Clinical Policy: Buprenorphine Injection (Sublocade, Brixadi)

Reference Number: CP.PHAR.289
Effective Date: 12.01.16
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Sublocade and Brixadi are indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine.

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

Sublocade and Brixadi are administered only by healthcare providers in a healthcare setting

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 Sublocade and Brixadi are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

A. Opioid Dependence (must meet all)**:**

1. Diagnosis of opioid dependence;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):
   a. Member is switching from another non-transmucosal buprenorphine-containing product (e.g., Sublocade, Brixadi);
   b. Member meets one of the following (i, ii, or iii):
      i. Member has tolerated a single 4 mg dose of a transmucosal buprenorphine-containing product;
      ii. For Brixadi requests, member is currently being treated with a transmucosal buprenorphine-containing product;
      iii. For Sublocade requests, member is currently being treated with 8 mg to 24 mg daily of transmucosal buprenorphine;

4. Medical justification supports inability to continue to use transmucosal (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 transmucosal formulations of buprenorphine;
   b. Treatment failure with transmucosal 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 transmucosal formulations of buprenorphine;
5. Dose does not exceed any of the following (a or b):
   a. Sublocade, both of the following (i and ii):
      i. Initiation doses (1 and 2):
         1) 300 mg on Day 1, followed by 300 mg between Day 8 to 1 Month;
         2) 2 injections;
      ii. Maintenance doses (1 and 2):
         1) 300 mg per month;
         2) 1 injection;
   b. Brixadi (i or ii):
      i. 32 mg (1 injection) per week;
      ii. 128 mg (1 injection) every 28 days.

Approval duration:
Medicaid/Commercial – 6 months *(12 months for New Hampshire)*
HIM – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

A. Opioid Dependence (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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 any of the following (a or b):
   a. Sublocade: 300 mg (1 injection) per month;
   b. Brixadi (i or ii):
      i. 32 mg (1 injection) per week;
      ii. 128 mg (1 injection) every 28 days.

Approval duration:
Medicaid/Commercial – 6 months *(12 months for New Hampshire)*
HIM – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for 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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;
- **B.** Pain management.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MAT: medication-assisted treatment
REMS: Risk Evaluation and Mitigation Strategy
SL: sublingual

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) sublingual (SL) tablet	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) 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	17.2 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 Sublocade or Brixadi

- Boxed warning(s): risk of serious harm or death with intravenous administration; available only through a restricted program called the Sublocade or Brixadi REMS Program

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
			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 (Sublocade)	Two[a] monthly initial doses of 300 mg subcutaneously followed by 100 mg monthly maintenance doses [a] *The second injection may be administered as early as 1 week and up to 1 month after the initial injection based on patient need* Increasing the maintenance to 300 mg monthly may be considered for patients in which the benefits outweigh the risks <u>Induction in patients not already receiving buprenorphine:</u>	300 mg per month

Drug Name	Dosing Regimen	Maximum Dose
	Patients should receive an initial dose (e.g., 4 mg of transmucosal buprenorphine and be observed for one hour to confirm tolerability before administering the first injection of Sublocade <u>Transition of patients already receiving transmucosal buprenorphine:</u> Patients who have been on 8 mg to 24 mg daily of transmucosal buprenorphine may be transitioned directly to the recommended starting dose of 300 mg of Sublocade.	
Buprenorphine (Brixadi)	<u>Patients not currently receiving buprenorphine treatment</u> • The recommended weekly dose is 24 mg subcutaneously weekly titrated over the first week as follows: ○ Administer a test dose of transmucosal buprenorphine 4 mg. If the test does is tolerated without precipitated withdrawal, administer the first dose of Brixadi (weekly) 16 mg. Administer an additional dose of 8 mg Brixadi (weekly) within 3 days of the first dose to achieve the recommended 24 mg Brixadi (weekly) dose. • If needed, during this week of treatment, administer an additional 8 mg dose of Brixadi (weekly), waiting at least 24 hours after the previous injection, for a total weekly dose of 32 mg. • Administer subsequent weekly injections based on the total weekly dose that was established in week one. Dose adjustments can be made at weekly appointments with the maximum weekly dose being 32 mg. <u>Patients switching from transmucosal buprenorphine-containing products</u> Patients currently treated with a transmucosal buprenorphine-containing product may be switched directly to either weekly or monthly Brixadi. Refer to Prescribing Information for suggested corresponding weekly or monthly Brixadi.	32 mg per week or 128 mg per 28 days

Drug Name	Dosing Regimen	Maximum Dose
	Patients transitioning between weekly and monthly Brixadi Refer to Prescribing Information for recommended dose when transitioning between weekly and monthly Brixadi. Dose adjustments of Brixadi An additional 8 mg of Brixadi (weekly) may be administered, based on clinical judgement during a dosing interval, up to a maximum dose of 32 mg per week or 128 mg per month. Other Brixadi (weekly) should be administered in 7-day intervals. Brixadi (monthly) should be administered in 28-day intervals. Weekly doses of Brixadi cannot be combined to yield a monthly dose. Administer Brixadi as a single injection, and do not divide	

VI. Product Availability

Drug Name	Availability
Buprenorphine (Sublocade)	Prefilled syringes: 100 mg/0.5 mL and 300 mg/1.5 mL
Buprenorphine (Brixadi)	• Prefilled single-dose syringes – weekly: 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, and 32 mg/0.64 mL • Prefilled single-dose syringes – monthly: 64 mg/0.18 mL, 96 mg/0.27 mL, and 128 mg/0.36 mL

VII. References

1. Sublocade Prescribing Information. North Chesterfield, VA: Indivior Inc.; February 2025. Available at https://www.sublocade.com/. Accessed February 26, 2025.
2. Brixadi Prescribing Information. Plymouth Meeting, PA: Braeburn Inc.; December 2023. Available at: https://www.brixadi.com/. Accessed February 26, 2025.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. Available at: http://www.clinicalkey.com/pharmacology/. Accessed November 14, 2024.
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 14, 2024.

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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.ncbi.nlm.nih.gov/books/NBK64164/. Accessed November 14, 2024.
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://store.samhsa.gov/product/TIP-45-Detoxification-and-Substance-Abuse-Treatment/SMA15-4131. Accessed November 14, 2024.
8. Kampman K and Jarvis M. American society of addiction medicine (ASAM): national practice guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med.* 2015 Oct; 9(5):358-367. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4605275/. Accessed November14, 2024.
9. Cunningham C, Edlund MJ, Gordon AJ et al. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. Available from: https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline. Accessed November 14, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Q9991	Injection, buprenorphine extended-release (Sublocade), less than or equal to 100 mg
Q9992	Injection, buprenorphine extended-release (Sublocade), greater than 100 mg
J0577	Injection, buprenorphine extended release (brixadi), less than or equal to 7 days of therapy
J0578	Injection, buprenorphine extended release (brixadi), greater than 7 days of therapy

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added coding implications; references reviewed and updated.	12.02.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added separate approval duration for initial and continued approval of 12 months for HIM lines of business to meet regulatory requirements; added that approval durations should be 12 months for NH for other lines of business.	11.02.21	
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.22.21	02.22
In Section IIB clarified approval duration by removing references to implants which do not apply to Sublocade injection requests.	06.09.22	
Template changes applied to other diagnoses/indications and continued therapy section.	09.20.22	
1Q 2023 annual review: no significant changes; removal of references to discontinued product Probuphine; references reviewed and updated.	11.16.22	02.23
3Q 2023 annual review: for initial criteria, changed buprenorphine or buprenorphine-naloxone to buprenorphine-containing products and changed sublingual tablets or film to transmucosal buprenorphine; clarified oral buprenorphine as transmucosal buprenorphine; references reviewed and updated. RT4: Brixadi is now FDA approved – combined from previously approved pre-emptive policy CP.PHAR.498; clarified that at least one dose of oral buprenorphine means member should have tolerated a single 4 mg dose of or is currently being treated with a transmucosal-containing product.	06.02.23	08.23
Added HCPCS code [J0576]	10.26.23	
1Q 2024 annual review: no significant changes; added HCPCS code [C9154] for Brixadi; references reviewed and updated.	10.19.23	02.24
Removed HCPCS codes [C9154, J0576] and added HCPCS codes [J0577, J0578] for Brixadi.	02.22.24	
Added disclaimer that medical management techniques, including quantity management, beyond step therapy is not allowed for members in NV per SB 439.	05.30.24	
1Q 2025 annual review: added pain management to section III as diagnoses/indication for which coverage is not authorized; references reviewed and updated.	10.31.24	02.25
RT4: for Sublocade, updated criteria to include FDA approved rapid initiation protocol per PI (previously required 7 days of transmucosal buprenorphine).	02.26.25	
For Sublocade, updated criteria to include option for second initiation dose between Day 8 to 1 Month per PI.	06.17.25	

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.

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