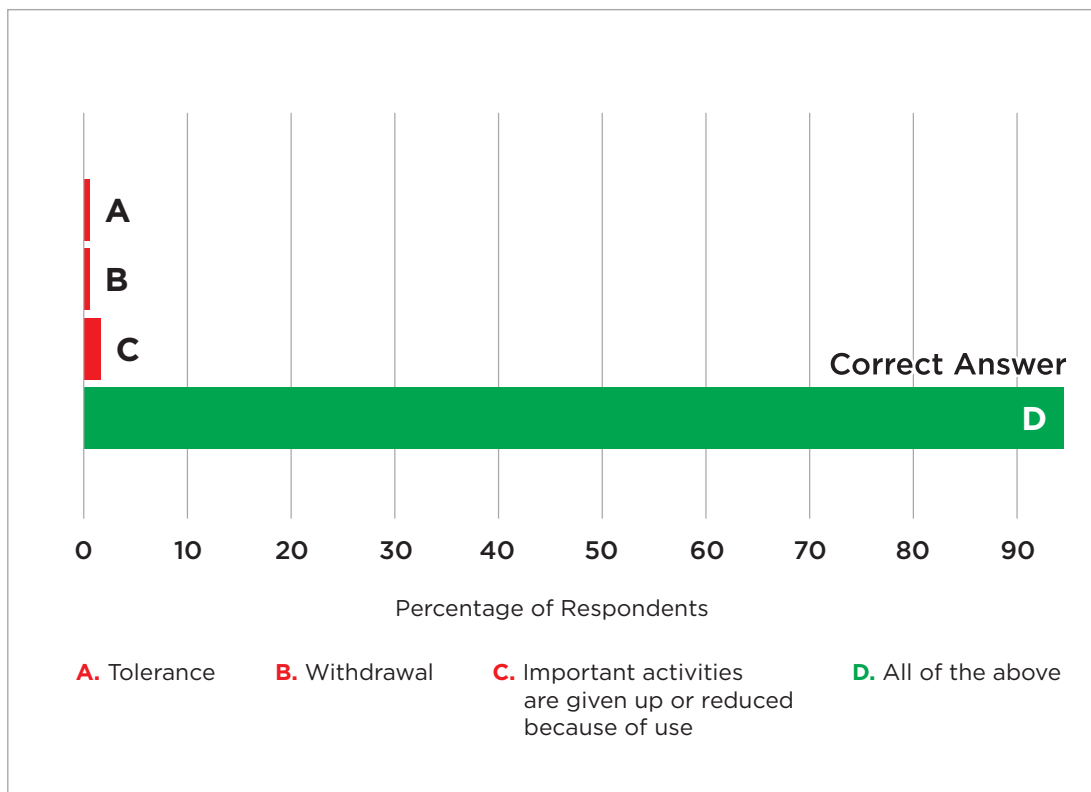


Meeting the Need

Doing more to help address the crisis of opioid and alcohol dependence

Question 2 of 5: Which of the following is included as part of the *DSM-IV-TR* criteria for opioid dependence?

Finding: The vast majority of respondents, but not all, appear to be well versed in the diagnostic criteria for opioid dependence described in the *DSM-IV-TR*. (Note that the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition*, has updated the criteria for opioid use disorders.)



Explanation

Opioid dependence is a maladaptive pattern of opioid use leading to clinically significant impairment or distress, as manifested by 3 (or more) of the following occurring in the same 12-month period:

- Tolerance
- Withdrawal
- Taking the substance in larger amounts or longer than intended
- Persistent desire or unsuccessful efforts to curb or control use
- Excessive time spent obtaining, using, or recovering from use
- Important activities are given up or reduced because of use
- Continued use despite acknowledged physical or psychological problem due to use

DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision.

For complete information, see:

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Text Revision. Washington, DC: American Psychiatric Association; 2000.

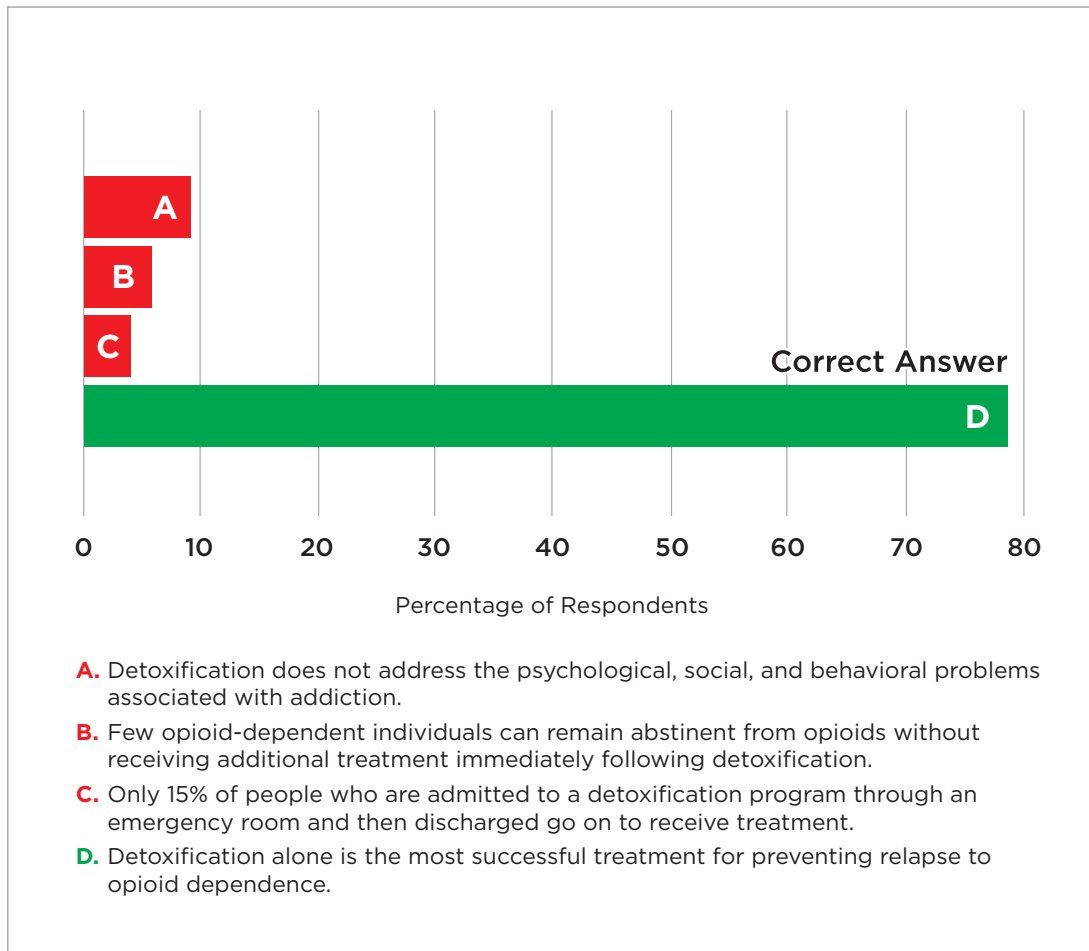


Meeting the Need

Doing more to help address the crisis of opioid and alcohol dependence

Question 3 of 5: Which of the following statements regarding detoxification for opioid dependence is FALSE?

Finding: More than 20% of respondents apparently do not recognize the limitations of detoxification alone in the treatment of opioid dependence.



Explanation

Very few people with opioid dependence can sustain abstaining from opioids without additional help following detoxification. Therefore, detoxification should be viewed as the first stage of treatment.¹ Importantly, some individuals may not agree to treatment following initial detoxification.^{1,2} Because of the relapsing nature of opioid dependence, formal detoxification may be required repeatedly for many individuals.¹

For complete information, see:

1. Galanter M, Kleber HD, eds. *Textbook of Substance Abuse Treatment*. 4th ed. Arlington, VA: American Psychiatric Publishing, Inc.; 2008.
2. Substance Abuse and Mental Health Services Administration. *Detoxification and Substance Abuse Treatment*. Treatment Improvement Protocol (TIP) Series, No. 45. HHS Publication No. (SMA) 06-4131. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2006.

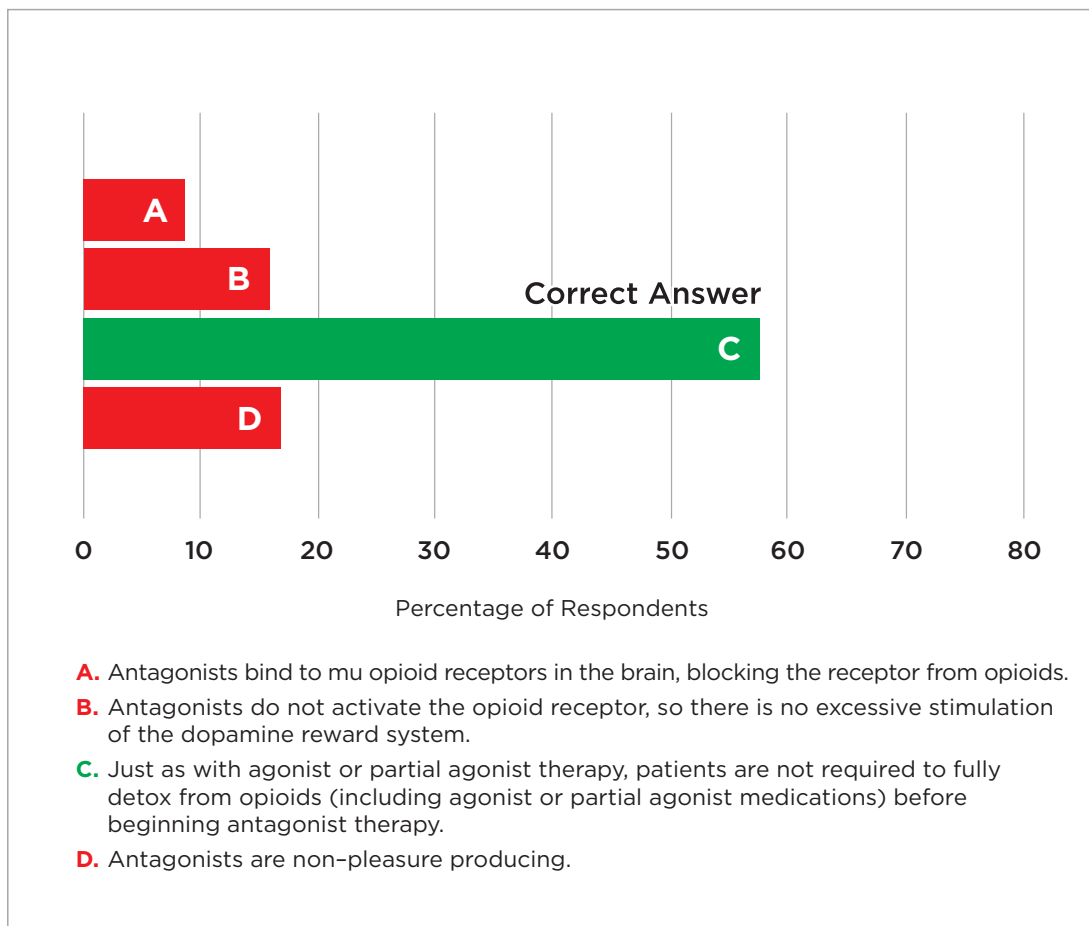


Meeting the Need

Doing more to help address the crisis of opioid and alcohol dependence

Question 4 of 5: Which of the following statements regarding characteristics of opioid antagonists is NOT true?

Finding: More than 40% of respondents had misconceptions about opioid antagonist treatment. In addition, it was not universally understood that patients must undergo complete detoxification from opioids before receiving an opioid antagonist.



Explanation

Opioid antagonists bind to mu opioid receptors in the brain, blocking the receptor from opioids. Antagonists do not activate the opioid receptor, so there is no excessive stimulation of the dopamine reward system. For this reason, patients must fully detox from opioids (including agonist or partial agonist medications) for 1 to 2 weeks before beginning antagonist therapy, or they could go into precipitated opioid withdrawal. Antagonists are non-pleasure producing. Therefore, there is no known abuse potential; patients do not experience a high; and if treatment is ceased, patients will not experience withdrawal symptoms.

For complete information, see:

Kosten TR, George TP. The neurobiology of opioid dependence: implications for treatment. *Sci Pract Perspect.* 2002;1(1):13-20.

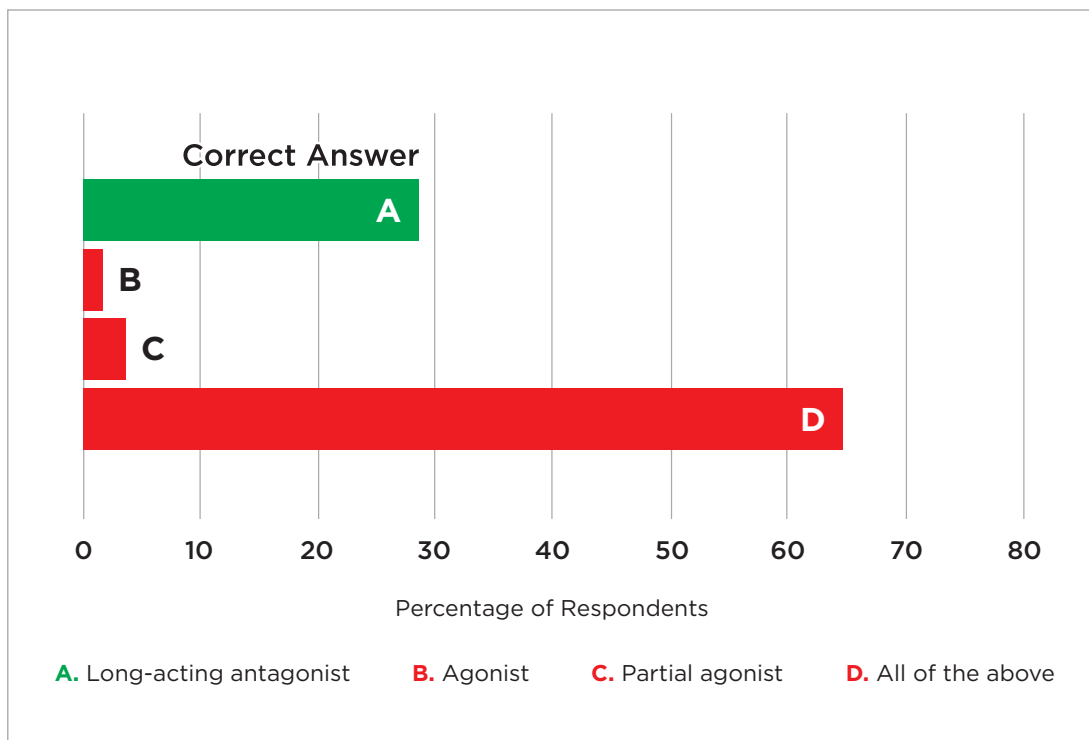


Meeting the Need

Doing more to help address the crisis of opioid and alcohol dependence

Question 5 of 5: When combined with counseling and other behavioral therapies, which medications are indicated for the prevention of relapse?

Finding: Most respondents apparently were unaware that, among medication-assisted treatments, only long-acting antagonist therapy is indicated specifically for the prevention of relapse to opioid dependence, following opioid detoxification, as part of a comprehensive management program that includes psychosocial support.



Explanation

Medications can be an important element of treatment for many patients, especially when combined with counseling and/or other behavioral therapies. Opioid-receptor antagonists, agonists, and partial agonists are used with behavioral therapies to treat opioid dependence.¹

Only extended-release naltrexone, a long-acting antagonist, is indicated for the prevention of relapse to opioid dependence, when combined with counseling, after detoxification.² Prior to initiating VIVITROL® (naltrexone for extended-release injectable suspension), 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 additional important safety information on page 6.

For complete information, see:

1. Stotts AL, Dodrill CL, Kosten TR. Opioid dependence treatment: options in pharmacotherapy. *Expert Opin Pharmacother.* 2009;10(11):1727-1740.
2. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc.; rev December 2015.

For more information on the impact, prevalence, and treatment of opioid dependence, please refer to the [Opioid Dependence Newsletter Series](#).

IMPORTANT SAFETY INFORMATION

INDICATIONS

VIVITROL[®] (naltrexone for extended-release injectable suspension) is indicated for:

- 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.
- Prevention of relapse to opioid dependence, following opioid detoxification.
- VIVITROL should be part of a comprehensive management program that includes psychosocial support.

CONTRAINDICATIONS

VIVITROL is contraindicated in patients:

- Receiving opioid analgesics
- With current physiologic opioid dependence
- In acute opioid withdrawal
- Who have failed the naloxone challenge test or have a positive urine screen for opioids
- Who have exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent

WARNINGS AND PRECAUTIONS

Vulnerability to Opioid Overdose:

- After opioid detoxification, patients are likely to have a reduced tolerance to opioids. VIVITROL blocks the effects of exogenous opioids for approximately 28 days after administration. As the blockade wanes and eventually dissipates completely, use of previously tolerated doses of opioids could result in potentially life-threatening opioid intoxication (respiratory compromise or arrest, circulatory collapse, etc.).
- Cases of opioid overdose with fatal outcomes have been reported in patients who used opioids at the end of a dosing interval, after missing a scheduled dose, or after discontinuing treatment. Patients and caregivers should be told of this increased sensitivity to opioids and the risk of overdose.
- Although VIVITROL is a potent antagonist with a prolonged pharmacological effect, the blockade produced by VIVITROL is surmountable. The plasma concentration of exogenous opioids attained immediately following their acute administration may be sufficient to overcome the competitive receptor blockade. This poses a potential risk to individuals who attempt, on their own, to overcome the blockade by administering large amounts of exogenous opioids.
- Any attempt by a patient to overcome the VIVITROL blockade by taking opioids may lead to fatal overdose. Patients should be told of the serious consequences of trying to overcome the opioid blockade.

Injection Site Reactions:

- VIVITROL injections may be followed by pain, tenderness, induration, swelling, erythema, bruising, or pruritus; however, in some cases injection site reactions may be very severe.
- Injection site reactions not improving may require prompt medical attention, including, in some cases, surgical intervention.
- Inadvertent subcutaneous/adipose layer injection of VIVITROL may increase the likelihood of severe injection site reactions.
- Select proper needle size for patient body habitus, and use only the needles provided in the carton.
- Patients should be informed that any concerning injection site reactions should be brought to the attention of their healthcare provider.

Precipitation of Opioid Withdrawal:

- When withdrawal is precipitated abruptly by administration of an opioid antagonist to an opioid-dependent patient, the resulting withdrawal syndrome can be severe. Some cases of withdrawal symptoms have been severe enough to require hospitalization, and in some cases, management in the ICU.
- To prevent occurrence of precipitated withdrawal, opioid-dependent patients, including those being treated for alcohol dependence, should be opioid-free (including tramadol) before starting VIVITROL treatment:

- An opioid-free interval of a minimum of 7-10 days is recommended for patients previously dependent on short-acting opioids.
- Patients transitioning from buprenorphine or methadone may be vulnerable to precipitated withdrawal for as long as two weeks.
- If a more rapid transition from agonist to antagonist therapy is deemed necessary and appropriate by the healthcare provider, monitor the patient closely in an appropriate medical setting where precipitated withdrawal can be managed.
- Patients should be made aware of the risk associated with precipitated withdrawal and be encouraged to give an accurate account of last opioid use.

Hepatotoxicity:

- Cases of hepatitis and clinically significant liver dysfunction have been observed in association with VIVITROL. Warn patients of the risk of hepatic injury; advise them to seek help if experiencing symptoms of acute hepatitis. Discontinue use of VIVITROL in patients who exhibit acute hepatitis symptoms.

Depression and Suicidality:

- Alcohol- and opioid-dependent patients taking VIVITROL should be monitored for depression or suicidal thoughts. Alert families and caregivers to monitor and report the emergence of symptoms of depression or suicidality.

When Reversal of VIVITROL Blockade Is Required for Pain Management:

- For VIVITROL patients in emergency situations, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required to reverse the VIVITROL blockade, patients should be closely monitored by trained personnel in a setting staffed and equipped for CPR.

Eosinophilic Pneumonia:

- Cases of eosinophilic pneumonia requiring hospitalization have been reported. Warn patients of the risk of eosinophilic pneumonia and to seek medical attention if they develop symptoms of pneumonia.

Hypersensitivity Reactions:

- Patients should be warned of the risk of hypersensitivity reactions, including anaphylaxis.

Intramuscular Injections:

- As with any IM injection, VIVITROL should be administered with caution to patients with thrombocytopenia or any coagulation disorder.

Alcohol Withdrawal:

- Use of VIVITROL does not eliminate nor diminish alcohol withdrawal symptoms.

ADVERSE REACTIONS

- Serious adverse reactions that may be associated with VIVITROL therapy in clinical use include severe injection site reactions, eosinophilic pneumonia, serious allergic reactions, unintended precipitation of opioid withdrawal, accidental opioid overdose, and depression and suicidality.
- The adverse events seen most frequently in association with VIVITROL therapy for alcohol dependence (ie, those occurring in $\geq 5\%$ 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.
- The adverse events seen most frequently in association with VIVITROL in opioid-dependent patients (ie, those occurring in $\geq 2\%$ and at least twice as frequently with VIVITROL than placebo) were hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.

You are encouraged to report side effects to the FDA.

Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see [Prescribing Information](#) and [Medication Guide](#). Review the [Medication Guide](#) with your patients.

Alkermes

ALKERMES and VIVITROL are registered trademarks of Alkermes, Inc.

All other marks are registered to their respective owners.

For U.S. healthcare providers only.

©2018 Alkermes, Inc. All rights reserved. VIV-003783