CARBAMAZEPINE (Epitol, Equetro, Tegretol, others) Fact Sheet [G]

Bottom Line:
Equetro is the only FDA-approved formulation of carbamazepine for bipolar disorder, but use of other formulations would result in the same effects at a lower price. Generally, carbamazepine is not considered a first-line treatment for bipolar disorder due to its side effect profile and high likelihood of significant drug interactions.

FDA Indications:
Bipolar disorder (Equetro: acute mania); seizures; trigeminal neuralgia.

Off-Label Uses:
Bipolar maintenance; impulse control disorders; violence and aggression.

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.

Dosage Guidance:
- Bipolar disorder: Start at 200 mg BID and gradually ↑ by 200 mg/day every three to four days, to target 400–600 mg BID (guided by clinical response). Max 800 mg BID. Dosing is the same for IR and ER versions of carbamazepine; both are BID.
- Extended-release formulations of carbamazepine are better tolerated than immediate release.

Monitoring: Carbamazepine level, complete blood count, sodium, LFT, pregnancy test, HLA-B*1502 in Asians.

Cost: $

Side Effects:
- Most common: Dizziness, somnolence, nausea, headache.
- 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.
- Pregnancy/breastfeeding: Avoid in pregnancy, can cause neural tube defects and other anomalies; relatively safe in breastfeeding.

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 within two to four weeks and then stabilizes).
- High potential for significant interactions: Potent inducer of CYP1A2, CYP2B6, CYP2C19, CYP2C8, CYP2C9, CYP3A4, P-glycoprotein; use caution with medications significantly metabolized through these pathways as their levels may become subtherapeutic; caution in patients taking strong CYP3A4 inducers or inhibitors that can affect carbamazepine levels.
- Avoid concomitant use with oral contraceptives (can lower serum levels of these contraceptives and cause unplanned pregnancies) and with clozapine (additive risk of agranulocytosis).

Clinical Pearls:
- ER capsules such as Carbatrol have been shown to cause less fluctuation in serum CBZ level and fewer side effects, so start with this formulation when possible (some insurance companies might require pre-authorization).
- Therapeutic levels: 4–12 mcg/mL in seizure disorders. Studies in bipolar haven't shown correlation between levels and clinical response, so it's best dosed clinically.
- Lab monitoring: Baseline and periodic (at six weeks and every three months) CBC and LFTs.
- Patients of Asian descent should be screened for the variant HLA-B*1502 allele prior to starting carbamazepine; this variant is associated with significantly increased risk of developing Stevens-Johnson syndrome and/or toxic epidermal necrolysis. Avoid use in such patients.

Fun Fact:
Carbamazepine may cause a false-positive serum TCA screen—indeed, its chemical structure contains the familiar tricyclic nucleus common to all TCAs.