
BUPRENORPHINE/NALOXONE (Bunavail, Suboxone, Zubsolv)

Fact Sheet [G]

Bottom Line:

Buprenorphine/naloxone is the definitive partial agonist treatment for opioid use disorder. The combination product is preferred over buprenorphine alone for maintenance because the addition of naloxone lowers its potential for injection abuse. The sublingual film formulation is priced a little higher than the sublingual tablets yet provides very little (if any) meaningful benefit; generic tablets should be used as a cost-saving measure.

FDA Indications:

Opioid dependence (induction and maintenance).

Dosage Forms:

- **SL tablets (G):** 2/0.5 mg, 8/2 mg (scored).
- **SL film strips (Suboxone, [G]):** 2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg.
- **SL tablets (Zubsolv):** 0.7/0.18 mg, 1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg.
- **Buccal film (Bunavail):** 2.1/0.3 mg, 4.2/0.7 mg, 6.3/1 mg.

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).
- Maintenance treatment: give combination product (Suboxone or [G]) daily in the equivalent buprenorphine dose on last day of induction; adjust dose in increments of 2 mg or 4 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms (usually 4–24 mg/day); max 32 mg/day.
- Zubsolv 5.7/1.4 mg SL tablet provides equivalent buprenorphine to a Suboxone 8/2 mg SL tablet.
- Bunavail 4.2/0.7 mg buccal film provides equivalent buprenorphine to a Suboxone 8/2 mg SL tablet.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: SL tablet, film, Bunavail: \$–\$\$ depending on dose; Zubsolv: \$\$\$

Side Effects:

- Most common: Headache, pain, vomiting, sweating.
- Serious but rare: Hepatitis reported rarely, ranging from transient, asymptomatic transaminase elevations to hepatic failure; in many cases, patients had preexisting hepatic dysfunction. Rare cases of dental problems including tooth decay, cavities, and infections; recommend swishing with water after dose completely dissolved and good dental care.
- Pregnancy/breastfeeding: Limited data suggest relative safety in pregnancy and breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Buprenorphine: Partial opioid agonist (mu receptors) and antagonist (kappa receptors); naloxone: Opioid antagonist (mu receptors).
- Metabolized primarily through CYP3A4; t_{1/2}: 24–48 hours (naloxone: 2–12 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 no longer limited as long as provider has an active DEA license.
- Naloxone is an opioid antagonist that is active only when injected; it is added to buprenorphine in order to reduce misuse via intravenous injection of a dissolved tablet.
- The SL film formulation's manufacturer claims it dissolves faster and tastes better than SL tablets. Actually, it is more likely a way for the manufacturer to switch users to a "new" product (with patent protection until 2025) rather than lose patients to generics.
- SL film should be placed at base of tongue to the side of midline; this allows patient to use two films at the same time if dose dictates.
- Zubsolv and Bunavail formulations have better bioavailability, hence the dose equivalencies noted above.
- Prescribers should be aware of the risk for diversion and sale of buprenorphine films and tablets. Buprenorphine is bought and sold on the streets and used to combat cravings and withdrawal symptoms.

Fun Fact:

The manufacturer of Suboxone, Reckitt Benckiser, generates most of its revenue from selling home and personal care products like Lysol cleaners and Durex condoms.