

Clinical Policy: Buprenorphine HCL (Probuphine Implant)

Reference Number: NH.PHAR.289

Effective Date: 11/2016

Last Review Date: 12/2017

[Revision Log](#)

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

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for buprenorphine (Probuphine® Implant).

Policy/Criteria

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

I. Initial Approval Criteria

A. Opioid Dependence (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 subdermally in the inner side of the upper arm.

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Opioid Dependence (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. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Probuphine (buprenorphine hydrochloride [HCL]) is designed to be implanted subdermally by a trained medical professional and to provide sustained delivery of buprenorphine for up to 6 months (each 6-month dose represents four implants). Buprenorphine is an opioid partial agonist at the mu opioid receptor and an antagonist at the kappa-opioid receptor and is regulated as a Schedule III controlled substance/narcotic (C-III) under the United States Controlled Substances Act.

Because of the risks associated with implant insertion and removal, Probuphine is available only through a restricted program called the PROBUPHINE REMS Program (see package insert for more details, including exception at Appendix E). Additionally, under the Drug Addiction Treatment Act (DATA) codified at 21 United States Code (U.S.C.) 823(g), use of Probuphine in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, have notified the Secretary of Health and Human Services of their intent to prescribe or dispense this product for the treatment of opioid dependence, and have been assigned a unique identification number that must be included on every prescription.

Formulations:

Each Probuphine implant kit contains the following:

- One individually packaged sterile disposable applicator (used to insert all four implants)
- Four individually packaged sterile implants
 - Each implant is 26 mm in length and 2.5 mm in diameter and contains 74.2 mg of buprenorphine (equivalent to 80 mg buprenorphine HCL) and ethylene vinyl acetate (EVA).
 - Four Probuphine implants (320 mg buprenorphine HCL) deliver circulating drug blood levels comparable to the average plasma concentrations observed following daily doses of ≤ 8 mg of Subutex/Suboxone sublingual tablet equivalencies.

FDA Approved Indications:

Probuphine (buprenorphine) is a partial opioid agonist/subdermal implant indicated for:

- 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 equivalent or generic equivalent).
 - *Probuphine should be used as part of a complete treatment program to include counseling and psychosocial support.*
 - *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 equivalent or generic equivalent.

Appendices

Appendix A: Abbreviation Key

DATA: Drug Addiction Treatment Act

HCL: Hydrochloric acid

U.S.C.: United States Code

EVA: Ethylene vinyl acetate

NOWS: Neonatal opioid withdrawal syndrome

Appendix B: 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 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)
			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 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	4 mg/1 mg (Suboxone)	
		8 mg/2 mg	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.

Appendix C: Dosing and Administration Information

- Probuphine subdermal implants are intended to be in place for 6 months and then removed by the end of the sixth month or earlier if needed.
- If continued treatment is desired new implants are inserted subdermally at the time of removal of the first implant. The new implants are placed in an area of the inner side of either upper arm that has not been previously used.

- If new implants are not inserted on the same day as the removal of implants, patients are maintained on their previous dosage of transmucosal buprenorphine (i.e., the dose from which they were transferred to Probuphine treatment) prior to additional Probuphine treatment.
- After one insertion in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment.
- Patients who elect to discontinue Probuphine treatment without continuing on other buprenorphine treatment should be monitored for withdrawal.
 - Withdrawal signs and symptoms can include restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, mydriasis, irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.
 - Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy and is a risk if members using Probuphine are pregnant (see package insert for more information).

Appendix D: Opioids and Opioid Antagonists

- Opioids
 - Naturally occurring opioids (opiates): Morphine, codeine
 - Semi-synthetic opioids: Heroin (a derivative of morphine not used therapeutically in the U.S.), hydrocodone, oxycodone
 - Synthetic opioids: Buprenorphine, fentanyl, methadone, tramadol
- Opioid antagonists
 - Naloxone
 - Naltrexone

Appendix E: Overdosage Information

- Clinical presentation:
 - The manifestations of acute buprenorphine overdose include pinpoint pupils, sedation, hypotension, respiratory depression, and death.
- Treatment of overdose:
 - In case of overdose, priorities are the re-establishment of a patent and protected airway and institution of assisted ventilation, if needed. Employ other supportive measures (including oxygen, vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life support techniques.
 - The opioid antagonist naloxone is a specific antidote to respiratory depression resulting from opioid overdose. Naloxone may be of value for the management of buprenorphine overdose. Higher than normal doses and repeated administration may be necessary.
 - Clinicians should consider the potential role and contribution of buprenorphine, other CNS depressant drugs, and other opioids in a patient's clinical presentation, in determining whether the implants should be removed. In an emergency situation, the removal procedure can be performed by a surgeon who is not certified in the REMS.

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 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.	12/17	12/17

References

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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.

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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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