MOOD STABILIZER

Carbamazepine

Tegretol, Tegretol-XR, Carbatrol, Epitol, Equetro

Sodium-channel anticonvulsant and antimanic agent whose value is offset by marrow suppression, severe rash, and potent enzyme induction.

USUAL ADULT RANGE	TARGET TROUGH	HALF-LIFE	METABOLISM
400-1200 mg/day PO divided	4-12 mcg/mL	36 h initial; 16 h induced	CYP3A4; potent 3A4 inducer

⚠ FDA BOXED WARNING

Serious and sometimes fatal dermatologic reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome, with markedly higher risk in carriers of HLA-B*1502, who should be screened before use in patients of Asian ancestry; also aplastic anemia and agranulocytosis at rates far above background.

INDICATIONS

- FDA-approved as extended-release capsules (Equetro) for acute manic and mixed episodes of bipolar I disorder in adults.
- FDA-approved for partial seizures with complex symptomatology, generalized tonic-clonic seizures, and mixed seizure patterns in adults and children.
- FDA-approved for the pain of trigeminal neuralgia and glossopharyngeal neuralgia, where it remains the established first-line drug.
- Off-label maintenance treatment of bipolar disorder, generally reserved for patients intolerant of or unresponsive to lithium and valproate.
- Off-label use for alcohol withdrawal, impulsive aggression, and neuropathic pain, with modest evidence relative to newer alternatives.
- Not effective and potentially worsening in absence and myoclonic seizures, which it can aggravate.

DOSING & TITRATION

- For bipolar mania start extended-release **200 mg** twice daily and increase by 200 mg per day as tolerated, with a maximum of **1600 mg/day**.
- For epilepsy start **200 mg** twice daily and titrate weekly by 200 mg to a usual adult range of **800-1200 mg/day** in divided doses.
- Trigeminal neuralgia starts lower at **100 mg** twice daily, titrated by 200 mg per day to pain control, rarely exceeding **1200 mg/day**.
- Expect to raise the dose after 3 to 5 weeks because autoinduction lowers levels; recheck a trough and adjust to **4-12 mcg/mL**.
- Reduce doses in hepatic impairment and avoid in significant liver disease; renal impairment needs no routine adjustment.
- Taper over several weeks when stopping, since abrupt withdrawal can precipitate seizures even in patients treated for mood symptoms.

MECHANISM OF ACTION

- Binds voltage-gated sodium channels in the inactivated state, slowing recovery and limiting sustained high-frequency neuronal firing.
- Use-dependent blockade means it suppresses pathologically rapid discharge while sparing normal transmission at physiologic firing rates.
- Reduces glutamate release and modulates calcium currents, contributing to antimanic and antineuralgic effects.
- Acts as an agonist at adenosine A1 receptors and dampens kindling, mechanisms proposed for its mood-stabilizing action.
- Antidiuretic hormone potentiation at the renal tubule explains the frequent hyponatremia that accompanies therapeutic use.

PHARMACOKINETICS

- Absorption is slow and erratic with peaks at 4 to 8 hours for immediate-release tablets and later for extended-release formulations.
- The half-life is 25 to 65 hours after a single dose but falls to roughly 12 to 17 hours once autoinduction completes at 3 to 5 weeks.
- Carbamazepine induces its own CYP3A4 metabolism, so a dose that was therapeutic in week one is often subtherapeutic by week four.
- The 10,11-epoxide metabolite is pharmacologically active and neurotoxic, and accumulates when valproate inhibits epoxide hydrolase.
- It is a potent inducer of CYP3A4, CYP1A2, CYP2C9, CYP2C19, UGT enzymes, and P-glycoprotein, affecting a very large number of drugs.

ADVERSE EFFECTS

- Dizziness, diplopia, ataxia, sedation, and nausea are common early and are usually dose-related and improved by slower titration.
- Hyponatremia occurs in up to a quarter of patients, more often in older adults and with concurrent diuretics or SSRIs.
- Benign leukopenia affects roughly 10 percent, while aplastic anemia and agranulocytosis are rare but potentially fatal.
- Morbilliform rash occurs in about 5 to 10 percent, and progression to Stevens-Johnson syndrome or toxic epidermal necrolysis is the feared outcome.
- Drug reaction with eosinophilia and systemic symptoms is associated with HLA-A*3101 and presents with fever, rash, and organ involvement.
- Hepatotoxicity, cardiac conduction delay, and dose-related cognitive slowing round out the effects that most often force a switch.

MONITORING

- Screen patients of Asian ancestry for HLA-B*1502 before the first dose and do not start carbamazepine if the allele is present.
- Obtain a baseline CBC with differential, liver enzymes, sodium, and renal function, and repeat at 2 to 4 weeks and periodically thereafter.
- Check a trough level after 3 to 5 days at a new dose and again after 4 to 6 weeks to capture the drop caused by autoinduction.
- Recheck sodium at 1 month and whenever confusion, headache, or new seizures appear, particularly in patients over 65.
- Instruct patients to report any rash, fever, sore throat, mouth ulcers, bruising, or jaundice immediately and to stop pending evaluation.

INTERACTIONS & CAUTIONS

- As a potent CYP3A4 inducer it lowers concentrations of oral contraceptives, direct oral anticoagulants, many antipsychotics, and immunosuppressants.
- It reduces lamotrigine levels by roughly half, so lamotrigine titration and target dose must be increased when the two are combined.
- Strong CYP3A4 inhibitors such as clarithromycin, fluconazole, diltiazem, and grapefruit juice raise levels quickly into the toxic range.
- Valproate inhibits epoxide hydrolase and raises the neurotoxic 10,11-epoxide even when the parent carbamazepine level looks normal.
- Contraindicated with nefazodone, within 14 days of an MAOI, and in patients with a history of bone marrow depression or prior hypersensitivity.

SPECIAL POPULATIONS

- First-trimester exposure raises the risk of neural tube defects to roughly 0.5 to 1 percent along with craniofacial and cardiac malformations.
- Supplement folic acid at **4 mg/day** before conception, and give vitamin K in late pregnancy given induced fetal clotting factor metabolism.
- Milk levels are moderate and breastfeeding is generally acceptable, with monitoring of the infant for sedation, poor feeding, and jaundice.
- Pediatric epilepsy use is established from infancy; children need weight-based dosing and clear faster than adults after induction.
- Older adults are especially prone to hyponatremia, ataxia, falls, and drug interactions, so start low and check sodium early.

PRESCRIBING PEARLS

- Recheck the level at 4-6 weeks; autoinduction routinely drops it into the subtherapeutic range.
- Any new rash on carbamazepine is Stevens-Johnson until proven otherwise; stop the drug and evaluate.
- It induces contraceptive metabolism, so counsel patients to add a non-hormonal method.

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.