

Clinical Policy: Buprenorphine Implant/Injection (Probuphine, Sublocade)

Reference Number: NH.PHAR.289

Effective Date: 11/2016

Last Review Date: 03.18

Line of Business: Medicaid, HIM

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Buprenorphine (Probuphine, Sublocade) is a partial opioid agonist.

FDA Approved Indication(s)

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).

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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Probuphine and Sublocade are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Probuphine (must meet all):

1. Diagnosis of opioid dependence;
2. Age \geq 16 years;
3. Currently on a maintenance dose of \leq 8 mg/day of buprenorphine or buprenorphine-naloxone sublingual tablet or Suboxone® film (members should not be tapered down to a lower dose for the sole purpose of transitioning to Probuphine) for 3 months or longer without any need for supplemental dosing or adjustments;
4. Medical justification supports why oral (e.g., sublingual, buccal) formulations of buprenorphine cannot be continued;
5. Dose does not exceed 4 implants/6 months.

Approval duration: 12 months (two sets of four implants)

The four implants are inserted sub dermally in the inner side of the upper arm.

B. Sublocade Injection (must meet all):

1. Diagnosis of opioid dependence;

2. Age \geq 18 years;
3. Currently on a dose of 8 to 24 mg/day of a buprenorphine or buprenorphine-naloxone sublingual tablet or film for 7 days or longer;
4. Medical justification supports inability to continue to use oral (e.g., sublingual, buccal) formulations of buprenorphine;
5. Dose does not exceed 300mg per month

Approval Duration: 12 Months

C. Other diagnoses/indications: Refer to CP.PMN.53 off-label use policy (Medicaid) or HIM.PHAR.21 (HIM) if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

A. Probuphine (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. One of the following conditions is met (a or b):
 - a. Member has NOT received an opioid analgesic since last approval;
 - b. Prescriber submits documentation acknowledging that the use of opioid during the last approval period was due to diagnosis of pain;
4. Dose does not exceed 4 implants/6 months.

Approval duration: 12 months (a maximum of four sets of four implants)

The four implants are inserted subdermally in the inner side of the OPPOSITE upper arm.

B. Sublocade Injection (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. One of the following conditions is met (I or II):
 - I. Member has NOT received an opioid analgesic since last approval;
 - II. Prescriber submits documentation acknowledging that the use of opioid during the last approval period was due to diagnosis of acute pain;
4. If request is for a dose increase, new dose does not exceed 300mg per month.

Approval Duration: 12 Months

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;

Approval Duration: 12 Months

or

2. Refer to CP.PMN.53 Off-Label Use Policy (Medicaid) or HIM.PHAR.21 (HIM) if the diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy HIM.PHAR.21 for health insurance marketplace or CP.PMN.53 for Medicaid.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|--|-------------------------------------|
| buprenorphine-naloxone (Suboxone) sublingual (SL) or buccal dissolving film, SL tablet | <u>Maintenance:</u> Target dose: buprenorphine 16 mg/naloxone 4 mg once daily; dosage should be adjusted in increments or decrements of 2 mg/ 0.5 mg or 4 mg/1 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 4 mg/1 mg to 24 mg/6 mg per day | 24 mg/6 mg per day |
| Bunavail® (buprenorphine-naloxone) buccal film | <u>Maintenance:</u> Target dose: buprenorphine 8.4 mg/naloxone 1.4 mg once daily; dosage should be adjusted in increments or decrements of 2.1 mg/ 0.3 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 2.1 mg/0.3 mg to 12.6 mg/2.1 mg per day | 12.6 mg/2.1 mg per day |
| Zubsolv® (buprenorphine-naloxone) SL tablet | <u>Maintenance:</u> Target dose: buprenorphine 11.4 mg/naloxone 2.9 mg once daily; dosage should be adjusted in increments or decrements of 2.9 mg/ 0.71 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 2.9 mg/0.71 mg to 17.2 mg/4.2 mg per day | 17.1 mg/4.2 mg per day |

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Probuphine carries a boxed warning for implant migration, protrusion, expulsion, and nerve damage associated with implant insertion and removal. Probuphine is available only through a restricted program called the Probuphine REMS Program.

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- There is no clinical experience with insertion of Probuphine beyond a single insertion in each arm. 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. Following 1 insertion in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment.

Appendix D: Brand/Generic Transmucosal Formulations Equivalent to Subutex or Suboxone Sublingual Tablets Containing ≤ 8 mg of Buprenorphine

| Drug | Transmucosal* | Brand/ Generic† | Brand/ Generic Strength | Subutex/Suboxone‡ Sublingual Tablet Strength |
|--------------------------------|----------------------------|--------------------|--|--|
| | | | <i>Buprenorphine/Naloxone§ Equivalency</i> | |
| Buprenorphine HCL | Tablet, sublingual | Generic | 2 mg | 2 mg (Subutex) |
| | | | 8 mg | 8 mg (Subutex) |
| Buprenorphine HCL/naloxone HCL | Tablet, sublingual | Generic | 2 mg/0.5 mg | 2 mg/0.5 mg (Suboxone) |
| | | | 8 mg/2 mg | 8 mg/2 mg (Suboxone) |
| | | | Zubsolv | 1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg |
| | Film, buccal | Bunavail | 2.1 mg/0.3 mg | 4 mg/1 mg (Suboxone) |
| | | | 4.2 mg/0.7 mg | 8 mg/2 mg (Suboxone) |
| | Film, sublingual or buccal | Suboxone | 2 mg/0.5 mg | 2 mg/0.5 mg (Suboxone) |
| 4 mg/1 mg 8 mg/2 mg | | | 4 mg/1 mg (Suboxone) 8 mg/2 mg (Suboxone) | |

*Transmucosal formulations include buprenorphine and buprenorphine/naloxone sublingual tablets and buccal/sublingual films.

†For a more comprehensive listing of brand/generic sublingual/buccal transmucosal formulations see the U.S. Food & Drug Administration Orange Book: Approved drug products with therapeutic equivalence evaluations at http://www.accessdata.fda.gov/scripts/cder/ob/search_product.cfm.

‡Subutex (buprenorphine) and Suboxone (buprenorphine/naloxone) sublingual tablets, while used as buprenorphine equivalency references, are no longer available in the U.S.

§Naloxone (an opioid antagonist) is minimally absorbed in sublingual/buccal transmucosal formulations and rather is added to discourage diversion or misuse.

V. Dosage and Administration

| Drug Name | Dosing Regimen | Maximum Dose |
|----------------------------|---|---------------------|
| Buprenorphine (Probuphine) | Each dose consists of 4 implants inserted subdermally in the inner side of the upper arm. The implants are intended to be in place for 6 months. New implants may be inserted subdermally in an area of the inner side of either upper arm that has not been previously used at the | 4 implants/6 months |

| Drug Name | Dosing Regimen | Maximum Dose |
|---------------------------|--|------------------|
| | time of removal, if continued treatment is desired. If new implants are not inserted on the same day as the removal of old implants, maintain patients on their previous dose of transmucosal buprenorphine prior to insert of the implant. Following 1 insertion in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment. | |
| Buprenorphine (Sublocade) | Two monthly initial doses of 300 mg subcutaneously followed by 100 mg monthly maintenance doses | 300 mg per month |

VI. Product Availability

| Drug Name | Availability |
|----------------------------|--|
| Buprenorphine (Probuphine) | 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) |
| Buprenorphine (Sublocade) | Subcutaneous Injection: 100 mg/0.5 mL and 300 mg/1.5 mL provided in a prefilled syringe with a 19 Gauge 5/8-inch needle |

VII. References

1. Probuphine Prescribing Information. Princeton, NJ: Braeburn Pharmaceuticals, Inc.; August 2017. Available at: <https://probuphine.com/>. Accessed November 9, 2017.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: <http://www.clinicalpharmacology-ip.com/>.
3. Sublocade Prescribing Information. North Chesterfield, VA: Indivior Inc.; November 2017. Available at <http://www.indivior.com/>. Accessed December 11, 2017.
4. Center for Substance Abuse Treatment. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2004. (Treatment Improvement Protocol (TIP) Series, No. 40.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK64245/>. Accessed November 9, 2017.

| Reviews, Revisions, and Approvals | Date | Approval Date |
|--|-------|---------------|
| New policy created. | 11/16 | 11/16 |
| Adjusted duration of approval to 12 months as well as criteria | 07/17 | 7/17 |
| Added age restriction as safety and effectiveness of Probuphine have not been established in children or adolescents < 16 years of age; removed “No evidence or reports of illicit opioid use (confirmed with at least one random urine drug screen within the last 3 months), significant withdrawal symptoms, significant desire/need to use illicit opioids, hospitalizations, emergency room visits or crisis interventions for addiction or mental health | 12/17 | 12/17 |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|--|-------|---------------|
| issues, and non-adherence to clinic visits or drug abuse counseling as recommended”; removed requirement for participation in drug abuse counseling to shift the responsibility of appropriate monitoring and use to the prescriber; added requirement for medical justification to support why oral (e.g., sublingual, buccal) formulations of buprenorphine cannot be continued; re-auth: removed that if a supplemental buprenorphine containing product was prescribed, it was prescribed only intermittently rather than on an ongoing basis. | | |
| Added new appendix section with updated information. Updated references. Added information for criteria of approval for Sublocade including FDA indications. Adjusted name of policy to include Sublocade formulation. | 03/18 | 03/18 |

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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