

RESEARCH MONOGRAPH . COMPOUND PROFILE

Pramipexole

A non-ergot benzothiazole D3-preferring dopamine receptor agonist; first-line for Parkinson disease and restless legs syndrome.

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RESEARCH USE ONLY

ABSTRACT

Pramipexole ((6S)-N6-propyl-4,5,6,7-tetrahydro-1,3-benzothiazole-2,6-diamine; CAS 104632-26-0; molecular formula C₁₀H₁₇N₃S; molecular weight 211.32) is a non-ergot benzothiazole dopamine receptor agonist developed at Boehringer Ingelheim and approved by the FDA in 1997 under the trade name Mirapex. The compound is D₃-preferring (D₃ K_i approximately 0.5 nM, D₂ K_i approximately 4 nM, ratio approximately 8) with minimal activity at non-dopaminergic receptors, distinguishing it from ergoline agonists by absence of the rare cardiac valvulopathy and serosal fibrosis associated with the ergot agonists. Plasma half-life is 8 to 12 hours; metabolism is minimal (90 percent renal excretion unchanged). Approved for Parkinson disease, restless legs syndrome. Off-label use in treatment-resistant unipolar and bipolar depression at higher doses (up to 4.5 mg/day) is supported by mechanistic rationale (D₃ receptor predominance in mesolimbic reward circuits) and small clinical trials. The dopaminergic activity produces a recognized risk of impulse control disorders (pathological gambling, hypersexuality) in approximately 14 percent of long-term users.

1. Compound Identification

Pramipexole is described as non-ergot d2/d3-preferring dopamine agonist. A non-ergot benzothiazole D3-preferring dopamine receptor agonist; first-line for Parkinson disease and restless legs syndrome.

1.1 Class summary

Non-ergot D2/D3-preferring dopamine agonist

1.2 Subtitle

A non-ergot benzothiazole D3-preferring dopamine receptor agonist; first-line for Parkinson disease and restless legs syndrome.

2. Abstract

Pramipexole ((6S)-N6-propyl-4,5,6,7-tetrahydro-1,3-benzothiazole-2,6-diamine; CAS 104632-26-0; molecular formula C₁₀H₁₇N₃S; molecular weight 211.32) is a non-ergot benzothiazole dopamine receptor agonist developed at Boehringer Ingelheim and approved by the FDA in 1997 under the trade name Mirapex. The compound is D3-preferring (D3 Ki approximately 0.5 nM, D2 Ki approximately 4 nM, ratio approximately 8) with minimal activity at non-dopaminergic receptors, distinguishing it from ergoline agonists by absence of the rare cardiac valvulopathy and serosal fibrosis associated with the ergot agonists. Plasma half-life is 8 to 12 hours; metabolism is minimal (90 percent renal excretion unchanged). Approved for Parkinson disease, restless legs syndrome. Off-label use in treatment-resistant unipolar and bipolar depression at higher doses (up to 4.5 mg/day) is supported by mechanistic rationale (D3 receptor predominance in mesolimbic reward circuits) and small clinical trials. The dopaminergic activity produces a recognized risk of impulse control disorders (pathological gambling, hypersexuality) in approximately 14 percent of long-term users.

3. Mechanism of Action

Non-ergot D3-preferring dopamine receptor agonist (~8-fold over D2). Minimal off-target activity. Risk of impulse control disorders.

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 0.125 to 4.5 mg per oral administration daily, in divided doses or once-daily ER. Rodent studies 0.1 to 3 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. Mierau J, et al. Pramipexole binding and activation of cloned and expressed dopamine D2, D3 and D4 receptors. Eur J Pharmacol 1995.
2. Rektorova I, et al. Pramipexole and pergolide in the treatment of depression in Parkinson's disease. Eur J Neurol 2003.
3. Voon V, et al. Impulse control disorders and dopaminergic medications in Parkinson's disease. Curr Opin Neurol 2006.

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