The Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD)

A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure that the benefits of a drug outweigh its risks.

The purpose of the BTOD REMS program is to inform healthcare professionals and patients about the safe use conditions and serious risks, including accidental overdose, misuse, and abuse, associated with buprenorphine-containing transmucosal products indicated for the treatment of opioid dependence.

**Prescribers should:**

- **Verify** that patients meet diagnostic criteria for opioid dependence
- **Counsel** patients and/or their caregivers on safe use of the product, including appropriate storage and disposal, and risks associated with treatment, at each visit
- **Monitor and document** safe use conditions for each patient by using the [Appropriate Use Checklist](#) (or by other means specific to office practice)
- **Assess** appropriateness of treatment and adequate progress towards treatment goals for each patient

To prescribe products covered under the BTOD REMS, a prescriber must be certified to treat opioid dependence under the Drug Addiction Treatment Act of 2000 (DATA 2000). For certification information, [click here](#).

[Click here for a complete list of products covered under the BTOD REMS program](#)

This REMS does not apply to buprenorphine-containing products indicated for the treatment of pain or for products dispensed to patients admitted to Opioid Treatment Programs (OTP) under 42 CFR part 8.
Important Safety Information

The drug products subject to the Buprenorphine-Containing Transmucosal products for Opioid Dependence (BTOD) REMS® includes:

- Generic equivalents of Subutex® (buprenorphine hydrochloride) sublingual tablet
- Generic equivalents of Suboxone® (buprenorphine hydrochloride/naloxone hydrochloride) sublingual tablet
- Zubsolv® (buprenorphine/naloxone) sublingual tablet
- Bunavail™ (buprenorphine hydrochloride/naloxone hydrochloride) buccal film

These products, collectively referred to as “buprenorphine-containing products”, are delivered by the oral transmucosal route and are indicated for use during treatment of opioid dependence as part of a comprehensive treatment plan to include counseling and psychological support. Treatment must be initiated under the direct or of prescribers qualified under the Drug Addict treatment Act of 2000.

Buprenorphine-containing products must not be used by patients with hypersensitivity to buprenorphine, and/or naloxone in the case of combination products.

Buprenorphine-containing products can be abused in a manner similar to other opioids, legal or illegal. Close monitoring appropriate to the patient’s level of stability is essential.

Children who ingest buprenorphine-containing products can have severe, possibly fatal, respiratory depressions. Emergency medical care is critical. Keep buprenorphine-containing products out of the sight and reach of children.

Buprenorphine-containing products can cause serious life-threatening respiratory depressions on death, particularly when taken by the intravenous (IV) route in combination with benzodiazepines or other central nervous system (CNS) depressants (e.g., sedatives, tranquilizers, or alcohol). It is extremely dangerous to self-administer nonprescribed benzodiazepines or other CNS depressants while taking buprenorphine-containing products. When buprenorphine-containing products are taken together with CNS depressants, dose reduction of either product(s) should be considered.

Death has been reported in intolerant, nondependent individuals who received a 2 mg dose for analgesia. The products covered under this REMS are not appropriate for use as an analgesic.

Chronic use of buprenorphine can cause physical dependence. A sudden or rapid decrease in dose may result in an opioid withdrawal syndrome that is typically milder than seen with full agonists (e.g., heroin, hydrocodone, methadone, morphine, oxycodone) and may be delayed in onset. Intravenous misuse or taking buprenorphine-containing products before the effects of full agonist opioids have subsided is highly likely to cause opioid withdrawal symptoms.

Liver function should be monitored before and during treatment.

Use of buprenorphine-containing products in pregnant women or during breast-feeding should only be considered if the potential benefit justifies the potential risk. Neonatal withdrawal has been reported.

Cautions should be exercised when driving vehicles or operating hazardous machinery, especially during dose adjustment.

Adverse events most commonly observed with the sublingual administration of buprenorphine during clinical trials and post-marketing experience are headache, nausea, vomiting, hypotension, constipation, signs and symptoms of withdrawal, insomnia, and pain. An additional adverse event among those most commonly observed with sublingual administration of buprenorphine/naloxone formulation is peripheral edema.

Cytolytic cholestatic jaundice, and allergic reactions, including anaphylaxis and shock, have been reported. Adverse events most commonly observed with the buccal administration of the buprenorphine/naloxone formulation were signs and symptoms of withdrawal and headache.

This is not a complete list of potential adverse events associated with buprenorphine-containing products. Please see Full Prescribing Information for each specific product for a complete list.

For more information on the BTOD REMS, including all program materials and instructions call 1-855-223-3922.

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

Please see Full Prescribing Information and Medication Guide for all buprenorphine-containing products.
### Buprenorphine Single Ingredient Products

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### Buprenorphine/Naltrexone Combination Ingredient Products

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The REMS attests that the table above will only include products listed in the link titled 'List of approved application numbers and sponsors' on the FDA Approved REMS website.

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Materials for Prescribers:
- **Dear Prescriber Letter**
- **Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers**
- **Appropriate Use Checklist**

Materials for Pharmacists:
- **Dear Pharmacist Letter**
- **Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists**

Materials for Patients:
- **Medication Guides**

For more information or to receive print copies of the materials, please call: 1-855-223-3922.
Getting Certified

Under the Drug Addiction Treatment Act of 2000 (DATA 2000), prescription use of buprenorphine-containing products in the treatment of opioid dependence is limited to prescribers who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.

To become certified to prescribe buprenorphine-containing products, you will need to follow certification guidelines set by DATA 2000.

Detailed information about DATA 2000, qualifications, notifying SAMHSA, and the general prescriber waiver process can be found at buprenorphine.samhsa.gov, or by contacting SAMHSA directly:

**SAMHSA Buprenorphine Information Center**  
Phone: 1-866-287-2729 (866-BUP-CSAT)  
E-mail: info@buprenorphine.samhsa.gov

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