
OXYBATES (Lumryz, Xyrem, Xywav) Fact Sheet [G]

Bottom Line:

The oxybates are often used by sleep specialists as first-line agents for narcolepsy with cataplexy. It's unlikely that many psychiatrists will prescribe them, given the side effect profile and potential for misuse. Pitolisant, which is easier to use and is not a controlled substance, may be a better option for most patients with both cataplexy and excessive daytime sedation (EDS) associated with narcolepsy.

FDA Indications:

Cataplexy and EDS in narcolepsy (ages 7 and up); idiopathic hypersomnia (Xywav).

Off-Label Uses:

Fibromyalgia; chronic pain; neuropathic pain.

Dosage Forms:

- **Sodium oxybate oral solution (Xyrem, [G]):** 0.5 g/mL.
- **ER sodium oxybate oral suspension (Lumryz):** 4.5 g, 7.5 g, 9 g.
- **Calcium, magnesium, potassium, and sodium oxybate oral solution (Xywav):** 0.5 g/mL.

Dosage Guidance:

- IR: Start 4.5 g nightly, given in two equal, divided doses (because of extremely short half-life): 2.25 g at bedtime and 2.25 g taken 2.5 to four hours later. Titrate to effect in increments of 1.5 g/night at weekly intervals (0.75 g at bedtime and 0.75 g taken 2.5 to four hours later). Usual dose 6–9 g per night. Max 9 g/night.
- ER: Start 4.5 g nightly, given QHS. Titrate to effect in increments of 1.5 g/night at weekly intervals; usual dose 6–9 g QHS. Max 9 g/night.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$\$\$\$

Side Effects:

- Most common: Nausea, dizziness, vomiting, somnolence, enuresis, tremor, parasomnias (sleepwalking).
- Serious but rare: Respiratory depression, depression and suicidality, impaired motor and cognitive function.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- CNS depressant.
- Metabolized primarily by conversion to carbon dioxide and then eliminated by expiration; $t_{1/2}$: 0.5–1 hour.
- Avoid concomitant use with alcohol, sedative hypnotics, and other CNS depressants. Valproic acid increases oxybate levels by 25%; adjust valproic acid dose by at least 20%.

Clinical Pearls:

- Sodium oxybate is the sodium salt of gamma hydroxybutyrate (GHB), a Schedule I controlled substance (“date rape” drug).
- Sodium oxybate is a Schedule III controlled substance and is available only through a restricted distribution program called the Xyrem REMS Program using a centralized pharmacy. Prescribers and patients must enroll in the program (www.xyremrems.com or 1-866-XYREM88).
- Patients must wait at least two hours after eating before taking a dose. Both doses should be prepared (dilute in provided vials with water) before bedtime. Dose must be taken while in bed, and patients are to lie down after dosing.
- Most patients find the taste of Xyrem to be awful.
- Xyrem alone was just as effective as modafinil alone for excessive daytime sedation, but the combination was significantly better than either medication used alone in one narcolepsy study.
- Xywav is the newer “mixed salts” version (patent extender for Xyrem’s manufacturer Jazz?) and delivers 92% less sodium than Xyrem.
- The FDA granted a new indication for using Xywav to treat idiopathic hypersomnia, a rare and debilitating neurologic sleep disorder characterized by EDS, prolonged but non-restorative nighttime sleep, and severe sleep inertia (prolonged difficulty waking).
- Newest to market is the once-nightly version of Xyrem, called Lumryz, which offers the huge benefit of not needing to set an alarm for middle-of-the-night dosing.

Fun Fact:

Xyrem, an orphan drug, is expensive, between \$108,000 and \$160,000 per year depending on the nightly dose. Jazz Pharmaceuticals is looking to expand its use by testing it in obstructive sleep apnea, Parkinson’s, chronic fatigue, schizophrenia, binge eating, and cluster headache.