

RESEARCH MONOGRAPH . COMPOUND PROFILE

Lamotrigine

A phenyltriazine voltage-gated sodium channel blocker; uniquely effective for bipolar depression and a first-line maintenance mood stabilizer.

DOCUMENT	KDC-MN-243
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	Phenyltriazine sodium channel blocker / mood stabilizer

ABSTRACT

Lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine; CAS 84057-84-1; molecular formula C₉H₇Cl₂N₅; molecular weight 256.09) is a phenyltriazine voltage-gated sodium channel blocker developed at Wellcome (now GSK) and approved by the FDA in 1994 under the trade name Lamictal. Mechanism: state-dependent inhibition of voltage-gated sodium channels (preferentially binding inactivated state), reducing release of presynaptic glutamate and aspartate. Secondary inhibition of high-voltage-activated calcium channels and weak antagonism at 5-HT₃ receptors contribute to the broader profile. Distinct among anticonvulsants for efficacy in bipolar depression and maintenance mood stabilization (more effective at preventing depressive than manic episodes, opposite the lithium pattern). Plasma half-life is 25 to 33 hours alone, shortened by enzyme-inducing comedications. Hepatic metabolism is primarily glucuronidation. The principal limitation is a benign rash incidence of approximately 10 percent and Stevens-Johnson syndrome at approximately 1 in 1000, both reduced by slow titration over 4 to 6 weeks. Approved for partial-onset seizures, primary generalized tonic-clonic seizures, Lennox-Gastaut syndrome, and bipolar I disorder maintenance. Used as the reference anticonvulsant mood stabilizer and as a clean voltage-gated sodium channel blocker.

1. Compound Identification

Lamotrigine is described as phenyltriazine sodium channel blocker / mood stabilizer. A phenyltriazine voltage-gated sodium channel blocker; uniquely effective for bipolar depression and a first-line maintenance mood stabilizer.

1.1 Class summary

Phenyltriazine sodium channel blocker / mood stabilizer

1.2 Subtitle

A phenyltriazine voltage-gated sodium channel blocker; uniquely effective for bipolar depression and a first-line maintenance mood stabilizer.

2. Abstract

Lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine; CAS 84057-84-1; molecular formula $C_9H_7Cl_2N_5$; molecular weight 256.09) is a phenyltriazine voltage-gated sodium channel blocker developed at Wellcome (now GSK) and approved by the FDA in 1994 under the trade name Lamictal. Mechanism: state-dependent inhibition of voltage-gated sodium channels (preferentially binding inactivated state), reducing release of presynaptic glutamate and aspartate. Secondary inhibition of high-voltage-activated calcium channels and weak antagonism at 5-HT₃ receptors contribute to the broader profile. Distinct among anticonvulsants for efficacy in bipolar depression and maintenance mood stabilization (more effective at preventing depressive than manic episodes, opposite the lithium pattern). Plasma half-life is 25 to 33 hours alone, shortened by enzyme-inducing comedications. Hepatic metabolism is primarily glucuronidation. The principal limitation is a benign rash incidence of approximately 10 percent and Stevens-Johnson syndrome at approximately 1 in 1000, both reduced by slow titration over 4 to 6 weeks. Approved for partial-onset seizures, primary generalized tonic-clonic seizures, Lennox-Gastaut syndrome, and bipolar I disorder maintenance. Used as the reference anticonvulsant mood stabilizer and as a clean voltage-gated sodium channel blocker.

3. Mechanism of Action

State-dependent voltage-gated sodium channel inhibition; reduces presynaptic glutamate/aspartate release. Secondary calcium channel and 5-HT₃ effects.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Clinical 100 to 400 mg per oral administration daily, with slow titration. Rodent studies 5 to 30 mg/kg/day.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Goldsmith DR, et al. Lamotrigine: a review of its use in bipolar disorder. *Drugs* 2003.
2. Calabrese JR, et al. A double-blind placebo-controlled study of lamotrigine monotherapy in outpatients with bipolar I depression. *J Clin Psychiatry* 1999.
3. Cheriyan J, et al. Lamotrigine and Stevens-Johnson syndrome. *Pediatr Dermatol* 2018.

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