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Injectable Buprenorphine:
Getting Started

This resource guide provides basic information about the two extended-release injectable forms of buprenorphine (BUP-XR) – Sublocade™ and Brixadi™ – and offers guidance on the clinical use of these buprenorphine formulations.

SL buprenorphine (SL-BUP) is very effective for opioid use disorder, but for a variety of reasons, some people have difficulty stabilizing on it. Long-acting injectable buprenorphine is an alternative form of buprenorphine that can potentially address some of those barriers.

Reasons to consider long-acting injectable buprenorphine include:

- Patients don't have to take daily medication, making adherence easier
- Cuts down on patient trips to the pharmacy and clinic
- Good alternative if a patient has a taste aversion to SL buprenorphine
- Some patients can benefit from higher serum concentrations than can be achieved with SL-BUP
- Patients and providers don't have to worry about lost/stolen medication
- Providers don't have to worry about diversion
- Injectable buprenorphine offers consistent and stable dosing

Injectable buprenorphine has been shown to have similar, if not greater effectiveness than SL-BUP. Many providers are interested in providing injectable buprenorphine and have asked for information on characteristics of the medications themselves, how to use these medications in practice, and the best practice logistics for a clinic offering injectable buprenorphine (for this, see the resource guide titled "Injectable Buprenorphine: Getting Your Clinic Ready"). References and further reading materials on injectable buprenorphine can be found at the end of this guide.

Best practice approaches to offering XR-BUP:

- Offer XR-BUP to all individuals with OUD – those new to treatment as well as those already taking SL-BUP
- Use a patient-centered approach that provides education about treatment options and tailors a patient's BUP formulation (SL vs. XR) to their clinical situation and their preferences

Disclaimer: We are using the trade names for the two available injectable buprenorphine formulations – Sublocade™ and Brixadi™. We do not endorse one medication over another, yet we do want providers to understand these medications so they can tailor their care to the individuals they treat. If this resource guide sounds as if we are supportive of these medications, it's because we have read the science behind them and have known people who have benefitted from them. We do not receive any funding from companies who develop or sell these medications. Our goal is to increase options for people who have opioid use disorder.

Table 1: Characteristics of Sublocade™ and Brixadi™

Characteristic	Sublocade	Brixadi
FDA-approved	2017	2023
Commercially available	2019	2024
Injection sites	Multiple subcutaneous injection sites (abdomen, thigh, buttock, back of upper arm) Rotate sites for each injection	Multiple subcutaneous injection sites (buttock, thigh, abdomen, upper arm) Rotate sites for each injection
Injection side effects	Pain at injection site, noticeable bump under skin, resolves slowly	Minimal pain at injection site, no noticeable bump under skin Upper arm with 10% lower plasma levels, so use after 4th dose
Dose strengths	Monthly dose strengths: 100mg, 300mg	Weekly dose strengths: 8-16-24-32 mg, Monthly dose strengths: 64-96-128 mg
Half-life	43-60 days	Weekly 3-5 days, Monthly 19-26 days
Steady state timing	4-6 months	Weekly 4-7 doses, Monthly 4 doses
Monitoring recommendations	Baseline LFTs and "periodically"	Baseline LFTs and "periodically"
Stopping treatment	Depot can be surgically removed within 14 days of injection	Depot cannot be surgically removed
Advantages	• High steady state concentrations may protect against the respiratory depression seen with potent opioids (e.g., fentanyl) (Moss) • Some patients using potent opioids may need the higher steady state concentrations that Sublocade provides to be stabilized on buprenorphine (Moss)	• More flexibility in dosing • No need for refrigeration • Weekly dosing can be used in pregnancy (Winhusen) • Possibility of induction without 7-day lead time is being investigated (Mariani)
Disadvantages	• Fewer injection sites • Bump at site of injection slow to resolve • Requirement for refrigeration unless using within 12 weeks	• Steady state concentrations lower with monthly dosing • Weekly dose less convenient • Shorter half-life, thus wears off before one month

**See table 3*

Table 2: Dose equivalents to different BUP formulations

SL-BUP doses	Sublocade (monthly)	Brixadi (weekly)	Brixadi (monthly)
≤ 6 mg	N/A	8 mg	N/A
8-10 mg	100 mg*	16 mg	64 mg
12-16 mg	100 mg*	24 mg	96 mg
18 mg	100 mg*	32 mg	128 mg
20-24 mg	100 or 300 mg*	32 mg	128 mg

After induction at steady state

Figure 1: MOUD treatment goals and average BUP concentrations

Pharmacokinetic parameters	*SL-BUP*		Sublocade		
Mean	*12mg (ss)*	*24mg (ss)*	*300mg* (1st injection)*	*100mg** (ss)*	*300mg** (ss)*
Cavg, ss (ng/mL)	*1.71*	*2.91*	*2.19*	*3.21*	*6.54*
Cmax, ss (ng/mL)	*5.35*	*8.27*	*5.37*	*4.88*	*10.12*
Cmin, ss (ng/mL)	*0.81*	*1.54*	*1.42*	*2.48*	*5.01*

Pharmacokinetic parameters	*Brixadi (weekly)*		*Brixadi (monthly)*	
Mean	*24mg*	*32mg*	*96mg*	*128mg*
Cavg, ss (ng/mL)	*2.9*	*4.2*	*2.9*	*3.9*
Cmax, ss (ng/mL)	*5.5*	*6.9*	*6.0*	*11.1*
Cmin, ss (ng/mL)	*1.4*	*2.6*	*2.0*	*2.1*

MOUD treatment goals	Serum concentration
Minimize withdrawal and cravings	at ≥1ng/mL (TM Bup > 4mg)
Reduce euphoria and drug-seeking	at ≥2-3ng/mL (TM Bup > 16-32mg)
Block toxicity of non-prescribed opioid use	at ≥5ng/mL

All forms and formulations of injectable buprenorphine attain higher trough (minimum) concentrations than SL-BUP, and thus are able to manage symptoms as well as drug-seeking effects of opioids.

Sublocade 300mg dosing attains higher trough (minimum) concentrations than other formulations and may be needed for individuals using high levels of opioids, especially fentanyl.

Table 3: FDA-approved induction protocols for XR-BUP

Patient status	Sublocade	Brixadi (weekly)	Brixadi (monthly)
Not currently using SL-BUP	**Week 1:** • Give 4mg TM Bup when objective signs of mild to moderate withdrawal appear • If no precipitated withdrawal after ~1 hour, give first 300mg injection • Monitor in a healthcare setting for signs of worsening withdrawal or sedation **Subsequent weeks:** • Second dose may be administered 1 week to 1 month after first injection • 300mg for doses 1 & 2 • 100mg monthly maintenance dose • Dose every 28 days (Range: 26-42 days)	**Week 1:** • Give 4mg TM Bup when objective signs of mild to moderate withdrawal appear • If no precipitated withdrawal after ~1 hour, give 16mg injection • Within 3 days of first dose (no sooner than 24 hours) give additional 8mg • Ok to give additional 8mg 24 hours after previous injection with max. first week dose of 32mg **Subsequent weeks:** • Give week 1 total dose: 16mg, 24mg, 32mg • Dose adjustments can be made up to a max. of 32 mg	• Not used for induction per the package insert • Once stabilized using weekly dosing (64-128 mg), dose every 28 days (Range: 21-35 days)
Using SL-BUP:	Based on SL-BUP maintenance dose *Can give supplemental SL-BUP as needed*	Week 1 and beyond, give equivalent SL-BUP dose	Month 1 and beyond, give equivalent SL-BUP dose
≤ 6 mg		8mg	
8-10 mg	Month 1: 300 Month 2: 100 Month 3: 100 and ongoing	16mg	64mg
12-16 mg	Month 1: 300 Month 2: 100 Month 3: 100 and ongoing	24mg	96mg
18 mg	Month 1: 300 Month 2: 100 Month 3: 100 and ongoing	32mg	128mg
20-24 mg	Month 1: 300 Month 2: 100 Month 3: 100 or 300 and ongoing	32mg	128mg

For both Sublocade and Brixadi, supplemental SL-BUP may be needed in the early weeks of induction for break-through symptoms. Symptom management can be accomplished with medications such as lofexidine, gabapentin, hydroxyzine, tizanidine, ondansetron for nausea, fluids, or NSAIDs for muscle aches (www.asam.org/quality-care/clinical-guidelines/national-practice-guideline).

Additional training can be found here:
www.learnabouttreatment.org/vidseries/using-extended-release-injectable-buprenorphine-for-oud

In Conclusion

Injectable buprenorphine offers an important option for treatment of OUD.

Clinical recommendations for injectable buprenorphine are straightforward, making it possible for both primary care providers and specialty providers to offer this important treatment option.

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Sublocade Prescribing Information
https://www.sublocade.com/Content/pdf/prescribing-information.pdf

Brixadi Medication Guide
https://www.brixadi.com/pdfs/brixadi-medication-guide.pdf

The ASAM National Practice Guideline For the Treatment of Opioid Use Disorder 2020 Focused Update
https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline