



BTOD|REMS

IMPORTANT DRUG WARNING

Subject: Risk Evaluation and Mitigation Strategy (REMS) for buprenorphine-containing transmucosal products for opioid dependence due to their risks of accidental overdose, misuse, and abuse.

Dear Prescriber:

You are receiving this letter because you are a prescriber certified to treat opioid dependence under the Drug Addiction Treatment Act of 2000 (DATA 2000).

The purpose of this letter is to inform you of a Risk Evaluation and Mitigation Strategy (REMS) called the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS program. This REMS does not apply to buprenorphine-containing products that are dispensed to patients in an Opioid Treatment Program (OTP) under 42 CFR Part 8.

The FDA has determined that a REMS is necessary to ensure that the benefits of buprenorphine-containing transmucosal products for opioid dependence outweigh the potential risks of accidental overdose, misuse, and abuse. Buprenorphine, like morphine and other opioids, has the potential for being abused and misused. Abuse of buprenorphine poses a risk of overdose and death. This risk is increased with the concomitant use of buprenorphine and alcohol and other central nervous system (CNS) depressants, especially benzodiazepines. Products containing buprenorphine only are indicated for the treatment of opioid dependence and are preferred for induction. Products containing buprenorphine with naloxone are indicated for the maintenance treatment of opioid dependence and may be appropriate for induction in patients physically dependent on heroin and other short-acting opioids. These products should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Prescriber Action

To meet the requirements of the REMS and to ensure the benefits of prescribing buprenorphine-containing products outweigh the risks of accidental overdose, misuse, and abuse, prescribers should take the following measures and document actions taken with each patient to ensure safe use conditions:

- Verify the patient meets appropriate diagnostic criteria for opioid dependence.
- Check patient's prescription profile in the Prescription Drug Monitoring Program, as appropriate, and review all medications (e.g., benzodiazepines, other opioids, CNS depressants) and illicit substances to assess for appropriateness of co-prescribing.
- **Discuss the risks** (including misuse and abuse) **and side effects** associated with buprenorphine-containing products, including those described in the Medication Guide.
- Explain what patients should do if they experience side effects.
- Explain how to store buprenorphine-containing products safely out of the sight and reach of all others, especially children.
- Strongly consider prescribing naloxone because patients being treated for opioid use disorder have the potential for relapse, putting them at risk for opioid overdose.
- Discuss the importance of having access to naloxone with patient and caregiver, if there are household members (including children) or other close contacts at risk for accidental ingestion or opioid overdose.
- If naloxone is prescribed, also advise patients and caregivers:
 - How to treat with naloxone in the event of an opioid overdose
 - To tell family and friends about their naloxone and to keep it in a place where family and friends can easily access it in an emergency
 - To read the Patient Information (or other educational material) that will come with their naloxone. Emphasize the importance of doing this before an opioid emergency happens, so the patient and caregiver will know what to do.
- Provide induction doses under appropriate supervision.
- Prescribe a limited amount of medication to the patient that will last until the next visit.
- Schedule patient appointments commensurate with patient stability (weekly or more frequent visits recommended for the first month).
- Consider "pill/film count"/dose reconciliation.
- Assess whether the patient is receiving the counseling/psychosocial support considered necessary for treatment **and if not, encourage them to do so.**
- Assess whether the patient is making progress toward treatment goals (including, as appropriate, urine toxicology testing).
- Continually assess appropriateness of maintenance dose.
- Continually assess whether or not benefits of treatment outweigh the risks.

Serious Risks of Buprenorphine-containing Products

The following key messages need to be communicated to patients about safe use of products covered under the REMS to mitigate **the serious risks of accidental overdose, misuse, and abuse**:

- **Instruct patients to keep buprenorphine-containing products in a secure place, out of the sight and reach of all others, especially children. Accidental or deliberate ingestion by a child may cause respiratory depression that can result in death. Advise patients to seek medical attention immediately if a child is exposed to one of these products.**
- Warn patients that it is extremely dangerous to self-administer non-prescribed benzodiazepines or other CNS depressants (including alcohol) with these products. Caution patients prescribed benzodiazepines or other CNS depressants to use them only as directed by their prescriber.
- Advise patients to never give buprenorphine-containing products to anyone else, even if he or she has the same signs and symptoms. They may cause harm or death.
- Discuss the availability of naloxone for the emergency treatment of opioid overdose for the patient, household members (including children), or other close contacts at risk for accidental ingestion or opioid overdose .
- Strongly consider prescribing naloxone along with buprenorphine-containing products. Consider the potential for relapse, the risk for opioid overdose, the risk to close contacts for accidental ingestion or opioid overdose, and the risk from concomitant use of CNS depressants.
- Advise patients that buprenorphine-containing products contain an opioid that can be a target for people who abuse prescription medications or street drugs. Caution patients to keep buprenorphine-containing products in a secure and safe place, out of the sight and reach of all others, especially children, and to protect them from theft.
- Advise patients that selling or giving away these products is against the law.
- **Use the contents of each BTOD drug product's Medication Guide**, in its entirety, with each patient to review the information noted above, including side effects and what to do if a patient has them. The Medication Guide will be dispensed with each prescription for a buprenorphine-containing transmucosal product.
- **Encourage patients to seek psychosocial counseling and support for safe and effective treatment.**

Patient Monitoring and Appropriate Dosing Info

An **Appropriate Use Checklist** is enclosed to assist you in performing and documenting the above prescriber actions of the BTOD REMS. Use the enclosed checklist or other means (e.g. electronic health record) specific to your office practice to document that the above actions have been completed for each patient.

Reporting Adverse Events

To report SUSPECTED ADVERSE EVENTS contact:

- The manufacturer of the product taken or
- FDA MedWatch program by phone at 1-800-FDA-1088 or online at www.fda.gov/medwatch/report.htm

This letter is not a comprehensive description of the risks associated with the use of buprenorphine-containing transmucosal products. Additional important safety information can be found in the **Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers** educational brochure and Prescribing Information.

Additional copies of the educational brochure, **Appropriate Use Checklist**, Prescribing Information, and Medication Guide for each product covered under the BTOD REMS, can be obtained at <https://www.btodrems.com/> or by contacting the toll-free call center at 1-855-223-3922.

Sincerely,

The Buprenorphine-containing Transmucosal products for Opioid Dependence Companies

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Enclosures: *Appropriate Use Checklist*
Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescriber