BUPRENORPHINE MONOTHERAPY (Subutex, others) 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 (OUD). 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, at least theoretically, decreases misuse and diversion.

FDA Indications:

OUD: induction, maintenance; moderate to severe pain (Belbuca, Buprenex, Butrans).

Dosage Forms:

- **SL tablets (Subutex, [G]):** 2 mg, 8 mg (scored).
- **Buccal film (Belbuca, [G]):** 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, 900 mcg (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).
- **Short-acting injection (Buprenex, [G]):** 0.3 mg/mL (used for pain).
- **Extended-release injection:** For OUD; see "Buprenorphine Extended-Release Injection Monotherapy" fact sheet.

Dosage Guidance for OUD:

- Induction procedure (SL tablets):
  - Begin when opioid withdrawal reaches moderate severity; otherwise, you may trigger withdrawal symptoms.
  - Start 4–8 mg SL day 1; increase up to 16 mg on day 2; then up to 24 mg on day 3. Some patients may need up to 12 mg in first 24 hours. Typical maintenance dose is 8–24 mg SL QD, though best evidence is for 16–24 mg; max 32 mg/day.
  - See separate fact sheets for more information about induction procedures.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: SL: $$

Side Effects:

- Most common: 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. QT prolongation, particularly with higher doses of transdermal patch. Rare cases of dental problems including tooth decay, cavities, and infections; recommend swishing with water after dose completely dissolved and good dental care.

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."
- Though buprenorphine/naloxone products are recommended for maintenance treatment, buprenorphine monoproduct can be used during pregnancy and for the handful of patients who may have adverse effects to the small amount of naloxone absorbed sublingually from the combination product (headache, anxiety, GI distress, palpitations).
- Patients with moderate to severe OUD and who have been stabilized with SL or buccal buprenorphine 8–24 mg for >7 days may convert to monthly or weekly subcutaneous injections.

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 of SL buprenorphine. Other implants currently in development include medications for schizophrenia, breast cancer, photosensitivity, and Parkinson's disease.