

RESEARCH MONOGRAPH . COMPOUND PROFILE

Clomipramine

A chloro-substituted TCA with the most potent SERT inhibition in the class; the only TCA with FDA approval for OCD.

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COMPOUND CLASS	Tricyclic antidepressant (chlorinated tertiary amine)

ABSTRACT

Clomipramine (3-(3-chloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine; CAS 303-49-1; molecular formula C₁₉H₂₃ClN₂; molecular weight 314.85) is a 3-chloro-substituted analog of imipramine developed at Geigy and approved by the FDA in 1989 under the trade name Anafranil. The chloro substitution shifts transporter selectivity sharply toward SERT (SERT K_i approximately 0.28 nM, the most potent in the TCA class; NET K_i approximately 38 nM). The active metabolite N-desmethyldesmethylclomipramine (formed via CYP3A4/CYP2C19) is a NET-preferring secondary amine, producing balanced steady-state monoaminergic activity from a SERT-dominant parent. Off-target activity parallels other tertiary amine TCAs: muscarinic, H₁, alpha-1, and sodium channel block. Plasma half-life is 19 to 37 hours. The compound is the only TCA with FDA approval for obsessive-compulsive disorder, an indication where the SSRI class typically requires higher doses; clomipramine remains a benchmark in treatment-resistant OCD. Used as the reference SERT-potent TCA in mechanism studies.

1. Compound Identification

Clomipramine is described as tricyclic antidepressant (chlorinated tertiary amine). A chloro-substituted TCA with the most potent SERT inhibition in the class; the only TCA with FDA approval for OCD.

1.1 Class summary

Tricyclic antidepressant (chlorinated tertiary amine)

1.2 Subtitle

A chloro-substituted TCA with the most potent SERT inhibition in the class; the only TCA with FDA approval for OCD.

2. Abstract

Clomipramine (3-(3-chloro-10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine; CAS 303-49-1; molecular formula C₁₉H₂₃ClN₂; molecular weight 314.85) is a 3-chloro-substituted analog of imipramine developed at Geigy and approved by the FDA in 1989 under the trade name Anafranil. The chloro substitution shifts transporter selectivity sharply toward SERT (SERT K_i approximately 0.28 nM, the most potent in the TCA class; NET K_i approximately 38 nM). The active metabolite N-desmethyldomipramine (formed via CYP3A4/CYP2C19) is a NET-preferring secondary amine, producing balanced steady-state monoaminergic activity from a SERT-dominant parent. Off-target activity parallels other tertiary amine TCAs: muscarinic, H₁, α-1, and sodium channel block. Plasma half-life is 19 to 37 hours. The compound is the only TCA with FDA approval for obsessive-compulsive disorder, an indication where the SSRI class typically requires higher doses; clomipramine remains a benchmark in treatment-resistant OCD. Used as the reference SERT-potent TCA in mechanism studies.

3. Mechanism of Action

Most potent SERT inhibition in TCA class; active metabolite N-desmethyl-clomipramine shifts steady-state to NET. Anticholinergic, antihistaminergic, alpha-1, and sodium channel block.

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 250 mg per oral administration daily. Rodent studies 5 to 30 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. DeVeugh-Geiss J, et al. Clomipramine hydrochloride in the treatment of obsessive compulsive disorder. Arch Gen Psychiatry 1989.
2. Trimble MR. Worldwide use of clomipramine. J Clin Psychiatry 1990.
3. Faravelli C, et al. Comparison of clomipramine with other TCAs and SSRIs. CNS Drugs 2003.

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.