BENZODIAZEPINE | C-IV

Lorazepam

Ativan, Loreev XR

Intermediate-acting benzodiazepine cleared by glucuronidation; the workhorse for catatonia, agitation and status epilepticus.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
2-6 mg/day PO (max 10)	12 h (10-20 h)	Glucuronidation; no CYP	PO 20-30 min; IV 1-3 min

⚠ FDA BOXED WARNING

Concomitant use with opioids may cause profound sedation, respiratory depression, coma, and death. Abuse, misuse, and addiction can lead to overdose and death. Continued use causes physical dependence; abrupt discontinuation or rapid dose reduction can precipitate life-threatening withdrawal reactions.

INDICATIONS

- FDA-approved orally for anxiety disorders, short-term relief of anxiety symptoms, and anxiety associated with depressive symptoms in adults.
- FDA-approved as an injection for status epilepticus and as a preanesthetic agent providing sedation and anterograde amnesia before procedures.
- Off-label but standard of care for catatonia, where a diagnostic lorazepam challenge often produces rapid and dramatic symptomatic response.
- Off-label as the benzodiazepine backbone of symptom-triggered alcohol withdrawal protocols, particularly when liver disease is present.
- Off-label for acute agitation, alone or with an antipsychotic, and for chemotherapy-induced anticipatory nausea and vomiting.
- Guidelines reserve benzodiazepines for short-term anxiety use, with SSRIs or SNRIs carrying the maintenance treatment of anxiety disorders.

DOSING & TITRATION

- Anxiety: start **0.5-1 mg PO two or three times daily**, usual range 2-6 mg/day, labeled maximum **10 mg/day** in divided doses.
- Insomnia due to anxiety or situational stress: 2-4 mg PO at bedtime, intended for a few nights rather than as continuing hypnotic therapy.
- Status epilepticus: **4 mg IV** given at no more than 2 mg/min, repeated once after 10-15 minutes if seizures continue; pediatric dose 0.1 mg/kg up to 4 mg.
- Catatonia: 1-2 mg IV, IM or PO every 4-12 hours, titrating as high as 8-24 mg/day; failure to respond should prompt consideration of ECT.
- Older adults or debilitated patients start at 0.5-1 mg/day in divided doses; no renal or hepatic dose reduction is formally required.
- Taper by about 10 percent of the current dose every 1-2 weeks after chronic use, slowing near the end, since abrupt stop can cause seizures and death.

MECHANISM OF ACTION

- Positive allosteric modulator at the GABA-A benzodiazepine site, increasing chloride channel opening frequency and dampening neuronal excitability.
- Intermediate lipophilicity gives slower brain entry than diazepam but longer CNS residence, which is why it outperforms diazepam in status epilepticus.
- Non-selective across alpha subunits, producing anxiolysis, sedation, amnesia, muscle relaxation and anticonvulsant effect as one package.
- Presumed correction of GABA-A hypofunction underlies its dramatic effect in catatonia and its suppression of alcohol withdrawal hyperexcitability.
- Repeated dosing downregulates GABA-A receptors, producing tolerance to sedation and the physiologic dependence that drives withdrawal.

PHARMACOKINETICS

- Oral bioavailability is about 90 percent with peak levels near 2 hours; intramuscular absorption is reliable, unlike chlordiazepoxide or diazepam.
- Elimination half-life is roughly **12 hours**, so oral dosing is typically two or three times daily with little day-to-day accumulation.
- Cleared solely by UGT2B15 glucuronidation to an inactive glucuronide, bypassing hepatic oxidation entirely and producing no active metabolites.
- Along with oxazepam and temazepam, this glucuronidation-only route makes lorazepam the preferred benzodiazepine in cirrhosis and in older adults.
- Kinetics are essentially unaffected by CYP inhibitors or inducers, so it is the safer choice when a patient is on ritonavir or carbamazepine.

ADVERSE EFFECTS

- Sedation is the most common effect at roughly 16 percent, followed by dizziness 7 percent, weakness 4 percent and unsteadiness 3 percent.
- Anterograde amnesia is dose-dependent and pronounced after intravenous use, which is useful before procedures but problematic in ward settings.
- Falls, hip fracture and delirium in older adults; benzodiazepine exposure is a common reversible contributor to hospital-acquired confusion.
- Paradoxical agitation, disinhibition and aggression, seen most often in children, older adults, dementia and traumatic brain injury.
- Rapid intravenous administration can cause apnea, hypotension and airway compromise, so push slowly with monitoring and resuscitation available.
- Withdrawal after chronic use brings rebound anxiety, insomnia, tremor, hallucinations and seizures, and can be fatal without a managed taper.

MONITORING

- Assess sedation level, respiratory rate and oxygen saturation after parenteral doses, especially when an opioid or antipsychotic is co-administered.
- Screen for substance use history and check the prescription monitoring program before initiating and periodically during outpatient therapy.
- Track falls, gait, cognition and driving safety at every visit in older adults, and revisit whether ongoing benzodiazepine use is still warranted.
- In alcohol withdrawal use a validated scale such as CIWA-Ar to drive symptom-triggered dosing rather than fixed standing orders.
- No routine laboratory monitoring is needed; propylene glycol toxicity is a concern only with prolonged high-dose continuous infusions.

INTERACTIONS & CAUTIONS

- Additive respiratory depression and death with opioids, the basis of the boxed warning; avoid the combination or use the lowest doses with naloxone available.
- Alcohol, gabapentinoids, sedating antihistamines, clozapine and other hypnotics all compound sedation and psychomotor impairment.
- Intramuscular olanzapine plus parenteral lorazepam has been linked to excess sedation and cardiorespiratory depression; separate doses by at least an hour.
- Valproate and probenecid inhibit glucuronidation and raise lorazepam levels, so reduce the dose by roughly half when either is added.
- Contraindicated in acute narrow-angle glaucoma, benzodiazepine hypersensitivity and, for the injection, in severe respiratory insufficiency.

SPECIAL POPULATIONS

- Pregnancy: crosses the placenta; late exposure causes neonatal sedation, hypotonia and withdrawal, so limit use and alert the delivery team.
- Lactation: low milk transfer and it is often considered acceptable, but monitor the nursing infant for sedation and poor feeding.
- Pediatrics: oral use is not established under age 12, though the injection is used for pediatric status epilepticus at 0.1 mg/kg.
- Older adults: the AGS Beers Criteria advise avoiding benzodiazepines, but when one is unavoidable lorazepam is preferred over oxidized agents.
- Hepatic and renal impairment: glucuronidation is relatively preserved in cirrhosis, making lorazepam the class choice in liver failure.

☆ PRESCRIBING PEARLS

- Lorazepam, oxazepam and temazepam skip hepatic oxidation, so they are safest in liver disease.
- A lorazepam challenge is both a diagnostic test and the first treatment for suspected catatonia.
- The only oral benzodiazepine here with reliable IM absorption and a widely stocked IV form.

References

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.