

LAMOTRIGINE (Lamictal, Lamictal XR, Subvenite) Fact Sheet [G]

Bottom Line:

Lamotrigine is a good choice for maintenance treatment of bipolar disorder, especially to prevent depressive episodes. It has a good side effect profile. Its main disadvantage is the very slow titration schedule recommended to decrease the risk of Stevens-Johnson syndrome—as well as its ineffectiveness in the treatment of manic episodes.

FDA Indications:

Bipolar disorder (maintenance) in adults; seizures in adults and children.

Off-Label Uses:

Bipolar depression; neuropathic pain; major depression.

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.

Dosage Guidance:

- Bipolar disorder: Start 25 mg QD for two weeks, ↑ to 50 mg QD for two weeks, then 100 mg QD; max 200 mg/day; can increase up to 400 mg/day if needed.
- Patients on valproic acid: 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. However, patients taking more than 200 mg should either split the dose or take the Lamictal XR formulation.
- Dose timing: Can be taken either in the morning or night; it rarely causes drowsiness.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: IR: \$; ER: \$\$

Side Effects:

- Most common: Dizziness, headache, nausea, sedation, benign rash (7%).
- Serious but rare: Skin reactions (black box warning): Severe, potentially life-threatening skin rashes requiring hospitalization reported; incidence is higher in pediatric patients; risk increased by co-administration with valproic acid, higher than recommended starting doses, and exceeding recommended dose titration. The majority of cases occur in the first eight weeks, but isolated cases may occur beyond eight weeks or even in patients without risk factors. Discontinue at first sign of rash and do not reinitiate unless rash is clearly not drug-related; rare cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and angioedema reported. Cardiac arrhythmias (slowed ventricular conduction and widening of the QRS) in susceptible patients.
- Pregnancy/breastfeeding: Considered relatively safe.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Sodium channel blocker.
- Metabolism primarily hepatic (non-CYP450); t_{1/2}: 25–33 hours (with VPA 48–70 hours; with carbamazepine 13–14 hours).
- Caution with enzyme-inducing medications (eg, carbamazepine), which may decrease lamotrigine levels. Caution with hormonal contraceptives, which may decrease lamotrigine levels; lamotrigine maintenance dose may need to be increased (two-fold). Gradual increases of lamotrigine levels may occur during the inactive “pill-free” week. Lamotrigine may decrease levels of some hormonal contraceptives (greater effect with estrogens than progestins); alternative birth control methods should be considered. Valproic acid may double lamotrigine levels, necessitating dosage adjustments (as above).

Clinical Pearls:

- Lamotrigine is useful for the maintenance treatment of bipolar disorder, with best efficacy in the prophylaxis of depressive episodes. Not useful in acute episodes.
- If lamotrigine has been stopped/missed for more than five half-lives (see above), consider restarting according to initial dosing recommendations to minimize rash risk.
- Routine baseline ECG is not necessary, but similar to use of other mood stabilizers that can affect heart rhythm (carbamazepine, lithium, oxcarbazepine), monitor or get consultation in patients with cardiac conduction delay or significant ischemic or structural heart disease.

Fun Fact:

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