

RESEARCH MONOGRAPH . COMPOUND PROFILE

Lurasidone

A benzisothiazole atypical antipsychotic with prominent 5-HT₇ receptor antagonism contributing to procognitive and antidepressant effects.

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AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Atypical antipsychotic with 5-HT ₇ antagonism

ABSTRACT

Lurasidone ((3aR,4S,7R,7aS)-2- $\{$ (1R,2R)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl]-cyclohexylmethyl $\}$ hexahydro-4,7-methano-2H-isoindole-1,3-dione; CAS 367514-87-2; molecular formula C₂₈H₃₆N₄O₂S; molecular weight 492.68) is a benzisothiazole atypical antipsychotic developed at Sumitomo Dainippon and approved by the FDA in 2010 under the trade name Latuda. The receptor profile features full D₂ antagonism (K_i approximately 1 nM), potent 5-HT_{2A} antagonism (K_i approximately 0.5 nM), 5-HT_{1A} partial agonism (K_i approximately 6.4 nM), and prominent 5-HT₇ antagonism (K_i approximately 0.5 nM, the most potent in clinical use). The 5-HT₇ antagonism is associated with procognitive effects and improvement in bipolar depression. H₁ and muscarinic activity is minimal, producing low sedation and metabolic burden compared to olanzapine and quetiapine; the principal limitation is dose-related akathisia. Plasma half-life is 18 hours; absorption requires food (approximately 350 kcal). Metabolism is via CYP3A4. Approved for schizophrenia (acute and maintenance), bipolar I depression (monotherapy or with lithium/valproate). Used as the reference 5-HT₇-prominent antipsychotic.

1. Compound Identification

Lurasidone is described as atypical antipsychotic with 5-HT₇ antagonism. A benzoisothiazole atypical antipsychotic with prominent 5-HT₇ receptor antagonism contributing to procognitive and antidepressant effects.

1.1 Class summary

Atypical antipsychotic with 5-HT₇ antagonism

1.2 Subtitle

A benzoisothiazole atypical antipsychotic with prominent 5-HT₇ receptor antagonism contributing to procognitive and antidepressant effects.

2. Abstract

Lurasidone ((3aR,4S,7R,7aS)-2-[(1R,2R)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl]-cyclohexylmethyl]hexahydro-4,7-methano-2H-isoindole-1,3-dione; CAS 367514-87-2; molecular formula C₂₈H₃₆N₄O₂S; molecular weight 492.68) is a benzisothiazole atypical antipsychotic developed at Sumitomo Dainippon and approved by the FDA in 2010 under the trade name Latuda. The receptor profile features full D₂ antagonism (K_i approximately 1 nM), potent 5-HT_{2A} antagonism (K_i approximately 0.5 nM), 5-HT_{1A} partial agonism (K_i approximately 6.4 nM), and prominent 5-HT₇ antagonism (K_i approximately 0.5 nM, the most potent in clinical use). The 5-HT₇ antagonism is associated with procognitive effects and improvement in bipolar depression. H₁ and muscarinic activity is minimal, producing low sedation and metabolic burden compared to olanzapine and quetiapine; the principal limitation is dose-related akathisia. Plasma half-life is 18 hours; absorption requires food (approximately 350 kcal). Metabolism is via CYP3A4. Approved for schizophrenia (acute and maintenance), bipolar I depression (monotherapy or with lithium/valproate). Used as the reference 5-HT₇-prominent antipsychotic.

3. Mechanism of Action

Full D2 antagonism, potent 5-HT_{2A} and 5-HT₇ antagonism, 5-HT_{1A} partial agonism. Minimal H₁ and muscarinic activity. Low metabolic burden.

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 20 to 160 mg per oral administration daily, with food (≥ 350 kcal). Rodent studies 1 to 20 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. Ishibashi T, et al. Pharmacological profile of lurasidone, a novel antipsychotic agent with potent 5-hydroxytryptamine 7 (5-HT7) and 5-HT1A receptor activity. J Pharmacol Exp Ther 2010.
2. Loebel A, et al. Lurasidone monotherapy in the treatment of bipolar I depression. Am J Psychiatry 2014.
3. Citrome L. Lurasidone for schizophrenia: a review of the efficacy and safety profile. Int J Clin Pract 2011.

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.