Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

Clinical Policy: Buprenorphine Injection (Brixadi)

Reference Number: ERX.SPA.410
Effective Date: FDA Approval Date
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

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

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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®, Probuphine®);*
   b. Medical justification supports inability to continue oral buprenorphine as evidenced by one of the following (i, ii, iii, or iv):*
      i. Non-compliance to oral buprenorphine;
      ii. Treatment failure with oral 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 a health plan affiliated with Envolve Pharmacy Solutions 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
OUD: opioid use disorder

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 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	17.1 mg/4.2 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	opioid withdrawal symptoms; usual range: 2.9 mg/0.71 mg to 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 [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 Name		Indication	Dosing Regimen	Maximum Dose
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 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 June 16, 2020.

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 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 June 16, 2020.
2. 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 June 16, 2020.
3. 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.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed June 23, 2020.
5. 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.
6. Medications for opioid use disorder: For healthcare and addiction professionals, policymakers, patients, and families. Updated 2020. Treatment improvement protocol 63. SAMHSA.
7. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	07.07.20	08.20
3Q 2021 annual review: no significant changes; product is still waiting for final FDA approval; references reviewed and updated.	05.12.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.