

RESEARCH MONOGRAPH . COMPOUND PROFILE

Zolpidem

An imidazopyridine Z-drug hypnotic; a selective alpha-1-containing GABA-A receptor positive modulator with reduced anxiolytic and muscle-relaxant effects.

DOCUMENT	KDC-MN-347
ISSUED	2026-05-09
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COMPOUND CLASS	Imidazopyridine selective alpha-1 GABA-A agonist (Z-drug)

ABSTRACT

Zolpidem (N,N,6-trimethyl-2-(4-methylphenyl)imidazo[1,2-a]pyridine-3-acetamide; CAS 82626-48-0; molecular formula C₁₉H₂₁N₃O; molecular weight 307.39) is an imidazopyridine Z-drug hypnotic developed at Synthelabo and approved by the FDA in 1992 (Ambien). The compound is a positive allosteric modulator of GABA-A receptors at the benzodiazepine site, but with selectivity for alpha-1-containing receptor subtypes (K_i approximately 20 nM) over alpha-2, alpha-3, and alpha-5 (lower affinity). The alpha-1 selectivity produces sedation/hypnosis without the anxiolytic, muscle-relaxant, and anticonvulsant effects of benzodiazepines (which engage all four alpha subtypes). Plasma half-life is approximately 2.5 hours; metabolism is via CYP3A4. Approved for short-term treatment of insomnia. The compound has well-documented complex sleep behaviors (sleepwalking, sleep-driving, sleep-eating) and amnestic effects, with notable case reports of bizarre nighttime behavior leading to FDA black-box warnings. Used as the canonical Z-drug in sleep pharmacology.

1. 1. Compound Identification

Zolpidem is described as imidazopyridine selective alpha-1 gaba-a agonist (z-drug). An imidazopyridine Z-drug hypnotic; a selective alpha-1-containing GABA-A receptor positive modulator with reduced anxiolytic and muscle-relaxant effects.

1.1. 1.1 Class summary

Imidazopyridine selective alpha-1 GABA-A agonist (Z-drug)

1.2. 1.2 Subtitle

An imidazopyridine Z-drug hypnotic; a selective alpha-1-containing GABA-A receptor positive modulator with reduced anxiolytic and muscle-relaxant effects.

2. 2. Abstract

Zolpidem (N,N,6-trimethyl-2-(4-methylphenyl)imidazo[1,2-a]pyridine-3-acetamide; CAS 82626-48-0; molecular formula C₁₉H₂₁N₃O; molecular weight 307.39) is an imidazopyridine Z-drug hypnotic developed at Synthelabo and approved by the FDA in 1992 (Ambien). The compound is a positive allosteric modulator of GABA-A receptors at the benzodiazepine site, but with selectivity for alpha-1-containing receptor subtypes (K_i approximately 20 nM) over alpha-2, alpha-3, and alpha-5 (lower affinity). The alpha-1 selectivity produces sedation/hypnosis without the anxiolytic, muscle-relaxant, and anticonvulsant effects of benzodiazepines (which engage all four alpha subtypes). Plasma half-life is approximately 2.5 hours; metabolism is via CYP3A4. Approved for short-term treatment of insomnia. The compound has well-documented complex sleep behaviors (sleepwalking, sleep-driving, sleep-eating) and amnestic effects, with notable case reports of bizarre nighttime behavior leading to FDA black-box warnings. Used as the canonical Z-drug in sleep pharmacology.

3. Mechanism of Action

Z-drug GABA-A positive allosteric modulator at the benzodiazepine site; selective for alpha-1-containing receptor subtypes (sedation/hypnosis) over alpha-2/3/5 (anxiolytic/muscle relaxant).

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. 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. 5. Reported Research Dose Ranges

Clinical 5 to 12.5 mg per oral administration at bedtime.

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. 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. 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. 9. References

1. Sanger DJ. The pharmacology and mechanisms of action of new generation, non-benzodiazepine hypnotic agents. CNS Drugs 2004.
2. Holm KJ, Goa KL. Zolpidem: an update of its pharmacology, therapeutic efficacy and tolerability in the treatment of insomnia. Drugs 2000.
3. Wong CK, et al. Zolpidem-induced complex sleep behaviors: a systematic review. Sleep Med 2017.

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.