MOOD STABILIZER

Oxcarbazepine

Trileptal, Oxtellar XR

Keto-analog of carbamazepine with fewer interactions and no marrow monitoring, but a higher rate of clinically significant hyponatremia.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
1200-2400 mg/day PO divided	**MHD ~9 h; parent 1-2.5 h**	**Cytosolic reduction to MHD**	**Days for seizure control**

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved as monotherapy for partial-onset seizures in adults and in children aged 4 years and older.
- FDA-approved as adjunctive therapy for partial-onset seizures in adults and in children as young as 2 years for the immediate-release form.
- The extended-release tablet is FDA-approved as adjunctive therapy for partial-onset seizures in adults and children aged 6 to 17 years.
- Off-label use as a mood stabilizer in bipolar disorder, where controlled trials have been largely negative and guidelines rank it low.
- Off-label first-line alternative to carbamazepine for trigeminal neuralgia, with comparable efficacy and easier monitoring.
- Off-label options include alcohol withdrawal and neuropathic pain, generally where carbamazepine interactions are unacceptable.

DOSING & TITRATION

- Start **300 mg** twice daily for adults and increase by no more than 600 mg per day at weekly intervals as tolerated.
- Usual maintenance for adjunctive epilepsy therapy is **1200 mg/day**, with the labeled maximum of **2400 mg/day** in divided doses.
- When converting from carbamazepine use roughly 1.5 times the carbamazepine dose, since **200 mg** carbamazepine approximates **300 mg** oxcarbazepine.
- Off-label mood or neuralgia use typically targets **900-1800 mg/day**, titrated by response rather than by a defined serum level.
- Halve the starting dose and titrate slowly if creatinine clearance is below 30 mL/min; no adjustment is needed for mild hepatic impairment.
- Taper over 1 to 2 weeks when discontinuing to avoid withdrawal seizures, even in patients treated for nonepileptic indications.

MECHANISM OF ACTION

- Blocks voltage-sensitive sodium channels in a use-dependent manner, stabilizing hyperexcited membranes and limiting repetitive firing.
- Most activity comes from the 10-monohydroxy derivative, so the parent compound behaves largely as a prodrug after oral dosing.
- Modulates high-voltage-activated calcium currents and increases potassium conductance, further reducing synaptic transmission.
- Unlike carbamazepine it is not converted to a 10,11-epoxide, which accounts for less neurotoxicity and fewer hematologic effects.
- Potentiation of antidiuretic hormone action at the collecting duct produces hyponatremia more often than with carbamazepine.

PHARMACOKINETICS

- Absorption is essentially complete, and the parent drug is rapidly reduced by cytosolic enzymes to the active monohydroxy derivative.
- The parent half-life is 1 to 2.5 hours while the active metabolite has a half-life near 9 hours, supporting twice-daily dosing.
- There is no autoinduction, so a stable dose keeps stable levels rather than drifting downward over the first month like carbamazepine.
- It is a weak inducer of CYP3A4 and CYP3A5 and an inhibitor of CYP2C19, giving a narrower interaction profile than carbamazepine.
- The metabolite is cleared renally as a glucuronide, so dose reduction is required when creatinine clearance falls below 30 mL/min.

ADVERSE EFFECTS

- Dizziness, somnolence, headache, diplopia, and ataxia are the most common effects and are dose-related during rapid titration.
- Hyponatremia below 125 mmol/L occurs in roughly 2 to 3 percent of patients and mild sodium drops are far more frequent.
- Nausea, vomiting, and abdominal discomfort are common early and often lessen when the dose is taken with food.
- Rash develops in about 3 percent, and 25 to 30 percent of patients with carbamazepine hypersensitivity react to oxcarbazepine as well.
- Stevens-Johnson syndrome, toxic epidermal necrolysis, and multiorgan hypersensitivity are rare but reported, with HLA-B*1502 raising risk.
- Cognitive slowing, tremor, and gait unsteadiness limit dosing in older adults and in those taking other sodium-channel drugs.

MONITORING

- Check serum sodium at baseline, at 2 to 4 weeks, after dose increases, and then periodically, especially in older or diuretic-treated patients.
- Recheck sodium promptly for new headache, nausea, confusion, lethargy, or increased seizure frequency, which suggest hyponatremia.
- Consider HLA-B*1502 testing in patients of Asian ancestry, since the allele raises risk of severe cutaneous reactions with this drug as well.
- Routine serum levels are not required, but monitoring the monohydroxy derivative can help assess adherence or unexplained toxicity.
- Assess renal function at baseline and review gait, balance, and cognition at each visit during titration.

INTERACTIONS & CAUTIONS

- Doses above 1200 mg per day meaningfully induce CYP3A4 and can lower ethinyl estradiol exposure enough to cause contraceptive failure.
- Inhibition of CYP2C19 raises phenytoin concentrations, sometimes requiring a phenytoin dose reduction of 20 to 30 percent.
- Strong enzyme inducers such as carbamazepine, phenytoin, phenobarbital, and rifampin lower monohydroxy derivative levels substantially.
- Additive hyponatremia with thiazides, SSRIs, and desmopressin, and additive sedation and ataxia with alcohol and other CNS depressants.
- Avoid in patients with prior severe cutaneous reactions to carbamazepine given the substantial cross-reactivity between the two drugs.

SPECIAL POPULATIONS

- Human pregnancy data are more limited than for older anticonvulsants, but registry signals suggest lower malformation risk than valproate.
- Clearance of the active metabolite increases substantially during pregnancy, so levels and seizure control should be followed each trimester.
- Breast milk transfer is modest and nursing is generally acceptable with monitoring for infant sedation and poor feeding.
- Pediatric use is established for adjunctive therapy from age 2 and monotherapy from age 4, with weight-based dosing and faster clearance.
- Older adults need lower doses and closer sodium monitoring because hyponatremia, dizziness, and falls are considerably more frequent.

PRESCRIBING PEARLS

- Check sodium at 2-4 weeks; hyponatremia is the effect most likely to force a stop.
- Not a carbamazepine substitute for bipolar disorder; controlled evidence is weak and mostly negative.
- Above **1200 mg/day** it induces enough CYP3A4 to compromise hormonal contraception.

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.