Clinical Policy: Buprenorphine Injection (Brixadi)

Reference Number: LA.PHAR.498
Effective Date: FDA Approval Date
Last Review Date: 05.01.23
Line of Business: Medicaid

Coding Implications
Revision Log

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

Please note: This policy is for medical benefit

Description

Buprenorphine Injection (Brixadi™) is a partial opioid agonist.

FDA Approved Indication(s) [Pending]

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

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Brixadi is administered only by healthcare providers in a healthcare setting and used as part of a complete treatment program that includes counseling and psychosocial support.

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 Louisiana Healthcare Connections® that Brixadi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Opioid Dependence/Opioid Use Disorder (must meet all)**:**

1. Diagnosis of opioid dependence or moderate to severe OUD;*
2. Age ≥ 18 years;*
3. Has initiated treatment with at least one dose of oral buprenorphine;*
4. Member meets one of the following (a or b):
   a. Member is switching from another non-oral buprenorphine product (e.g., Sublocade®);*
   b. Medical justification supports inability to continue oral (e.g, sublingual, buccal) formulations of buprenorphine as evidenced by one of the following (i, ii, iii, or iv):*
      i. Documentation of non-compliance to oral formulations of buprenorphine;
      ii. Treatment failure with oral formulations of buprenorphine;
      iii. History of buprenorphine diversion;
      iv. Contraindication(s) or clinically significant adverse effects to oral buprenorphine excipients;

5. Dose does not exceed 32 mg (one syringe) per week or 128 mg (one syringe) per month.*

Approval duration: 6 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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Opioid Dependence/Opioid Use Disorder (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections 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 a diagnosis of acute pain;
4. If request is for a dose increase, new dose does not exceed 32 mg (one syringe) per week or 128 mg (one syringe) per month.*

Approval duration: 6 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 LA.PMN.255
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: LA.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 – LA.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
OUD: opioid use disorder
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/buccal 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 [Pending]
- Contraindication(s): pending
- Boxed warning(s): pending

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, SL	Generic	2 mg 8 mg	2 mg (Subutex) 8 mg (Subutex)
Buprenorphine HCL/naloxone HCL	Tablet, SL	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, SL/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 SL tablets and SL tablets/buccal film respectively.*
†For a more comprehensive listing of brand/generic SL/buccal 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) SL tablets, while used as buprenorphine equivalency references, are no longer available in the U.S.
§Naloxone (an opioid antagonist) is minimally absorbed in SL/buccal formulations and rather is added to discourage diversion or misuse.

Appendix E: General Information

- In December 2018, Brixadi was tentatively approved for the treatment of moderate to severe OUD but is not eligible for marketing in the U.S. until December 1, 2020, because of exclusivity considerations. With tentative approval, FDA concluded that Brixadi met all required quality, safety, and efficacy standards necessary for approval.
- The pivotal Phase 3 efficacy and safety trial demonstrates that Brixadi met the primary endpoint of non-inferiority for responder rate ($p < 0.001$) versus treatment with the current standard of care, sublingual buprenorphine/naloxone, and demonstrated superiority for the secondary endpoint for the percentage of negative opioid assessments from week 4 through 24 ($p = 0.004$). Brixadi also was effective in reducing opioid withdrawal and cravings and maintaining low withdrawal and craving scores. Brixadi is

the only injectable buprenorphine studied against the current standard of care, sublingual buprenorphine/naloxone.

Braeburn receives new Complete Response Letter for Brixadi in the US. Camurus Press Release. December 15, 2021. Available at https://mb.cision.com/Main/13456/3473281/1510618.pdf. Accessed April 12, 2022.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
OUD *	Weekly or monthly SC injection administered in the buttock, thigh, stomach (abdomen) or upper arm. (*Refer to conversion chart for optimal dosing.*)* Weekly: 8 mg, 16 mg, 24 mg, 32 mg Monthly: 64 mg, 96 mg, 128 mg	Weekly: 32 mg* Monthly: 128 mg*

VI. Product Availability [Pending]

Prefilled syringes: weekly: 8 mg, 16 mg, 24 mg, 32 mg; monthly: 64 mg, 96 mg, 128 mg*

VII. References

1. Braeburn receives new Complete Response Letter for Brixadi in the US. Camurus Press Release. December 15 2021. Available at: https://mb.cision.com/Main/13456/3473281/1510618.pdf . Accessed April 12, 2022.
2. Braeburn submits request for final approval of Brixadi™ (buprenorphine) extended-release injection for the treatment of opioid use disorder. Braeburn Press Release. June 1, 2020. Available at https://braeburnrx.com/braeburn-submits-request-for-final-approval-of-brixadi-buprenorphine-extended-release-injection-for-the-treatment-of-opioid-use-disorder/. Accessed April 12, 2022.
3. FDA Grants Braeburn's Citizen Petition Allowing BRIXADI (buprenorphine) Extended-Release Injection for Opioid Use Disorder to be Available in December 2020. November 7, 2019. Available at: https://braeburnrx.com/fda-grants-braeburns-citizen-petition-allowing-brixadi-buprenorphine-extended-release-injection-for-opioid-use-disorder-to-be-available-in-december-2020/. Accessed April 12, 2022.
4. Lofwall MR, Walsh SL, Nunes EV, et al. Weekly and monthly subcutaneous buprenorphine depot formulations vs daily sublingual buprenorphine with naloxone for treatment of opioid use disorder: A randomized clinical trial. *JAMA Intern Med.* 2018;178(6):764-773. doi:10.1001/jamainternmed.2018.1052.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed April 12, 2022.
6. The ASAM national practice guideline for the treatment of opioid use disorder - 2020 focused updated. Available at: https://www.asam.org/Quality-Science/quality/2020-national-practice-guideline.
7. Medications for opioid use disorder: For healthcare and addiction professionals, policymakers, patients, and families. Updated 2020. Treatment improvement protocol 63. SAMHSA.

8. Compton WM, Dawson DA, Goldstein RB, Grant BF. Crosswalk between DSM-IV dependence and DSM-5 substance use disorders for opioids, cannabis, cocaine and alcohol. Drug and Alcohol Dependence. 2013;132:387-390. http://dx.doi.org/10.1016/j.drugalcdep.2013.02.036.

Coding Implications [Pending]
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
Pending	Pending

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.