



Alkermes Supports White House Declaration of Nationwide Public Health Emergency to Combat Opioid Crisis

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In response to today's White House news conference, Alkermes fully supports the President's declaration of a nationwide public health emergency to more aggressively address the growing opioid crisis. Drug overdose deaths exceeded 64,000 in 2016.¹ This is the crisis of our time, and we must work together to reverse the trend.

Alkermes has been on the frontlines of the opioid epidemic for years, and we commend the administration for providing additional resources and support to help combat this devastating epidemic that continues to impact our communities and families. Expanded access to services, such as telemedicine, will help bolster increased access to treatment for patients.

Richard Pops, Chief Executive Officer of Alkermes, commented, "Alkermes is committed to ensuring all Americans have access to treatment, including all FDA-approved medications. Patients need information about and access to all available options."

In addition to today's declaration, Alkermes supports the advancements made by the Comprehensive Addiction Recovery Act (CARA), which was enacted last year. CARA requires office-based opioid addiction providers to have the capacity to offer all FDA-approved medications, either directly or by referral, and requires these same providers to complete training on all approved medication options, detoxification, relapse prevention, and overdose reversal. We look forward to further implementation of this important law.

Alkermes manufactures VIVITROL[®] (naltrexone for extended-release injectable suspension), an FDA-approved medicine for the prevention of relapse to opioid dependence, following opioid detoxification.

About VIVITROL[®]

VIVITROL (naltrexone for extended-release injectable suspension) is a once-monthly medication for the treatment of alcohol dependence as well as for the prevention of relapse to opioid dependence, following opioid detoxification. VIVITROL is a non-narcotic, non-addictive, once-monthly medication approved for the treatment of opioid dependence. Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support.

IMPORTANT SAFETY INFORMATION

INDICATIONS

VIVITROL 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 [Full Prescribing Information](#) for VIVITROL.

About Alkermes

Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines for the treatment of central nervous system (CNS) diseases. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for chronic diseases that include schizophrenia, depression, addiction and multiple sclerosis. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

¹CDC. Drugs, Brains, and Behavior: Provisional Counts of Drug Overdose Deaths, as of 8/6/2017. Accessed on Oct. 26, 2017 from https://www.cdc.gov/nchs/data/health_policy/monthly-drug-overdose-death-estimates.pdf.