

RESEARCH MONOGRAPH . COMPOUND PROFILE

Venlafaxine

A bicyclic SNRI with dose-dependent transporter selectivity; the prototype dual-action antidepressant.

DOCUMENT	KDC-MN-207
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Serotonin-norepinephrine reuptake inhibitor

RESEARCH USE ONLY

ABSTRACT

Venlafaxine ((R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexan-1-ol; CAS 93413-69-5; molecular formula C₁₇H₂₇NO₂; molecular weight 277.40) is a bicyclic phenethylamine SNRI developed at Wyeth and approved by the FDA in 1993 under the trade name Effexor. The compound is the prototype clinical SNRI, exhibiting dose-dependent transporter selectivity: at doses below 150 mg daily it functions as an SSRI (SERT inhibition predominates with NET inhibition becoming clinically meaningful only at higher doses); at 150 to 375 mg daily, NET engagement adds a noradrenergic component. The active metabolite O-desmethylvenlafaxine (desvenlafaxine, marketed separately as Pristiq) carries comparable transporter activity and contributes substantially to the steady-state effect. Plasma half-life of the parent compound is approximately 5 hours; the metabolite half-life is approximately 11 hours. Metabolism is via CYP2D6 (primary) and CYP3A4 (secondary). The compound exhibits a pronounced discontinuation syndrome, attributed to the short half-life and combined serotonergic-noradrenergic withdrawal. Used as the reference SNRI in mechanism studies and as a positive control in dual-action antidepressant pharmacology research.

1. 1. Compound Identification

Venlafaxine is described as serotonin-norepinephrine reuptake inhibitor. A bicyclic SNRI with dose-dependent transporter selectivity; the prototype dual-action antidepressant.

1.1. 1.1 Class summary

Serotonin-norepinephrine reuptake inhibitor

1.2. 1.2 Subtitle

A bicyclic SNRI with dose-dependent transporter selectivity; the prototype dual-action antidepressant.

2. Abstract

Venlafaxine ((R/S)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexan-1-ol; CAS 93413-69-5; molecular formula C₁₇H₂₇NO₂; molecular weight 277.40) is a bicyclic phenethylamine SNRI developed at Wyeth and approved by the FDA in 1993 under the trade name Effexor. The compound is the prototype clinical SNRI, exhibiting dose-dependent transporter selectivity: at doses below 150 mg daily it functions as an SSRI (SERT inhibition predominates with NET inhibition becoming clinically meaningful only at higher doses); at 150 to 375 mg daily, NET engagement adds a noradrenergic component. The active metabolite O-desmethylvenlafaxine (desvenlafaxine, marketed separately as Pristiq) carries comparable transporter activity and contributes substantially to the steady-state effect. Plasma half-life of the parent compound is approximately 5 hours; the metabolite half-life is approximately 11 hours. Metabolism is via CYP2D6 (primary) and CYP3A4 (secondary). The compound exhibits a pronounced discontinuation syndrome, attributed to the short half-life and combined serotonergic-noradrenergic withdrawal. Used as the reference SNRI in mechanism studies and as a positive control in dual-action antidepressant pharmacology research.

3. Mechanism of Action

Dose-dependent dual SERT/NET inhibition; SSRI-like at low doses, true SNRI at higher doses. Active metabolite O-desmethylvenlafaxine drives steady-state effect.

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 75 to 375 mg per oral administration daily. Rodent studies 5 to 50 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. Holliday SM, Benfield P. Venlafaxine. A review of its pharmacology and therapeutic potential. Drugs 1995.
2. Bymaster FP, et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters. Neuropsychopharmacology 2001.
3. Roseboom PH, Kalin NH. Neuropharmacology of venlafaxine. Depress Anxiety 2000.

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.