Medication Guide

PROBUPHINE®
(pro-bú-feen)
PROBUPHINE (buprenorphine HCl) Implant CIII

IMPORTANT:

Read this Medication Guide before starting PROBUPHINE and before each subsequent PROBUPHINE treatment. There may be new information. This Medication Guide does not take the place of talking to your doctor. Talk to your doctor if you have questions about PROBUPHINE.

Share the important information in this Medication Guide with members of your household.

What is the most important information I should know about PROBUPHINE?

PROBUPHINE can cause serious and life-threatening breathing problems. Call your doctor right away or **get emergency help if you**:

- Feel faint, dizzy, or confused
- Have slower breathing than you normally have
- Feel sleepy and uncoordinated
- Have blurred vision
- Have slurred speech
- Cannot think well or clearly
- Have slowed reflexes

These can be signs of an overdose or other serious problems.

Overdose or death can happen if you take anxiety medicines or benzodiazepines (such as Valium® or Xanax®), sleeping pills, tranquilizers, or sedatives (such as Ambien®), antidepressants, or antihistamines, or drink alcohol while using PROBUPHINE. Ask your doctor what you should do if you are taking one of these drugs or if you drink alcohol.

Since PROBUPHINE is implanted in your body, it provides a slow, continuous release of buprenorphine into your body. Even if you do not "feel" the effects, you are receiving buprenorphine around-the-clock. ANY additional opioid narcotics that you take will add to the effects of buprenorphine and could cause a medical emergency and even death.

In an emergency, have family members tell the emergency medical staff that you are physically dependent on an opioid and are being treated with PROBUPHINE.

What is PROBUPHINE?

PROBUPHINE is an FDA-approved implant that contains buprenorphine hydrochloride, a Category III controlled substance, which is used to treat adults who are dependent on (addicted to) opioid drugs (either prescription or street drugs).

PROBUPHINE is one part of a complete treatment program that also includes counseling and behavioral therapy. PROBUPHINE should be used only in patients who are opioid tolerant and are currently on a maintenance dose of 8 mg or less of buprenorphine.

PROBUPHINE is inserted by a healthcare provider just under the skin of the inside of the patient's upper arm through a minor surgical procedure. The implants are small, soft, flexible, and about the size of a matchstick.

A single treatment of PROBUPHINE implants lasts for 6 months. PROBUPHINE is removed by a healthcare provider through a minor office based surgical procedure. The implants **cannot** be seen by X-ray and will require an ultrasound or MRI for the implants that cannot be located by simple palpation. The effect of PROBUPHINE remaining in your body for longer than the recommended treatment time of 6 months has not been studied.

What if I need treatment with PROBUPHINE for more than 6 months?

You should discuss with your treating physician the benefit of continuing treatment with PROBUPHINE for more than 6 months. Your doctor can insert new implants under your skin (in the opposite arm, if possible) after taking out the old ones.

What if I change my mind about PROBUPHINE and want to stop treatment before 6 months?

Your healthcare professional can remove the implants at any time.

Who should not be treated with PROBUPHINE?

PROBUPHINE should not be used if you are allergic to buprenorphine or any ingredients in PROBUPHINE.

What should I tell my doctor before starting PROBUPHINE treatment?

PROBUPHINE may not be right for you. Before being treated with PROBUPHINE, tell your doctor if you have any of these medical issues:

- Trouble breathing or lung problems
- An enlarged prostate gland (men)
- A head injury or brain problem
- Problems urinating
- A curve in your spine that affects your breathing
- Liver or kidney problems
- Gallbladder problems

- Adrenal gland problems
- Addison's disease
- Low thyroid hormone levels (hypothyroidism)
- A history of alcoholism
- History of keloid formation, connective tissue disease, e.g. scleroderma, or history of recurrent MRSA infections.
- Mental problems such as hallucinations (seeing or hearing things that are not there).
- An allergy to numbing medicines (anesthetics) or medicines used to clean your skin (antiseptics). These medicines will be used when the implants are placed into and removed from your arm.
- Are pregnant or plan to become pregnant. It is not known if PROBUPHINE will harm your unborn baby. If you take PROBUPHINE while pregnant, your baby may have symptoms of opioid withdrawal at birth. Talk to your doctor if you are pregnant or plan to become pregnant.
- Are breast-feeding or plan to breast-feed. The buprenorphine in PROBUPHINE can pass into your breast milk and may harm your baby. Talk to your doctor about the best way to feed your baby if you are being treated with PROBUPHINE. Monitor your baby for increased drowsiness and breathing problems.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins and herbal supplements. PROBUPHINE may affect the way other medicines work and other medicines may affect how PROBUPHINE works. Some medicines may cause serious or life-threatening medical problems when taken with PROBUPHINE.

Sometimes the doses of certain medicines may need to be changed if used together. Do not take any medicine while being treated with PROBUPHINE until you have talked with your doctor. Your doctor will tell you if it is safe to take other medicines while being treated with PROBUPHINE. If you are scheduled for surgery or are admitted to the Emergency Department, tell the doctors you are being treated with PROBUPHINE.

Be especially careful about taking other medicines that may make you sleepy, such as pain medicines, anxiety medicines or benzodiazepines (such as Valium® or Xanax®), sleeping pills, tranquilizers, or sedatives (such as Ambien®), antidepressants, or antihistamines.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist each time you get a new medicine.

Do not try to remove PROBUPHINE implants yourself. This could lead to serious infection that may be difficult to treat. You could also go into withdrawal and become sick because your body has become used to the medicine in PROBUPHINE. Ask your doctor how to stop PROBUPHINE treatment the right way.

What should I avoid while being treated with PROBUPHINE?

Do not drive, operate heavy machinery, or perform any other dangerous activities until you know how this medication affects you. Buprenorphine can cause drowsiness and slow reaction times. This may happen more often in the first few days of treatment.

You should not drink alcohol while being treated with PROBUPHINE, as this can lead to drowsiness, delayed reaction time, loss of consciousness or even death.

You should not take anxiety medicines or benzodiazepines (such as Valium® or Xanax®), sleeping pills, tranquilizers, or sedatives (such as Ambien®) that are not prescribed to you while being treated with PROBUPHINE, as this can lead to drowsiness, delayed reaction time, loss of consciousness or even death. In the event that a health care provider is considering prescribing such a medication for you, remind the health care provider that you are being treated with PROBUPHINE.

What are the possible side effects of PROBUPHINE?

PROBUPHINE can cause serious side effects including:

- Respiratory problems. You have a higher risk of death and coma if you are treated with PROBUPHINE along with other medicines, including anxiety medicines or benzodiazepines (such as Valium® or Xanax®).
- Sleepiness, dizziness, and problems with coordination.
- Drug dependency.
- Liver problems. Call your doctor right away if you notice any of these signs of liver problems: your skin or the white part of your eyes turning yellow (jaundice), urine turning dark, stools turning light in color, you have less of an appetite, or you have stomach (abdominal) pain or nausea.
- Allergic reaction. If you have a rash, hives, swelling of your face, wheezing, low blood pressure, dizziness or decrease in consciousness, seek emergency help right away.
- Opioid withdrawal. This can include: shaking, sweating more than normal, feeling hot or cold more than normal, runny nose, watery eyes, goose bumps, diarrhea, vomiting and muscle aches. Tell your doctor if you develop any of these symptoms.
- Decrease in blood pressure. You may feel dizzy when you get up from sitting or lying down.
- Common side effects of PROBUPHINE include:
    - Headache
    - Decrease in sleep (insomnia)
    - Runny nose
    - Upper respiratory tract infection
    - Nausea
    - Anxiety
    - Back pain
    - Depression
    - Constipation
    - Vomiting

Tell your doctor about any side effect that bothers you or that does not go away.

These are not all the possible side effects of PROBUPHINE. For more information, talk to your doctor.

Call your doctor for medical advice about side effects. You may also report side effects to the Food and Drug Administration (FDA) at 1-800-332-1088.

See "What is the most important information I should know about PROBUPHINE?"

How are the PROBUPHINE implants inserted and removed?

Either your doctor or another healthcare professional will insert and remove the PROBUPHINE implants in your treating physician's office. After your arm has been numbed with an anesthetic, the implants are placed just under the skin on the inside of your upper arm.

Your healthcare professional will cover the site where PROBUPHINE was inserted with 2 bandages. Leave the top bandage on for 24 hours. Keep the smaller, bottom bandage clean, dry, and in place for 3 to 5 days.

You will also get a PATIENT IDENTICATION CARD to carry with you. Your healthcare professional will fill out the PATIENT IDENTICATION CARD with the date the implants were inserted and the date the implants are to be removed. Keep track of the date the implants are to be removed. Schedule an appointment with your healthcare professional to remove the implants on or before the removal date. You should also discuss with your physician continuing treatment with PROBUPHINE.

Be sure to have checkups as advised by your doctor.

Are there risks associated with the minor surgical procedures for the insertion and removal of PROBUPHINE?

Yes, common risks associated with any minor surgical procedure are:

- Itching, pain, irritation, redness, swelling, bleeding, or bruising at the insertion site;
- Scarring around the insertion site; and
- Infection at the site of the insertion or removal.

Appropriate care of the incision is important to reduce the risk of complications associated with the insertion of PROBUPHINE.

Are there risks associated with the improper insertion and removal of PROBUPHINE?

Yes, there are possible risks associated with improper insertion and removal of the implant which include:

- An implant may come out by itself, or an end of an implant may begin sticking out of the skin;
- Injury to nerves or blood vessels in your arm;
- Implants may be difficult to locate if they were inserted too deeply, or manipulated by you, or if you have gained significant weight since insertion; and
- Special procedures or a referral to a specialist may be needed to remove the implants if they are difficult to locate.

What should I pay attention to after the PROBUPHINE insertion procedure?

Monitor the implant site and call your healthcare provider right away if you are experiencing any of the following:

- If you are no longer able to feel all four of the implants under your skin;
- If the implant comes out or the end of the implant starts sticking out of the skin; or
- If you have excessive or worsening itching, pain, irritation, redness, swelling, bleeding, bruising, numbness, or scarring at the insertion site.

Are there risks of accidental overdose, misuse and abuse associated with the use of PROBUPHINE?

Yes, there are risks of accidental overdose, misuse, and abuse associated with the use of PROBUPHINE if an implant comes out of the skin or the end of an implant starts sticking out of the skin.

Do not try to remove PROBUPHINE implants yourself. Improper removal carries risk of implant-site infection and may induce opioid withdrawal symptoms.

If a PROBUPHINE implant protrudes or comes out:

- Wash your hands if you touch the PROBUPHINE implant;
- Cover the area where the implants were inserted with a clean bandage;
- Do not allow others to touch or use the PROBUPHINE implants, since they contain buprenorphine and would expose others to any infection you may have; and
- If the PROBUPHINE implants come out, put them in a plastic bag and take the implants to your healthcare provider right away. Keep them away from others, especially children.

General information about PROBUPHINE.

This Medication Guide summarizes important information about PROBUPHINE. If you would like more information, talk to your doctor. You can ask your doctor for information that is written for healthcare professionals. For more information, call 1-844-859-6341.

What are the ingredients in PROBUPHINE?

Active Ingredients: buprenorphine HCl

Inactive Ingredients: ethylene vinyl acetate (EVA)

Distributed by Braeburn Pharmaceuticals, Inc., 47 Hulfish St., Princeton, NJ 08542, USA.

For more information, go to www.PROBUPHINE.com or call 1-844-859-6341.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Approval date: