MOOD STABILIZER

Topiramate

Topamax, Trokendi XR, Qudexy XR, Eprontia, Qsymia (with phentermine)

Broad anticonvulsant used in psychiatry chiefly for migraine, alcohol use disorder, binge eating, and weight offset rather than for mania.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
50-400 mg/day PO divided	**~21 h; renal elimination**	**Minimal; 70% renal unchanged**	**Migraine benefit by 4-8 wks**

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved as monotherapy for partial-onset and primary generalized tonic-clonic seizures in patients aged 2 years and older.
- FDA-approved as adjunctive therapy for partial-onset seizures, generalized tonic-clonic seizures, and seizures of Lennox-Gastaut syndrome.
- FDA-approved for migraine prophylaxis in patients aged 12 and older, and in combination with phentermine for chronic weight management.
- Off-label but well supported for alcohol use disorder, where it reduces heavy drinking days at doses of 200 to 300 mg per day.
- Off-label use for binge eating disorder, antipsychotic-induced weight gain, and cocaine use disorder, with modest supporting trial data.
- Off-label use in bipolar disorder is not supported; controlled monotherapy trials in acute mania were negative.

DOSING & TITRATION

- For migraine prophylaxis start **25 mg** at bedtime and increase by 25 mg weekly to a usual target of **100 mg/day** in two divided doses.
- For epilepsy monotherapy titrate over 6 weeks toward **400 mg/day** divided twice daily, which is the labeled adult target dose.
- For alcohol use disorder, off-label practice titrates by 25 to 50 mg weekly to **200-300 mg/day**, balancing efficacy against cognitive effects.
- Slow titration is the key to tolerability, since paresthesias and word-finding problems track with the speed of dose escalation.
- Halve the dose when creatinine clearance falls below 70 mL/min, and give a supplemental dose on hemodialysis days.
- Taper over at least 2 to 3 weeks when stopping, since abrupt withdrawal can precipitate seizures even in nonepileptic patients.

MECHANISM OF ACTION

- Blocks voltage-gated sodium channels and reduces sustained repetitive firing, the shared mechanism of most broad-spectrum anticonvulsants.
- Antagonizes AMPA and kainate glutamate receptors, dampening excitatory transmission implicated in craving and migraine generation.
- Enhances GABA-A receptor activity at a site distinct from the benzodiazepine site, adding inhibitory tone without benzodiazepine tolerance.
- Weakly inhibits carbonic anhydrase isoenzymes, producing metabolic acidosis, paresthesias, and calcium phosphate kidney stones.
- Appetite suppression and dose-dependent weight loss follow from combined glutamatergic, GABAergic, and taste-related effects.

PHARMACOKINETICS

- Absorption is rapid and nearly complete, is not affected by food, and gives peak plasma levels within about 2 hours.
- The elimination half-life is roughly 21 hours, supporting twice-daily immediate-release or once-daily extended-release dosing.
- Approximately 70 percent of a dose is excreted unchanged in urine, so renal function rather than hepatic metabolism drives clearance.
- Protein binding is low at 15 to 41 percent and metabolism is minor, which limits the number of pharmacokinetic interactions.
- It weakly induces CYP3A4 at doses above 200 mg per day and weakly inhibits CYP2C19, effects that matter mainly for contraceptives.

ADVERSE EFFECTS

- Paresthesias affect up to half of patients at higher doses and are the most common reason for early discontinuation.
- Cognitive effects with word-finding difficulty, slowed processing, and memory complaints are dose-related and often dose-limiting.
- Dose-dependent weight loss averages 2 to 5 kilograms and is sometimes the reason the drug is chosen in psychiatric practice.
- Taste alteration, especially of carbonated beverages, plus fatigue, dizziness, and somnolence are common early complaints.
- Metabolic acidosis from carbonic anhydrase inhibition occurs in a substantial minority, with kidney stones in about 1.5 percent.
- Acute angle-closure glaucoma and oligohidrosis with hyperthermia are rare but urgent, the former usually in the first month.

MONITORING

- Check serum bicarbonate at baseline, after titration, and periodically thereafter, and evaluate any unexplained hyperventilation or fatigue.
- Advise immediate evaluation for acute eye pain, blurred vision, or red eye, which may indicate secondary angle-closure glaucoma.
- Monitor weight and, in patients where weight loss is undesirable, track intake and consider a different agent if loss is excessive.
- Assess renal function at baseline, encourage generous fluid intake, and ask about flank pain or hematuria suggesting stones.
- In children and in hot climates, monitor for decreased sweating and elevated body temperature during exercise or heat exposure.

INTERACTIONS & CAUTIONS

- Doses above 200 mg per day can lower ethinyl estradiol exposure enough to reduce oral contraceptive reliability, so counsel on backup methods.
- Carbamazepine and phenytoin induce topiramate clearance and can lower its concentrations by roughly 40 to 50 percent.
- Combined with valproate, topiramate can precipitate hyperammonemia and encephalopathy even when both levels appear therapeutic.
- Other carbonic anhydrase inhibitors such as zonisamide and acetazolamide compound the risk of acidosis and nephrolithiasis.
- Alcohol adds sedation and cognitive impairment, and the extended-release Trokendi formulation should not be used within 6 hours of alcohol.

SPECIAL POPULATIONS

- First-trimester exposure raises the risk of cleft lip and palate roughly threefold and increases the rate of small-for-gestational-age infants.
- Discuss contraception and pregnancy planning before starting in anyone who can become pregnant, and use the lowest effective dose.
- Topiramate passes into breast milk in meaningful amounts; monitor the infant for sedation, poor feeding, and diarrhea if nursing.
- Children clear topiramate faster than adults and are more susceptible to oligohidrosis, hyperthermia, and metabolic acidosis.
- In older adults and any patient with reduced creatinine clearance, halve the dose and titrate more slowly to limit cognitive effects.

PRESCRIBING PEARLS

- Titrate 25 mg per week; almost all the paresthesia and cognitive complaints come from moving faster.
- Best psychiatric evidence is for alcohol use disorder and binge eating, not for bipolar disorder.
- New eye pain or blurred vision in month one means urgent evaluation for angle-closure glaucoma.

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.