Buprenorphine (Probuphine® & Sublocade®) (for Ohio Only)

Policy Number: CSOH2023D0057A
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Instructions for Use

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Related Policies
None

Application

This Medical Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

This policy provides information about the use of buprenorphine formulations administered by either the subcutaneous (SC) or by subdermal implant. This policy refers to the following buprenorphine products:

- Probuphine®
- Sublocade®

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 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*

Buprenorphine extended-release injection (e.g., Sublocade) is proven and medically necessary for the treatment of moderate to severe opioid use disorder in patients who meet all of the following criteria:

- For initial therapy, all of the following:
  - Patient is currently maintained on an 8 mg to 24 mg per day dose of oral, sublingual, or transmucosal buprenorphine product equivalent for at least 7 days prior to initiation of extended-release buprenorphine injection; and
  - Patient has not, nor will receive supplemental, oral, sublingual, or transmucosal buprenorphine; and
  - Sublocade dosing is in accordance with the U.S. Food and Drug Administration approved labeling; and
  - Initial authorization will be for no more than 6 months
- For continuation of therapy, all of the following:
  - Provider documentation that the patient has experienced a positive clinical response to buprenorphine extended-release therapy, as defined by the provider; and
  - Patient has not, nor will receive supplemental, oral, sublingual, or transmucosal buprenorphine; and
  - Sublocade dosing is in accordance with the U.S. Food and Drug Administration approved labeling; and
  - Continuation authorization will be for no more than 12 months

*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 sustained, 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).

Buprenorphine extended-release injection is unproven and not medically necessary for pain management.[1,3,6]

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 sublingual 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, drug-delivery implant (i.e., bioresorbable, biodegradable, non-biodegradable)
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
Q9991	Injection, buprenorphine extended-release (Sublocade), less than or equal to 100 mg
Q9992	Injection, buprenorphine extended-release (Sublocade), greater than 100 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.

Four Probuphine implants 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.

Sublocade (buprenorphine-extended release) is a sterile solution for subcutaneous injection only. It is designed to deliver buprenorphine at a controlled rate over a one month period.

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]

Clinical Evidence

The efficacy of Sublocade for the treatment of opioid use disorder was evaluated in a Phase 3, 24-week, randomized, double-blind, placebo-controlled, multicenter trial in treatment-seeking patients with moderate or severe opioid use disorder.[6,7] Patients (n = 504 patients) were randomized 4:4:1:1 to one of following dosing regimens: 6 once-monthly 300 mg doses (n = 203), 2 once-monthly 300 mg doses followed by 4 once-monthly 100 mg doses (n = 201), or 6 once-monthly SC injections of placebo (n = 100). All doses were administered by a physician or suitably qualified designee and were separated by 28 ±2 days. In addition to study medication, all subjects received manual-guided psychosocial support at least once a week (Individual Drug Counseling = IDC). Prior to the first dose, treatment was initiated with buprenorphine/naloxone sublingual film; doses were adjusted from 8/2 mg to 24/6 mg per day over a period of 7-14 days. Patients were randomized to Sublocade injection or placebo after cravings and withdrawal symptoms were clinically controlled. After randomization, supplemental dosing with buprenorphine/naloxone film was not permitted during the study. Efficacy was evaluated over Weeks 5 through 24 based on weekly urine drug screens combined with self-reported use of illicit opioid use. A “grace period” was applied for Weeks 1 through 4 to allow patients to stabilize in treatment. During this period, opioid use, if it occurred, was not considered in the analysis. Missing urine drug screen samples and/or self-reports during Weeks 5-24 were counted as positive for illicit opioids. Based on the cumulative distribution function (CDF) of the percentage of urine samples negative for illicit opioids combined with self-reports negative for illicit opioid use collected from Week 5 through Week 24, regardless of dose, Sublocade was superior to the placebo group with statistical significance. The proportion of patients achieving treatment success (defined as patients with ≥ 80% opioid-free weeks) was statistically significantly higher in both groups receiving Sublocade compared to the placebo group (28.4% [300 mg/100 mg], 29.1% [300 mg/300mg], 2% [placebo].

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 8 mg/d or less of sublingual buprenorphine for 90 days or longer, and were determined to be clinically stable by their physician. Eligible participants also showed no evidence of opioid withdrawal or illicit opioid-positive urine samples for at least 90 days prior to study entry. Participants were randomized to receive either sublingual buprenorphine plus four 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.

Sublocade is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days. Sublocade should be used as part of a complete treatment plan that includes counseling and psychosocial support.[6]

Sublocade is available only through a restricted REMS program, called the "Sublocade REMS Program," because of the risk of serious harm or death that could result from intravenous self-administration. Healthcare settings and pharmacies that order and dispense Sublocade must be certified in this program and comply with the REMS requirements.

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

Removal of DATA Waiver (X-Waiver) Requirement

Section 1262 of the Consolidated Appropriations Act, 2023 (also known as Omnibus bill), removes the federal requirement for practitioners to submit a Notice of Intent (have a waiver) to prescribe medications, like buprenorphine, for the treatment of opioid use disorder. All practitioners who have a current DEA registration that includes Schedule III authority may now prescribe buprenorphine for Opioid Use Disorder in their practice if permitted by applicable state law. All prescriptions for buprenorphine only require a standard DEA registration number. The previously used DATA-Waiver registration numbers are no longer needed for any prescription. There are no longer any limits or patient caps on the number of patients a prescriber may treat for opioid use disorder with buprenorphine. The Act does not impact existing state laws or regulations that may be applicable.

References

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Policy History/Revision Information

Date	Summary of Changes
06/01/2023	**Template Update** • Created state-specific policy version **Coverage Rationale** • Revised coverage criteria; removed criterion requiring the prescriber meets DATA 2000 requirements and has been assigned a unique identification number specific to the prescription of medication assisted therapy (DEA-X) **Supporting Information** • Updated *FDA* and *References* sections to reflect the most current information • Archived previous policy version CS2022D0057N

Instructions for Use

This Medical Benefit Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical 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.