

RESEARCH MONOGRAPH . COMPOUND PROFILE

Vilazodone

A dual-mechanism antidepressant combining SSRI activity with 5-HT1A partial agonism intended to accelerate clinical response.

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ABSTRACT

Vilazodone (5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]piperazin-1-yl]benzofuran-2-carboxamide; CAS 163521-12-8; molecular formula C₂₆H₂₇N₅O₂; molecular weight 441.53) is an SSRI plus 5-HT_{1A} partial agonist developed at Merck KGaA and Forest Pharmaceuticals, approved by the FDA in 2011 under the trade name Viibryd. SERT affinity is approximately 0.1 nM; 5-HT_{1A} affinity is approximately 0.2 nM (intrinsic activity approximately 70 percent), producing partial agonism at the autoreceptor. The dual mechanism was designed to bypass the autoreceptor desensitization period that delays SSRI response: by directly activating 5-HT_{1A} receptors while blocking SERT, vilazodone aims to produce faster clinical effect. Real-world clinical trials have shown modest response acceleration. Plasma half-life is approximately 25 hours; metabolism is via CYP3A4 (primary). Approved for major depressive disorder. The compound is administered with food, which doubles bioavailability compared to fasted dosing. Used as a reference compound for 5-HT_{1A} partial agonist plus SSRI pharmacology.

1. 1. Compound Identification

Vilazodone is described as ssri + 5-ht1a partial agonist. A dual-mechanism antidepressant combining SSRI activity with 5-HT1A partial agonism intended to accelerate clinical response.

1.1. 1.1 Class summary

SSRI + 5-HT1A partial agonist

1.2. 1.2 Subtitle

A dual-mechanism antidepressant combining SSRI activity with 5-HT1A partial agonism intended to accelerate clinical response.

2. Abstract

Vilazodone (5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]piperazin-1-yl]benzofuran-2-carboxamide; CAS 163521-12-8; molecular formula C₂₆H₂₇N₅O₂; molecular weight 441.53) is an SSRI plus 5-HT_{1A} partial agonist developed at Merck KGaA and Forest Pharmaceuticals, approved by the FDA in 2011 under the trade name Viibryd. SERT affinity is approximately 0.1 nM; 5-HT_{1A} affinity is approximately 0.2 nM (intrinsic activity approximately 70 percent), producing partial agonism at the autoreceptor. The dual mechanism was designed to bypass the autoreceptor desensitization period that delays SSRI response: by directly activating 5-HT_{1A} receptors while blocking SERT, vilazodone aims to produce faster clinical effect. Real-world clinical trials have shown modest response acceleration. Plasma half-life is approximately 25 hours; metabolism is via CYP3A4 (primary). Approved for major depressive disorder. The compound is administered with food, which doubles bioavailability compared to fasted dosing. Used as a reference compound for 5-HT_{1A} partial agonist plus SSRI pharmacology.

3. Mechanism of Action

Combined SERT inhibition and 5-HT_{1A} partial agonism. Designed to accelerate clinical response by bypassing autoreceptor desensitization.

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 10 to 40 mg per oral administration daily, with food. Rodent studies 1 to 10 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. Khan A, Macaluso M, et al. Vilazodone, a novel dual-acting serotonergic antidepressant for managing major depression. Expert Opin Investig Drugs 2012.
2. Heinrich T, et al. Synthesis and structure-activity relationships in a class of serotonergic N-acylated amine ligands. J Med Chem 2004.
3. Reinhold JA, Mandos LA, Rickels K, Lohoff FW. Pharmacological treatment of generalized anxiety disorder. Expert Opin Pharmacother 2011.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.