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

Quiz Results
Update on the Impact and Treatment of Opioid Dependence

Note: A total of 1034 completed quizzes were received as of August 28, 2018.

Question 1 of 5: In 2016, nearly ____ American adults had an opioid use disorder, about ____ of whom had a heroin use disorder.

Finding: About one-third of respondents underestimated the number of Americans with a heroin use disorder.

Commentary from Laura P. Bamford, M.D., M.S.C.E.*: We also should not overlook the impact of synthetic opioids. According to the Centers for Disease Control and Prevention (CDC), among opioid-involved deaths in 2016, the most commonly involved drugs were synthetic opioids other than methadone† (primarily illicitly manufactured fentanyl). In fact, rates of drug overdose deaths involving synthetic opioids other than methadone increased by 87% annually from 2013 to 2016. Unfortunately, National Vital Statistics System data are unable to distinguish between deaths involving pharmaceutical versus illicit synthetic opioids.

Explanation
According to the Substance Abuse and Mental Health Services Administration (SAMHSA) National Survey on Drug Use and Health, approximately 1,991,000 American adults had an opioid use disorder in 2016, about 625,000 of whom had a heroin use disorder. Compared with the 2015 SAMHSA survey, the latest data represent a decline in opioid use disorder overall (from 2,248,000 in 2015) but an increase in heroin use disorder (from 585,000 in 2015). For further discussion of the prevalence and mortality associated with opioid use disorder, see Issue 1 of the Opioid Dependence Newsletter Series, available on this website.

For complete information, see:

*Member of the Meeting the Need Steering Committee and paid consultant of Alkermes, Inc.
†This analysis also excluded buprenorphine formulations used for the treatment of opioid use disorder.

Please see Prescribing Information and Medication Guide. Review the Medication Guide with your patients.
Question 2 of 5: A retrospective cohort study found that from 2010 to 2014 the proportion of commercially insured Americans diagnosed with opioid use disorder ______ and the proportion of months that this population received medication for opioid use disorder ______.

Finding: More than half of respondents did not realize that the proportion of patients receiving medication-assisted treatment (MAT) for diagnosed opioid use disorder appears to be trending down.

Commentary from Dr. Bamford*: The finding of MAT underutilization in this study is consistent with the SAMHSA estimate that nearly 80% of those with opioid use disorder do not receive treatment. However, more recent data suggest that this estimate might be changing for the better: A published review of prescription data found that new starts of MAT for opioid dependence nearly doubled from December 2015 to December 2017, from 44,000 to 82,000 new starts per month.

Commentary from Dr. Jeffrey A. Berman, M.D., DFASAM*: In Treatment Improvement Protocol (TIP) 63, published in 2018, SAMHSA notes that, although patients can take medication for opioid use disorder on a short- or long-term basis, those who discontinue treatment generally return to illicit opioid use. SAMHSA advises providers and patients to base decisions about discontinuing medication on knowledge of the evidence base for the use of these medications, individualized assessments, and an individualized treatment plan that is collaboratively developed and agreed upon. SAMHSA notes that arbitrary time limits on the duration of treatment with medication for opioid use disorder are inadvisable.

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Please see Prescribing Information and Medication Guide. Review the Medication Guide with your patients.
Explanation

A retrospective cohort study published in 2018 examined the prevalence of opioid use disorder from 2010 to 2014, along with prescribing patterns during this time period for extended-release naltrexone, oral naltrexone, sublingual or oral-mucosal buprenorphine/naloxone, and sublingual and transdermal buprenorphine. This analysis utilized a nationally representative, claims-based database of commercially insured Americans.

The study found that although the proportion of commercially insured individuals diagnosed with opioid use disorder increased 4-fold from 2010 to 2014, the proportion of months that this population received medication actually decreased during this time period, from 25% to 16%. Note that this study included medications available only from an outpatient pharmacy. Therefore, methadone use was not considered in this analysis.

For a discussion of barriers to medication-assisted treatment, see Issue 2 of the Opioid Dependence Newsletter Series, available on this website.

For complete information, see:
Question 3 of 5: Which of the following is true about partial agonist medications for the treatment of opioid dependence?

**Finding:** Most respondents were familiar with these properties of partial agonist medications. However, 5% of respondents were apparently unaware that partial agonist medications can be used for maintenance treatment as well as for management of withdrawal symptoms during opioid detoxification.

**Commentary from Dr. Bamford**: As prescribers, it is important for us to be aware of the specific properties of medications for the treatment of opioid dependence.

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**Correct Answer**

A. They can suppress opioid withdrawal and block the effects of other opioids; therefore they are effective for managing withdrawal symptoms during detoxification as well as for maintenance treatment.

B. Some dosage forms require that each dose be administered by a licensed healthcare provider.

C. They are Schedule III controlled substances.

D. All of the above.

**Explanation**

Because partial agonist medications can suppress opioid withdrawal, they are effective for managing withdrawal symptoms during opioid detoxification. In addition, because they can block the effects of other opioids, they are an effective option for maintenance treatment of opioid dependence. Furthermore, while some dosage forms of partial agonist medication require only initial administration by a healthcare provider (HCP), others require that each dose be given by an HCP. Finally, all partial agonist medications are Schedule III controlled substances.

For further discussion of medication-assisted treatment options, see [Issue 2 of the Opioid Dependence Newsletter Series](https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/substanceuse.pdf), available on this website.

For complete information, see:


*Member of the [Meeting the Need](#) Steering Committee and paid consultant of Alkermes, Inc.*
Question 4 of 5: Which of the following is TRUE about opioid antagonist medications used to treat opioid dependence?

**Finding:** Most respondents were familiar with these properties of opioid antagonist medications. However, nearly 20% of respondents were unaware that these medications have no known abuse potential, 15% were unaware that they do not produce withdrawal symptoms after discontinuation, and more than 10% were unaware that they are not associated with tolerance or dependence.

**Commentary from Dr. Bamford:** All prescribers also should be aware that, as opioid antagonist medication effects wane and eventually dissipate completely, the use of previously tolerated doses of opioids could result in potentially life-threatening opioid intoxication. Please refer to the Important Safety Information below for more information.

**Commentary from Dr. Berman:** I think we also should point out that opioid antagonist medications are not scheduled by the Drug Enforcement Agency, and they do not require a special waiver to be prescribed.

**Explanation**

Opioid antagonist medications used for MAT bind to mu opioid receptors in the brain, blocking the receptor from opioid agonist drugs. They do not activate the opioid receptor, so there is no excessive stimulation of the dopamine reward system.

For further discussion of opioid antagonist medication, see Issue 2 of the Opioid Dependence Newsletter Series, available on this website.

For complete information, see:


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Question 5 of 5: True or False: Opioid antagonist medication for opioid dependence has never been compared with partial agonist medication in a head-to-head study.

Finding: Half of respondents were unaware that opioid antagonist and partial agonist medications have now been compared in multiple head-to-head studies.

Commentary from Dr. Berman*: It’s terrific that we now have more data to help guide us when presenting MAT options to our patients with opioid dependence. All prescribers of MAT should become familiar with these studies.

Explanation
In 2017, the results of 2 multicenter, open-label, randomized clinical trials were published comparing an antagonist medication (extended-release naltrexone) with a partial agonist combination medication (buprenorphine-naloxone) for the prevention of relapse to opioid dependence after detoxification.\(^1^,\(^2\) One was a 12-week Norwegian trial that enrolled 159 patients, and the other was a 24-week US trial that enrolled 570 patients.\(^2\) In both trials, antagonist treatment was found to be non-inferior to treatment with the partial agonist combination medication in terms of relapse rates in patients who had successful detoxification before treatment.\(^2\) (In the 24-week trial, which included the detoxification step after randomization, difficulty initiating antagonist treatment in some patients negatively affected overall relapse rates.\(^2\))

To learn more about these recent publications, see Issue 4 of the Opioid Dependence Newsletter Series.

For complete information, see:

*Member of the Meeting the Need Steering Committee and paid consultant of Alkermes, Inc.

For more information on the impact, prevalence, and treatment of opioid dependence, please refer to the Opioid Dependence Newsletter Series.
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 intramuscular 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
The adverse events seen most frequently in association with VIVITROL therapy for alcohol dependence (ie, those occurring in ≥25% 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.

The adverse events seen most frequently in association with VIVITROL 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.

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.