This brochure is intended for healthcare professionals only.

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.**

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

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.

Important Safety Information (Continued)

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.

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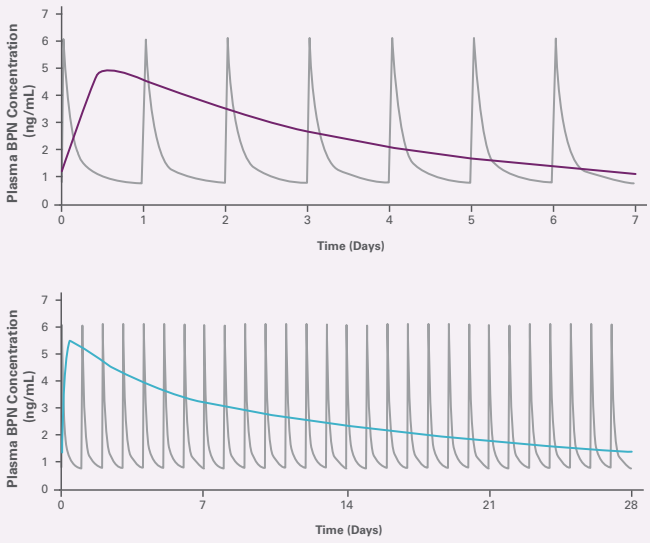
A steady release of buprenorphine without daily peaks and troughs[3]

BRIXADI provided sustained buprenorphine plasma levels throughout the weekly and monthly dosing intervals at steady state.[3]*

Buprenorphine Plasma Level Profile at Steady State[5]*



Population pharmacokinetics (PK) model based on 236 subjects and >10,000 observations from 4 clinical studies.

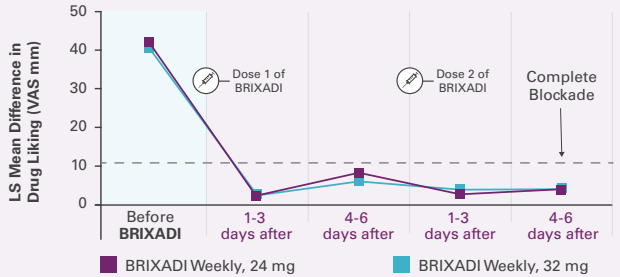
SL BPN, sublingual buprenorphine.
*Steady state is achieved after 4 consecutive doses.[3]

BRIXADI blocked the effects of a high potency opioid throughout the entire dosing interval[3]

BRIXADI demonstrated complete blockade of the drug-liking effect of hydromorphone, a high potency opioid. This was sustained throughout the first and second dosing intervals.[3]

Study objective: Assess the blockade of drug-liking effects, pharmacokinetics, and safety of 24 mg and 32 mg BRIXADI Weekly when patients were administered hydromorphone (6 mg and 18 mg) intramuscularly compared with administration of placebo in patients with OUD.[3]

Mean Difference in Placebo-Corrected Peak Drug Liking[3]



This graph represents the results for hydromorphone 18 mg.[6] LS, least squares.

Primary endpoint: The maximum effect (E_{max}) as rated on a 100-mm bipolar Visual Analog Scale (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.[3]

Study design: Phase 2, randomized, double-blind, multicenter, 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.[3,6] **Learn more about the phase 2 study design on page 14 of this document.**

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.

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.

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BRIXADI is the ONLY injectable buprenorphine studied against daily SL BPN/NX[3]*

A pivotal phase 3 head-to-head clinical study evaluated BRIXADI in patients characteristic of the patient population with OUD.[4]

>25% had urine toxicology positive for fentanyl

>70% were using heroin

>71% were also using nonopioid substances

>52% were injecting opioids

Study objective: To determine whether treatment involving BRIXADI Weekly and BRIXADI Monthly and individual drug counseling is noninferior to daily SL BPN/NX in the treatment of moderate to severe OUD based on opioid assessments using urine screens and self-reports.[3]

Study design: Phase 3, randomized, double-blind, double-dummy, active-controlled, multicenter trial.[3]

Learn more about the phase 3 study design on page 14 of this document.

SL BPN/NX, sublingual buprenorphine/naloxone.
*In a pivotal phase 3 trial.[3]

Patient response to treatment with BRIXADI was noninferior to treatment with SL BPN/NX[3]

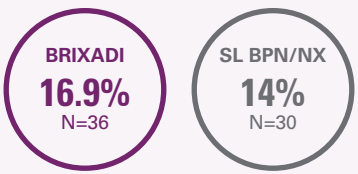
BRIXADI met the primary endpoint of noninferiority to daily SL BPN/NX in responder rates for patients who received both weekly and monthly injections.[3,4]*

Treatment response 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.[3]

Responders met all the following criteria[3,4]

- At least 8 of 10 (80%) negative opioid assessments from weeks 9 to 24
- Negative opioid assessments in:
  - Phase 1 for at least 2 of 3 assessments from weeks 9 to 11
  - Phase 2 for at least 5 of 6 assessments from weeks 12 to 24
- Week 12 and month 6 (weeks 21 to 24) opioid assessments must be negative

Primary Endpoint:
Percentage of Patients Who Met the Responder Definition[3,5]



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

*Patients in the BRIXADI arm received BRIXADI Weekly during weeks 1 to 12 and BRIXADI Monthly during weeks 13 to 24 of the study.
†Proportion difference BRIXADI minus SL BPN/NX; 95% CI (-3.9%, 9.8%).[3]

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.

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.

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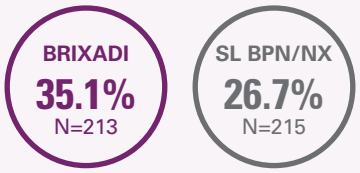
Patients treated with BRIXADI were more likely to achieve negative opioid assessments[3]

BRIXADI demonstrated statistical superiority to daily SL BPN/NX based on the cumulative distribution function (CDF) of the percentage of negative opioid assessments during weeks 4 to 24 (secondary endpoint).[3]

- In patients reporting mostly negative opioid assessments (80% or greater), there was little to no difference between BRIXADI and SL BPN/NX[3]

Mean Percentage of Opioid-Free Assessments (Weeks 4 to 24[3,4])



P=0.004

In an exploratory analysis, a decline in opioid cravings and **withdrawal symptoms*** was observed throughout the treatment period in patients who received BRIXADI. These endpoints were not controlled for multiplicity; therefore, no statistical comparisons (or significance) can be drawn.[4]

*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 [strongest possible need]). Opioid withdrawal was evaluated using the Clinical Opiate Withdrawal Scale (COWS) score.[4]

A post hoc analysis of patients using fentanyl observed outcomes consistent to those seen in the overall study. 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 trial 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.[7]

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.

A comparable clinical safety profile[3]

In the phase 3 double-blind study:

- Excluding injection site reactions, the safety profile of BRIXADI was generally comparable to that of SL BPN/NX[4]
- No injection site reactions were reported as being severe in intensity[3]

Over 48 weeks of treatment in a long-term safety study, BRIXADI had a safety profile consistent with the phase 3 double-blind study.[3,8]

Adverse Reactions Occurring in ≥2% of Patients Receiving BRIXADI in the Phase 3 Double-Blind Study[3]

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.[3]

*Patients are represented once per preferred term.[3]
†This group includes all subjects exposed to varying doses of both BRIXADI Weekly and BRIXADI Monthly.[3]
‡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.[3]

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Multiple weekly and monthly doses to support individualized treatment

Patients currently on transmucosal buprenorphine treatment can be switched directly to BRIXADI Weekly or BRIXADI Monthly.[3]

Daily Sublingual Buprenorphine Dose*	BRIXADI Weekly	BRIXADI Monthly
≤6 mg	8 mg	-
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 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.[3]

Patients can be transitioned between BRIXADI Monthly and BRIXADI Weekly based on clinical judgment.[3]

For patients not currently receiving buprenorphine treatment: Administer a test dose of oral 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.[3]

Sections 2.1 and 2.3 of the Prescribing Information provide additional important information for these patients.[3]

Features to consider when prescribing BRIXADI to patients

BRIXADI has a unique delivery system providing key attributes.[4]

FluidCrystal®* Injection Depot Technology allows for[3,4]:

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

*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 areas 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).[3]

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.[3]

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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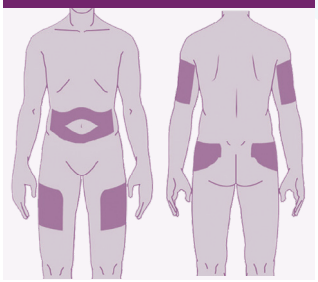
Administering BRIXADI

BRIXADI is for subcutaneous injection only.

- **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 areas should be alternated/rotated between injections for BRIXADI Weekly

Areas where BRIXADI can be injected



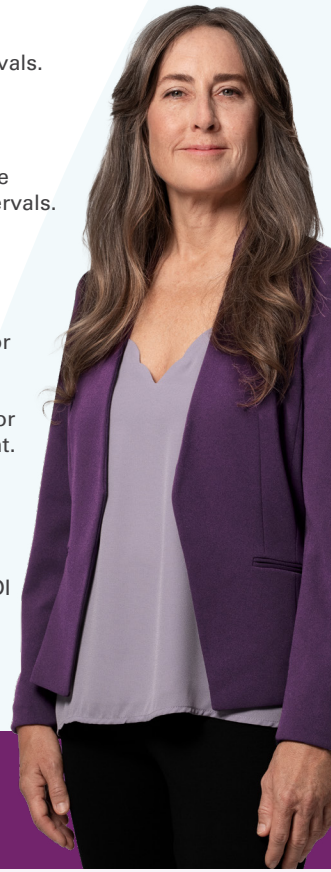
Scan the QR code to watch the How to Administer video.

*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).[3]

Dosing considerations

Consider the following when choosing the dosing option that is right for your patients:

- BRIXADI Weekly should be administered in 7-day intervals.
- BRIXADI Monthly should be administered in 28-day intervals.
- The weekly dose may be given up to 2 days before or after the weekly time point. The monthly dose may be given up to 1 week before or after the monthly time point.
- Doses of BRIXADI Weekly cannot be combined to yield an equivalent BRIXADI Monthly dose.



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.

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.

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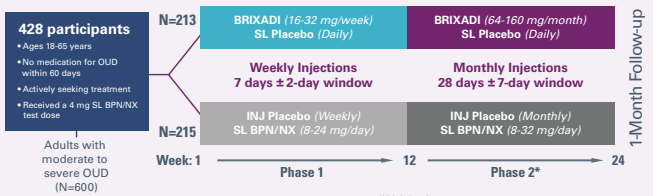
Additional study details

Phase 2 study design: Phase 2, randomized, double-blind, multicenter, 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 the 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.[3,6]

Phase 3 study design: Phase 3, randomized, double-blind, double-dummy, active-controlled, multicenter study.[3]

Phase 3 Study Design[3,4]



*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.[3]

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.

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.

BRIXADI Copay Savings Program

Eligible* patients may pay as little as

$0 per injection

BRAEBURN ByYourSide

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

Call 877-279-7367 or scan the 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

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

*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.

References: 1. Hyman SE, Malenka RC. Addiction and the brain: the neurobiology of compulsion and its persistence. *Nat Rev Neurosci.* 2001;2(10):695-703. **2.** *Medications for Opioid Use Disorder: For Healthcare and Addiction Professionals, Policymakers, Patients, and Families.* Treatment Improvement Protocol 63. Substance Abuse and Mental Health Services Administration, US Dept of Health and Human Services; 2018. Updated 2021. Accessed May 1, 2024. https://www.ncbi.nlm.nih.gov/books/NBK574910/pdf/Bookshelf_NBK574910.pdf **3.** BRIXADI. Prescribing information. Braeburn Inc; 2023. **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. **5.** Data on file. Plymouth Meeting, PA; Braeburn Inc. 2020. **6.** Walsh SL, Comer SD, Lofwall MR, et al. Effect of buprenorphine weekly depot (CAM2038) and hydromorphone blockade in individuals with opioid use disorder: a randomized clinical trial. *JAMA Psychiatry.* 2017;74(9):894-902. **7.** Nunes EV, Comer SD, Lofwall MR, et al. Extended-release injection vs sublingual buprenorphine for opioid use disorder with fentanyl use: a post hoc analysis of a randomized clinical trial. *JAMA Netw Open.* 2024;7(6):e24173777. **8.** Frost M, Bailey GL, Lintzeris N, et al. Long-term safety of a weekly and monthly subcutaneous buprenorphine depot (CAM2038) in the treatment of adult out-patients with opioid use disorder. *Addiction.* 2019;114(8):1416-1426.

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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.

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.

Important Safety Information (Continued)

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.

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 the BRIXADI Full Prescribing Information, including Boxed Warning, at brixadihcp.com or accompanying this document.

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

The ONLY injectable buprenorphine that offers multiple weekly and monthly dosing options to support individualized treatment[3,4]

BRIXADI is indicated for the treatment of moderate to severe OUD 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.[3]

- Upon injection, BRIXADI releases buprenorphine at a steady rate over the weekly or monthly dosing interval[3]
- In a clinical study, BRIXADI demonstrated noninferiority to SL BPN/NX based on responder rate[3,5]
- BRIXADI also demonstrated superiority to daily SL BPN/NX based on the CDF of the percentage of negative opioid assessments during weeks 4 to 24 (secondary endpoint)[3,4]
- Excluding injection site reactions, the safety profile of BRIXADI was generally comparable to that of SL BPN/NX. No injection site reactions were reported as being severe in intensity[3,4]

Scan the QR code to learn more and find resources on BRIXADIhcp.com.

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 Important Safety Information throughout, including Boxed Warning, and Full Prescribing Information at brixadihcp.com or accompanying this document.

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