

RESEARCH MONOGRAPH . COMPOUND PROFILE

Risperidone

A benzisoxazole atypical antipsychotic; the most prescribed atypical worldwide and the prototype combined D2 / 5-HT2A antagonist.

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COMPOUND CLASS	Atypical antipsychotic

ABSTRACT

Risperidone (3-{2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)piperidin-1-yl]ethyl}-2-methyl-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-one; CAS 106266-06-2; molecular formula C₂₃H₂₇FN₄O₂; molecular weight 410.49) is a benzisoxazole atypical antipsychotic developed at Janssen and approved by the FDA in 1993 under the trade name Risperdal. The receptor profile is the prototype combined D₂/5-HT_{2A} antagonist: D₂ (K_i approximately 4 nM), 5-HT_{2A} (K_i approximately 0.16 nM, ratio approximately 25:1 favoring 5-HT_{2A}), with secondary α -1, α -2, and H₁ antagonism. At doses below 6 mg the 5-HT_{2A} predominates and EPS is minimal; above 6 mg the D₂ antagonism produces dose-dependent EPS approaching haloperidol-like profile. The active metabolite 9-hydroxyrisperidone (paliperidone, marketed as Invega) carries similar receptor profile and contributes substantially to steady-state activity. Risperidone is the most prescribed atypical antipsychotic worldwide. Plasma half-life is 3 hours for parent, 24 hours for paliperidone metabolite. Long-acting injectables (Risperdal Consta, Perseris) provide biweekly or monthly administration. Approved for schizophrenia, bipolar mania, autism-associated irritability. Used as the canonical D₂/5-HT_{2A} reference atypical.

1. Compound Identification

Risperidone is described as atypical antipsychotic. A benzisoxazole atypical antipsychotic; the most prescribed atypical worldwide and the prototype combined D2 / 5-HT_{2A} antagonist.

1.1 Class summary

Atypical antipsychotic

1.2 Subtitle

A benzisoxazole atypical antipsychotic; the most prescribed atypical worldwide and the prototype combined D2 / 5-HT_{2A} antagonist.

2. Abstract

Risperidone (3-{2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)piperidin-1-yl]ethyl}-2-methyl-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-one; CAS 106266-06-2; molecular formula C₂₃H₂₇FN₄O₂; molecular weight 410.49) is a benzisoxazole atypical antipsychotic developed at Janssen and approved by the FDA in 1993 under the trade name Risperdal. The receptor profile is the prototype combined D₂/5-HT_{2A} antagonist: D₂ (K_i approximately 4 nM), 5-HT_{2A} (K_i approximately 0.16 nM, ratio approximately 25:1 favoring 5-HT_{2A}), with secondary α-1, α-2, and H₁ antagonism. At doses below 6 mg the 5-HT_{2A} predominates and EPS is minimal; above 6 mg the D₂ antagonism produces dose-dependent EPS approaching haloperidol-like profile. The active metabolite 9-hydroxyrisperidone (paliperidone, marketed as Invega) carries similar receptor profile and contributes substantially to steady-state activity. Risperidone is the most prescribed atypical antipsychotic worldwide. Plasma half-life is 3 hours for parent, 24 hours for paliperidone metabolite. Long-acting injectables (Risperdal Consta, Perseris) provide biweekly or monthly administration. Approved for schizophrenia, bipolar mania, autism-associated irritability. Used as the canonical D₂/5-HT_{2A} reference atypical.

3. Mechanism of Action

D2 antagonism plus 5-HT_{2A} antagonism (~25:1 5-HT_{2A}/D2 ratio); secondary alpha-1, alpha-2, H1 antagonism. Active metabolite paliperidone (9-hydroxyrisperidone).

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 0.5 to 8 mg per oral administration daily. Long-acting injectable 25 to 50 mg biweekly. 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. Leysen JE, et al. Biochemical profile of risperidone, a new antipsychotic. J Pharmacol Exp Ther 1988.
2. Mauri MC, et al. Clinical pharmacology of atypical antipsychotics: an update. EXCLI J 2014.
3. Csernansky JG, et al. A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. N Engl J Med 2002.

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