



December 6, 2010

Dear Prescriber:

The purpose of this communication is to notify you that a Risk Evaluation and Mitigation Strategy (REMS) has been instituted for Butrans™.

The Butrans™ REMS is deemed necessary by the U.S. Food and Drug Administration (FDA) to ensure that the benefits of Butrans™ outweigh its potential risk of misuse, abuse, overdose and addiction to Butrans™. Butrans™ contains buprenorphine, a partial agonist at the mu-opioid receptor and a Schedule III controlled substance. Butrans™ can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Butrans™ in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, overdose, and addiction.

Butrans™ is indicated for the management of moderate to severe chronic pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. Butrans™ has not been studied and is not approved for use in the management of addictive disorders.

The goals of the Butrans™ REMS program are:

Goal 1: To inform patients and healthcare professionals about the potential for misuse, abuse, and overdose from, and addiction to Butrans™.

Goal 2: To inform patients and healthcare professionals about the safe use of Butrans™.

Butrans™ is contraindicated in:

- patients who have significant respiratory depression
- patients who have severe bronchial asthma
- patients who have or are suspected of having paralytic ileus
- patients with known hypersensitivity to any of its components or the active ingredient, buprenorphine
- the management of acute pain or in patients who require opioid analgesia for a short period of time
- the management of post-operative pain, including use after out-patient or day surgeries
- the management of mild pain
- the management of intermittent pain (e.g., use on an as-needed basis [prn])

Safe Use, Storage and Disposal

The buprenorphine contained in Butrans™ is supplied in sealed transdermal systems in packages which pose little risk of exposure to health care workers. If the adhesive from the drug matrix accidentally contacts the skin, the area should be washed with water. Do not use soap, alcohol, or other

solvents to remove the adhesive because they may enhance the absorption of the drug.

When changing the system, remove the Butrans™ patch, fold it over on itself, and flush it down the toilet. Alternatively, Butrans™ can be sealed in the Patch-Disposal Unit provided and then disposed of in the trash. Butrans™ should never be thrown away in the trash without sealing it in the Patch-Disposal Unit. Apply immediately after removal from the individually sealed package. Do not use a Butrans™ patch if the pouch seal is broken or the patch is cut, damaged, or changed in any way.

Misuse and Abuse

Abuse may occur by applying the transdermal system in the absence of legitimate purpose, or by ingesting buprenorphine extracted from the transdermal system. The risk of fatal overdose is further increased when buprenorphine is abused concurrently with alcohol or other CNS depressants, including other opioids and benzodiazepines.

In cases of overdose, remove Butrans™ immediately. Even in the face of improvement, continued medical monitoring is required because of the possibility of extended effects as opioid continues to be absorbed from the skin.

Due to the long terminal half-life of buprenorphine (approximately 26 hours) and the relatively short half-life of opioid antagonists, keep the patient under continued surveillance (at least 24 hours) and administer repeated doses of the antagonist according to the antagonist labeling as needed to maintain adequate respiration.

Naloxone may not be effective in reversing any respiratory depression produced by buprenorphine. High doses of naloxone, 10-35 mg/70 kg, may be of limited value in the management of buprenorphine overdose. The onset of naloxone effect may be delayed by 30 minutes or more. Doxapram hydrochloride (a respiratory stimulant) has also been used. Maintenance of adequate ventilation is essential when managing Butrans™ overdose and more important than specific antidote treatment with an opioid antagonist such as naloxone. Please see the full prescribing information for more information about treating overdose.

Patient Counseling

Patients should also be advised to store opioid analgesics, including Butrans™, safely and out of the reach of children, other household members, visitors and pets.

Patients should be instructed against use by individuals other than the patient for whom it was prescribed.

You are strongly advised to discuss the risks associated with Butrans™ with your patients and/or their caregivers and encourage them to read the Medication Guide. This Medication Guide (including Instructions for Use) contains important information on the safe and effective use of Butrans™. The Butrans™ Medication Guide should be provided by the pharmacist to patients every time Butrans™ is dispensed.

A REMS packet containing important information regarding the prescribing of Butrans™ accompanies this letter. Purdue Pharma L.P. encourages you to review the educational material that discuss the risk of misuse, abuse, overdose and addiction from exposure to opioids, how to identify patients who are at risk

for addiction, information to counsel patients on proper safe storage of medications and patch application, removal and disposal.

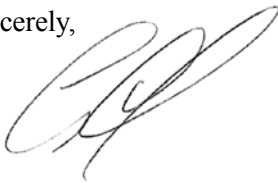
Content of the Butrans™ REMS packet:

- Prescribing Butrans™ (buprenorphine) Transdermal System CIII: A Training Guide for Healthcare Providers
- Butrans™ Training Confirmation Form
- Butrans™ Medication Guide (including Instructions for Use)

As part of the REMS, the FDA has required that Purdue Pharma L.P. provide a Training Guide to healthcare providers. Healthcare providers are asked to please read the training guide received by mail or available at the Butrans™ REMS website (www.butransrems.com). The FDA has also required that a confirmation form be sent to healthcare providers to verify prescriber's understanding of the risks associated with Butrans™ and other information. After reading the Training Guide, healthcare providers are asked to please sign the confirmation form included in this mailing and to mail the confirmation form back in the self-addressed envelope. The confirmation form can also be completed online at the Butrans™ REMS website. Completion of this form does not affect your ability to prescribe Butrans™. There is also an online training course containing the same word-for-word content as the Training Guide available on the Butrans™ REMS website.

Please report any adverse event information associated with the use of Butrans™ to Purdue Pharma L.P., at (888)726-7535 (prompt #2), or to the FDA MedWatch system by phone at (800)FDA-1088, by fax at (800) FDA-0178, or via the Internet at www.FDA.gov/medwatch.

Sincerely,



Craig J. Landau, MD
Chief Medical Officer