This brochure is intended for healthcare professionals only.

Brixadi®
(buprenorphine) extended-release injection for subcutaneous use (CIII)
Weekly 8 • 16 • 24 • 32 mg **Monthly** 64 • 96 • 128 mg

FOR MODERATE TO SEVERE OUD

IT MAY BE POSSIBLE TO OFFER PATIENTS

A MONTH OF MORNINGS

WITHOUT DAILY MEDICATION REMINDING THEM OF THEIR ADDICTION[1-4]

LAI, long-acting injectable; OUD, opioid use disorder.
Not actual patient.

BRIXADI is the fastest-growing LAI for OUD.*

*Based on units from Symphony Health, an ICON plc Company, Metys®, March 1, 2024 to June 30, 2025, month over prior year month.

INDICATIONS AND USAGE

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.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS HARM OR DEATH WITH INTRAVENOUS ADMINISTRATION; BRIXADI RISK EVALUATION AND MITIGATION STRATEGY

- **Serious harm or death could result if administered intravenously. BRIXADI forms a liquid crystalline gel upon contact with body fluids and may cause occlusion, local tissue damage, and thrombo-embolic events, including life-threatening pulmonary emboli, if administered intravenously.**
- **Because of the risk of serious harm or death that could result from intravenous self-administration, BRIXADI is only available through a restricted program called the BRIXADI REMS. Healthcare settings and pharmacies that order and dispense BRIXADI must be certified in this program and comply with the REMS requirements.**

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

For patients with OUD, taking medication daily may come with challenges[2,3,5,6]

Patients may start their recovery journey with daily medication, but could face obstacles.[7-11]

Common obstacles include:

- Remembering or choosing to take doses
- Feeling dependent on a substance
- Taking it as directed
- Diversion, theft, or loss
- Secure storage/safe disposal
- Concerns about dental issues

~30% to 60% of patients prescribed daily buprenorphine products discontinued within 30 days in a claims database study.[12]

OUD, opioid use disorder.

Research shows that even brief interruptions in buprenorphine treatment can lead to relapse[6]

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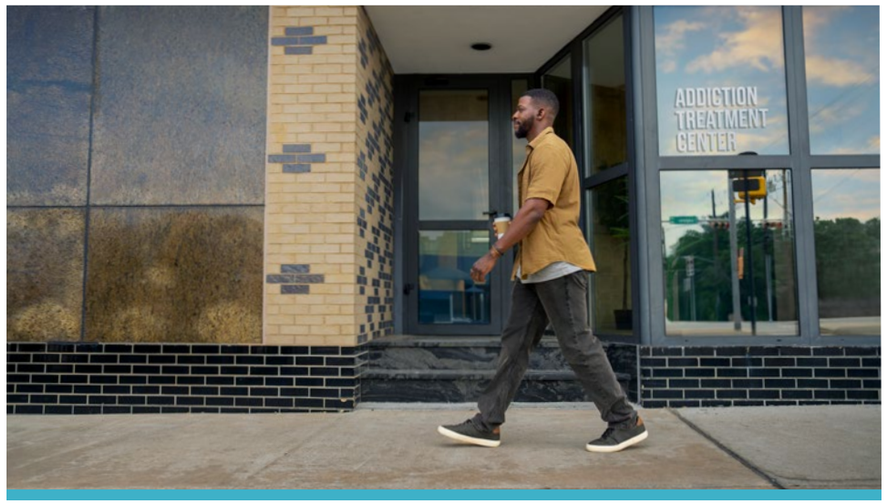
Adherence to treatment is considered an important part of a recovery journey.[13]

- Nonadherent patients were 10× more likely to relapse[6]
- Nonadherent patients overdosed almost 3× as often as adherent patients[14]



Multiple guidelines for OUD state that treatment retention and reducing illicit opioid use are key factors for patients in OUD recovery.[13,15,16]

Is it time to consider another treatment option for your patients?

Important Safety Information (Continued)

BRIXADI (buprenorphine) extended-release injection (weekly, 50 mg/mL buprenorphine) and BRIXADI (monthly, 356 mg/mL buprenorphine) are different formulations. Doses of BRIXADI (weekly) cannot be combined to yield an equivalent monthly dose.

BRIXADI is contraindicated in patients with hypersensitivity (e.g. anaphylactic shock) to buprenorphine or any other ingredients in the solution for injection.

Warnings and Precautions

Addiction, Abuse, and Misuse: BRIXADI contains buprenorphine, a Schedule III controlled substance that can be abused in a manner similar to other opioids. Buprenorphine is sought by people with opioid use disorder and is subject to criminal diversion. Monitor all patients for progression of opioid dependence and addictive behaviors.

Important Safety Information (Continued)

Warnings and Precautions

Respiratory and CNS Depression: Buprenorphine has been associated with life-threatening respiratory depression and death. Use BRIXADI with caution in patients with compromised respiratory function. Due to its extended-release characteristics, if BRIXADI is discontinued as a result of compromised respiratory function, monitor patients for ongoing buprenorphine effects for approximately 1 month for BRIXADI (weekly) and for approximately 4 months for BRIXADI (monthly). Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose.

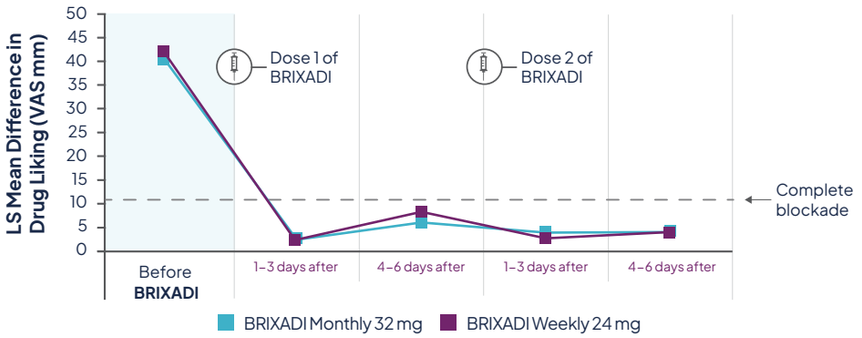
Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

BRIXADI blocked the effects of a high-potency opioid throughout the entire dosing interval[1]

Starting after the first injection, and lasting through the end of the dosing interval: BRIXADI demonstrated complete blockade of the rewarding effects of hydromorphone. This was sustained throughout the first and second dosing intervals.

MEAN DIFFERENCE IN PLACEBO-CORRECTED PEAK DRUG LIKING

This graph represents the results for hydromorphone 18 mg.



Primary endpoint[1]

The maximum rating (E_{max}) as rated on a 100-mm bipolar VAS for drug liking, with scores ranging from 0 (strong disliking) to 100 (strong liking), 50 being neutral. The predefined upper bound of the 95% CI for complete blockade of drug liking was an 11-mm difference between VAS E_{max} scores obtained for hydromorphone doses compared with placebo.

Study design[1,17]

Phase 2, randomized, double-blind, 2-dose opioid challenge study of 24 mg and 32 mg BRIXADI Weekly in 47 patients with moderate or severe OUD not actively seeking treatment. After stabilization on immediate-release morphine, all patients completed a 3-day qualification/baseline hydromorphone challenge session consisting of 3 intramuscular doses of hydromorphone (0 mg [placebo], 6 mg, and 18 mg) once daily for 3 consecutive days. Following qualification phase, eligible patients were randomly assigned to receive 2 injections of BRIXADI Weekly of either 24 mg (22 patients) or 32 mg (24 patients), with each dose administered 1 week apart. Two hydromorphone challenge sessions (3 consecutive days each) were conducted after each weekly injection of BRIXADI.

LS, least squares; VAS, visual analog scale.

BRIXADI delivers a continuous, steady release of buprenorphine over a month or a week[1]

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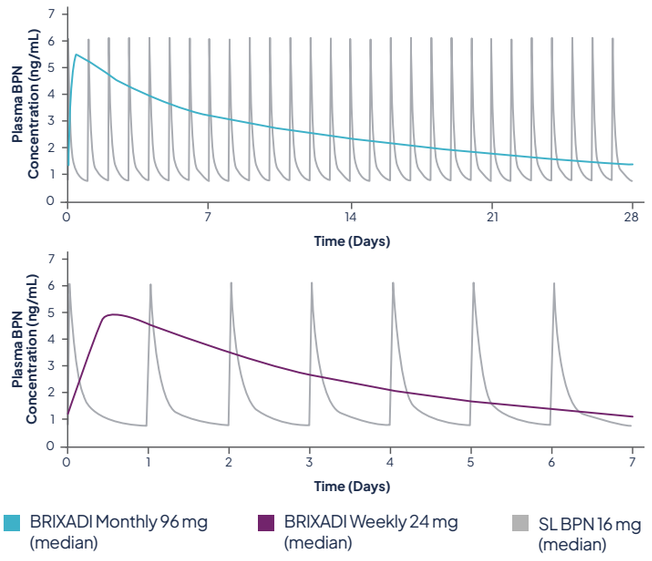
BRIXADI transforms into a liquid crystalline gel upon injection that steadily releases buprenorphine as the depot biodegrades over the monthly or weekly dosing interval.

BUPRENORPHINE PLASMA LEVEL PROFILE AT STEADY STATE[18]*

Population PK model based on 236 participants and >10,000 observations from 4 clinical studies.



With BRIXADI, the levels of buprenorphine remained above the C_{trough} of the corresponding sublingual doses at steady state.[1]*

*Steady state is achieved after 4 consecutive doses.

BPN, buprenorphine; PK, pharmacokinetic; SL BPN, sublingual buprenorphine.

Important Safety Information (Continued)

Warnings and Precautions

Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose: Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver. Because patients being treated for opioid use disorder have the potential for relapse, putting them at risk for opioid overdose, strongly consider prescribing naloxone for the emergency treatment of opioid overdose, both when initiating and renewing treatment with BRIXADI. If naloxone is prescribed, educate patients and caregivers on how to treat with naloxone, and emphasize the importance of calling 911 or getting emergency medical help, even if naloxone is administered.

Important Safety Information (Continued)

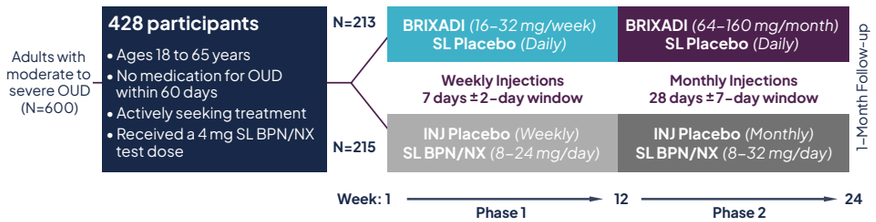
Warnings and Precautions

Concomitant Use of Benzodiazepines or other CNS Depressants: Concomitant use of buprenorphine and benzodiazepines or other CNS depressants increase the risk of adverse reactions including respiratory depression, overdose and death. Ensure that other healthcare providers prescribing benzodiazepines or other CNS depressants are aware of the patient's buprenorphine treatment and coordinate care to minimize the risk associated with concomitant use. Inform patients and caregivers that potentially fatal additive effects may occur if BRIXADI is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a healthcare provider.

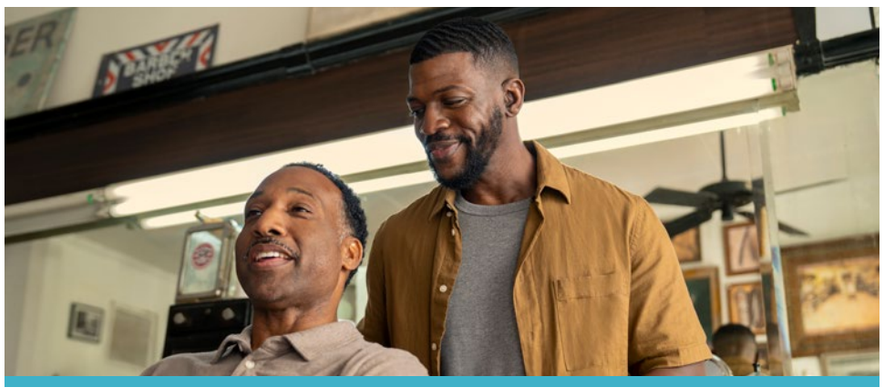
Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

BRIXADI is the ONLY injectable buprenorphine studied against daily SL BPN/NX in a pivotal phase 3 study[1]

PHASE 3, HEAD-TO-HEAD, 24-WEEK, RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY, ACTIVE-CONTROLLED, MULTICENTER STUDY[1,19]



- To allow for individualized treatment, patient doses could be adjusted throughout the study based on clinical judgment. Most patients, including those who tested positive for fentanyl at baseline, were titrated to 16 mg and 24 mg SL BPN/NX per day or the equivalent BRIXADI doses[1,19,20]
- 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[1]



INJ, injection; SL, sublingual; SL BPN/NX, sublingual buprenorphine/naloxone.

Important Safety Information (Continued)

Warnings and Precautions

Neonatal Opioid Withdrawal Syndrome, Pregnancy, and Lactation: Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy. NOWS may be life-threatening if not recognized and treated in the neonate. Healthcare providers should observe newborns for signs of NOWS and manage accordingly. Advise pregnant women receiving opioid addiction treatment with BRIXADI of the risk of neonatal opioid withdrawal syndrome. Warn patients that buprenorphine passes into breast milk. Advise the nursing mother taking buprenorphine to monitor the infant for increased drowsiness and breathing difficulties.

Patient characteristics and additional study information

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Study population was characteristic of people with OUD.[1,19]

>25%
had a urine toxicology positive for fentanyl

>71%
were also using nonopioid substances

>70%
were using heroin

>52%
were injecting opioids

~70% of patients completed the 24-week study period (69.0% in the BRIXADI arm [n=147/213] and 72.6% in the SL BPN/NX arm [n=156/215]).[1]

In a different open-label, phase 3 safety study of 227 patients[21]:

- **82.8%** of patients receiving BRIXADI completed 24 weeks of treatment
- **73.6%** of patients receiving BRIXADI completed 48 weeks of treatment

Important Safety Information (Continued)

Warnings and Precautions

Adrenal Insufficiency: If adrenal insufficiency is diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.

Risk of Opioid Withdrawal with Abrupt Discontinuation: Patients who elect to discontinue BRIXADI treatment should be monitored for withdrawal signs and symptoms with consideration given to the product's extended-release characteristics.

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

Primary endpoint

Patient response to treatment with BRIXADI was noninferior to treatment with SL BPN/NX[1,18]

Treatment response was evaluated using urine drug screens combined with self-reported illicit opioid use. Missing urine drug screen samples and/or self-reports were counted as positive for illicit opioids.

PRIMARY ENDPOINT: PERCENTAGE OF PATIENTS WHO MET THE RESPONDER DEFINITION

BRIXADI	SL BPN/NX
16.9%	14.0%
N=36	N=30

Treatment difference of 2.9 percentage points* (*P*<0.001; noninferiority)

*Proportion difference of BRIXADI minus SL BPN/NX; 95% CI (-3.9%, 9.8%).

Responders met all the following criteria[1,19]:

- At least 8 of 10 (80%) negative opioid assessments from weeks 9 to 24
- Opioid assessment must be negative at the end of both Phase 1 and Phase 2
- Negative opioid assessments for at least 2 of 3 assessments from weeks 9 to 11 (Phase 1) and for at least 5 of 6 assessments from weeks 12 to 24 (Phase 2)

Secondary endpoint

Patients treated with BRIXADI were more likely to achieve negative opioid assessments[1,19]

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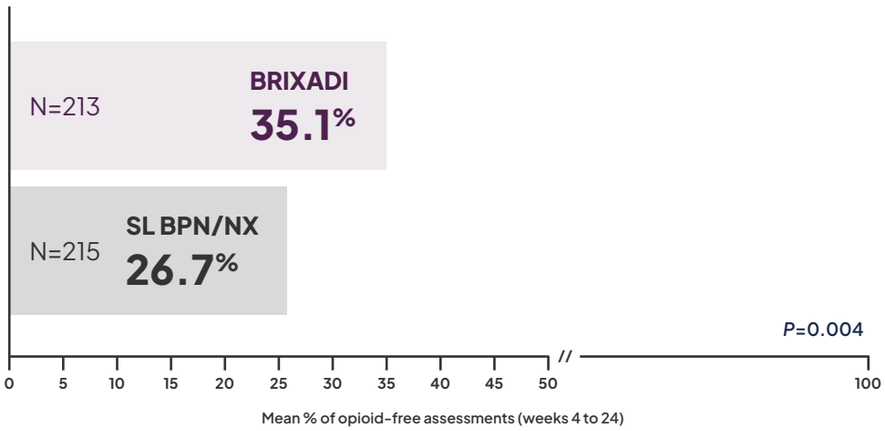
BRIXADI demonstrated statistical superiority to daily SL BPN/NX based on the CDF of the percentage of negative opioid assessments during weeks 4 to 24.

- For patients reporting mostly negative opioid assessments (80% or greater), there was little to no difference between BRIXADI and SL BPN/NX

ADDITIONAL ANALYSIS: MEAN PERCENTAGE OF OPIOID-FREE ASSESSMENTS (WEEKS 4 TO 24)



CDF, cumulative distribution function.

Important Safety Information (Continued)

Warnings and Precautions

Risk of Hepatitis, Hepatic Events, and Use in Patients with Impaired Hepatic Function: Liver function tests should be performed on all patients prior to initiation, during treatment, and if a hepatic event is suspected. Because buprenorphine levels cannot be rapidly decreased, patients with pre-existing moderate to severe hepatic impairment are not candidates for treatment with BRIXADI. Patients who develop moderate to severe hepatic impairment while being treated with BRIXADI should be monitored for signs and symptoms of toxicity or overdose of buprenorphine and may require a dose adjustment.

Important Safety Information (Continued)

Warnings and Precautions

Hypersensitivity Reactions: Cases of bronchospasm, angioneurotic edema, and anaphylactic shock have been reported in patients receiving buprenorphine-containing products. The most common signs and symptoms include rashes, hives, and pruritus. The BRIXADI needle cap is synthetically derived from natural rubber latex which may cause allergic reactions in latex-sensitive individuals.

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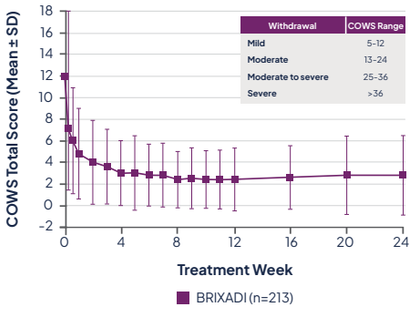
Exploratory analysis

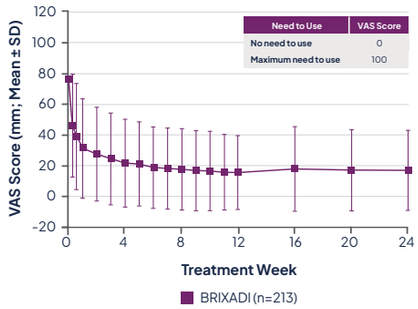
A decline in opioid withdrawal symptoms and cravings* was observed throughout the treatment period with BRIXADI[19]

These endpoints were not controlled for multiplicity; therefore, no statistical comparisons (or significance) can be drawn.

EXPLORATORY ENDPOINT:
OPIOID WITHDRAWAL



EXPLORATORY ENDPOINT:
OPIOID CRAVING



*Opioid withdrawal was evaluated at the end of the dosing interval using the COWS score. Opioid craving was assessed using unipolar 100–mm VAS, indicating strongest need to use opioids since the last scheduled assessment visit (range 0 [no need to use] to 100 [maximum need to use]).

A post hoc analysis of patients using fentanyl observed outcomes consistent to those seen in the overall study[22]

The fentanyl-positive subgroup included 123 participants: 64 in the BRIXADI arm and 59 in the SL BPN/NX arm. The analysis was not prespecified, and the original study was not designed to assess the differences in treatment response between treatment arms in this subgroup; therefore, no statistical conclusions should be made. Differences in outcomes could be related to the overall disease severity rather than fentanyl use.

COWS, Clinical Opiate Withdrawal Scale.

Important Safety Information (Continued)

Warnings and Precautions

Precipitation of Opioid Withdrawal in Patients Dependent on Full Opioid Agonists: BRIXADI injection may precipitate opioid withdrawal signs and symptoms in individuals physically dependent on full opioid agonists such as heroin, morphine, or methadone before the effects of the full opioid agonist have subsided. In patients who are new entrants to treatment, to avoid precipitating an opioid withdrawal syndrome, administer a 4 mg test dose of transmucosal buprenorphine when objective signs of mild to moderate withdrawal appear and monitor for precipitated withdrawal before injecting BRIXADI.

The safety profile of BRIXADI was generally comparable to that of SL BPN/NX, excluding injection site reactions[1]

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No injection site reactions were reported as severe in intensity.

ADVERSE REACTIONS OCCURRING IN ≥2% OF PATIENTS RECEIVING BRIXADI IN THE PHASE 3 DOUBLE-BLIND STUDY

System Organ Class (SOC) Preferred Term†	BRIXADI Total‡ (N=213) n (%)	SL BPN/NX§ (N=215) n (%)
Cardiac disorders	**6 (2.8%)**	**9 (4.2%)**
Tachycardia	5 (2.3)	5 (2.3)
Gastrointestinal disorders	**43 (20.2%)**	**45 (20.9%)**
Constipation	16 (7.5)	16 (7.4)
Diarrhea	6 (2.8)	7 (3.3)
Nausea	15 (7.0)	17 (7.9)
Vomiting	9 (4.2)	8 (3.7)
Infections and infestations	**42 (19.7%)**	**50 (23.3%)**
Urinary tract infection	11 (5.2)	10 (4.7)
Upper respiratory tract infection	9 (4.2)	9 (4.2)
Musculoskeletal and connective tissue disorders	**20 (9.4%)**	**22 (10.2%)**
Arthralgia	7 (3.3)	3 (1.4)
Nervous system disorders	**27 (12.7%)**	**27 (12.6%)**
Headache	16 (7.5)	17 (7.9)
Psychiatric disorders	**20 (9.4%)**	**20 (9.3%)**
Anxiety	6 (2.8)	7 (3.3)
Insomnia	12 (5.6)	6 (2.8)
Injection Site Reactions Preferred Term†	**BRIXADI Total‡ (N=213) n (%)**	**SL BPN/NX§ (N=215) n (%)**
Administration site reactions	**44 (20.7%)**	**49 (22.8%)**
Injection site pain	21 (9.9%)	17 (7.9%)
Injection site erythema	14 (6.6%)	12 (5.6%)
Injection site pruritus	13 (6.1%)	13 (6.0%)
Injection site swelling	10 (4.7%)	7 (3.3%)
Injection site reaction	9 (4.2%)	7 (3.3%)

All patients received a single test dose of 4 mg SL BPN/NX before randomization into either arm.[1]

†Patients are represented once per preferred term.[1]
‡This group includes all patients exposed to varying doses of both BRIXADI Monthly and BRIXADI Weekly.[1]
§This group includes patients assigned to daily SL BPN/NX with placebo injections. Patients randomized to this group could also receive a "booster" injection of BRIXADI Weekly, 8 mg, per protocol.[1]

- Zero overdoses were reported in patients treated with BRIXADI in the clinical development program[19]
- The safety profile of BRIXADI across 48 weeks in a long-term safety study was consistent with the results from the phase 3 double-blind study[21]

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

BRIXADI is designed with the treatment experience in mind[1]

BRIXADI uses FluidCrystal®* depot technology, which transforms into a liquid crystalline gel upon injection and steadily releases buprenorphine over the monthly or weekly dosing interval.

This unique delivery system allows for [1]:

- **Needle size: 23 G**
- **No refrigeration**
- **Small injection volume (≤0.64 mL)**
- **Multiple subcutaneous injection areas†**

*FluidCrystal® trademark is owned by Camurus and used by Braeburn under license.

†The options include buttock, thigh, abdomen, and upper arm. For BRIXADI Weekly, injection sites should be alternated/rotated. In patients who are not currently receiving buprenorphine treatment, for BRIXADI Weekly, the upper-arm area should only be used after steady state has been achieved (4 consecutive doses).

For subcutaneous use only. Do not administer BRIXADI intravenously, intramuscularly, or intradermally. BRIXADI is available through a restricted distribution via the BRIXADI REMS Program and is administered only by a healthcare professional. BRIXADI should never be dispensed directly to a patient because of the serious harm or death that could result from intravenous administration.[1]

Administering BRIXADI[1]

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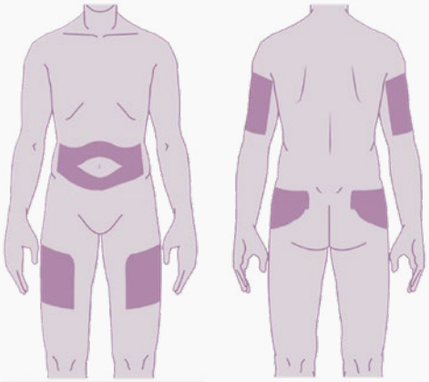
BRIXADI is for subcutaneous injection only.

Areas of Administration



- **DO NOT ADMINISTER BRIXADI INTRAVENOUSLY, INTRAMUSCULARLY, OR INTRADERMALLY**
- Only healthcare professionals should prepare and administer BRIXADI
- BRIXADI should be injected slowly into the subcutaneous tissue of the buttock, thigh, abdomen, or upper arm‡
- Injection sites should be alternated/rotated between injections for BRIXADI Weekly

‡In patients who are not currently receiving buprenorphine treatment, for BRIXADI Weekly, the upper-arm area should only be used after steady state has been achieved (4 consecutive doses). Please refer to Section 2 of the BRIXADI Full Prescribing Information for additional details on dosage and administration.

Scan the QR code to watch the How to Administer video.

Important Safety Information (Continued)

Warnings and Precautions

Risks Associated with Treatment of Emergent Acute Pain: While on BRIXADI, situations may arise where patients need acute pain management, or may require anesthesia. Treat patients receiving BRIXADI with non-opioid analgesic whenever possible. Patients requiring opioid therapy for analgesia may be treated with a high-affinity full opioid analgesic under the supervision of a healthcare provider, with particular attention to respiratory function. Higher doses may be required for analgesic effect. Therefore, a higher potential for toxicity exists with opioid administration. Advise patients of the importance of instructing their family members, in the event of emergency, to inform the treating healthcare provider or emergency room staff that the patient is being treated with BRIXADI.

Important Safety Information (Continued)

Warnings and Precautions

Use in Opioid Naïve Patients: There have been reported deaths of opioid naïve individuals who received a 2 mg dose of buprenorphine as a sublingual tablet. BRIXADI is not appropriate for use in opioid naïve patients.

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

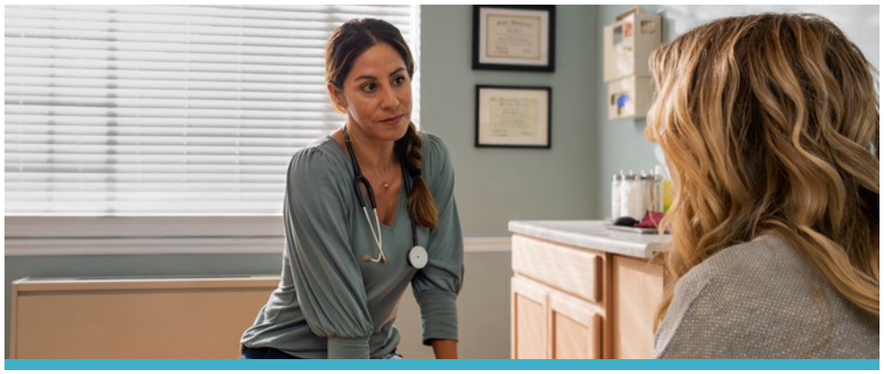
Individualization of treatment plans is possible with BRIXADI[1]

BRIXADI is the ONLY injectable buprenorphine that offers multiple monthly and weekly dosing options.

Patients currently on transmucosal buprenorphine treatment can be switched directly to BRIXADI Monthly or BRIXADI Weekly.

Daily Sublingual Buprenorphine Dose*	BRIXADI Monthly	BRIXADI Weekly
Less than or equal to 6 mg	–	8 mg
8-10 mg	64 mg	16 mg
12-16 mg	96 mg	24 mg
18-24 mg	128 mg	32 mg

*One Suboxone® (buprenorphine and naloxone) 8 mg/2 mg sublingual tablet provides equivalent buprenorphine exposure to one Subutex® (buprenorphine HCl) 8 mg sublingual tablet or one Zubsolv® (buprenorphine and naloxone) 5.7 mg/1.4 mg sublingual tablet.



- **Patients not currently receiving buprenorphine treatment** can start BRIXADI after receiving a test dose of transmucosal buprenorphine (4 mg) when objective signs of mild to moderate withdrawal appear. If the dose is tolerated without precipitated withdrawal, administer the first dose of BRIXADI Weekly 16 mg followed by BRIXADI Weekly 8 mg within 3 days of the first dose. Titrate patients as needed. Refer to Sections 2.1 and 2.3 of the Prescribing Information for additional information for these patients

Dosing considerations for BRIXADI Monthly and BRIXADI Weekly[1]

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Once on BRIXADI, patients can be switched between BRIXADI Monthly and Weekly based on clinical judgment.

28 BRIXADI Monthly should be administered in 28-day intervals.

7 BRIXADI Weekly should be administered in 7-day intervals.

+/– The monthly dose may be given up to 1 week before or after the monthly time point. The weekly dose may be given up to 2 days before or after the weekly time point.

Doses of BRIXADI Weekly cannot be combined to yield an equivalent BRIXADI Monthly dose.

The nature of OUD demands options. There is no one-size-fits-all approach. With BRIXADI Monthly and Weekly, you have the power to individualize treatment to meet your patients' needs.[1,15]

Important Safety Information (Continued)

Warnings and Precautions

Patients at Risk for Arrhythmia: Thorough QT studies with buprenorphine products have demonstrated QT prolongation ≤ 15 msec. This QTc prolongation effect does not appear to be mediated by hERG channels. Based on these two findings, buprenorphine is unlikely to be pro-arrhythmic when used alone in patients without risk factors. The risk of combining buprenorphine with other QT-prolonging agents is not known.

Impairment of Ability to Drive and Operate Machinery: BRIXADI may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Caution patients about driving or operating hazardous machinery until they are reasonably certain that BRIXADI does not adversely affect their ability to engage in such activities.

Important Safety Information (Continued)

Warnings and Precautions

Orthostatic Hypotension: Buprenorphine may produce orthostatic hypotension in ambulatory patients.

Elevation of Cerebrospinal Fluid Pressure: Buprenorphine may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions, and other circumstances when cerebrospinal pressure may be increased.

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

Braeburn ByYourSide is available for support with your patients' access to BRIXADI

BRAEBURN ByYourSide

Call 877-279-7367 or scan QR code for access support, including:

- Investigation of patient insurance coverage and potential out-of-pocket costs for BRIXADI
- Assistance in understanding prior authorization and appeal process
- Answers to other questions related to patient access

Eligible* commercially insured patients may pay as little as

$0 per injection with the BRIXADI Copay Savings Program

*Patients are not eligible for copay savings if they participate in a federal or state healthcare program, including, but not limited to, Medicaid, Medicare, Veterans Affairs (VA), Department of Defense (DoD), TRICARE, or other federal and state patient or pharmaceutical assistance program. Void where prohibited by law. Program terms and conditions apply.

Visit BRIXADIhcp.com for access resources, including a full list of specialty pharmacies and specialty distributors in the network.

Important Safety Information

Brixadi® (buprenorphine) extended-release injection for subcutaneous use (III)
Weekly 8 • 16 • 24 • 32 mg Monthly 64 • 96 • 128 mg

WARNING: RISK OF SERIOUS HARM OR DEATH WITH INTRAVENOUS ADMINISTRATION; BRIXADI RISK EVALUATION AND MITIGATION STRATEGY

- **Serious harm or death could result if administered intravenously. BRIXADI forms a liquid crystalline gel upon contact with body fluids and may cause occlusion, local tissue damage, and thrombo-embolic events, including life-threatening pulmonary emboli, if administered intravenously.**
- **Because of the risk of serious harm or death that could result from intravenous self-administration, BRIXADI is only available through a restricted program called the BRIXADI REMS. Healthcare settings and pharmacies that order and dispense BRIXADI must be certified in this program and comply with the REMS requirements.**

BRIXADI (buprenorphine) extended-release injection (weekly, 50 mg/mL buprenorphine) and BRIXADI (monthly, 356 mg/mL buprenorphine) are different formulations. Doses of BRIXADI (weekly) cannot be combined to yield an equivalent monthly dose.

BRIXADI is contraindicated in patients with hypersensitivity (e.g. anaphylactic shock) to buprenorphine or any other ingredients in the solution for injection.

Warnings & Precautions

Addiction, Abuse, and Misuse: BRIXADI contains buprenorphine, a Schedule III controlled substance that can be abused in a manner similar to other opioids. Buprenorphine is sought by people with opioid use disorder and is subject to criminal diversion. Monitor all patients for progression of opioid dependence and addictive behaviors.

Respiratory and CNS Depression: Buprenorphine has been associated with life-threatening respiratory depression and death. Use BRIXADI with caution in patients with compromised respiratory function. Due to its extended-release characteristics, if BRIXADI is discontinued as a result of compromised respiratory function, monitor patients for ongoing buprenorphine effects for approximately 1 month for BRIXADI (weekly) and for approximately 4 months for BRIXADI (monthly). Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose.

Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose: Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver. Because patients being treated for opioid use disorder have the potential for relapse, putting them at risk for opioid overdose, strongly consider prescribing naloxone for the emergency treatment of opioid overdose, both when initiating and renewing treatment with BRIXADI. If naloxone is prescribed, educate patients and caregivers on how to treat with naloxone, and emphasize the importance of calling 911 or getting emergency medical help, even if naloxone is administered.

Concomitant Use of Benzodiazepines or other CNS Depressants: Concomitant use of buprenorphine and benzodiazepines or other CNS depressants increase the risk of adverse reactions including respiratory depression, overdose and death. Ensure that other healthcare providers prescribing benzodiazepines or other CNS depressants are aware of the patient's buprenorphine treatment and coordinate care to minimize the risk associated with concomitant use. Inform patients and caregivers that potentially fatal additive effects may occur if BRIXADI is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a healthcare provider.

Neonatal Opioid Withdrawal Syndrome, Pregnancy, and Lactation: Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy. NOWS may be life-threatening if not recognized and treated in the neonate. Healthcare providers should observe newborns for signs of NOWS and manage accordingly. Advise pregnant women receiving opioid addiction treatment with BRIXADI of the risk of neonatal opioid withdrawal syndrome. Warn patients that buprenorphine passes into breast milk. Advise the nursing mother taking buprenorphine to monitor the infant for increased drowsiness and breathing difficulties.

Adrenal Insufficiency: If adrenal insufficiency is diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.

Important Safety Information (Continued)

Risk of Opioid Withdrawal with Abrupt Discontinuation: Patients who elect to discontinue BRIXADI treatment should be monitored for withdrawal signs and symptoms with consideration given to the product's extended-release characteristics.

Risk of Hepatitis, Hepatic Events, and Use in Patients with Impaired Hepatic Function: Liver function tests should be performed on all patients prior to initiation, during treatment, and if a hepatic event is suspected. Because buprenorphine levels cannot be rapidly decreased, patients with pre-existing moderate to severe hepatic impairment are not candidates for treatment with BRIXADI. Patients who develop moderate to severe hepatic impairment while being treated with BRIXADI should be monitored for signs and symptoms of toxicity or overdose of buprenorphine and may require a dose adjustment.

Hypersensitivity Reactions: Cases of bronchospasm, angioneurotic edema, and anaphylactic shock have been reported in patients receiving buprenorphine-containing products. The most common signs and symptoms include rashes, hives, and pruritus. The BRIXADI needle cap is synthetically derived from natural rubber latex which may cause allergic reactions in latex-sensitive individuals.

Precipitation of Opioid Withdrawal in Patients Dependent on Full Opioid Agonists: BRIXADI injection may precipitate opioid withdrawal signs and symptoms in individuals physically dependent on full opioid agonists such as heroin, morphine, or methadone before the effects of the full opioid agonist have subsided. In patients who are new entrants to treatment, to avoid precipitating an opioid withdrawal syndrome, administer a 4 mg test dose of transmucosal buprenorphine when objective signs of mild to moderate withdrawal appear and monitor for precipitated withdrawal before injecting BRIXADI.

Risks Associated with Treatment of Emergent Acute Pain: While on BRIXADI, situations may arise where patients need acute pain management, or may require anesthesia. Treat patients receiving BRIXADI with non-opioid analgesic whenever possible. Patients requiring opioid therapy for analgesia may be treated with a high-affinity full opioid analgesic under the supervision of a healthcare provider, with particular attention to respiratory function. Higher doses may be required for analgesic effect. Therefore, a higher potential for toxicity exists with opioid administration. Advise patients of the importance of instructing their family members, in the event of emergency, to inform the treating healthcare provider or emergency room staff that the patient is being treated with BRIXADI.

Use in Opioid Naïve Patients: There have been reported deaths of opioid naïve individuals who received a 2 mg dose of buprenorphine as a sublingual tablet. BRIXADI is not appropriate for use in opioid naïve patients.

Patients at Risk for Arrhythmia: Thorough QT studies with buprenorphine products have demonstrated QT prolongation ≤ 15 msec. This QTc prolongation effect does not appear to be mediated by hERG channels. Based on these two findings, buprenorphine is unlikely to be pro-arrhythmic when used alone in patients without risk factors. The risk of combining buprenorphine with other QT-prolonging agents is not known.

Impairment of Ability to Drive and Operate Machinery: BRIXADI may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Caution patients about driving or operating hazardous machinery until they are reasonably certain that BRIXADI does not adversely affect their ability to engage in such activities.

Orthostatic Hypotension: Buprenorphine may produce orthostatic hypotension in ambulatory patients.

Elevation of Cerebrospinal Fluid Pressure: Buprenorphine may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions, and other circumstances when cerebrospinal pressure may be increased.

Elevation of Intracholedochal Pressure: Buprenorphine has been shown to increase intracholedochal pressure, as do other opioids, and thus should be administered with caution to patients with dysfunction of the biliary tract.

Effects in Acute Abdominal Conditions: Buprenorphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Important Safety Information (Continued)

Unintentional Pediatric Exposure: Buprenorphine can cause severe, possibly fatal, respiratory depression in children who are accidentally exposed to it.

Adverse Reactions

Adverse reactions commonly associated with BRIXADI administration (in ≥ 5% of patients) were injection site pain, headache, constipation, nausea, injection site erythema, injection site pruritus, insomnia, and urinary tract infection.

To report SUSPECTED ADVERSE REACTIONS, contact Braeburn at 1-833-274-9234 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional Important Safety Information throughout and the BRIXADI Full Prescribing Information, including Boxed Warning, at BRIXADIhcp.com or accompanying this document.

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HELP YOUR PATIENTS FOCUS ON WHERE THEY'RE GOING, VERSUS WHERE THEY'VE BEEN

BRIXADI blocked the rewarding effects of a high-potency opioid throughout the entire dosing interval in a hydromorphone challenge study.[1]

~70% of patients completed the 24-week study period in the double-blind, pivotal phase 3 study (69.0% in the BRIXADI arm [n=147/213] and 72.6% in the SL BPN/NX arm [n=156/215]).[1]

Upon injection, BRIXADI transforms into a liquid crystalline gel that steadily releases buprenorphine as the depot biodegrades over the monthly or weekly dosing interval.[1]

The safety profile of BRIXADI was generally comparable to that of SL BPN/NX, excluding injection site reactions. No injection site reactions were reported as being severe in intensity.[1]

BRIXADI is the ONLY injectable buprenorphine studied against daily SL BPN/NX in a pivotal phase 3 head-to-head clinical study.[1]

BRIXADI is the ONLY injectable buprenorphine that offers multiple monthly and weekly dosing options to support individualized treatment.[1]

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