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

Reference Number: AZ.CP.PHAR.289
Effective Date: 11.19
Last Review Date: 02.22
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st) 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.

AHCCCS preferred drugs in this class include: Sublocade

AHCCCS non-preferred drugs in this class include: Probuphine

FDA approved indications
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.

Both should be used as part of a complete treatment program to include 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.

It is the policy of Arizona Complete Health-Complete Care Plan and Care1st 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. 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;
3. Member has co-occurring serious mental illness and medical justification supports inability to continue to use oral (e.g., sublingual, buccal) formulations of buprenorphine as evidenced by one of the following:
   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;
4. Member is receiving psychosocial interventions as part of a comprehensive medication assisted treatment (MAT) program;
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. 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;
3. Member will not receive supplemental, oral, sublingual, or transmucosal buprenorphine;
4. Member is receiving psychosocial interventions as part of a comprehensive medication assisted treatment (MAT) program;
5. Prescriber provides confirmation they have checked the Arizona State Board of Pharmacy Controlled Substance Prescription Monitoring Program (CSPMP) database prior to each monthly injection.
6. Dose does not exceed 300 mg per month.

Approval duration: 6 months

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): AZ.CP.PMN.53 for Arizona Medicaid.

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. Prescriber documents checks of the Arizona State Board of Pharmacy Controlled Substance Prescription Monitoring Program (CSPMP) database are regularly occurring.
3. Member is responding positively to therapy;
4. One of the following conditions is met (a or b):
   a. Member has NOT received supplemental, oral, sublingual, transmucosal buprenorphine, or 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;
5. 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]);
6. 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 Centene benefit or member has previously met initial approval criteria;
2. Prescriber documents checks of the Arizona State Board of Pharmacy Controlled Substance Prescription Monitoring Program (CSPMP) database are regularly occurring.
3. Member is responding positively to therapy;
4. One of the following conditions is met (a or b):
   a. Member has NOT received supplemental, oral, sublingual, transmucosal buprenorphine since last approval;
   b. Prescriber submits documentation acknowledging that the use of any opioid during the last approval period was due to a diagnosis of acute pain;
5. 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 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): AZ.CP.PMN.53 for Arizona Medicaid.

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 – AZ.CP.PMN.53 for Arizona Medicaid.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
EVA: ethylene vinyl acetate
FDA: Food and Drug Administration
MAT: medication-assisted treatment

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 (Subutex) oral tablets	Maintenance: Target dose: 16 mg PO once daily; dosage should be adjusted in increments or decrements of 2 mg or 4 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 4 mg to 24 mg per day	24 mg per day
buprenorphine-naloxone (Suboxone) sublingual (SL) or buccal dissolving film, SL tablet	Maintenance: Target dose: buprenorphine 16 mg/naloxone 4 mg PO 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 PO 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 PO 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):
  - Probuphine: hypersensitivity to buprenorphine or any other ingredients in Probuphine (e.g., EVA)
  - Sublocade: hypersensitivity to buprenorphine or any other ingredients in Sublocade
- Boxed warning(s):
  - Probuphine: implant migration, protrusion, expulsion, and nerve damage associated with insertion and removal; available only through a restricted program called the Probuphine REMS Program
  - Sublocade: 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	**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.
‡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)	Prefilled syringe: 100 mg/0.5 mL and 300 mg/1.5 mL

VII. References

1. Probuphine Prescribing Information. Princeton, NJ: Braeburn 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 https://www.sublocade.com/. Accessed November 22, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed November 22, 2021.
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 December 2, 2020.
5. Center for Substance Abuse Treatment. Medications for opioid use disorder. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2020. (Treatment Improvement Protocol (TIP) Series, No. 63) Available from: https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP20-02-01-006. Accessed December 2, 2020.
6. Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. DHHS Publication No. (SMA) 05-4048. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005. Available at: https://www.asam.org/docs/advocacy/samhsa_tip43_matforopioidaddiction.pdf?sfvrsn=0. Accessed December 3, 2020.
7. Center for Substance Abuse Treatment. Detoxification and Substance Abuse Treatment. Treatment Improvement Protocol (TIP) Series, No. 45. HHS Publication No. (SMA) 15-4131. Rockville, MD: Center for Substance Abuse Treatment, 2006. Available at: https://www.samhsa.gov/search-samhsa/featured/tip-45. Accessed December 3, 2020.
8. American Society of Addiction Medicine (ASAM). National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. Available at: https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf. Accessed December 3, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/2019	10/2019
1Q 2020 annual review: added Probuphine implant to criteria; updated references.	01.15.2020	01.2020
Removed requirement for concurrent SMI diagnosis for Sublocade per AHCCCS FFS criteria; Removed age requirement for >18 years for Probuphine and Sublocade.	5.1.2020	n/a
Reviewed clinical content and updated references	9.19.2020	

CLINICAL POLICY
Buprenorphine Implant/Injection

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references reviewed and updated	01.26.21	01.21
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21
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. 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.

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.

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.