LORAZEPAM (Ativan, Loreev XR) Fact Sheet [G]

Bottom Line:
When a benzodiazepine is appropriate for use (short-term; minimal risk of abuse), we consider lorazepam to be a first-line agent.

FDA Indications:
Generalized anxiety disorder; status epilepticus (IV route).

Off-Label Uses:
Other anxiety disorders; insomnia; acute mania or psychosis; catatonia; preoperative sedation; chemotherapy-related nausea and vomiting.

Dosage Forms:
- **Tablets (G):** 0.5 mg (scored), 1 mg (scored), 2 mg (scored).
- **ER capsules (Loreev XR):** 1 mg, 1.5 mg, 2 mg, 3 mg.
- **Oral concentrate (G):** 2 mg/mL.
- **Injection (G):** 2 mg/mL, 4 mg/mL.

Dosage Guidance:
- Anxiety: Start 1 mg BID, ↑ by 0.5–1 mg/day increments every two to four days up to 6 mg/day divided BID–TID. Max 10 mg/day divided BID–TID.
- ER capsules for patients taking stable, evenly divided TID dosing with IR; to be taken once daily in morning.
- Insomnia (off-label use): Start 0.5–1 mg QHS, 20–30 minutes before bedtime; max 4 mg nightly.
- Use lower doses in elderly.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $; Loreev XR: $$$$

Side Effects:
- Most common: Somnolence, dizziness, weakness, ataxia.
- Serious but rare: Anterograde amnesia, increased fall risk, paradoxical reaction (irritability, agitation), respiratory depression (avoid in patients with sleep apnea or on opioids).
- Pregnancy/breastfeeding: Potential risks with exposure in early and late pregnancy; use caution in breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Binds to benzodiazepine receptors to enhance GABA effects.
- Metabolism primarily hepatic (non-CYP450) to inactive compounds; t ½: 10–20 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). No risk for CYP450 drug interactions.

Clinical Pearls:
- Schedule IV controlled substance.
- Lorazepam does not have a long half-life or active metabolites that could accumulate, and poses no CYP450 drug interaction risk.
- Withdrawal symptoms are usually seen on the first day after abrupt discontinuation and last five to seven days in patients receiving benzodiazepines with short to intermediate half-lives, such as lorazepam. A gradual taper is highly recommended, particularly if the patient is receiving prolonged treatment on a high dose.
- Tolerance to sedative effect may develop within two to four weeks of use, and benzodiazepines affect sleep architecture; thus, long-term use is discouraged.

Fun Fact:
Early Ativan marketing efforts included clever direct-to-consumer advertising campaigns. These included "Now it can be yours—the Ativan experience" in 1977 and "In a world where certainties are few . . . no wonder Ativan is prescribed by so many caring clinicians" in 1987.