Medical Benefit Drug Policy

Buprenorphine (Sublocade® and Brixadi™) Subcutaneous

Policy Number: MC/PC 004
Effective Date: June 1, 2025

Instructions for Use

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Related Policies

- n/a

Coverage Rationale

Moderate to Severe Opioid Use Disorder

For initial coverage of Buprenorphine extended release injection (i.e, Brixadi, Sublocade) for the treatment of moderate to severe opioid use disorder, the following will be required:

- Patient is being treated for opioid use disorder **and**
- Patient is on a complete treatment plan that includes counseling and psychosocial support **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 will not receive additional supplemental buprenorphine

For reauthorization coverage of Buprenorphine extended release injection (i.e., Brixadi, Sublocade) the following will be required:

- Patient demonstrates positive clinical response to therapy
- Patient will not receive additional supplemental buprenorphine

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 the member specific benefit plan

document and applicable laws that may require coverage for a specific service ...ly any right to reimbursement or guarantee claim payment. Other Policies and G...

HCPCS Code	Description
C9154	Injection, buprenorphine extended-release (Brixadi), 1 mg
Q9991	Injection, buprenorphine extended-release (Sublocade), less than or equal to 100 mg
Q9992	Injection, buprenorphine extended-release (Sublocade), greater than 100 mg

ICD-10 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

Buprenorphine hydrochloride is an opioid partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor, thus exhibiting a ceiling to its effects. The danger of overdose, abuse liability, and toxicity may be less than with full opioid agonists.

Clinical Evidence

Clinical Evidence for Opioid Use Disorder

The efficacy of Sublocade for the treatment of opioid use disorder was evaluated in a Phase 3, 24-week, randomized, double-blind, placebo-controlled, multicenter trial in treatment-seeking patients with moderate or severe opioid use disorder (Haight et al 2019, Sublocade Package insert, 2023). Patients (n = 504 patients) were randomized 4:4:1:1 to one of following dosing regimens: 6 once-monthly 300 mg doses (n = 203), 2 once-monthly 300 mg doses followed by 4 once-monthly 100 mg doses (n = 201), or 6 once-monthly SC injections of placebo (n = 100). All doses were administered by a physician or suitably qualified designee and were separated by 28 ±2 days. In addition to study medication, all subjects received manual-guided psychosocial support at least once a week (Individual Drug Counseling = IDC). Prior to the first dose, treatment was initiated with buprenorphine/naloxone sublingual film; doses were adjusted from 8/2mg to 24/6 mg per day over a period of 7-14 days. Patients were randomized to Sublocade injection or placebo after cravings and

withdrawal symptoms were clinically controlled. After randomization, supplem oxone film was not permitted during the study. Efficacy was evaluated over Weeks drug screens combined with self-reported use of illicit opioid use. A "grace period" was applied for Weeks 1 through 4 to allow patients to stabilize in treatment. During this period, opioid use if it occurred, was not considered in the analysis. Missing urine drug screen samples and/or self-reports during Weeks 5-24 were counted as positive for illicit opioids. Based on the cumulative distribution function (CDF) of the percentage of urine samples negative for illicit opioids combined with self-reports negative for illicit opioid use collected from Week 5 through Week 24, regardless of dose, Sublocade was superior to the placebo group with statistical significance. The proportion of patients achieving treatment success (defined as patients with ≥ 80% opioid-free weeks) was statistically significantly higher in both groups receiving Sublocade compared to the placebo group (28.4% [300 mg/100 mg], 29.1% [300 mg/300mg], 2% [placebo].

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. 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).

Clinical Guidelines

The American Academy of Pediatrics (AAP), American Psychiatric Association (APA), American Society of Addiction Medicine (ASAM), CDC, Society for Adolescent Health and Medicine (SAHM), SAMHSA, and the Veterans Health Administration (VHA) have published guidelines for the treatment of opioid dependence. In general, these guidelines support access to all FDA-approved pharmacological therapies for the management of opioid use disorder. Buprenorphine/naloxone combination products may be used for induction and maintenance. In pregnant women for whom buprenorphine therapy is selected, buprenorphine alone (i.e., without naloxone) is recommended. Naltrexone may

be considered for the prevention of relapse, although outcomes with this medi poor adherence. Extended-release injectable naltrexone may reduce, but not eli oral naltrexone adherence. The VHA guideline offers a weak recommendation fo the use of extended-release injectable naltrexone; it does not recommend for or against oral naltrexone. Furthermore, the VHA guideline suggests offering clonidine or lofexidine as a second-line agent for opioid withdrawal management in patients with OUD for whom withdrawal management is indicated and for whom methadone and buprenorphine are contraindicated, unacceptable, or unavailable, or for whom extended-release injectable naltrexone is planned (CSUP 2016 [policy expired, but currently under review], Cunningham et al 2020, Dowell et al 2022, Kampman et al 2015, Kleber et al 2006, SAHM 2021, SAMHSA treatment improvement protocol 2021, VHA 2021).

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.

Sublocade is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days. Sublocade should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Sublocade is available only through a restricted REMS program, called the "Sublocade REMS Program," because of the risk of serious harm or death that could result from intravenous self-administration. Healthcare settings and pharmacies that order and dispense Sublocade must be certified in this program and comply with the REMS requirements.

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.

References

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Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
5/16/2024	Name change of Policy from Subloclade to Buprenophine, addition of Brixadi to the criteria
5/15/2025	Annual Review. Updated references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance 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.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx 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.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).