

RESEARCH MONOGRAPH . COMPOUND PROFILE

Milnacipran

An SNRI marketed in Europe and Japan for depression and FDA-approved for fibromyalgia, with balanced SERT/NET inhibition.

DOCUMENT	KDC-MN-192
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Serotonin-norepinephrine reuptake inhibitor

ABSTRACT

Milnacipran (Savella, Ixel; CAS 92623-85-3; molecular formula $C_{15}H_{22}N_2O$; molecular weight 246.35) is a serotonin-norepinephrine reuptake inhibitor (SNRI) marketed in Europe, Japan, and Australia for major depressive disorder and FDA-approved in 2009 (Savella) for fibromyalgia. The compound has more balanced SERT and NET inhibition than venlafaxine or duloxetine (which are SERT-biased), with NET inhibition more prominent at lower doses. Approved doses are 100 mg per day in two divided administrations.

1. Compound Identification

Milnacipran is described as serotonin-norepinephrine reuptake inhibitor. An SNRI marketed in Europe and Japan for depression and FDA-approved for fibromyalgia, with balanced SERT/NET inhibition.

1.1 Class summary

Serotonin-norepinephrine reuptake inhibitor

1.2 Subtitle

An SNRI marketed in Europe and Japan for depression and FDA-approved for fibromyalgia, with balanced SERT/NET inhibition.

2. Abstract

Milnacipran (Savella, Ixel; CAS 92623-85-3; molecular formula $C_{15}H_{22}N_2O$; molecular weight 246.35) is a serotonin-norepinephrine reuptake inhibitor (SNRI) marketed in Europe, Japan, and Australia for major depressive disorder and FDA-approved in 2009 (Savella) for fibromyalgia. The compound has more balanced SERT and NET inhibition than venlafaxine or duloxetine (which are SERT-biased), with NET inhibition more prominent at lower doses. Approved doses are 100 mg per day in two divided administrations.

3. Mechanism of Action

Balanced SNRI with NET inhibition more prominent at lower doses.

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

100 mg per day in divided doses.

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. Mendlewicz J. Pharmacologic profile and efficacy of milnacipran. Eur Neuropsychopharmacol 1995.

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.