BUPRENORPHINE EXTENDED-RELEASE INJECTION MONOTHERAPY (Brixadi, Sublocade) Fact Sheet

Bottom Line:

Extended-release injectable formulations of buprenorphine allow patients to receive doses weekly, monthly, or every eight weeks for patients maintained on a low dose—which improves medication adherence. Brixadi has the advantage over Sublocade due to its more flexible dosing options.

FDA Indications:

Opioid use disorder (maintenance).

Dosage Forms:

- **Monthly injection (Sublocade):** 100 mg/0.5 mL, 300 mg/1.5 mL prefilled syringes.
- **Weekly or monthly injection (Brixadi):** 8 mg, 16 mg, 24 mg, 32 mg (weekly) and 64 mg, 96 mg, 128 mg (monthly) prefilled syringes.

Dosage Guidance:

- After patient is stabilized on sublingual (SL) buprenorphine for seven days:
  - Sublocade:
    - Injections are given subcutaneously in the abdomen.
    - For patients maintained on 8–18 mg: Start with 300 mg then 100 mg monthly or 300 mg Q8wks.
    - For patients maintained on 20–24 mg: Start with 300 mg monthly for two months, then give 100 mg monthly maintenance doses.
    - Patients commonly have opioid cravings or withdrawal symptoms when dropping down to the 100 mg dose. For these patients, you can give 300 mg every month.
    - Doses may be given early if clinically indicated, though no closer than 26 days apart.
  - Brixadi:
    - Injections are given subcutaneously in the buttocks, thigh, abdomen, or upper arms (upper arm should be avoided for first four doses).
    - Rotate administration sites for weekly injections and avoid administering into same site for at least eight weeks. No site rotation needed for monthly injections.
    - For patients maintained on ≤6 mg: Give 8 mg weekly.
    - For patients maintained on 8–10 mg: Give 16 mg weekly or 64 mg monthly.
    - For patients maintained on 12–16 mg: Give 24 mg weekly or 96 mg monthly.
    - For patients maintained on 18–24 mg: Give 32 mg weekly or 128 mg monthly.

Monitoring: Baseline and monthly LFTs.

Cost: $$$$$

Side Effects:

- Most common: Injection site itching and pain, constipation, headache, insomnia, nausea, anxiety.
- Serious but rare: Hepatitis reported rarely, ranging from transient, asymptomatic transaminase elevations to hepatic failure; in many cases, patients had preexisting hepatic dysfunction. Respiratory depression and orthostatic hypotension possible.
- Boxed warning emphasizes the risk of administering the drug intravenously rather than the intended subcutaneous route. Their gel formulations could cause occlusion, local tissue damage, or thrombotic events if injected intravenously, potentially causing severe harm or death.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Partial opioid agonist (delta and mu receptors) and antagonist (kappa receptors).
- Metabolized primarily through CYP3A4; t ½: 24–48 hours.
- Avoid concomitant use with opioid analgesics (diminished pain control). Additive effects with CNS depressants. CYP3A4 inhibitors and inducers may affect levels of buprenorphine.

Clinical Pearls:

- Schedule III controlled substance. Prescribing buprenorphine for OUD no longer requires having a special "X-license."
- Extended-release injectable formulations are only available through a REMS program.
- Of the two formulations, Brixadi offers more flexibility in terms of dosing and injection sites.
- If needed in first week, can give an additional 8 mg weekly injection of Brixadi (at least 24 hours after previous injection). Dose adjustments can be made weekly with a maximum weekly dose of 32 mg.
- Brixadi can be switched from weekly to monthly or vice versa based on the following equivalencies: 16 mg weekly = 64 mg monthly, 24 mg weekly = 96 mg monthly, 32 mg weekly = 128 mg monthly.
- Brixadi weekly can be initiated in patients not currently receiving SL buprenorphine, but a 4 mg SL test dose is recommended to help determine appropriate dose.

Fun Fact:

- The development of long-lasting buprenorphine injections represents a milestone in "depot technology," where the medication is stored and gradually released in the body, reducing the need for daily dosing and potentially improving treatment outcomes.