Buprenorphine (Brixadi™) (for Indiana Only)

Policy Number: CSIND0057.08
Effective Date: April 1, 2024

Ü Instructions for Use

Table of Contents **Page**

Application 1
Coverage Rationale 1
Applicable Codes 2
Background 2
Clinical Evidence 2
U.S. Food and Drug Administration 3
References 3
Policy History/Revision Information 4
Instructions for Use 4

Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Indiana.

Coverage Rationale

This policy provides information about the use of buprenorphine formulations administered by subcutaneous (SC) injection. This policy refers to the following buprenorphine products:

- Brixadi™

Buprenorphine extended-release injection (e.g., Brixadi) is proven and medically necessary for the treatment of moderate to severe opioid use disorder in patients who meet all of the following criteria:

- For **initial therapy**, **all** of the following:
  - Patient is being treated for opioid dependence; **and**
  - **One** of the following:
    - **Both** of the following:
      - Patient is not currently receiving maintenance buprenorphine treatment; **and**
      - Patient has received a test dose of buprenorphine to establish that buprenorphine is tolerated without precipitated withdrawal

      or
    - Patient is currently maintained on oral, sublingual, or transmucosal buprenorphine product

    and
  - Patient has not, nor will receive supplemental, oral, sublingual, or transmucosal buprenorphine; **and**
  - Brixadi dosing is in accordance with the U. S. Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response to buprenorphine extended-release therapy; **and**
  - Patient has not, nor will receive supplemental, oral, sublingual, or transmucosal buprenorphine; **and**
  - Brixadi dosing is in accordance with the U. S. Food and Drug Administration approved labeling; **and**
  - Continuation authorization will be for no more than 12 months

Buprenorphine extended-release injection is unproven and not medically necessary for pain management.[1,3,6]

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
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 and up to 28 days of therapy

Diagnosis Code	Description
F11.20	Opioid dependence, uncomplicated
F11.21	Opioid dependence, in remission
F11.220	Opioid dependence with intoxication, uncomplicated
F11.221	Opioid dependence with intoxication delirium
F11.222	Opioid dependence with intoxication with perceptual disturbance
F11.229	Opioid dependence with intoxication, unspecified
F11.24	Opioid dependence with opioid-induced mood disorder
F11.250	Opioid dependence with opioid-induced psychotic disorder with delusions
F11.251	Opioid dependence with opioid-induced psychotic disorder with hallucinations
F11.259	Opioid dependence with opioid-induced psychotic disorder, unspecified
F11.28	Opioid dependence with other opioid-induced disorder (Incomplete code - additional digit required)
F11.281	Opioid dependence with opioid-induced sexual dysfunction
F11.282	Opioid dependence with opioid-induced sleep disorder
F11.288	Opioid dependence with other opioid-induced disorder
F11.29	Opioid dependence with unspecified opioid-induced disorder

Background

Brixadi (buprenorphine extended-release) injection is a sterile solution intended for subcutaneous injection only. Brixadi is designed to deliver buprenorphine at a controlled rate over either one week or one month.[10]

Clinical Evidence

The efficacy and safety of Brixadi for the treatment of opioid use disorder was evaluated in a Phase 3, 24-Week, randomized, double-blind, double-dummy, active controlled, multicenter study in patients who met the DSM-5 criteria for moderate or severe opioid use disorder and who were actively seeking but not currently receiving buprenorphine treatment.[10] Patients were randomized to receive either Brixadi injections with placebo sublingual tablets or sublingual buprenorphine/naloxone (SL BPN/NX) tablets with placebo injections. All patients received individual drug counseling for the duration of the study. On the first day of treatment patients received an open-label 4 mg test dose of sublingual buprenorphine. Patients who tolerated the test dose (two patients did not tolerate the test dose) were randomized and given a 16 mg injection of Brixadi (weekly) or matched placebo. During the next 6 days patients were allowed up to two further 8 mg injections as needed. Patients received an injection of 16, 24, or 32 mg on Day 8 matched to the dose they received in the previous seven days. Patients received injections weekly (every 7 days ±2-day window) for twelve weeks total and then transitioned to an equivalent dose of Brixadi (monthly) (every 28 days, ±7-day window) for the remaining twelve weeks. Dose adjustments were permitted for the duration of

the study. Supplemental 8 mg Brixadi (weekly) injections were allowed during the second phase of the study and were also used in the active-controlled group. Overall, supplemental 8 mg injections were given to 14 patients (6.6%) in the Brixadi arm and 17 patients (7.9%) in the SL BPN/NX arm. For the first twelve weeks patients completed weekly visits. For the final twelve weeks patients were transitioned to monthly visits. Patients were also required to complete three additional randomly scheduled visits during the final twelve weeks. Efficacy was evaluated using urine drug screens combined with self-reported use of illicit opioid use. Missing urine drug screen samples and/or self-reports were counted as positive for illicit opioids. A total of 428 patients were randomized equally (215 patients in the SL BPN/NX group and 213 in the Brixadi group). Of the randomized patients, 69.0% (147/213) of the patients in Brixadi treatment group and 72.6% (156/215) of the patients in the SL BPN/NX treatment group completed the 24-week period. A patient was a responder if they met all of the following criteria:

- Negative opioid assessment (urinalysis and self-report) during week 12 (evaluated during week 13 visit)
- No more than one positive opioid assessment in the three illicit opioid use assessments performed during week 9 to 11 (evaluated during visits at weeks 10 to 12)
- Negative opioid assessment during the final month of the study
- No more than one positive opioid assessment at the three scheduled monthly visits and three random site visits

This responder definition was designed to identify patients who were successfully treated with both Brixadi (weekly) (administered in the first 12 weeks of treatment) and Brixadi (monthly) (administered in the second 12 weeks of treatment). Therefore, patients were required to have negative opioid assessments at the end of each treatment phase. Each phase also included an allowable grace period (an initial period of time when positive opioid assessments were not taken into account), and the definition also allowed for sporadic positive assessments. Brixadi met the primary endpoint of non-inferiority for responder rate vs. Daily SL BPN/NX (16.9% vs. 14.0%; treatment difference of 2.9; 95% CI: -3.9, 9.8).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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

Brixadi is available only through a restricted program called the Brixadi REMS because of the risk of serious harm or death that could result from intravenous self-administration. The goal of the REMS is to mitigate serious harm or death that could result from intravenous self-administration by ensuring that healthcare settings and pharmacies are certified and only dispense Brixadi directly to a healthcare provider for administration by a healthcare provider. Healthcare Settings and Pharmacies that order and dispense Brixadi must be certified in the Brixadi REMS.

Substance Abuse and Mental Health Services Administration (SAMHSA)[4,8]

Removal of DATA Waiver (X-Waiver) Requirement

Section 1262 of the Consolidated Appropriations Act, 2023 (also known as Omnibus bill), removes the federal requirement for practitioners to submit a Notice of Intent (have a waiver) to prescribe medications, like buprenorphine, for the treatment of opioid use disorder. All practitioners who have a current DEA registration that includes Schedule III authority may now prescribe buprenorphine for Opioid Use Disorder in their practice if permitted by applicable state law. All prescriptions for buprenorphine only require a standard DEA registration number. The previously used DATA-Waiver registration numbers are no longer needed for any prescription. There are no longer any limits or patient caps on the number of patients a prescriber may treat for opioid use disorder with buprenorphine. The Act does not impact existing state laws or regulations that may be applicable.

References

1. Probuphine [package insert]. South San Francisco, CA: Titan Pharmaceuticals, Inc., June 2022.
2. Gold Standard, Inc. Probuphine®. Clinical Pharmacology [database online]. Available at: http://www.clinicalpharmacology.com. Accessed: October 9, 2022.
3. Rosenthal RN, Lofwall MR, Kim S, Chen M, Effect of Buprenorphine Implants on Illicit Opioid Use Among Abstinent Adults

With Opioid Dependence Treated With Sublingual Buprenorphine: A Randomized Clinical Trial. JAMA. 2016 Jul 19;316(3):282-90.

4. Buprenorphine Treatment Physician Locator. (n.d.). Retrieved October 9, 2022, from http://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator.
5. Probuphine Insertion & Removal Instruction Booklet. Princeton, NJ: Braeburn Pharmaceuticals, Inc., May 2016. Available at: http://probuphinerems.com/wp-content/uploads/2016/04/ifu.pdf.
6. Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2019 Feb 23;393(10173):778-790.
7. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update [published correction appears in J Addict Med. 2020 May/Jun;14(3):267]. J Addict Med. 2020;14(2S Suppl 1):1-91. doi:10.1097/ADM.0000000000000633.
8. SAMHSA. Removal of data waiver (X-waiver) requirement. SAMHSA. https://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement. Last updated: January 25, 2023. Accessed: February 3, 2023.
9. Brixadi [package insert]. Plymouth Meeting, PA: Braeburn Inc., May 2023.

Policy History/Revision Information

Date	Summary of Changes
04/01/2024	**Applicable Codes** • Updated list of applicable HCPCS codes to reflect quarterly edits: o Added J0577 and J0578 o Removed J0576 **Supporting Information** • Archived previous policy version CSIND0057.07

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.