

RESEARCH MONOGRAPH . COMPOUND PROFILE

Desvenlafaxine

*The major active metabolite of venlafaxine;
a pure SNRI marketed separately to bypass
CYP2D6 polymorphism.*

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COMPOUND CLASS	Active metabolite of venlafaxine (SNRI)

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ABSTRACT

Desvenlafaxine (4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol; CAS 93413-62-8; molecular formula C₁₆H₂₅NO₂; molecular weight 263.38) is the O-desmethylated active metabolite of venlafaxine, marketed as Pristiq by Wyeth/Pfizer after FDA approval in 2008. The compound is a structurally similar SNRI to venlafaxine with comparable SERT (K_i approximately 40 nM) and NET (K_i approximately 558 nM) affinity but a more balanced ratio than the parent compound, producing meaningful NET inhibition at lower doses. The principal pharmacokinetic advantage is bypass of CYP2D6 metabolism: desvenlafaxine is conjugated and excreted directly without further hepatic transformation, producing flat steady-state concentrations across CYP2D6 phenotypes and minimal drug-drug interaction potential. Plasma half-life is approximately 11 hours; the standard clinical dose is 50 mg daily with a flat dose-response above 50 mg. Discontinuation syndrome is comparable to venlafaxine. Used as a reference SNRI compound when CYP2D6 variability is undesirable.

1. Compound Identification

Desvenlafaxine is described as active metabolite of venlafaxine (snri). The major active metabolite of venlafaxine; a pure SNRI marketed separately to bypass CYP2D6 polymorphism.

1.1 Class summary

Active metabolite of venlafaxine (SNRI)

1.2 Subtitle

The major active metabolite of venlafaxine; a pure SNRI marketed separately to bypass CYP2D6 polymorphism.

2. Abstract

Desvenlafaxine (4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol; CAS 93413-62-8; molecular formula C₁₆H₂₅NO₂; molecular weight 263.38) is the O-desmethylated active metabolite of venlafaxine, marketed as Pristiq by Wyeth/Pfizer after FDA approval in 2008. The compound is a structurally similar SNRI to venlafaxine with comparable SERT (K_i approximately 40 nM) and NET (K_i approximately 558 nM) affinity but a more balanced ratio than the parent compound, producing meaningful NET inhibition at lower doses. The principal pharmacokinetic advantage is bypass of CYP2D6 metabolism: desvenlafaxine is conjugated and excreted directly without further hepatic transformation, producing flat steady-state concentrations across CYP2D6 phenotypes and minimal drug-drug interaction potential. Plasma half-life is approximately 11 hours; the standard clinical dose is 50 mg daily with a flat dose-response above 50 mg. Discontinuation syndrome is comparable to venlafaxine. Used as a reference SNRI compound when CYP2D6 variability is undesirable.

3. Mechanism of Action

Direct SNRI activity, more balanced SERT/NET ratio than venlafaxine. Bypasses CYP2D6, providing flat PK across phenotypes.

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 50 to 100 mg per oral administration daily. Rodent studies 3 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. Sopko MA Jr, et al. Desvenlafaxine: another me-too drug? Ann Pharmacother 2008.
2. Liebowitz MR, et al. Efficacy of desvenlafaxine 50 mg/day and 100 mg/day in major depressive disorder. Neuropsychiatr Dis Treat 2013.
3. Preskorn S, et al. Comparison of duloxetine, escitalopram, and sertraline effects on cytochrome P450 2D6. J Clin Psychopharmacol 2007.

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