

Buprenorphine Subcutaneous Injection SA (BRIXADI)* Mini-Monograph Nov 2023

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

*NOTE – Buprenorphine injection SA marketed in U.S. as BRIXADI has been available overseas since 2019 and may be referenced to in peer reviewed literature as BUVIDAL or CAM2038.

Abbreviations: MOA=mechanism of action; TBD=to be determined; VANF=VA National Formulary; PADR-F = Prior Authorization-Facility; SL = sublingual

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| FDA Approval | Description/MOA | Opioid receptor partial agonist |
| | Indication(s) Under Review | Treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of transmucosal buprenorphine product or who are already being treated with buprenorphine. ¹ |
| | Dosage Form(s)¹ | BRIXADI weekly is available in 8mg, 16mg, 24mg, and 32mg doses. BRIXADI monthly is available in 64mg, 96mg, and 128mg doses. <i>*NOTE: BRIXADI weekly and monthly dosage forms are NOT interchangeable.</i> |

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| Clinical Evidence | Study/Design | For purposes of monograph preparation, studies considered included: a pharmacokinetic/pharmacodynamic (PK/PD) study in patients with opioid use disorder ² (OUD), a PK study in healthy volunteers receiving naltrexone blockade ³ , a PD study in non-prescribed opioid using volunteers ⁴ , a double-blinded, active comparator RCT ⁵ , and a phase 3 open-label, 48-week safety and tolerability trial. ⁶ |
| | Demographics | Phase 1, 2 studies -- Hassan, et al., (n=42) Healthy patients with OUD aged 18-65 years on stable maintenance therapy; Albayaty et al., (n=87) healthy volunteers (receiving naltrexone blockade) aged 18-64 years; Walsh, et al. (n=47) Patients with moderate to severe OUD and physical dependence to short acting opioids not interested in OUD treatment. Phase 3 studies -- Lowfall et al., (n=428) Patients age 18-65, treatment seeking with moderate to severe OUD; Frost et al., (n=228) PK/PD Patients aged 18-65 years with moderate to severe OUD, the majority of whom (84%) were on stable treatment with sublingual buprenorphine/naloxone. |
| | Intervention | Phase 1, 2 studies -- <ul style="list-style-type: none"> Hassan, et al., (n=42) Following 48-hour washout, treatment with BRIXADI weekly 8mg, 16mg, 24mg or 32mg and assessed for plasma levels of buprenorphine, opioid withdrawal symptoms, and need for buprenorphine rescue. Albayaty et al., All patients received naltrexone blockade and I.V. buprenorphine. After washout, subjects were randomized 1:1:1 to either SL buprenorphine, BRIXADI weekly, or BRIXADI monthly. Plasma levels of buprenorphine and norbuprenorphine were assessed. Walsh, et al., Patients randomized 1:1 to BRIXADI weekly 16 or 32mg dose and assessed for hydromorphone “liking,” opioid withdrawal symptoms, and buprenorphine plasma levels. Phase 3 studies -- <ul style="list-style-type: none"> Lowfall et al., Twenty-four week study where patients were randomized to either daily SL buprenorphine or BRIXADI qWeek with weekly follow up for 12 weeks (phase 1), then continued on monthly BRIXADI or daily SL buprenorphine with monthly follow-up for 12 weeks (phase 2). Percent negative urine drug screen (UDS) and FDA responder rate* were assessed as primary endpoints. Opioid negative UDS weeks 4-24 and study retention were secondary endpoints. Frost et al., Patients open-label initiated on BRIXADI (n=37, 16%) or transitioned from sublingual buprenorphine (n=190, 84%) to assess over 48 weeks the occurrence of Treatment Emergent Adverse Events (TEASs) and Serious Adverse Events (SAEs) <i>*NOTE – FDA responder rate is defined as no evidence of illicit opioids for 2 of 3 assessments week 9-11 and week 12, and no illicit opioids for 5 of 6 assessments weeks 12-24 including final assessment.</i> |
| | Results | Phase 1, 2 studies -- In PK / PD trials, BRIXADI demonstrated half-life sufficient to allow for adequate plasma levels throughout dosing interval, reduced withdrawal symptoms, successfully reduced need for rescue buprenorphine doses, and blocked “liking” of hydromorphone challenge. Phase 3 studies -- |

Conclusions/Projected Place in Therapy

- BRIXADI was shown in phase 3 clinical trials to provide similar clinical benefit to active comparator of sublingual buprenorphine/naloxone in patients with moderate-to-severe opioid use disorder
- BRIXADI weekly and monthly dosage forms are NOT interchangeable
- BRIXADI may have benefit in patients at higher risk (e.g. history of overdose) or at risk of non-adherence
- BRIXADI is cost similar to its market competitor (e.g. SUBLOCADE)
- BRIXADI is stored at room temperature, offers multiple sites for subcutaneous injection, and more dose flexibility vs. market competitor
- **BRIXADI is a REMS drug and must never be dispensed directly to a patient and must only be administered by a healthcare professional in a healthcare setting**

References

1. BRIXADI full prescribing information [brixadi-prescribing-information.pdf](#) Accessed August 2023
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5. Lofwall M.R., Walsh S.L., Nunes E.V., Bailey G.L., Sigmon S.C., Kampman K.M., , Kim S.: Weekly and monthly subcutaneous buprenorphine depot formulations vs daily sublingual buprenorphine with naloxone for treatment of opioid use disorder: A randomized clinical trial. *JAMA Internal Medicine* 2018; 178: pp. 764-773
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