CARBAMAZEPINE (Tegretol) Fact Sheet [G]

BOTTOM LINE:
Not a first-line treatment for bipolar disorder in kids due to limited data, side effect profile, and high likelihood of significant interactions. Used in kids for seizure disorders, so we have some basis of safety information. Equetro is FDA approved for bipolar disorder (in adults), but other cheaper formulations give similar results.

PEDIATRIC FDA INDICATIONS:
Seizure disorders.

ADULT FDA INDICATIONS:
Seizures; trigeminal neuralgia; bipolar disorder (Equetro: acute mania).

OFF-LABEL USES:
Bipolar maintenance; impulse control disorders; violence and aggression; migraine prophylaxis.

DOSAGE FORMS:
- **Chewable tablets (G):** 100 mg, 200 mg (scored).
- **Tablets (Tegretol, Epitol, [G]):** 100 mg, 200 mg, 300 mg, 400 mg (scored).
- **ER tablets (Tegretol XR, [G]):** 100 mg, 200 mg, 400 mg.
- **ER capsules (Equetro, Carbatrol, [G]):** 100 mg, 200 mg, 300 mg.
- **Oral solution (Tegretol, Teril, [G]):** 100 mg/5 mL.

PEDIATRIC DOSAGE GUIDANCE:
- Age <6 years: Start 10–20 mg/kg/day divided BID–QID, increase by 5–10 mg/kg/day in weekly intervals; max 35 mg/kg/day.
- Age 6–12 years: Start 100 mg BID, increase by 100 mg/day in weekly intervals; max 1000 mg/day in divided doses.
- Age >12 years: Start 200 mg BID and gradually ↑ by 200 mg/day in weekly intervals; max 1200 mg/day.
- Dosing is the same for IR and ER versions of carbamazepine; both are BID.

MONITORING: CBC, electrolytes (sodium), LFTs, pregnancy test, serum level, HLA-B*1502 (Asians), ECG if cardiac risk.

COST: $

SIDE EFFECTS:
- Most common: Dizziness, somnolence, nausea, headache. (ER versions may cause fewer side effects in some patients, but the evidence is not clear.)
- Serious but rare: Hematologic abnormalities including agranulocytosis, aplastic anemia, neutropenia, leukopenia, thrombocytopenia, and pancytopenia reported; hepatic complications including slight increases in hepatic enzymes, cholestatic and hepatocellular jaundice, hepatitis (and, rarely, hepatic failure), hyponatremia, SIADH; rash (5%–10%), including exfoliation, reported. Severe reactions, including toxic epidermal necrolysis and Stevens-Johnson syndrome, are rare but can be fatal.

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:
- Sodium channel blocker. Metabolized primarily through CYP3A4; t ½: 15 hours (initially 25–65 hours but induces its own metabolism over approximately two to four weeks with each dosage change and then stabilizes).
- Highly significant interactions: Potent inducer of CYP1A2, CYP2B6, CYP2C19, CYP2C8, CYP2C9, CYP3A4, P-glycoprotein; medications significantly metabolized through these pathways may become subtherapeutic; caution in patients taking strong CYP3A4 inducers or inhibitors that can affect carbamazepine levels.
- Avoid use with oral contraceptives (lowers levels/unplanned pregnancies) and clozapine (agranulocytosis).

EVIDENCE AND CLINICAL PEARLS:
- Pediatric bipolar data limited to open-label studies with only modest response rates (38%–44%).
- Therapeutic level: 4–12 mcg/mL in seizure disorders. No correlation in bipolar disorder—best dosed clinically. Check levels five days and a few weeks after changes due to induction of enzymes that affect levels.
- Avoid use if variant HLA-B*1502 allele (Asians): Risk of Stevens-Johnson syndrome/toxic epidermal necrolysis.

FUN FACT:
May cause false-positive TCA screen as its chemical structure contains the tricyclic nucleus common to TCAs.