BUPRENORPHINE (Brixadi, Sublocade) Fact Sheet [G]

Bottom Line:

Buprenorphine (Subutex, available now only as generic) is the active ingredient in Suboxone (buprenorphine/naloxone) and is responsible for the effectiveness of the combination medication in opioid use disorder. In the past, buprenorphine alone was preferred for the initial (induction) phase of treatment, while Suboxone was preferred for maintenance treatment (unsupervised administration). Currently, the combination is favored for both induction and maintenance as it decreases abuse and diversion potential.

FDA Indications:

Opioid dependence: induction, maintenance (Sublocade); moderate-severe pain (Belbuca, Buprenex, Butrans).

Dosage Forms:

- **SL tablets (G):** 2 mg, 8 mg (scored).
- **Extended-release injection (Sublocade):** 100 mg, 300 mg prefilled syringes.
- **Extended-release injection (Brixadi):** 8 mg, 16 mg, 24 mg, 32 mg (weekly) and 64 mg, 96 mg, 128 mg (monthly) prefilled syringes.
- **Buccal film (Belbuca, [G]):** 0.075 mg, 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg, 0.75 mg, 0.9 mg (used for pain).
- **Injection (Buprenex, [G]):** 0.3 mg/mL (used for pain).
- **Transdermal patch (Butrans):** 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr (used for pain).

Dosage Guidance:

- Induction procedure:
  - Begin at least four hours after last use of heroin or other short-acting opioids and when first signs of withdrawal appear; otherwise, you may trigger withdrawal symptoms.
  - Start 2–8 mg SL day one; then 8–16 mg SL QD (usual initial dose range is 12–16 mg/day and accomplished over three to four days).
  - Other than extended-release injection, not for maintenance treatment; patients should be switched to the buprenorphine/naloxone combination product for maintenance and unsupervised therapy.
- Patients with moderate to severe opioid use disorder who have been stabilized with SL or buccal buprenorphine for greater than seven days may convert to monthly or weekly subcutaneous injections. Sublocade: Start 300 mg monthly for two months, then give 100 mg monthly maintenance doses; Brixadi: 8–32 mg weekly or 64–128 mg monthly, based on daily dose of SL. Brixadi weekly can be initiated in patients not currently receiving SL, but a 4 mg SL test dose is recommended to help determine appropriate dose.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: SL: $$; extended-release injection: $$$$$

Side Effects:

- Most common: Headache, pain, 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. QT prolongation with higher doses of transdermal patch.
- Pregnancy/breastfeeding: Limited data suggest relative safety in pregnancy and breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Partial opioid agonist (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 for opioid dependence no longer requires any special training
- Weekly and monthly injection options offer alternative that may be convenient for some patients.

Fun Fact:

The subcutaneous implant formulation of buprenorphine (Probuphine) was discontinued. Its use was severely limited as it was invasive, expensive, and an option only for patients stable on ≤8 mg/day. Other implants currently in development include medications for schizophrenia, breast cancer, photosensitivity, and Parkinson's disease.