CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022410Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SUBOXONE® sublingual film safely and effectively. See full prescribing information for SUBOXONE sublingual film.

SUBOXONE (buprenorphine and naloxone) sublingual film for sublingual administration CIII.
Initial U.S. Approval: 2002

----------INDICATIONS AND USAGE----------

SUBOXONE sublingual film is indicated for maintenance treatment of opioid dependence. Prescription use of this product is limited under the Drug Addiction Treatment Act. (1)

----------DOSAGE AND ADMINISTRATION----------

Administer SUBOXONE sublingual film sublingually as a single daily dose. (2)

The recommended daily dose for maintenance is 16/4 mg.

----------DOSAGE FORMS AND STRENGTHS----------

Sublingual film: 2 mg buprenorphine with 0.5 mg naloxone and 8 mg buprenorphine with 2 mg naloxone. (3)

----------CONTRAINDICATIONS----------

Hypersensitivity to buprenorphine or naloxone. (4)

----------WARNINGS AND PRECAUTIONS----------

- Buprenorphine can be abused in a similar manner to other opioids. Clinical monitoring appropriate to the patient's level of stability is essential. Multiple refills should not be prescribed early in treatment or without appropriate patient follow-up visits. (5.1)
- Significant respiratory depression and death have occurred in association with buprenorphine, particularly when taken by the intravenous (IV) route in combination with benzodiazepines or other CNS depressants (including alcohol). (5.2)
- Consider dose reduction of CNS depressants, SUBOXONE sublingual film, or both in situations of concomitant prescription. (5.3)
- Store SUBOXONE sublingual film safely out of the sight and reach of children. Buprenorphine can cause severe, possibly fatal, respiratory depression in children. (5.4)
- Chronic administration produces opioid-type physical dependence. Abrupt discontinuation or rapid dose taper may result in opioid withdrawal syndrome. (5.5)
- Monitor liver function tests prior to initiation and during treatment and evaluate suspected hepatic events. (5.6)
- Do not administer SUBOXONE sublingual film to patients with known hypersensitivity to buprenorphine or naloxone. (5.7)
- A marked and intense opioid withdrawal syndrome is highly likely to occur with parenteral misuse of SUBOXONE sublingual film by individuals physically dependent on full opioid agonists or by sublingual administration before the agonist effects of other opioids have subsided. (5.8)
- Neonatal withdrawal has been reported following use of buprenorphine by the mother during pregnancy. (5.9)
- SUBOXONE sublingual film is not appropriate as an analgesic. There have been reported deaths of opioid naïve individuals who received a 2 mg sublingual dose. (5.10)
- Caution patients about the risk of driving or operating hazardous machinery. (5.11)

----------ADVERSE REACTIONS----------

Adverse events commonly observed with the sublingual administration of the SUBOXONE sublingual film was oral hypoesthesia, glossodynia, oral mucosal erythema, headache, nausea, vomiting, hyperhidrosis, constipation, signs and symptoms of withdrawal, insomnia, pain, and peripheral edema. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Reckitt Benckiser Pharmaceuticals Inc. at 1-877-782-6966,FDA at 1-800-FDA-1088, or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Monitor patients starting or ending CYP3A4 inhibitors or inducers for potential over or under dosing. (7.1)
- Use caution in prescribing SUBOXONE sublingual film for patients receiving benzodiazepines or other CNS depressants and warn patients against concomitant self-administration/misuse. (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- SUBOXONE sublingual film is not indicated for use during pregnancy unless potential benefit justifies potential risk. (8.1)
- Buprenorphine passes into the mother's milk. Breast-feeding is not advised while taking SUBOXONE sublingual film. (8.3)
- Safety and effectiveness of SUBOXONE sublingual film in patients below the age of 16 has not been established. (8.4)
- Administer SUBOXONE sublingual film with caution to elderly or debilitated patients. (8.5)
- Administer SUBOXONE sublingual film with caution to patients with liver dysfunction. (8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised August 2010

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections and subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

SUBOXONE sublingual film is indicated for maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians 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.

2 DOSAGE AND ADMINISTRATION

SUBOXONE sublingual film is administered sublingually as a single daily dose. SUBOXONE sublingual film should be used in patients who have been initially inducted using Subutex (buprenorphine) sublingual tablets.

2.1 Maintenance

- SUBOXONE sublingual film is indicated for maintenance treatment. The recommended target dosage of SUBOXONE sublingual film is 16/4 mg buprenorphine/naloxone/day as a single daily dose.
- The dosage of SUBOXONE sublingual film should be progressively adjusted in increments/decrements of 2/0.5 mg or 4/1 mg buprenorphine/naloxone to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.
- The maintenance dose of SUBOXONE sublingual film is generally in the range of 4/1 mg buprenorphine/naloxone to 24/6 mg buprenorphine/naloxone per day depending on the individual patient. Dosages higher than this have not been demonstrated to provide any clinical advantage.

2.2 Method of Administration

Place the SUBOXONE sublingual film under the tongue. If an additional sublingual film is necessary to achieve the prescribed dose, place the additional sublingual film sublingually on the opposite side from the first film. Place the sublingual film in a manner to minimize overlapping as much as possible. The sublingual film must be kept under the tongue until the film is completely dissolved. SUBOXONE sublingual film should NOT be chewed, swallowed, or moved after placement.

Proper administration technique should be demonstrated to the patient.

2.3 Clinical Supervision

Treatment should be initiated with supervised administration, progressing to unsupervised administration as the patient's clinical stability permits. SUBOXONE sublingual film is subject to diversion and abuse. When determining the prescription quantity for unsupervised administration, consider the patient's level of stability, the security of his or her home situation, and other factors likely to affect the ability to manage supplies of take-home medication.

Ideally patients should be seen at reasonable intervals (e.g., at least weekly during the first month of treatment) based upon the individual circumstances of the patient. Medication should be prescribed in consideration of the frequency of visits. Provision of multiple refills is not advised early in treatment or without appropriate patient follow-up visits. Periodic assessment is necessary to determine compliance with the dosing regimen, effectiveness of the treatment plan, and overall patient progress.

Once a stable dosage has been achieved and patient assessment (e.g., urine drug screening) does not indicate illicit drug use, less frequent follow-up visits may be appropriate. A once-monthly visit schedule may be reasonable for patients on a stable dosage of medication who are making progress toward their treatment objectives. Continuation or modification of pharmacotherapy should be based on the physician's evaluation of treatment outcomes and objectives such as:

1. Absence of medication toxicity.

2. Absence of medical or behavioral adverse effects.

3. Responsible handling of medications by the patient.

4. Patient's compliance with all elements of the treatment plan (including recovery-oriented activities, psychotherapy, and/or other psychosocial modalities).

5. Abstinence from illicit drug use (including problematic alcohol and/or benzodiazepine use).

If treatment goals are not being achieved, the physician should re-evaluate the appropriateness of continuing the current treatment.

2.4 Unstable Patients

Physicians will need to decide when they cannot appropriately provide further management for particular patients. For example, some patients may be abusing or dependent on various drugs, or unresponsive to psychosocial intervention such that the physician does not feel that he/she has the expertise to manage the patient. In such cases, the physician may want to assess whether to refer the patient to a specialist or more intensive behavioral treatment environment. Decisions should be based on a treatment plan established and agreed upon with the patient at the beginning of treatment.

Patients who continue to misuse, abuse, or divert buprenorphine products or other opioids should be provided with, or referred to, more intensive and structured treatment.

2.5 Stopping Treatment

The decision to discontinue therapy with SUBOXONE sublingual film after a period of maintenance should be made as part of a comprehensive treatment plan. Both gradual and abrupt discontinuation of buprenorphine has been used, but the data are insufficient to determine the best method of dose taper at the end of treatment.

2.6 Switching between SUBOXONE (buprenorphine and naloxone) Sublingual Tablets and SUBOXONE Sublingual Film

Patients being switched between SUBOXONE (buprenorphine and naloxone) sublingual tablets and SUBOXONE sublingual film should be started on the same dosage as the previously administered product. However, dosage adjustments may be necessary when switching between products. Because of the potentially greater relative bioavailability of SUBOXONE sublingual film compared to SUBOXONE (buprenorphine and naloxone) sublingual tablets, patients switching from SUBOXONE (buprenorphine and naloxone) sublingual tablets to SUBOXONE sublingual film should be monitored for over-medication. Those switching from SUBOXONE sublingual film to SUBOXONE (buprenorphine and naloxone) sublingual tablets should be monitored for withdrawal or other indications of under-dosing. In clinical studies, pharmacokinetics of SUBOXONE sublingual film was similar to the respective dosage strengths of SUBOXONE (buprenorphine and naloxone) sublingual tablets, although not all doses and dose combinations met bioequivalence criteria.

3 DOSAGE FORMS AND STRENGTHS

SUBOXONE sublingual film is supplied as an orange rectangular sublingual film with a white printed logo in two dosage strengths:

- buprenorphine/naloxone 2 mg/0.5 mg, and
- buprenorphine/naloxone 8 mg/2 mg.

4 CONTRAINDICATIONS

SUBOXONE sublingual film should not be administered to patients who have been shown to be hypersensitive to buprenorphine or naloxone as serious adverse reactions, including anaphylactic shock, have been reported *[see Warnings and Precautions (5.7)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Abuse Potential

Buprenorphine can be abused in a manner similar to other opioids, legal or illicit. Prescribe and dispense buprenorphine with appropriate precautions to minimize risk of misuse, abuse, or diversion, and ensure

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