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

Reference Number: ERX.SPA.254
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Line of Business: Commercial, Medicaid

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 buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.

Both should be used as part of a complete treatment program that includes counseling and psychosocial support.

Limitation(s) of use: 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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 16 years;
3. Currently on a maintenance dose of ≤ 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. Medical justification supports inability to continue to use oral (e.g., sublingual, buccal) formulations of buprenorphine as evidenced by one of the following (a, b, c, or d):
   a. Documentation of non-compliance to oral formulations of buprenorphine;
   b. Treatment failure with oral formulations of buprenorphine;
   c. History of diversion with buprenorphine medication-assisted treatment (MAT) products;
   d. Contraindication(s) or clinically significant adverse effects to the excipients of oral formulations of buprenorphine;
5. Dose does not exceed 4 implants per 6 months.

Approval duration: 6 months

B. Sublocade Injection (must meet all)**:**
1. Diagnosis of opioid dependence;
2. Age ≥ 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 as evidenced by one of the following (a, b, c, or d):
   a. Documentation of non-compliance to oral formulations of buprenorphine;
   b. Treatment failure with oral formulations of buprenorphine;
   c. History of diversion with buprenorphine MAT products;
   d. Contraindication(s) or clinically significant adverse effects to the excipients of oral formulations of buprenorphine;
5. Dose does not exceed 300 mg per month.

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Probuphine Implant (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 a diagnosis of acute pain;
4. 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]);
5. Dose does not exceed 4 implants per 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 a health plan affiliated with Envolve Pharmacy Solutions 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 a diagnosis of acute pain;
4. If request is for a dose increase, new dose does not exceed 300 mg per month.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EVA: ethylene vinyl acetate
FDA: Food and Drug Administration
MAT: medication-assisted treatment
REMS: Risk Evaluation and Mitigation Strategy

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
buprenorphine/ naloxone (Suboxone) sublingual (SL) or buccal dissolving film, SL tablet	Maintenance: 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	Maintenance: 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	Maintenance: 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	17.2 mg/4.2 mg per day
buprenorphine SL tablet (Subutex)	Maintenance: Target dose: 16 mg once daily; dosage should be adjusted in increments of to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 4-24 mg/day	24 mg/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: Contraindications/Boxed Warnings

Probuphine:

- Contraindication(s): hypersensitivity to buprenorphine or any other ingredients in Probuphine (e.g., EVA)
- Boxed warning(s): implant migration, protrusion, expulsion, and nerve damage associated with insertion and removal; Probuphine Risk Evaluation and Mitigation Strategy (REMS)

Sublocade:

- Contraindication(s): hypersensitivity to buprenorphine or any other ingredients in Sublocade
- Boxed warning(s): risk of serious harm or death with intravenous administration; available only through a restricted program called the Sublocade REMS program

Appendix D: General Information

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

Drug Name	Transmucosal* Formulation	Brand/ Generic†	Brand/ Generic Strength	Subutex/Suboxone‡ Sublingual Tablet Strength
			Buprenorphine/Naloxone§ Equivalency	
Buprenorphine HCL	Tablet, sublingual	Generic	2 mg 8 mg	2 mg (Subutex) 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.
‡Brand versions of 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

Indication	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/month

VI. Product Availability

Drug Name	Availability
Buprenorphine (Probuphine)	Ethylene vinyl acetate (EVA) implant, 26 mm in length and 2.5 mm in diameter: 74.2 mg of buprenorphine (equivalent to 80 mg of buprenorphine hydrochloride)

Drug Name	Availability
Buprenorphine (Sublocade)	Prefilled syringe: 100 mg/0.5 mL and 300 mg/1.5 mL

VII. References

1. Probuphine Prescribing Information. South San Francisco, CA: Titan Pharmaceuticals, Inc.; March 2021. Available at: https://probuphine.com. Accessed November 22, 2021.
2. Sublocade Prescribing Information. North Chesterfield, VA: Indivior Inc.; June 2021. Available at http://www.sublocade.com. Accessed November 22, 2021.
3. Center for Substance Abuse Treatment. Medications for opioid use disorder. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2018. (Treatment Improvement Protocol (TIP) Series, No. 63.) Available from: https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document-Including-Executive-Summary-and-Parts-1-5-/SMA18-5063FULLDOC. Accessed December 2, 2020.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.12.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.25.19	11.19
1Q 2020 annual review: updated requirement related to medical justification; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	12.02.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.22.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.