BENZODIAZEPINE | C-IV

# Oxazepam

Serax (brand discontinued in the US)

*Short-acting benzodiazepine cleared by glucuronidation with slow onset and low reinforcement; suited to liver disease.*

| USUAL ADULT RANGE | HALF-LIFE | METABOLISM | ONSET |
|---|---|---|---|
| 30-120 mg/day PO divided | 5-15 h (mean ~8 h) | Glucuronidation; no CYP | Slow; peak 2-4 h |

**⚠ 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 for anxiety, tension, agitation and irritability, including anxiety associated with depression, in adults.
- FDA-approved specifically for anxiety, tension, agitation and irritability in older patients, an unusual labeled geriatric indication.
- FDA-approved for acute alcohol withdrawal, covering tremulousness, anxiety and agitation in patients with acute inebriation.
- Preferred over chlordiazepoxide or diazepam for alcohol withdrawal when cirrhosis or significant hepatic impairment is present.
- Off-label as a substitution agent during benzodiazepine tapers when a low-reinforcement, oxidation-independent option is wanted.
- Not a maintenance treatment for anxiety disorders; SSRIs, SNRIs and psychotherapy remain first line by APA, NICE and CANMAT guidance.

## DOSING & TITRATION

- Mild to moderate anxiety: **10-15 mg PO three or four times daily**, titrated to symptom control and tolerability.
- Severe anxiety syndromes and acute alcohol withdrawal: **15-30 mg PO three or four times daily**, up to 120 mg/day in divided doses.
- Older adults: begin at 10 mg three times daily and increase cautiously to 15 mg three or four times daily only if clearly needed.
- No dose adjustment is required for hepatic impairment, which is the practical reason to select this agent in cirrhotic patients.
- Available as oral capsules in 10, 15 and 30 mg strengths; there is no parenteral, liquid or extended-release formulation.
- Taper by 10-25 percent every 1-2 weeks after chronic use; abrupt discontinuation can produce withdrawal seizures, delirium and death.

## MECHANISM OF ACTION

- Positive allosteric modulator at the GABA-A benzodiazepine site, increasing chloride channel opening frequency and reducing neuronal excitability.
- Slow absorption and modest lipophilicity give a gradual rise in brain concentration, which blunts the euphoric rush and lowers misuse appeal.
- Non-selective alpha subunit binding still delivers sedation, amnesia and ataxia along with anxiolysis, so impairment is not avoided.
- Cross-tolerance at GABA-A with alcohol provides symptomatic control and seizure protection during acute alcohol withdrawal.
- As the terminal active metabolite of diazepam and temazepam, it represents the endpoint of that oxidative pathway with nothing further to accumulate.

## PHARMACOKINETICS

- Absorption is slower than other benzodiazepines with peak levels at 2-4 hours, so it is a poor choice for rapid symptom relief.
- Elimination half-life is roughly **8 hours**, giving three or four times daily dosing and little accumulation between days.
- Conjugated directly by UGT2B15 glucuronidation to an inactive glucuronide excreted in urine, with no active metabolites at all.
- Hepatic oxidation is bypassed entirely, so clearance is largely preserved in cirrhosis and is not altered by CYP inhibitors or inducers.
- With lorazepam and temazepam, this glucuronidation-only pathway defines the three benzodiazepines preferred in liver disease and in older adults.

## ADVERSE EFFECTS

- Mild transient drowsiness is the most common effect early in therapy, along with dizziness, vertigo and headache.
- Ataxia, slurred speech and impaired coordination at higher doses, with measurable psychomotor and driving impairment.
- Falls, fracture, confusion and delirium in older adults, the same class risk despite the labeled geriatric indication.
- Paradoxical excitement, disinhibition and rage reactions, reported particularly in older adults and patients with brain injury.
- Rare leukopenia, hepatic dysfunction and jaundice have been reported; syncope has occurred rarely at higher doses.
- Additive respiratory depression and overdose death with opioids or alcohol, and full withdrawal syndrome including seizures after chronic use.

## MONITORING

- Assess sedation, gait, cognition and falls at each visit, and reconfirm that the indication still justifies continued benzodiazepine exposure.
- Use CIWA-Ar or a similar validated instrument to guide symptom-triggered dosing during acute alcohol withdrawal.
- Screen for substance use disorder and check the prescription drug monitoring program before initiating and periodically thereafter.
- Obtain periodic CBC and liver enzymes during prolonged therapy given rare reports of leukopenia and hepatic dysfunction.
- In alcohol withdrawal give thiamine before glucose and correct magnesium, potassium and phosphate alongside benzodiazepine dosing.

## INTERACTIONS & CAUTIONS

- Additive respiratory depression and death with opioids, plus compounding sedation with alcohol, gabapentinoids, antipsychotics and hypnotics.
- Essentially free of CYP-mediated interactions, making it a practical choice for patients on ritonavir, rifampin or carbamazepine.
- Probenecid and valproate inhibit glucuronidation and can raise exposure; consider reducing the dose when either is co-prescribed.
- Contraindicated in known benzodiazepine hypersensitivity and in psychoses where benzodiazepine monotherapy is not appropriate.
- Avoid in untreated obstructive sleep apnea, severe respiratory insufficiency and acute narrow-angle glaucoma.

## SPECIAL POPULATIONS

- Pregnancy: benzodiazepine exposure late in pregnancy causes neonatal sedation, hypotonia and withdrawal; avoid or use the lowest effective dose.
- Lactation: transfer into milk is low and there are no active metabolites, but monitor the infant for sedation and poor feeding.
- Pediatrics: dosage is not established below age 6 and no dosing recommendation exists for children aged 6 to 12 years.
- Older adults: the AGS Beers Criteria advise avoiding benzodiazepines, though oxazepam is among the least problematic when one is required.
- Hepatic impairment: the preferred benzodiazepine in cirrhosis along with lorazepam and temazepam because oxidation is not required.

## PRESCRIBING PEARLS

- Slow onset makes it less reinforcing than alprazolam but also poor for as-needed panic relief.
- It is the terminal active metabolite of diazepam, so nothing accumulates downstream of it.
- Glucuronidation only, so no CYP interactions and no dose change needed in liver disease.

# References

American Geriatrics Society Beers Criteria Update Expert Panel. (2023). American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society, 71*(7), 2052-2081. https://doi.org/10.1111/jgs.18372

American Society of Addiction Medicine. (2020). *The ASAM clinical practice guideline on alcohol withdrawal management*. https://www.asam.org/quality-care/clinical-guidelines/alcohol-withdrawal-management-guideline

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National Institute for Health and Care Excellence. (2020). *Generalised anxiety disorder and panic disorder in adults: Management* (Clinical guideline CG113). https://www.nice.org.uk/guidance/cg113

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Stahl, S. M. (2021). *Stahl's essential psychopharmacology* (5th ed.). Cambridge University Press.

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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.