

RESEARCH MONOGRAPH . COMPOUND PROFILE

Vigabatrin

An irreversible suicide inhibitor of GABA transaminase; uniquely effective in infantile spasms and refractory complex partial seizures, limited by retinal toxicity.

DOCUMENT	KDC-MN-246
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	GABA transaminase inhibitor (irreversible)

ABSTRACT

Vigabatrin ((R/S)-4-aminohept-5-enoic acid; CAS 60643-86-9; molecular formula $C_6H_{11}NO_2$; molecular weight 129.16) is a vinyl-GABA suicide inhibitor of GABA transaminase developed at Marion Merrell Dow and approved by the FDA in 2009 under the trade name Sabril (later than European registration in 1989). Mechanism: the vinyl group at the alpha-carbon converts vigabatrin into a substrate that the GABA transaminase enzyme begins to process but cannot release; the result is irreversible covalent enzyme inactivation, requiring de novo enzyme synthesis to recover GABA degradation capacity. The consequence is sustained elevation of brain GABA concentrations. Effective in infantile spasms (West syndrome) where conventional anticonvulsants often fail, and as adjunctive therapy in refractory complex partial seizures. The principal limitation is irreversible bilateral concentric visual field constriction in approximately 30 to 50 percent of long-term users, attributed to retinal photoreceptor damage; the FDA REMS program requires baseline and periodic visual field assessment. Plasma half-life is 5 to 13 hours, but the irreversible enzyme inhibition produces effective activity beyond the plasma window. Used as the canonical GABA transaminase suicide inhibitor.

1. 1. Compound Identification

Vigabatrin is described as gaba transaminase inhibitor (irreversible). An irreversible suicide inhibitor of GABA transaminase; uniquely effective in infantile spasms and refractory complex partial seizures, limited by retinal toxicity.

1.1. 1.1 Class summary

GABA transaminase inhibitor (irreversible)

1.2. 1.2 Subtitle

An irreversible suicide inhibitor of GABA transaminase; uniquely effective in infantile spasms and refractory complex partial seizures, limited by retinal toxicity.

2. 2. Abstract

Vigabatrin ((R/S)-4-aminohex-5-enoic acid; CAS 60643-86-9; molecular formula C₆H₁₁NO₂; molecular weight 129.16) is a vinyl-GABA suicide inhibitor of GABA transaminase developed at Marion Merrell Dow and approved by the FDA in 2009 under the trade name Sabril (later than European registration in 1989). Mechanism: the vinyl group at the alpha-carbon converts vigabatrin into a substrate that the GABA transaminase enzyme begins to process but cannot release; the result is irreversible covalent enzyme inactivation, requiring de novo enzyme synthesis to recover GABA degradation capacity. The consequence is sustained elevation of brain GABA concentrations. Effective in infantile spasms (West syndrome) where conventional anticonvulsants often fail, and as adjunctive therapy in refractory complex partial seizures. The principal limitation is irreversible bilateral concentric visual field constriction in approximately 30 to 50 percent of long-term users, attributed to retinal photoreceptor damage; the FDA REMS program requires baseline and periodic visual field assessment. Plasma half-life is 5 to 13 hours, but the irreversible enzyme inhibition produces effective activity beyond the plasma window. Used as the canonical GABA transaminase suicide inhibitor.

3. Mechanism of Action

Irreversible suicide inhibition of GABA transaminase via vinyl-GABA mechanism.
Sustained elevation of brain GABA concentrations.

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. 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. 5. Reported Research Dose Ranges

Clinical 1 to 3 g per oral administration daily, in divided doses. Rodent studies 100 to 500 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. 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. 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. 9. References

1. Lippert B, et al. 4-amino-hex-5-enoic acid, a selective catalytic inhibitor of 4-aminobutyric-acid aminotransferase. Eur J Biochem 1977.
2. Riikonen R. Long-term outcome of West syndrome: a study of adults with a history of infantile spasms. Epilepsia 1996.
3. Wild JM, et al. Vigabatrin and epilepsy: lessons learned. Epilepsia 2009.

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