

## Comparison of Buprenorphine (BUP) Long-Acting Subcutaneous Injections

	<b>Monthly Sublocade®</b>	<b>Weekly &amp; monthly Brixadi®</b>
<b>Indication</b>	Treatment of moderate to severe opioid use disorder (OUD) among patients tolerating transmucosal buprenorphine containing product for at least 1 week	Treatment of moderate to severe OUD in patients who have initiated treatment with a single dose of transmucosal buprenorphine or are already on buprenorphine
<b>FDA approval</b>	November 2017	May 2023
<b>Dosage</b>	<ul style="list-style-type: none"> <li>▪ 2 initial monthly doses of 300mg SQ followed by 100mg maintenance dose. Max dose: 300 mg a month</li> <li>▪ Doses should be separated by at least 26 days</li> </ul>	See dosing section below
<b>Administration site</b>	SUBQ: abdomen	SUBQ: abdomen, arm, leg, buttock
<b>Administration</b>	<ul style="list-style-type: none"> <li>▪ Rotate injection sites &amp; expect the formation of a solid depot after injection for gradual release of BUP</li> <li><u>Tips to minimize discomfort</u></li> <li>▪ Allow the inj to reach room temperature for at least 15 minutes before administration</li> <li>▪ Lidocaine injection 10 to 15 minutes before Sublocade</li> </ul>	<ul style="list-style-type: none"> <li>▪ no rotation required for <u>monthly</u> injection</li> <li>▪ do not administer weekly injection at the same site for at least 8 weeks</li> <li>▪ for pts not on BUP treatment, administer weekly formulation in upper arm (10% lower plasma levels vs other sites) only after 4 consecutive weekly doses (steady state reached)</li> </ul>
<b>Dosing interval</b>	<ul style="list-style-type: none"> <li>▪ doses should be separated by at least 26 days</li> <li>▪ occasional up to 2-week dosing delays may not be clinically significant</li> </ul>	<ul style="list-style-type: none"> <li>▪ Weekly injection can be given up to 2 days before or after the weekly time point</li> <li>▪ Monthly injection can be given up to 1 week before or after the monthly time point</li> </ul>
<b>How supplied</b>	pre-filled syringe with 19 Gauge 5/8 inch needle 100 mg/0.5 mL 300 mg/1.5 mL	pre-filled syringe with 23 Gauge ½ inch needle <b>Weekly:</b> 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, & 32 mg/0.64 mL <b>Monthly:</b> 64 mg/0.18 mL, 96 mg/0.27 mL, and 128 mg/0.36 mL.
<b>Mean BUP concentration at steady state (ng/mL)</b>	100 mg dose: 3.21 300 mg dose: 6.54	Variable depending on dose weekly: 2.1 to 4.2; monthly: 2 to 3.9
<b>Half-life</b>	43-60 days	weekly: 3 to 5 days, monthly: 19 to 26 days
<b>Tmax</b>	24 hours	24 hours (weekly), 6-10 hours (monthly)
<b>Steady state</b>	<ul style="list-style-type: none"> <li>▪ attained at 4-6 months</li> <li>▪ detectable levels can last &gt; a year after cessation (steady state)</li> </ul>	attained upon administration of the fourth weekly or monthly dose
<b>Formulation technology</b>	depot formulation contains BUP dissolved in biodegradable delivery system using Atrigel® technology that releases BUP at controlled rate over one-month period	FluidCrystal® injection depot technology enables low-volume injection solution that transforms into a nanostructured liquid-crystalline gel upon injection (gel allows for BUP controlled gradual release over one-week or one-month period)
<b>Refrigerated</b>	Yes	No
<b>Most common adverse effects</b>	Constipation, headache, nausea, injection site pruritus/pain, vomiting, increased hepatic enzymes, & fatigue	Headache, constipation, nausea, injection site erythema / pruritus / pain, insomnia, and UTI
<b>Similarities between Brixadi &amp; Sublocade</b>	▪ Both Brixadi and Sublocade are approved for the treatment of moderate to severe OUD	

	<ul style="list-style-type: none"> <li>▪ to be used as part of comprehensive treatment plan that includes counseling &amp; psychosocial support</li> <li>▪ administered by a healthcare provider in a healthcare setting, minimizing the risk for patient diversion or misuse (schedule III-controlled substance)</li> <li>▪ record site of administration in pt's medical record</li> <li>▪ less fluctuation in BUP levels compared to daily doses</li> <li>▪ not recommended for patients with moderate to severe hepatic impairment</li> <li>▪ use with alcohol, benzodiazepines, sleeping pills, antidepressants, or certain other medications can lead to drowsiness or overdose</li> <li>▪ consider prescribing naloxone when initiating or renewing Brixadi or Sublocade (potential for relapse, putting pts at risk for overdose)</li> <li>▪ Administer as a single subcutaneous injection only. Do NOT administer intravenously, intramuscularly, or intradermally. Doses should not be divided</li> <li>▪ Healthcare settings &amp; pharmacies must be certified in the REMS program, comply with the REMS requirements, and dispense the medication directly to a healthcare provider for administration</li> <li>▪ Patients should inform their provider if they become pregnant during treatment</li> <li>▪ Advise pts that IV self-injection can cause death</li> </ul>	
<b>Role in therapy</b>	<ul style="list-style-type: none"> <li>▪ Long-acting medications like Brixadi &amp; Sublocade hold significant promise in improving treatment entry, retention, and patient outcomes</li> <li>▪ Figuring out how to make these therapies more accessible to both patients and healthcare providers remains a significant challenge</li> <li>▪ ongoing research will offer further insights into the application and effectiveness of these therapies in real-world settings</li> <li>▪ BUP is also available as up to 6-month subdermal implant and weekly transdermal patches (5 mcg to 20 mcg/hr)</li> </ul>	
<b>Comments</b>	<ul style="list-style-type: none"> <li>▪ Requires patients to be on a stable dose of transmucosal BUP for at least 7 days</li> <li>▪ available in 2 doses only</li> <li>▪ Maintenance dose may be increased to 300 mg/month for patients tolerating 100 mg dose without satisfactory clinical response</li> <li>▪ For clts on 100 mg monthly dose, a 2-month dosing interval may be considered in certain situations, and a single 300 mg dose can be given to cover the 2-month period, followed by a return to 100 mg monthly dose</li> <li>▪ Advise pts that they must first be on 8 to 24 mg of SL BUP for a at least 7 days</li> <li>▪ a lump may develop at the injection site for a few weeks that gradually reduces in size. Advise not to rub or massage the lump or let belts/ waistbands rub against it</li> </ul>	<ul style="list-style-type: none"> <li>▪ Only a single prior dose of BUP SL is required before starting treatment</li> <li>▪ flexibility in weekly and monthly dosing</li> <li>▪ range of dosage options</li> <li>▪ flexibility in administration sites</li> <li>▪ overall safety profile comparable to BUP SL, except possible injection site reactions</li> <li>▪ anticipated availability September 2023</li> <li>▪ does not require refrigeration</li> <li>▪ weekly and monthly are different formulations (cannot be combined to yield monthly dose)</li> <li>▪ Pts may be transitioned from weekly to monthly or from monthly to weekly dosing</li> <li>▪ Weekly or Monthly instead of daily medication compliance</li> <li>▪ Brixadi was not available in the US due to Sublocade's exclusivity which lasted until 2020</li> </ul>
<b>Removal</b>	Depot can be surgically removed within 14 days, if needed	Not recommended. SUBQ injection forms a biodegradable gel depot that releases BUP over time. The depot may not be detectable or suitable for surgical removal
<b>Potential candidates</b>	<ul style="list-style-type: none"> <li>▪ patients dealing with challenging transitions (eg. leaving a hospital, ER, or jail)</li> <li>▪ concerns about diversion or misuse of BUP SL formulation</li> </ul>	

- difficulty accessing a local provider
- Patients at risk of non-adherence and misuse (unstable or frequently miss visits, unstable living situations, transportation issues, injection addiction)
- Patients preference (less frequent visits or supervised dosing, don't want to take daily medication)
- patients facing buprenorphine access challenges (eg during incarceration)
- concerns about safe storage (risk of medication being stolen or accessible to children)
- pts concerned about the stigma related to daily BUP use

**Brixadi Dosing**

Recommended weekly dose in patients not currently receiving BUP is 24 mg

1. Give test dose of 4 mg transmucosal BUP to ensure BUP is tolerated without precipitated withdrawal
2. If tolerated, administer the first dose of 16 mg Brixadi weekly
3. Add 8 mg weekly dose within 3 days to reach the recommended 24 mg weekly dose
4. An additional 8 mg (at least 24 hours apart) can be given for a total of 32 mg weekly (max dose), if needed

Switching from Transmucosal Buprenorphine-containing Products to Brixadi

Daily dose of SL BUP	Brixadi (weekly)	Brixadi (monthly)
≤6 mg	8 mg (0.16 ml)	---
8 mg to 10 mg	16 mg (0.32 ml)	64 mg (0.18 ml)
12 mg to 16 mg	24 mg (0.48 ml)	96 mg (0.27 ml)
18 mg to 24 mg	32 mg (0.64 ml)	128 mg (0.36 ml)

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

Transitioning between Brixadi weekly and monthly

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

Price Comparison

Drug	30-day cost at max dose	Formulary Status
Brixadi Monthly	\$1595	Recommend ADD
Brixadi Weekly	\$1660	Recommend ADD
Buprenorphine SL Bup/naloxone Film/tab	\$144 - \$750 (generic)	BHRS, CA, DHCS
Sublocade Monthly	\$1920	BHRS, CA, DHCS

Formulary Recommendation

ADD Brixadi to BHRS/CA/HealthWorkx formularies with quantity limit #1/28DS on monthly injections

## References

- Brixadi package insert
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- Micromedex Online. Accessed June 28, 2023
- Substance Abuse and Mental Health Services Administration (SAMHSA). Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63. Publication No. PEP21-02-01-002. Substance Abuse and Mental Health Services Administration; 2021.
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