OXCARBAZEPINE (Oxtellar XR, Trileptal) Fact Sheet [G]

BOTTOM LINE:
Compared to carbamazepine, oxcarbazepine poses less concern for drug interactions and for hepatic or hematologic toxicities; it also does not require serum level monitoring. However, due to lack of efficacy data in pediatric bipolar disorder, we do not recommend its general use for that disorder. Still, some clinicians use oxcarbazepine to try to reduce irritability in a wider range of clinical circumstances. It is reserved for third-line use after lithium and valproic acid, and even after carbamazepine.

PEDIATRIC FDA INDICATIONS:
Seizures.

ADULT FDA INDICATIONS:
Seizure disorders.

OFF-LABEL USES:
Bipolar disorder.

DOSAGE FORMS:
- **Tablets (G):** 150 mg, 300 mg, 600 mg (scored).
- **Oral suspension (G):** 300 mg/5 mL.
- **ER tablets (Oxtellar XR):** 150 mg, 300 mg, 600 mg.

PEDIATRIC DOSAGE GUIDANCE:
- Start 8–10 mg/kg/day divided BID, increase by 5 mg/kg/day in weekly intervals to usual 600–900 mg/day divided BID; max 2400 mg/day.
- No data on use of XR for bipolar disorder; caution as higher doses of XR likely needed when converting from IR to XR (not interchangeable on dose-for-dose basis).

MONITORING: Electrolytes (sodium), HLA-B*1502 in Asians.

COST: IR: $; ER: $$$$$

SIDE EFFECTS:
- Most common: Dizziness, somnolence, headache, ataxia, nausea, vomiting.
- Serious but rare: Potentially serious, sometimes fatal, dermatologic reactions (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis) reported; monitor for skin reactions. Rare cases of anaphylaxis and angioedema reported, even after initial dosing; permanently discontinue should symptoms occur.
- Use caution in patients with previous hypersensitivity to carbamazepine (cross-sensitivity occurs in 25%–30%). Clinically significant hyponatremia (serum sodium <125 mmol/L) may develop (1%–3%; higher rate than with carbamazepine); monitor serum sodium, particularly during the first three months of therapy, especially in patients at risk for hyponatremia.

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:
- Sodium channel blocker and neuronal membrane stabilizer.
- Metabolized primarily through CYP450; potent inducer of CYP3A4 and inhibitor of CYP2C19; t ½: 2 hours (9 hours for active metabolite).
- No auto-induction of metabolism and fewer interactions than with carbamazepine. Avoid concomitant use with medications metabolized by CYP3A4 since oxcarbazepine may reduce their levels. Reduces efficacy of oral contraceptives; try nonhormonal measures.

EVIDENCE AND CLINICAL PEARLS:
- In a double-blind study in pediatric mania, it was not statistically better than placebo.
- Oxcarbazepine is the 10-keto analog of carbamazepine (its "chemical cousin"); it is thought of as a gentler carbamazepine due to its more favorable side effect and drug interaction profile.
- Not bioequivalent to carbamazepine. Increase total daily dose by 20%–30% if switching from carbamazepine to oxcarbazepine.
- Screen and avoid using in patients of Asian descent who have HLA-B*1502 allele; risk of Stevens-Johnson syndrome and/or toxic epidermal necrolysis.

FUN FACT:
Synthesized in 1965, oxcarbazepine appeared on the US market in 2000. In 2010, Novartis pled guilty to marketing it for non-FDA-approved uses, eg, neuropathic pain and bipolar disorder.