

RESEARCH MONOGRAPH . COMPOUND PROFILE

Quetiapine

A dibenzothiazepine atypical antipsychotic with broad receptor binding; the active metabolite norquetiapine is a NET inhibitor contributing to antidepressant efficacy.

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ABSTRACT

Quetiapine (2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-piperazin-1-yl)ethoxy]ethanol; CAS 111974-69-7; molecular formula C₂₁H₂₅N₃O₂S; molecular weight 383.51) is a dibenzothiazepine atypical antipsychotic developed at AstraZeneca and approved by the FDA in 1997 under the trade name Seroquel. The receptor profile is broad: D₂ (K_i approximately 770 nM, the weakest of the antipsychotic class), 5-HT_{2A} (K_i approximately 295 nM), H₁ (K_i approximately 11 nM), α-1 (K_i approximately 22 nM), 5-HT_{1A} partial agonism. The active metabolite norquetiapine (formed via CYP3A4) is a potent NET inhibitor (K_i approximately 35 nM) and a 5-HT_{2C} antagonist, contributing to antidepressant efficacy and supporting the FDA-approved adjunctive use in major depressive disorder. Plasma half-life is 6 to 7 hours; metabolism is via CYP3A4. Approved for schizophrenia, bipolar I disorder (mania, depression, maintenance), and adjunctive in MDD. Off-label use as a hypnotic at 25 to 100 mg is widespread despite a poor efficacy-to-side-effect ratio for that indication. Used as a reference broad-spectrum atypical antipsychotic in mechanism studies.

1. Compound Identification

Quetiapine is described as atypical antipsychotic. A dibenzothiazepine atypical antipsychotic with broad receptor binding; the active metabolite norquetiapine is a NET inhibitor contributing to antidepressant efficacy.

1.1 Class summary

Atypical antipsychotic

1.2 Subtitle

A dibenzothiazepine atypical antipsychotic with broad receptor binding; the active metabolite norquetiapine is a NET inhibitor contributing to antidepressant efficacy.

2. Abstract

Quetiapine (2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethoxy]ethanol; CAS 111974-69-7; molecular formula C₂₁H₂₅N₃O₂S; molecular weight 383.51) is a dibenzothiazepine atypical antipsychotic developed at AstraZeneca and approved by the FDA in 1997 under the trade name Seroquel. The receptor profile is broad: D₂ (K_i approximately 770 nM, the weakest of the antipsychotic class), 5-HT_{2A} (K_i approximately 295 nM), H₁ (K_i approximately 11 nM), α-1 (K_i approximately 22 nM), 5-HT_{1A} partial agonism. The active metabolite norquetiapine (formed via CYP3A4) is a potent NET inhibitor (K_i approximately 35 nM) and a 5-HT_{2C} antagonist, contributing to antidepressant efficacy and supporting the FDA-approved adjunctive use in major depressive disorder. Plasma half-life is 6 to 7 hours; metabolism is via CYP3A4. Approved for schizophrenia, bipolar I disorder (mania, depression, maintenance), and adjunctive in MDD. Off-label use as a hypnotic at 25 to 100 mg is widespread despite a poor efficacy-to-side-effect ratio for that indication. Used as a reference broad-spectrum atypical antipsychotic in mechanism studies.

3. Mechanism of Action

Weak D2 antagonism, broad receptor profile (5-HT2A, H1, alpha-1, 5-HT1A partial agonism). Active metabolite norquetiapine is a NET inhibitor and 5-HT2C antagonist.

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 25 to 800 mg per oral administration daily (low for off-label hypnotic, high for psychosis/mania). Rodent studies 5 to 50 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. Goldstein JM. Quetiapine fumarate: a new atypical antipsychotic. *Drugs Today* 1999.
2. Jensen NH, et al. N-desalkylquetiapine, a potent norepinephrine reuptake inhibitor and partial 5-HT_{1A} agonist, as a putative mediator of quetiapine's antidepressant activity. *Neuropsychopharmacology* 2008.
3. Maneeton N, et al. Quetiapine monotherapy for major depressive disorder: a systematic review and meta-analysis. *CNS Drugs* 2014.

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