RXADVANCE
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Clinical Policy Title:	buprenorphine Implant/Injection
Policy Number:	RxA.441
Drug(s) Applied:	Probuphine®, Sublocade®
Original Policy Date:	03/06/2020
Last Review Date:	09/14 /2020
Line of Business Policy Applies to:	All lines of business

Background

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

Probuphine: It 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). It should be used as part of a complete treatment program to include counselling and psychosocial support.

It 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.

Sublocade: It 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. It should be used as part of a complete treatment program that includes counselling and psychosocial support.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Buprenorphine (Probuphine)	Opioid dependence	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 sub dermally 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	4 implants/6 months (one insertion in to each arm i.e. 2 sets of 4 implants)

		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)	Opioid dependence	Two monthly initial doses of 300 mg subcutaneously followed by 100 mg monthly maintenance doses. Increasing the maintenance dose to 300 mg monthly may be considered for patients in which the benefits outweigh the risks.	100 mg per month (maintenance dose)

Dosage Forms

- 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.

Clinical Policy

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

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. Dose does not exceed 4 implants/6 months.

Approval Duration
Commercial: 6 months
Medicaid: 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. Dose does not exceed 300 mg per month.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Probuphine Implant (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial :6 months (a second [and last] set of four implants)
Medicaid: 6 months (a second [and last] set of four implants)

B. Sublocade Injection (must meet all)**:**

1. Currently receiving medication via RxAdvance 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
Commercial :6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
EVA: Ethylene vinyl acetate
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
buprenorphinenaloxone (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® (buprenorphinenaloxone) 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® (buprenorphinenaloxone) 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	17.1 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: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to buprenorphine or any other ingredients in Probuphine and Sublocade

- Boxed Warning(s):
  - **Probuphine Implant**
  - Insertion and removal of Probuphine are associated with the risk of implant migration, protrusion, expulsion, and nerve damage resulting from the procedure.
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  - **Sublocade Injection**
  - Serious harm or death could result if administered intravenously.

APPENDIX D: 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 buprenorphinecontaining product for continued treatment.

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
Buprenorphine	Tablet,	Generic	2 mg	2 mg (Subutex)
		Geberic	8mg	8mg (Subutex)

HCL Buprenorphine HCL/naloxone HCL	sublingual tablet, sublingual		2mg/0.5mg 8mg/2mg	2mg/0.5mg (Suboxone)
		Zubsolv	1.4 mg/0.36 mg 2.9 mg/0.71mg 5.7 mg/1.4 mg	8 mg/2 mg (Suboxone) 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 4mg/1mg 8mg/2mg	2 mg/0.5mg (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.

References

1. Probuphine Prescribing Information. Princeton, NJ: Braeburn Pharmaceuticals, Inc.;December,2019. Available at: https://probuphine.com/. Accessed July 17,2020.
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.; February 2020. Available at http://www.indivior.com/. Accessed July 17,2020.
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 July 17,2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1) Policy description table was updated 2) Background updated for Probuphine and Sublocade according to latest prescribing information 3) Dosing regimen updated for Sublocade; Maximum dose for Probuphine and Sublocade were updated.	07/17/2020	09/14/2020

4) Initial therapy and continued therapy approval duration was added for Medicaid 5) Continuation therapy criteria II.A.1. was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance.." 6) Approval duration changes 7) Appendix A:Abbreviation/Acronym Key added 8) Appendix C, contraindications updated; Boxed Warnings added separately for Probuphine and Sublocade 9) References were updated		