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

Bottom Line:
Oxcarbazepine, an analog of carbamazepine, is popular because of its reputation as a kinder, gentler carbamazepine, which it's gained due to its more favorable side effect and drug interaction profile. However, due to the paucity of efficacy data in bipolar disorder, it is reserved for second-line use after lithium and valproic acid, and even after carbamazepine.

FDA Indications:
Seizure disorders in adults and children.

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.

Dosage Guidance:
- Bipolar disorder (off-label): Start 300 mg BID; ↑ by 300 mg/day every three days or 600 mg/day weekly to target dose 600–1200 mg 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).
- Dose timing: It can cause sedation; the entire dose can be taken at bedtime if needed.

Monitoring: 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 first three months of therapy, especially in patients at risk for hyponatremia.
- Pregnancy/breastfeeding: Limited data suggest relative safety.

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. However, there is still potential for interactions. Avoid concomitant use with medications metabolized by CYP3A4 since oxcarbazepine may reduce their levels. Oxcarbazepine may reduce efficacy of oral contraceptives; nonhormonal measures recommended.

Clinical Pearls:
- Oxcarbazepine is the 10-keto analog of carbamazepine (its "chemical cousin").
- Not bioequivalent to carbamazepine. Increase total daily dose by 20%–30% if switching from carbamazepine to oxcarbazepine.
- Patients of Asian descent should be screened for the variant HLA-B*1502 allele prior to starting oxcarbazepine; this variant may increase risk of developing Stevens-Johnson syndrome and/or toxic epidermal necrolysis. Avoid use in such patients.
- Oxcarbazepine failed to work in patients with bipolar disorder in two small and flawed placebo-controlled studies. Some limited data suggest it may fare better when used as augmentation with other mood stabilizers.

Fun Fact:
While first synthesized in 1965, oxcarbazepine first appeared on the US market in 2000. In 2010, Novartis pleaded guilty to marketing oxcarbazepine for non-FDA-approved uses, including neuropathic pain and bipolar disorder, in 2000 and 2001.