Probuphine

(buprenorphine implant)

Probuphine®
(buprenorphine) implant

New Product
Slideshow

MPR

Introduction

- **Brand name:** Probuphine
- **Generic name:** Buprenorphine
- **Pharmacological class:** Opioid (partial agonist-antagonist)
- **Strength and Formulation:** 74.2mg (equivalent to 80mg buprenorphine HCl); per implant; for subdermal use
- **Manufacturer:** Braeburn Pharmaceuticals
- **How supplied:** Kit—1 (4 implants with applicator)
- **Legal Classification:** CIII

PROBUPHINE

Indications

- Maintenance treatment of **opioid dependence** in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of transmucosal buprenorphine-containing product (eg, ≤8mg/day Subutex, Suboxone, or generic equivalent), as part of a complete treatment plan to include counseling and psychosocial support

Dosage & Administration

- See full labeling
- For opioid-tolerant patients only
- Insert 4 implants subdermally in the upper arm for 6 months, then remove
- Examine insertion site 1 week after procedure for infection or impaired wound healing

Dosage & Administration

- After first 6-month cycle, implants may be replaced by new implants at time of removal in the contralateral arm, if continuing treatment; maintain on previous dose of transmucosal buprenorphine if not inserted on same day as removal

Considerations for Special Populations

- **Pregnancy:** May cause fetal harm
- **Nursing mothers:** Monitor infant for increased drowsiness and breathing difficulties
- **Pediatric:** <16 years: not established
- **Geriatric:** Prescribe with caution; monitor for toxicity or overdose
- **Hepatic impairment:** Moderate or severe impairment: plasma levels may be higher

Warnings/Precautions

- Risk of serious complications from insertion/removal of implants; see full labeling
- Abuse potential (monitor)
- Risk of significant respiratory depression
- Compromised respiratory function (eg, COPD, cor pulmonale, decreased respiratory reserve, hypoxia, hypercapnia, pre-existing respiratory depression)

Warnings/Precautions

- Monitor LFTs prior to initiation and periodically during therapy; evaluate if a hepatic event is suspected
- Moderate or severe hepatic impairment; avoid
- Head injury
- Intracranial lesions
- Biliary tract dysfunction
- Acute abdomen
- Myxedema

Warnings/Precautions

- Hypothyroidism
- Adrenal cortical insufficiency
- CNS depression
- Coma
- Toxic psychoses
- GI or GU obstruction
- Acute alcoholism
- Delirium tremens

Warnings/Precautions

- Kyphoscoliosis
- History of keloid formation, connective tissue disease (eg, scleroderma), or recurrent MRSA infections
- Avoid abrupt cessation
- Opioid-naïve
- Debilitated
- Unintentional pediatric exposure

Interactions

- Potentiated by **CYP3A4 inhibitors** (eg, azole antifungals, macrolides, HIV protease inhibitors): monitor and may need dose adjustments or discontinuation
- Antagonized by **CYP3A4 inducers**: monitor for opioid withdrawal and consider dose adjustments or discontinuation
- Concomitant **NNRTIs** (eg, efavirenz, nevirapine, etravirine, delavirdine) or **PIs** (eg, atazanavir with/without ritonavir): monitor

Interactions

- Risk of **respiratory or CNS depression** with concomitant opioid analgesics, general anesthetics, benzodiazepines, phenothiazines, other tranquilizers, sedative/hypnotics, alcohol, or other CNS depressants; caution and consider dose reduction of one or both drugs

Interactions

- Risk of **serotonin syndrome** with concomitant SSRIs, SNRIs, TCAs, 5-HT3receptor antagonists, mirtazapine, trazodone, tramadol, MAO inhibitors; monitor and discontinue if suspected

Adverse Reactions

- Implant-site pain/pruritus/erythema
- Headache
- Depression
- Constipation
- Nausea
- Vomiting
- Back pain
- Toothache
- Oropharyngeal pain
- Signs/symptoms of opioid withdrawal
- Insertion/removal complications
- Orthostatic hypotension
- Hepatitis
- Hypersensitivity reactions

Mechanism of Action

- Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor

Clinical Trials

- The efficacy of Probuphine was demonstrated in a randomized double-blind, double-dummy study in adults who met DSM-IV-TR criteria for opioid dependence as their primary diagnosis, and were considered clinically stable on a sublingual buprenorphine dose of ≤8mg/day

Clinical Trials

- In the study, stable subjects on maintenance treatment were randomized to either:
  - Probuphine + placebo sublingual tabs (n=87)
  - Sublingual buprenorphine/naloxone tabs + placebo implants (n=89)
- Efficacy was evaluated with through urine toxicology screening and patient self-report to detect opioid use over the 6-month treatment period

Clinical Trials

- In the **Probuphine Only** group (no supplemental dosing), **63%** of patients successfully maintained clinical stability with no evidence of illicit opioid use
- In the **Sublingual Buprenorphine** group, **64%** of patients maintained clinical stability with no evidence of illicit opioid use
  - Treatment difference -1% (95% CI: -15%, 13%)

Clinical Trials

- Additionally, 11 patients in the Probuphine Only group required supplemental sublingual buprenorphine but had no evidence of opioid use

- For more clinical study data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/probuphine/drug/34590/