Buprenorphine (Probuphine®) (for Indiana Only)

Policy Number: CSIND0057.01
Effective Date: April 1, 2021

Instructions for Use

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Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Indiana.

Coverage Rationale

This policy provides information about the use of buprenorphine formulations administered by subdermal implant. This policy refers to the following buprenorphine products:

- Probuphine®

Probuphine (buprenorphine) subdermal implant is proven and medically necessary for the maintenance treatment of opioid dependence in patients who meet all of the following criteria:[1]

- Patient has achieved and sustained prolonged clinical stability on transmucosal buprenorphine; and
- Patient is currently maintained on a dose of 8mg per day or less of oral, sublingual, or transmucosal buprenorphine product equivalent [e.g., Subutex 8 mg or less, Suboxone (or generic equivalent) 8 mg/2 mg or less, Bunavail 4.2 mg/0.7 mg or less, or Zubsolv 5.7 mg/1.4 mg or less]; and
- Patient has been on a stable oral, sublingual, or transmucosal buprenorphine dose for six months or longer without any need for supplemental dosing or adjustments; and
- Prescriber meets DATA 2000 requirements and has been assigned a unique identification number specific to the prescription of medication assisted therapy (DEA-X); and
- Prescriber and/or the healthcare provider performing insertion has successfully completed a live training program specific to Probuphine insertion; and
- Submission of medical records (e.g., chart notes, laboratory values) documenting one of the following:
  - Initial therapy with Probuphine when meeting all of the following:[1,3]
    - Patient has a viable site for implant on the upper arm (inner side of the upper arm about 8-10 cm (3-4 inches) above the medial epicondyle of the humerus in the sulcus between the biceps and triceps muscle)
    - Patient will not be receiving supplemental, oral, sublingual, or transmucosal buprenorphine
    - Patient has not had an opioid-positive urine drug screen within the previous ninety days prior to insertion *

    or
  - Continuation of therapy with Probuphine when meeting all of the following:[1,3]

- Patient has only had one Probuphine implant and has a viable, unused site in the contralateral arm
- Patient has not, nor will receive supplemental, oral, sublingual, or transmucosal buprenorphine
- Probuphine is not being inserted into a previously used arm or insertion site
- Probuphine is only to be used in a maximum of 2 insertions (once in each arm)
- Patient shows no evidence of tampering, extraction, or attempted removal of the previous Probuphine implant
- Patient has not had an opioid-positive urine drug screen since starting Probuphine therapy*

*Note: Patients screening positive for opioid use outside of an opioid dependence treatment regimen is evidence that the patient has not achieved or is no longer in susatained, prolonged, clinical stability with their treatment program. Use of Probuphine is not indicated in this population. Patients should use sublingual or transmucosal buprenorphine until the patient can achieve sustained, prolonged, clinical stability on a low-to-moderate dose (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent).

Probuphine is unproven and not medically necessary for:[1,3]

- Patients who have not achieved and sustained prolonged clinical stability and tolerance to opioids for at least six months
- Patients who are maintained on sublinqual or transmucosal buprenorphine at doses greater than 8 mg per day
- Patients who are recently tapered to a lower dose of sublingual or transmucosal buprenorphine for the sole purpose of transitioning to Probuphine
- Patients who are new entrants to opioid dependence treatment
- Patients who have already had one insertion in each arm
- Patient who do not have viable sites for insertion in the upper arm
- Patients who have an opioid-positive urine drug screen within the previous ninety days
- Patient is currently being treated for chronic pain requiring opioids

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
11981	Insertion, non-biodegradable drug delivery implant
11982	Removal, non-biodegradable drug delivery implant

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HCPCS Code	Description
G0516	Insertion of non-biodegradable drug delivery implants, 4 or more (services for subdermal rod implant)
G0517	Removal of non-biodegradable drug delivery implants, 4 or more (services for subdermal implants)
G0518	Removal with reinsertion, non-biodegradable drug delivery implants, 4 or more (services for subdermal implants)
J0570	Buprenorphine implant, 74.2 mg

Diagnosis Code	Description
F11.20	Opioid dependence, uncomplicated
F11.21	Opioid dependence, in remission

Background

Probuphine (buprenorphine) implant is a sterile, single, off-white, soft, flexible rod-shaped drug product. It is 26 mm in length and 2.5 mm in diameter. Each implant contains 74.2 mg buprenorphine (equivalent to 80 mg buprenorphine hydrochloride) and

ethylene vinyl acetate (EVA). Probuphine is designed to be implanted subdermally by a trained medical professional and to provide sustained delivery of buprenorphine for up to six months.

Buprenorphine hydrochloride is an opioid partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor, thus it exhibits a ceiling to its effects. The danger of overdose, abuse liability, and toxicity may be less than with full opioid agonists.[2]

Four Probuphine rods deliver circulating drug blood levels comparable to the average plasma concentrations observed following daily doses of ≤ 8 mg buprenorphine or buprenorphine/naloxone sublingual or transmucosal products.

Clinical Evidence

The efficacy of Probuphine was demonstrated in an outpatient, randomized, active controlled, double-blind, double-dummy, multi-center, 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 no more than 8 mg per day, by their treating Healthcare Provider.[1,3] Patients included in the study were those prescribed daily sublingual buprenorphine for 6 months or more, were abstinent while taking 8mg/d or less of sublingual buprenorphine for 90 days or longer, and were determined to be clinically stable by their physician. Eligible particpants also showed no evidence of opioid withdrawal or illicit opioid-positive urine samples for at least 90 days prior to study entry. Participants were to randomized to receive either sublingual buprenorphine plus 4 placebo implants or sublingual placebo plus four 80mg buprenorphine implants for a 24 week trial period. Of 177 participants (mean age, 39 years; 40.9%female), 90 were randomized to sublingual buprenorphine with placebo implants and 87 to buprenorphine implants with sublingual placebo. Exclusion criteria included, but weren't limited to lack of appropriate implant sites (recent scars, history of keloids); primary diagnosis of substance dependence other than opioids or nicotine; or pending legal action or other factors/conditions that could adversely affect participant safety and adequate adherence. Patients were seen monthly for six months and were also required to provide four randomly-scheduled urine samples for toxicology. Efficacy was evaluated through urine toxicology screening and patient self-report to detect opioid use, over the 6-month treatment period. Supplemental dosing with open-label sublingual buprenorphine/naloxone tablets was permitted as clinically indicated. Of the 177 participants, 165 of 177 (93.2%) completed the trial. Eighty-one of 84 (96.4%) receiving buprenorphine implants and 78 of 89 (87.6%) receiving sublingual buprenorphine were responders, an 8.8% difference (1-sided 97.5%CI, 0.009 to ∞; P < .001 for noninferiority). Over 6 months, 72 of 84 (85.7%) receiving buprenorphine implants and 64 of 89 (71.9%) receiving sublingual buprenorphine maintained opioid abstinence (hazard ratio, 13.8; 95%CI, 0.018-0.258; P=.03). Non–implant-related and implant-related adverse events occurred in 48.3% and 23% of the buprenorphine implant group and in 52.8% and 13.5% of participants in the sublingual buprenorphine group, respectively. The authors concluded that the use of buprenorphine implants compared with continued sublingual buprenorphine did not result in an inferior likelihood of remaining a responder. However, the study population had an exceptionally high response rate in the control group, and further studies are needed in broader populations to assess the efficacy in other settings.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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 sublingual or transmucosal buprenorphine containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent).[1] Each Probuphine implant is an ethylene vinyl acetate (EVA) implant, 26 mm in length and 2.5 mm in diameter, containing 74.2 mg of buprenorphine (equivalent to 80 mg of buprenorphine hydrochloride).

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.

Probuphine is available only through a restricted REMS program, called the "Probuphine REMS Program," because of the risk of complications of migration, protrusion and expulsion, and nerve damage associated with the insertion and removal of Probuphine.

Notable requirements of the "Probuphine REMS Program" include the following:

- Healthcare providers who prescribe Probuphine must be certified with the program by enrolling and completing live training
- Healthcare providers who insert Probuphine:
  - Must meet the prerequisite requirements
  - Be certified with the program by enrolling and completing live training, including demonstrating competency in Probuphine procedures
- Patients must be monitored to ensure that Probuphine is removed by a healthcare provider certified to insert/remove Probuphine implants
- Probuphine will only be distributed to certified prescribers through a restricted distribution program

There is no experience with inserting additional implants into other sites in the arm to recommend an approach to a second insertion into a previously-used arm. Neither re-insertion into previously-used administration sites, nor into sites other than the upper arm, have been studied. It is important to avoid previously-implanted sites because the effect of scarring and fibrosis in previously-used insertion sites on either the effectiveness of Probuphine or the safety of insertion have not been evaluated. After one insertion in each arm, additional cycles of treatment should only be considered if the potential benefits of continuing Probuphine outweigh the potential risks of additional insertion and removal procedures, taking into account the experience of the health care provider with Probuphine procedures and related procedures, and the clinical need of the patient for ongoing treatment with subdermal medication. In most cases, patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment.

Substance Abuse and Mental Health Services Administration (SAMHSA)[4]

Verification of DATA-Certified Physicians

Effective July 25, 2005, physicians must include their DATA 2000 waiver ID number on prescriptions for opioid addiction treatment medications. The practitioner's DEA registration number and the unique identification number (DATA 2000 waiver ID number or "X" number) must be on the prescription 21 CFR 1306.05(a). The identification number is not in lieu of the DEA registration number, it is an addition. If the prescription is telephoned to the pharmacy, the pharmacist must have both of these numbers on the prescription record so the physician can provide the numbers or the pharmacist may have them on file.

The SAMHSA Buprenorphine Physician Locator website lists the physicians in each state who have DATA 2000 waivers. A physician listed on the site can be considered to have a valid DATA 2000 waiver. Note, however, that the site does not list every physician with a valid waiver, only those who have agreed to be listed on the site. Physicians with valid waivers may choose not to be listed on the site.

A person desiring to verify that a physician who is not listed on the site has a valid DATA 2000 waiver can contact SAMHSA by phone at 1-866-BUP-CSAT (1-866-287-2728) or by e-mail at infobuprenorphine@samhsa.hhs.gov. The verifying person should convey their DEA registration number with these requests.

References

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6. Sublocade [package insert]. Burlington, MA: Indivior Inc., February 2020.
7. Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2019 Feb 23;393(10173):778-790.

Policy History/Revision Information

Date	Summary of Changes
04/01/2021	• New Medical Benefit Drug Policy

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.