Don’t miss this important presentation

Are We Doing All We Can to Help Reinforce Recovery?

Meeting the Need

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

Friday, June 21, 2019 | 12:00 PM – 1:15 PM
Sagamore Ballroom 6
Indiana Convention Center, Indianapolis, IN

ABOUT THE SPEAKERS

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During this interactive program, these esteemed addiction-treatment professionals will review the management of opioid and alcohol dependence, with a focus on VIVITROL® (naltrexone for extended-release injectable suspension).

Lunch will be served.

Guests and spouses of attendees may not attend the presentation or consume any meals associated with it. This is a promotional program sponsored by Alkermes, Inc. Dr. Leahy and Dr. Cohen are paid consultants of Alkermes, Inc. This is a non-CE presentation and is not eligible for CE credits.

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

For additional Important Safety Information about VIVITROL, please see Brief Summary of Prescribing Information on adjacent pages.

This promotional, non-CE program is sponsored by: Alkermes® Vivitrol® (naltrexone for extended-release injectable suspension)

For related resources, visit MeetingTheNeed.com.

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VIV-004065-v2

Vivitrol®

(naltrexone for extended-release injectable suspension)

VIVITROL® (naltrexone for extended-release injectable suspension) Intramuscular

BRIEF SUMMARY See package insert for full prescribing information (rev. Dec. 2018).

INDICATIONS AND USAGE: VIVITROL contains naltrexone, an opioid antagonist, and 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. In addition, VIVITROL is indicated for the 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, patients with current physiologic opioid dependence, patients in acute opioid withdrawal, any individual who has failed the naloxone challenge test or has a positive urine screen for opioids, and patients who have previously 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 reduced tolerance to opioids. VIVITROL blocks the effects of exogenous opioids for approximately 28 days after administration. However, as the blockade wanes and eventually dissipates completely, patients who have been treated with VIVITROL may respond to lower doses of opioids than previously used, just as they would have shortly after completing detoxification. This could result in potentially life threatening opioid intoxication (respiratory compromise or arrest, circulatory collapse, etc.) if the patient uses previously tolerated doses of opioids. 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 should be alerted that they may be more sensitive to opioids, even at lower doses, after VIVITROL treatment is discontinued, especially at the end of a dosing interval (i.e., near the end of the month that VIVITROL was administered), or after a dose of VIVITROL is missed. It is important that patients inform family members and the people closest to the patient of this increased sensitivity to opioids and the risk of overdose. There is also the possibility that a patient who is treated with VIVITROL could overcome the opioid blockade effect of VIVITROL. 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 antagonism by taking opioids is especially dangerous and may lead to life-threatening opioid intoxication or 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. In the clinical trials, one patient developed an area of induration that continued to enlarge after 4 weeks, with subsequent development of necrotic tissue that required surgical excision. In the post marketing period, additional cases of injection site reaction with features including induration, cellulitis, hematoma, abscess, sterile abscess, and necrosis, have been reported. Some cases required surgical intervention, including debridement of necrotic tissue. Some cases resulted in significant scarring. The reported cases occurred primarily in female patients. VIVITROL is administered as an intramuscular gluteal injection, and inadvertent subcutaneous injection of VIVITROL may increase the likelihood of severe injection site reactions. 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 the proper needle is selected and that the needle length is adequate for intramuscular administration. Healthcare professionals 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. Patients should be informed that any concerning injection site reactions should be brought to the attention of the healthcare professional. Patients exhibiting signs of abscess, cellulitis, necrosis, or extensive swelling should be evaluated by a physician to determine if referral to a surgeon is warranted. **Precipitation of Opioid Withdrawal:** The symptoms of spontaneous opioid withdrawal (which are associated with the discontinuation of opioid in a dependent individual) are uncomfortable, but they are not generally believed to be severe or necessitate hospitalization. However, when withdrawal is precipitated abruptly by the administration of an opioid antagonist to an opioid-dependent patient, the resulting withdrawal syndrome can be severe enough to require hospitalization. Review of postmarketing cases of precipitated opioid withdrawal in association with naltrexone treatment has identified cases with symptoms of withdrawal severe enough to require hospital admission, and in some cases, management in the intensive care unit. To prevent occurrence of precipitated withdrawal in patients dependent on opioids, or exacerbation of a pre-existing subclinical withdrawal syndrome, 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 precipitation of withdrawal symptoms 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. In every case, healthcare providers should always be prepared to manage withdrawal symptomatically with non-opioid medications because there is no completely reliable method for determining whether a patient has had an adequate opioid-free period. A naloxone challenge test may be helpful; however, a few case reports have indicated that patients may experience precipitated withdrawal despite having a negative urine toxicology screen or tolerating a naloxone challenge test (usually in the setting of transitioning from buprenorphine treatment). Patients should be made aware of the risks associated with precipitated withdrawal and encouraged to give an accurate account of last opioid use. Patients treated for alcohol dependence with VIVITROL should also be assessed for underlying opioid dependence and for any recent use of opioids prior to initiation of treatment with VIVITROL. Precipitated opioid withdrawal has been observed in alcohol-dependent patients in circumstances where the prescriber had been unaware of the additional use of opioids or co-dependence on opioids. **Hepatotoxicity:** Cases of hepatitis and clinically significant liver dysfunction were observed in association with VIVITROL exposure during the clinical development program and in the postmarketing period. Transient, asymptomatic hepatic transaminase elevations were also observed in the clinical trials and postmarketing period. Although patients with clinically significant liver disease were not systematically studied, clinical trials did include patients with asymptomatic viral hepatitis infections. When patients presented with elevated transaminases, there were often other potential causative or contributory etiologies identified, including pre-existing alcoholic liver disease, hepatitis B and/or C infection, and concomitant usage of other potentially hepatotoxic drugs. Although clinically significant liver dysfunction is not typically recognized as a manifestation of opioid withdrawal, opioid withdrawal that is precipitated abruptly may lead to systemic sequelae including acute liver injury. Patients should be warned of the risk of hepatic injury and advised to seek medical attention if they experience symptoms of acute hepatitis. Use of VIVITROL should be discontinued in the event of symptoms and/or signs of acute hepatitis. **Depression and Suicidality:** Alcohol- and opioid-dependent patients, including those taking VIVITROL, should be monitored for the development of depression or suicidal thinking. Families and caregivers of patients being treated with VIVITROL should be alerted to the need to monitor patients for the emergence of symptoms of depression or suicidality, and to report such symptoms to the patient's healthcare provider. Alcohol Dependence: In controlled clinical trials of VIVITROL administered to adults with alcohol dependence, adverse events of a suicidal nature (suicidal ideation, suicide attempts, completed suicides) were infrequent overall, but were more common in patients treated with VIVITROL than in patients treated with placebo (1% vs 0%). In some cases, the suicidal thoughts or behavior occurred after study discontinuation, but were in the context of an episode of depression that began while the patient was on study drug. Two completed suicides occurred, both involving patients treated with VIVITROL. Depression-related events associated with premature discontinuation of study drug were also more common in patients treated with VIVITROL (~1%) than in placebo-treated patients (0%). In the 24-week, placebo-controlled pivotal trial in 624 alcohol-dependent patients, adverse events involving depressed mood were reported by 10% of patients treated with VIVITROL 380 mg, as compared to 5% of patients treated with placebo injections. Opioid Dependence: In an open-label, long-term safety study conducted in the US, adverse events of a suicidal nature (depressed mood, suicidal ideation, suicide attempt) were reported by 5% of opioid-dependent patients treated with VIVITROL 380 mg (n=101) and 10% of opioid-dependent patients treated with oral naltrexone (n=20). In the 24-week, placebo-controlled pivotal trial that was conducted in Russia in 250 opioid-dependent patients, adverse events involving depressed mood or suicidal thinking were not reported by any patient in either treatment group (VIVITROL 380 mg or placebo).

Vivitrol®

(naltrexone for extended-release injectable suspension)

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. If opioid therapy is required as part of anesthesia or analgesia, patients should be continuously monitored in an anesthesia care setting by persons not involved in the conduct of the surgical or diagnostic procedure. The opioid therapy must be provided by individuals specifically trained in the use of anesthetic drugs and the management of the respiratory effects of potent opioids, specifically the establishment and maintenance of a patent airway and assisted ventilation. Irrespective of the drug chosen to reverse VIVITROL blockade, the patient should be monitored closely by appropriately trained personnel in a setting equipped and staffed for cardiopulmonary resuscitation. **Eosinophilic Pneumonia:** In clinical trials with VIVITROL, there was one diagnosed case and one suspected case of eosinophilic pneumonia. Both cases required hospitalization, and resolved after treatment with antibiotics and corticosteroids. Similar cases have been reported in postmarketing use. Should a person receiving VIVITROL develop progressive dyspnea and hypoxemia, the diagnosis of eosinophilic pneumonia should be considered. Patients should be warned of the risk of eosinophilic pneumonia, and advised to seek medical attention should they develop symptoms of pneumonia. Clinicians should consider the possibility of eosinophilic pneumonia in patients who do not respond to antibiotics. **Hypersensitivity Reactions Including Anaphylaxis:** Cases of urticaria, angioedema, and anaphylaxis have been observed with use of VIVITROL in the clinical trial setting and in postmarketing use. Patients should be warned of the risk of hypersensitivity reactions, including anaphylaxis. In the event of a hypersensitivity reaction, patients should be advised to seek immediate medical attention in a healthcare setting prepared to treat anaphylaxis. The patient should not receive any further treatment with VIVITROL. **Intramuscular Injections:** As with any intramuscular injection, VIVITROL should be administered with caution to patients with thrombocytopenia or any coagulation disorder (eg, hemophilia and severe hepatic failure). **Alcohol Withdrawal:** Use of VIVITROL does not eliminate nor diminish alcohol withdrawal symptoms. **Interference with Laboratory Tests:** VIVITROL may be cross-reactive with certain immunoassay methods for the detection of drugs of abuse (specifically opioids) in urine. For further information, reference to the specific immunoassay instructions is recommended.

ADVERSE REACTIONS: Clinical Studies Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In all controlled and uncontrolled trials during the premarketing development of VIVITROL, more than 1100 patients with alcohol and/or opioid dependence have been treated with VIVITROL. Approximately 700 patients have been treated for 6 months or more, and more than 400 for 1 year or longer. Adverse Events Leading to Discontinuation of Treatment: *Alcohol Dependence*: In controlled trials of 6 months or less in alcohol-dependent patients, 9% of alcohol-dependent patients treated with VIVITROL discontinued treatment due to an adverse event, as compared to 7% of the alcohol-dependent patients treated with placebo. Adverse events in the VIVITROL 380-mg group that led to more dropouts than in the placebo-treated group were injection site reactions (3%), nausea (2%), pregnancy (1%), headache (1%), and suicide-related events (0.3%). In the placebo group, 1% of patients withdrew due to injection site reactions, and 0% of patients withdrew due to the other adverse events. *Opioid Dependence*: In a controlled trial of 6 months, 2% of opioid-dependent patients treated with VIVITROL discontinued treatment due to an adverse event, as compared to 2% of the opioid-dependent patients treated with placebo. Common Adverse Reactions: *Alcohol Dependence*: The adverse events seen most frequently in association with VIVITROL therapy for alcohol dependence (ie, 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), arthralgia, arthritis, or joint stiffness, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders. *Opioid Dependence*: The adverse events seen most frequently in association with VIVITROL therapy in opioid dependent patients (ie, those occurring in ≥2% and at least twice as frequently with VIVITROL than placebo) were hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.

DRUG INTERACTIONS: Patients taking VIVITROL may not benefit from opioid-containing medicines. Naltrexone antagonizes the effects of opioid-containing medicines, such as cough and cold remedies, antidiarrheal preparations and opioid analgesics.

USE IN SPECIFIC POPULATIONS: Pregnancy: Risk Summary: The available data from published case series with VIVITROL use in pregnant women are insufficient to identify a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are clinical considerations (see *Clinical Considerations*). Reproduction and developmental animal studies have not been conducted for VIVITROL. Daily oral administration of naltrexone to female rats and rabbits increased the incidence of early fetal loss at exposures ≥ 11 times and ≥ 2 times the human exposure, respectively. Daily oral administration of naltrexone to pregnant rats and rabbits during the period of organogenesis did not induce malformation at exposures up to 175 times and 14 times the human exposure, respectively (*see Data*). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Clinical Considerations: *Disease-associated maternal and embryo-fetal risk*: Untreated opioid addiction in pregnancy is associated with adverse obstetrical outcomes such as low birth weight, preterm birth, and fetal death. In addition, untreated opioid addiction often results in continued or relapsing illicit opioid use. Published studies have demonstrated that alcohol is associated with fetal harm including growth restriction, facial abnormalities, central nervous system abnormalities, behavioral disorders, and impaired intellectual development. Data: *Animal Data*: Reproduction and developmental studies have not been conducted for VIVITROL. Studies with naltrexone administered via the oral route have been conducted in pregnant rats and rabbits. Daily oral administration of naltrexone has been shown to increase the incidence of early fetal loss when given to rats at doses ≥30 mg/kg/day (11 times the human exposure based on an $AUC_{(0\text{-}28d)}$ comparison) and to rabbits at oral doses ≥60 mg/kg/day (2 times the human exposure based on an AUC(0-28d) comparison). Daily oral administration of naltrexone to rats and rabbits during the period of organogenesis did not induce malformations at doses up to 200 mg/kg/day (175- and 14-times the human exposure based on an $AUC_{(0\text{-}28d)}$ comparison, respectively). **Lactation**: Risk Summary: Naltrexone and its major metabolite, 6-naltrexol, are present in human milk. There are no data on the effects on the breastfed infant or the effects on milk production. The developmental health benefits of breastfeeding should be considered along with the mother's clinical need for naltrexone and any potential adverse effects on the breastfed infant from naltrexone or the mother's underlying maternal condition. **Pediatric Use:** The safety and efficacy of VIVITROL have not been established in the pediatric population. The pharmacokinetics of VIVITROL have not been evaluated in a pediatric population. **Geriatric Use:** In trials of alcohol-dependent subjects, 2.6% (n=26) of subjects were >65 years of age, and one patient was >75 years of age. Clinical studies of VIVITROL did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects. No subjects over age 65 were included in studies of opioid-dependent subjects. The pharmacokinetics of VIVITROL have not been evaluated in the geriatric population. This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function. **Renal Impairment:** Pharmacokinetics of VIVITROL are not altered in subjects with mild renal insufficiency (creatinine clearance of 50-80 mL/min). Dose adjustment is not required in patients with mild renal impairment. VIVITROL pharmacokinetics have not been evaluated in subjects with moderate and severe renal insufficiency. Because naltrexone and its primary metabolite are excreted primarily in the urine, caution is recommended in administering VIVITROL to patients with moderate to severe renal impairment. **Hepatic Impairment:** The pharmacokinetics of VIVITROL are not altered in subjects with mild to moderate hepatic impairment (Groups A and B of the Child-Pugh classification). Dose adjustment is not required in subjects with mild or moderate hepatic impairment. VIVITROL pharmacokinetics were not evaluated in subjects with severe hepatic impairment.

OVERDOSAGE: There is limited experience with overdose of VIVITROL. Single doses up to 784 mg were administered to 5 healthy subjects. There were no serious or severe adverse events. The most common effects were injection site reactions, nausea, abdominal pain, somnolence, and dizziness. There were no significant increases in hepatic enzymes. In the event of an overdose, appropriate supportive treatment should be initiated.

This brief summary is based on VIVITROL Full Prescribing Information (rev. December 2018).

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