

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

Reference Number: HNCA.CP.PHAR.289

Effective Date: 11.01.18

Last Review Date: 05.18

Line of Business: Commercial – HNCA

[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 Implant (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 oral buprenorphine or buprenorphine-naloxone sublingual tablet or 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. Dose does not exceed 4 implants/6 months.

Approval duration: 6 months

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. Dose does not exceed 300 mg per month.

Approval duration: 6 months or the member's renewal date, whichever is longer

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Probuphine Implant (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. The following condition is met:
 - Member is NOT receiving supplemental buprenorphine since initial approval;
3. Member has not had prior implants inserted in the contralateral arm (i.e., member has not previously received 2 sets of implants [one set is defined as four implants per arm]);
4. Dose does not exceed 4 implants/6 months.

Approval duration: 6 months (a second [and last] set of four implants)

B. Sublocade Injection (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Prescriber submits documentation acknowledging treatment success defined as greater than or equal to 80% opioid-free weeks following the first 4 weeks of stabilization;
3. If request is for a dose increase, new dose does not exceed 300 mg per month.

Approval duration: 6 months or member's renewal date, whichever is longer

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: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

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 policies – CP.CPA.09 for commercial or evidence of coverage documents.

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.
- 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* Formulation	Brand/ Generic†	Brand/ Generic Strength	Subutex/Suboxone‡ Sublingual Tablet Strength
			<i>Buprenorphine/Naloxone§ Equivalency</i>	
Buprenorphine	Tablet,	Generic	2 mg	2 mg (Subutex)

Drug	Transmucosal* Formulation	Brand/ Generic†	Brand/ Generic Strength	Subutex/Suboxone‡ Sublingual Tablet Strength
			<i>Buprenorphine/Naloxone§ Equivalency</i>	
HCL	sublingual		8 mg	8 mg (Subutex)
Buprenorphine HCL/naloxone HCL	Tablet, sublingual	Generic	2 mg/0.5 mg 8 mg/2 mg	2 mg/0.5 mg (Suboxone) 8 mg/2 mg (Suboxone)
		Zubsolv	1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg	2 mg/0.5mg (Suboxone) 4 mg/1 mg (Suboxone) 8 mg/2 mg (Suboxone)
	Film, buccal	Bunavail	2.1 mg/0.3 mg 4.2 mg/0.7 mg	4 mg/1 mg (Suboxone) 8 mg/2 mg (Suboxone)
	Film, sublingual or buccal	Suboxone	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg	2 mg/0.5 mg (Suboxone) 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 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.	4 implants/6 months
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	P&T Approval Date
Policy split from CP.PHAR.289 for CA commercial; removed requirement for medical justification why oral formulation cannot be used; removed positive response to therapy for continued approval.	10.25.18	
Changed Probuphine continuation approval criteria to “member not receiving buprenorphine SL supplementation since initial approval”. Removed checking for the use of opioids for acute pain. Changed Sublocade continuation approval criteria to remove “the member has not received opioid medications” and added “treatment success defined as greater than or equal to 80% opioid-free weeks after first 4 weeks of stabilization.”	10.30.18	11.30.18
Changed length of approval for Sublocade to 6 months or renewal date, whichever is longer.	11.1.18	11.30.18

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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