

RESEARCH MONOGRAPH . COMPOUND PROFILE

Maprotiline

*A tetracyclic NRI with TCA-like side effects
but selective noradrenergic action;
significant seizure risk at high dose.*

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COMPOUND CLASS	Tetracyclic norepinephrine reuptake inhibitor

ABSTRACT

Maprotiline (N-methyl-9,10-ethanoanthracene-9(10H)-propylamine; CAS 10262-69-8; molecular formula C₂₀H₂₃N; molecular weight 277.40) is a tetracyclic norepinephrine reuptake inhibitor developed at Ciba-Geigy and approved in the US in 1980 under the trade name Ludiomil. NET affinity is approximately 11 nM with very weak SERT activity (K_i greater than 1 µM), making the compound a selective NRI structurally classed with the tetracyclics owing to its bridged anthracene scaffold. Significant H₁ (K_i approximately 2 nM) and muscarinic activity produces a side effect profile resembling tricyclic antidepressants: sedation, anticholinergic effects, weight gain. Plasma half-life is 21 to 52 hours, the longest of the antidepressant class, owing to the bridged scaffold's resistance to CYP metabolism. The compound carries the highest seizure risk of any commonly used antidepressant (approximately 0.4 percent at therapeutic doses, increasing sharply in overdose). The seizure risk and TCA-like adverse profile have led to declining use in favor of mirtazapine and SSRIs.

1. Compound Identification

Maprotiline is described as tetracyclic norepinephrine reuptake inhibitor. A tetracyclic NRI with TCA-like side effects but selective noradrenergic action; significant seizure risk at high dose.

1.1 Class summary

Tetracyclic norepinephrine reuptake inhibitor

1.2 Subtitle

A tetracyclic NRI with TCA-like side effects but selective noradrenergic action; significant seizure risk at high dose.

2. Abstract

Maprotiline (N-methyl-9,10-ethanoanthracene-9(10H)-propylamine; CAS 10262-69-8; molecular formula C₂₀H₂₃N; molecular weight 277.40) is a tetracyclic norepinephrine reuptake inhibitor developed at Ciba-Geigy and approved in the US in 1980 under the trade name Ludiomil. NET affinity is approximately 11 nM with very weak SERT activity (K_i greater than 1 µM), making the compound a selective NRI structurally classed with the tetracyclics owing to its bridged anthracene scaffold. Significant H₁ (K_i approximately 2 nM) and muscarinic activity produces a side effect profile resembling tricyclic antidepressants: sedation, anticholinergic effects, weight gain. Plasma half-life is 21 to 52 hours, the longest of the antidepressant class, owing to the bridged scaffold's resistance to CYP metabolism. The compound carries the highest seizure risk of any commonly used antidepressant (approximately 0.4 percent at therapeutic doses, increasing sharply in overdose). The seizure risk and TCA-like adverse profile have led to declining use in favor of mirtazapine and SSRIs.

3. Mechanism of Action

Selective NET inhibition with significant H1 and muscarinic antagonism. Highest seizure risk among antidepressants.

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 75 to 225 mg per oral administration daily. Rodent studies 5 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. Pinder RM, et al. Maprotiline: a review of its pharmacological properties and therapeutic efficacy in mental depressive states. *Drugs* 1977.
2. Park J, Beck JR. Therapeutic and adverse effects of maprotiline. *Hosp Formul* 1986.
3. Yamashita H, et al. Seizures during long-term maprotiline therapy. *J Clin Psychiatry* 1986.

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