

RESEARCH MONOGRAPH . COMPOUND PROFILE

Amantadine

An adamantane derivative with NMDA receptor antagonism and dopamine release activity; used in Parkinson disease dyskinesia and (historically) influenza A.

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ABSTRACT

Amantadine (1-aminoadamantane; CAS 768-94-5; molecular formula C₁₀H₁₇N; molecular weight 151.25) is a tricyclic amine adamantane derivative developed at DuPont in 1959 and approved by the FDA in 1968 originally as an influenza A antiviral. Mechanism is multifactorial: weak NMDA receptor antagonism (K_i approximately 50 microM, similar to memantine), dopamine release and reuptake inhibition, and (the original mechanism) inhibition of the M2 ion channel in influenza A virus. Influenza A resistance to amantadine became near-universal by 2008, eliminating the antiviral utility. Pharmacological repurposing for Parkinson disease (modest motor benefit; the principal modern use is in levodopa-induced dyskinesia, where the NMDA antagonism reduces involuntary movements) and traumatic brain injury (cognitive recovery, accelerated emergence from minimally conscious state). Plasma half-life is approximately 17 hours; renal excretion is the principal clearance pathway. Used as a reference NMDA antagonist and dopaminergic enhancer.

1. Compound Identification

Amantadine is described as adamantane nmda antagonist + dopamine releaser. An adamantane derivative with NMDA receptor antagonism and dopamine release activity; used in Parkinson disease dyskinesia and (historically) influenza A.

1.1 Class summary

Adamantane NMDA antagonist + dopamine releaser

1.2 Subtitle

An adamantane derivative with NMDA receptor antagonism and dopamine release activity; used in Parkinson disease dyskinesia and (historically) influenza A.

2. Abstract

Amantadine (1-aminoadamantane; CAS 768-94-5; molecular formula C₁₀H₁₇N; molecular weight 151.25) is a tricyclic amine adamantane derivative developed at DuPont in 1959 and approved by the FDA in 1968 originally as an influenza A antiviral. Mechanism is multifactorial: weak NMDA receptor antagonism (K_i approximately 50 µM, similar to memantine), dopamine release and reuptake inhibition, and (the original mechanism) inhibition of the M2 ion channel in influenza A virus. Influenza A resistance to amantadine became near-universal by 2008, eliminating the antiviral utility. Pharmacological repurposing for Parkinson disease (modest motor benefit; the principal modern use is in levodopa-induced dyskinesia, where the NMDA antagonism reduces involuntary movements) and traumatic brain injury (cognitive recovery, accelerated emergence from minimally conscious state). Plasma half-life is approximately 17 hours; renal excretion is the principal clearance pathway. Used as a reference NMDA antagonist and dopaminergic enhancer.

3. Mechanism of Action

Weak NMDA receptor antagonism (similar to memantine); dopamine release and reuptake inhibition. Multi-target activity in Parkinson dyskinesia and TBI cognitive recovery.

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 100 to 400 mg per oral administration daily.

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. Moskowitz BM, et al. Amantadine therapy for Parkinson's disease. Neurology 1978.
2. Giacino JT, et al. Placebo-controlled trial of amantadine for severe traumatic brain injury. N Engl J Med 2012.
3. Kornhuber J, et al. Memantine pharmacological action: relevance for amantadine. Neuropharmacology 1991.

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