Probuphine
(buprenorphine) implant

Questions & Answers About Probuphine

Here are the answers to some questions you may have about the Probuphine implant:

1. Can my doctor prescribe and insert Probuphine?	Doctors are required to be trained on the appropriate use and insertion of Probuphine and certified as a Probuphine provider. To be certified, healthcare providers go through a training program called Risk Evaluation and Mitigation Services (REMS). You can see if your doctor has been trained by visiting the "Find a Doctor" tab on this website. If not, you will be able to find another doctor in your area.
2. What should I do after the Probuphine implant has been inserted?	Follow your doctor's instructions for wound care around the area where the implant was inserted. Your physician will discuss follow up visits after the procedure. Probuphine should be used as part of a complete treatment program that may include counseling and psychosocial support. Probuphine should be used as part of a complete treatment program that includes counseling and psychosocial support.
3. Do I need to let other healthcare providers know that I am being treated with Probuphine?	It is important that any healthcare provider treating you is aware of all medications you are taking. As a helpful tool after insertion of Probuphine, your doctor will give you a patient identification card to carry with you. In an emergency, have family members tell the emergency medical staff that you are being treated with buprenorphine and/or Probuphine.
4. How do I know that Probuphine is working?	Once Probuphine has been inserted, the medication, buprenorphine, will immediately start to be continuously released into your

	bloodstream for up to 6 months,helping to reduce your cravings.
5. What should I avoid while being treated with Probuphine?	For some, buprenorphine can cause drowsiness and slow reaction times during dose adjustment periods. For Probuphine, this may happen more often in the first few days after insertion. Until you know how the medication affects you, do not drive, operate heavy machinery, or perform any other dangerous activities. You should not drink alcohol during treatment with Probuphine or any buprenorphine medication, as this can lead to slowed breathing, drowsiness, slow reaction time, loss of consciousness or even death.
6. What if I need additional buprenorphine while on Probuphine?	82.1% of the patients on Probuphine went through the 6-month clinical study without a supplemental dose of buprenorphine. However, if necessary, the dosage of buprenorphine can be adjusted upward. If symptoms persist during the initial 2 weeks of treatment, your doctor may provide supplemental sublingual buprenorphine.
7. What if I want to stop treatment with the Probuphine implant before the 6 months is up?	Probuphine implant can be removed before the end of 6-months by your doctor if you or your doctor decides to change your treatment plan. Do not try to remove Probuphine implant yourself. The improper removal carries the risk of implant site infection. You could also experience moderate withdrawal signs and symptoms if you discontinue treatment abruptly because your body has become used to this medicine.
8. What happens after 6 months?	After the 6-month period, your doctor should remove the implant. If you wish to continue Probuphine, your doctor may replace it with a new Probuphine implant. Before each new set of implants you should discuss the benefits of continuing therapy with your doctor.

	If new implants are not inserted on the same day as the removal, you should take sublingual buprenorphine again under the guidance of your doctor.
9. Is Probuphine an Opioid? Is it addictive?	The medicine in Probuphine is buprenorphine, a partial opioid agonist, which may cause physical dependence. Physical dependence means that the body relies on an external source to prevent withdrawal. Physical dependence is predictable, easily managed with medication, and may ultimately be resolved with a slow taper off of the partial opioid agonist. [explanation sourced from National Alliance] The withdrawal syndrome is typically milder than seen with full agonists and illicit opioids, and may be delayed in onset.
10. Does Probuphine work as well as oral products with buprenorphine?	Yes, in order to earn FDA approval, in a clinical study, Probuphine efficacy and safety were compared to sublingual buprenorphine among patients who had been clinically stable. At the end of the 6 months, 75.8% of the patients (or people?) on Probuphine were free from illicit drug use As the first buprenorphine implant for the maintenance treatment of opioid dependence, Probuphine offers people who are stable on buprenorphine, a unique and convenient benefit—freedom from daily dosing for up to 6 months. Ask your doctor if Probuphine could be right for you.

IMPORTANT SAFETY INFORMATION:

PROBUPHINE INDICATIONS AND USAGE

Probuphine contains buprenorphine, a partial opioid agonist. Probuphine is indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent).

Probuphine should be used as part of a complete treatment program to include counseling and psychosocial support.

Probuphine is not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent.

WARNING: IMPLANT MIGRATION, PROTRUSION, EXPULSION and NERVE DAMAGE ASSOCIATED WITH INSERTION and REMOVAL

Risk associated with Insertion and Removal

Insertion and removal of Probuphine are associated with the risk of implant migration, protrusion, expulsion, and nerve damage resulting from the procedure. Serious but rare complications including nerve damage and migration resulting in embolism and death may result from improper insertion of drug implants inserted in the upper arm. Additional complications may include local migration, protrusion and expulsion. Incomplete insertions or infections may lead to protrusion or expulsion. All Healthcare Providers must successfully complete a live training program and become certified prior to performing insertion and/or removal of Probuphine implants.

Because of the risks associated with insertion and removal, Probuphine is available only through a restricted program called the Probuphine REMS Program. All Healthcare Providers must successfully complete a live training program on the insertion and removal procedures and become certified, prior to performing insertions or prescribing Probuphine implants. Patients must be monitored to ensure that Probuphine is removed by a healthcare provider certified to perform insertions.

CONTRAINDICATIONS

- Hypersensitivity to buprenorphine or any other ingredients in PROBUPHINE (e.g., EVA).

WARNINGS AND PRECAUTIONS

- Serious Complications from Insertion and Removal: Rare but serious complications including nerve damage and migration resulting in embolism and death may result from improper insertion of drug implants inserted in the upper arm. Additional complications may include local migration, protrusion and expulsion. Incomplete insertions or infections may lead to protrusion or expulsion. All Healthcare Providers must successfully complete a live training program on the insertion and removal procedures and become certified in the PROBUPHINE REMS program, prior to performing insertions or prescribing PROBUPHINE implants.
- Addiction, Abuse and Misuse: Buprenorphine can be abused in a manner similar to other opioids. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.
- Respiratory and CNS Depression: 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). Consider dose reduction of CNS depressants when used concomitantly.
- Neonatal Opioid Withdrawal Syndrome: Neonatal opioid withdrawal syndrome(NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy.
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.
- Unintentional Pediatric Exposure: In the event an implant protrudes or comes out, keep the implant away from children. Buprenorphine can cause severe, possibly fatal, respiratory depression in children.
- Risk of Opioid Withdrawal with Abrupt Discontinuation: If treatment is temporarily interrupted or discontinued, monitor patients for withdrawal and treat appropriately.
- Risk of Hepatitis, Hepatic Events: Monitor liver function tests prior to initiation and during treatment.
- Risk of Withdrawal in Patients Dependent on Full Agonist Opioids: Verify that patient is clinically stable on transmucosal buprenorphine and not dependent on full agonists before inserting Probuphine.
- Treatment of Emergent Acute Pain: Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect.
- Impairment of Ability to Drive and Operate Machinery: Probuphine may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery.
- Other systemic effects: Probuphine may cause orthostatic hypotension in ambulatory patients. Buprenorphine, may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions,

and other circumstances when cerebrospinal pressure may be increased. Buprenorphine can produce miosis and changes in the level of consciousness that may interfere with patient evaluation. Buprenorphine has been shown to increase intracholedochal pressure, as do other opioids, and thus should be administered with caution to patients with dysfunction of the biliary tract.

- Infection at Implant Site: Infection may occur at the site of the insertion or removal. Excessive palpation may increase an opportunity for infection. Improper removal carries risk of implant-site infection.
- General Precautions: Probuphine should be administered with caution in debilitated patients and those with myxedema or hypothyroidism; adrenal cortical insufficiency (e.g., Addison's disease); CNS depression or coma; toxic psychoses; prostatic hypertrophy or urethral stricture; acute alcoholism; delirium tremens; or kyphoscoliosis. Probuphine should also be administered with caution in patients with a history of keloid formation, connective tissue disease, e.g., scleroderma or history of recurrent MRSA infections.
- Most common side effects of Probuphine include: headache, insomnia, rhinorrhea, upper respiratory tract infection, nausea, anxiety, back pain, depression, constipation, and vomiting.

PLEASE READ THE FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING AND MEDICATION GUIDE

To report SUSPECTED ADVERSE REACTIONS, contact Braeburn at 1-844-859-6341 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch