NEW DRUG APPROVAL

Brand Name	Brixadi™
Generic Name	buprenorphine
Drug Manufacturer	Braeburn Inc.

Indications for Use

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.

New Drug Approval

FDA Approval Date: May 23, 2023

Dispensing restriction: N/A

Therapeutic Class

Analgesic, Opioid; Analgesic, Opioid Partial Agonist

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Opioids, used medically for pain relief, have analgesic and central nervous system depressant effects as well as the potential to cause euphoria. Opioid use disorder (OUD) can involve misuse of prescribed opioid medications, use of diverted opioid medications, or use of illicitly obtained heroin. OUD is typically a chronic, relapsing illness, associated with significantly increased rates of morbidity and mortality.

In patients with OUD who have achieved abstinence through medically supervised withdrawal or by other means, maintenance treatment aims to prevent relapse. Options for long-term maintenance treatment include an opioid agonist (ie, methadone or buprenorphine), an opioid antagonist (naltrexone), or nonmedication, abstinence-based treatment.

Efficacy

The safety and efficacy of Brixadi™ was established in a randomized, double-blind, active-controlled clinical trial in 428 adults with a diagnosis of moderate-to-severe OUD. Patients were randomized to treatment with Brixadi™ plus a sublingual placebo, or active sublingual buprenorphine plus placebo injections after initial test dose on transmucosal buprenorphine. Over the first week, after titration, patients were treated with weekly injections over 12 weeks and then transitioned to monthly injections for an additional 12 weeks. A response to treatment was measured by urine drug screening and self-reporting of illicit opioid use during the treatment period. Patients

were considered responders if they had negative opioid assessments at the end of each of the two treatment phases. The proportion of patients meeting the responder definition was 16.9% in the Brixadi™ group and 14.0% in the sublingual buprenorphine group (treatment difference of 2.9; 95% CI: -3.9, 9.8).

Safety

ADVERSE EVENTS

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.

WARNINGS & PRECAUTIONS

- Addiction, Abuse, and Misuse: Buprenorphine can be abused in a manner similar to other opioids. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.
- Respiratory Depression: Life-threatening respiratory depression and death have occurred in association with buprenorphine. Warn patients of the potential danger of self-administration of benzodiazepines or other CNS depressants while under treatment with Brixadi™.
- Neonatal Opioid Withdrawal Syndrome: Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy.
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.
- Risk of Opioid Withdrawal with Abrupt Discontinuation: If treatment with Brixadi™ is discontinued, monitor patients for withdrawal and treat appropriately.
- Risk of Hepatitis, Hepatic Events: Monitor liver function tests prior to and during treatment.
- Latex Allergy: The packaging of this product contains natural rubber latex which may cause allergic reactions.
- Risk of Withdrawal in Patients Dependent on Full Agonist Opioids: Administer a test dose of transmucosal buprenorphine and monitor for precipitated withdrawal before injecting Brixadi™.
- Treatment of Emergent Acute Pain: Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect.

CONTRAINDICATIONS

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

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

Brixadi™ is only available through the BRIXADI Risk Evaluation and Mitigation Strategy (REMS)

- 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.

Clinical Pharmacology

MECHANISMS OF ACTION

Buprenorphine exerts its analgesic effect via high-affinity binding to mu opiate receptors in the CNS; displays partial mu agonist and weak kappa antagonist activity. Due to it being a partial mu agonist, its analgesic effects plateau at higher doses and it then behaves like an antagonist. The extended-release formulation is injected subcutaneously as a liquid; subsequent precipitation following injection results in a solid depot which will gradually release buprenorphine via diffusion and biodegradation of the depot.

Dose & Administration

ADULTS

Patients Not Currently Receiving Buprenorphine Treatment

The recommended weekly dose in patients not currently receiving buprenorphine treatment is 24 mg of Brixadi™(weekly) titrated up over the first week of treatment as follows:

- To avoid precipitating an opioid withdrawal syndrome, administer a test dose of transmucosal buprenorphine 4 mg when objective signs of mild to moderate withdrawal appear.
- If the dose of transmucosal buprenorphine is tolerated without precipitated withdrawal, administer the first dose of Brixadi™(weekly), 16 mg.
- Administer an additional dose of 8 mg Brixadi™(weekly) within 3 days of the first dose to achieve the recommended 24 mg Brixadi™(weekly) dose.

If needed, during this first week of treatment, administer an additional 8 mg dose of Brixadi™(weekly), waiting at least 24 hours after the previous injection, for a total weekly dose of 32 mg Brixadi™(weekly).

Administer subsequent Brixadi™(weekly) injections based on the total weekly dose that was established during Week One. Dosage adjustments can be made at weekly appointments with the maximum Brixadi™(weekly) dose being 32 mg.

A patient who misses a dose of Brixadi™ (weekly) should receive the next dose as soon as possible. Brixadi™(weekly) should be administered in 7-day intervals.

Patients Switching from Transmucosal Buprenorphine-containing Products to Brixadi™

Table 6: Daily doses of sublingual buprenorphine (Subutex, Suboxone, or generic product equivalents) and suggested corresponding Brixadi™ (weekly) or Brixadi™ (monthly) doses

Daily dose of sublingual buprenorphine	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

Note: 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 Transitioning Between Brixadi™(weekly) and Brixadi™(monthly)

Table 7: Recommended dose when transitioning between Brixadi™(weekly) and Brixadi™(monthly)

Brixadi™(weekly)	Brixadi™(monthly)
16 mg	64 mg
24 mg	96 mg
32 mg	128 mg

A patient who misses a dose of Brixadi™ should receive the next dose as soon as possible. Brixadi™(weekly) should be administered in 7-day intervals. Brixadi™ (monthly) should be administered in 28-day intervals.

Dose Adjustments of Brixadi™

An additional Brixadi™(weekly) 8 mg injection may be administered, based on clinical judgment during a dosing interval, up to a maximum dose of 32 mg per week of Brixadi™ (weekly) or 128 mg per month of Brixadi™ (monthly).

PEDIATRICS

N/A

GERIATRICS

N/A

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

NEW DRUG APPROVAL

Brixadi™ is a weekly and monthly injection provided in a pre-filled single dose syringe with a 23-gauge ½ inch needle.

- Brixadi™ (weekly) is available in 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, and 32 mg/0.64 mL;
- Brixadi™ (monthly) is available in 64 mg/0.18 mL, 96 mg/0.27 mL, and 128 mg/0.36 mL.