

RESEARCH MONOGRAPH . COMPOUND PROFILE

Mianserin

A first-generation tetracyclic antidepressant; the structural and mechanistic precursor to mirtazapine.

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COMPOUND CLASS	Tetracyclic alpha-2 adrenergic antagonist

ABSTRACT

Mianserin (1,2,3,4,10,14b-hexahydro-2-methyldibenzo[c,f]pyrazino[1,2-a]azepine; CAS 24219-97-4; molecular formula C₁₈H₂₀N₂; molecular weight 264.37) is a tetracyclic antidepressant developed at Organon in the 1960s and marketed in Europe and Asia from 1976 (never FDA approved for the US market). The compound is the structural and mechanistic precursor to mirtazapine, sharing the alpha-2 adrenergic auto/heteroreceptor antagonism that increases monoaminergic release. Mianserin additionally exhibits 5-HT_{2A}, 5-HT_{2C}, H₁, and alpha-1 antagonism but with a less favorable receptor selectivity profile than mirtazapine. Notable for a higher incidence of agranulocytosis and aplastic anemia than mirtazapine (estimated 1 in 1500 to 1 in 5000 cases) which contributed to its replacement in clinical practice. Plasma half-life is 21 to 61 hours; metabolism is via CYP2D6 with active demethyl-mianserin metabolite. Used as a reference tetracyclic and alpha-2 antagonist in mechanism studies; less common in clinical use today owing to mirtazapine availability.

1. Compound Identification

Mianserin is described as tetracyclic alpha-2 adrenergic antagonist. A first-generation tetracyclic antidepressant; the structural and mechanistic precursor to mirtazapine.

1.1 Class summary

Tetracyclic alpha-2 adrenergic antagonist

1.2 Subtitle

A first-generation tetracyclic antidepressant; the structural and mechanistic precursor to mirtazapine.

2. Abstract

Mianserin (1,2,3,4,10,14b-hexahydro-2-methyldibenzo[c,f]pyrazino[1,2-a]azepine; CAS 24219-97-4; molecular formula C₁₈H₂₀N₂; molecular weight 264.37) is a tetracyclic antidepressant developed at Organon in the 1960s and marketed in Europe and Asia from 1976 (never FDA approved for the US market). The compound is the structural and mechanistic precursor to mirtazapine, sharing the alpha-2 adrenergic auto/heteroreceptor antagonism that increases monoaminergic release. Mianserin additionally exhibits 5-HT_{2A}, 5-HT_{2C}, H₁, and alpha-1 antagonism but with a less favorable receptor selectivity profile than mirtazapine. Notable for a higher incidence of agranulocytosis and aplastic anemia than mirtazapine (estimated 1 in 1500 to 1 in 5000 cases) which contributed to its replacement in clinical practice. Plasma half-life is 21 to 61 hours; metabolism is via CYP2D6 with active demethyl-mianserin metabolite. Used as a reference tetracyclic and alpha-2 antagonist in mechanism studies; less common in clinical use today owing to mirtazapine availability.

3. Mechanism of Action

Alpha-2 adrenergic auto/heteroreceptor antagonism, 5-HT_{2A/2C} antagonism, H₁ antagonism. Structural precursor to mirtazapine with broader off-target profile.

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 30 to 90 mg per oral administration nightly. 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. 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. de Jonghe F, Swinkels JA. The safety of mianserin. Drug Saf 1992.
2. Pinder RM, van Delft AM. The potential therapeutic role of the enantiomers of mianserin. Br J Pharmacol 1983.
3. Brogden RN, et al. Mianserin: a review of its pharmacological properties and therapeutic efficacy in depressive illness. Drugs 1978.

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.