LAMOTRIGINE (Lamictal, Subvenite) Fact Sheet [G]

BOTTOM LINE:
Not for first-line use for most kids due to limited data (open-label studies only), long titration required, and increased relative risk of rash in pediatric population.

PEDIATRIC FDA INDICATIONS:
Seizures.

ADULT FDA INDICATIONS:
Bipolar disorder (maintenance) in adults; seizures.

OFF-LABEL USES:
Bipolar depression; neuropathic pain; major depression; borderline personality disorder.

DOSAGE FORMS:
- **Tablets (Lamictal, Subvenite, [G]):** 25 mg, 50 mg, 100 mg, 150 mg, 200 mg (scored).
- **Chewable tablets (Lamictal CD, [G]):** 2 mg, 5 mg, 25 mg.
- **Orally disintegrating tablets (Lamictal ODT, [G]):** 25 mg, 50 mg, 100 mg, 200 mg.
- **ER tablets (Lamictal XR, [G]):** 25 mg, 50 mg, 100 mg, 200 mg, 250 mg, 300 mg.

PEDIATRIC DOSAGE GUIDANCE (BASED ON DOSING IN KIDS WITH SEIZURES):
- Bipolar disorder: Start 25 mg QD for two weeks, ↑ to 50 mg QD for two weeks, then 100 mg QD; max 200 mg/day.
- Patients on valproate: Start 25 mg QOD (every other day) for two weeks, ↑ to 25 mg QD for two weeks, then 50 mg QD; max 100 mg/day (VPA doubles lamotrigine levels).
- Dosing is the same with all versions of lamotrigine.

MONITORING: While some clinicians get blood levels, no specific monitoring is needed unless you are checking for compliance or toxicity.

COST: IR: $; ER: $$

SIDE EFFECTS:
- Most common: Dizziness, headache, nausea, sedation, benign rash (7%).
- Serious but rare: Rare, potentially life-threatening skin reactions (black box warning) requiring hospitalization reported, including Stevens-Johnson syndrome/toxic epidermal necrolysis; incidence higher in pediatric patients; risk increased by co-administration with valproic acid, higher-than-recommended starting doses, and exceeding recommended dose titration. Other risk factors include infections (herpes simplex, herpes zoster, HIV, hepatitis A, pneumonia), compromised immunity, and HLA-B*1502 (common in India, China, and Southeast Asia). Usually occurs before eight weeks, with isolated cases beyond eight weeks and without risk factors. Have patients take skin precautions (eg, use sunscreen; don't change detergents, soaps, or cosmetics; and avoid contact with poisonous plants). Discontinue at first sign of rash and do not reinitiate unless rash is clearly not drug related; rare cases of hemophagocytic lymphohistiocytosis (HLH) and angioedema reported. Cardiac arrhythmias (slowed ventricular conduction and widening of the QRS) in susceptible patients.

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:
- Sodium channel blocker. Metabolism primarily hepatic (non-P450); t ½: 25–33 hours (with VPA 48–70 hours; with carbamazepine 13–14 hours).
- Enzyme-inducing medications (eg, carbamazepine) and hormonal contraceptives decrease lamotrigine levels; lamotrigine may need to be increased (two-fold). Gradual increases of lamotrigine levels may occur during the inactive "pill-free" week. Lamotrigine may decrease hormonal contraceptives (estrogens more than progestins); consider alternative birth control methods. Valproic acid may double lamotrigine levels, necessitating much slower titration or dosage adjustments (as above).

EVIDENCE AND CLINICAL PEARLS:
- One open-label response: Monotherapy in pediatric bipolar disorder, 54% for manic symptoms.
- For maintenance in adult bipolar disorder; prophylaxis of depression. Not useful in acute episodes.
- If stopped/missed >5 half-lives (see above), restart with initial dosing protocol to minimize rash risk.
- FDA warning: Rare cases of HLH, a life-threatening immune reaction. Refer immediately for persistent fever (>101°F); rash; pain, tenderness, or swelling in the area of the liver; swollen lymph nodes; jaundice; unusual bleeding; and nervous system problems such as seizures, trouble walking, or visual difficulties.

FUN FACT:
The first FDA-approved drug for bipolar disorder in adults (not just acute mania) since lithium, a drug approved more than 30 years earlier (2003 for lamotrigine, 1970 for lithium).