

RESEARCH MONOGRAPH . COMPOUND PROFILE

Cetirizine

A second-generation peripheral H1 antihistamine; the principal active metabolite of hydroxyzine without CNS penetration.

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COMPOUND CLASS	Second-generation H1 antihistamine (peripheral)

ABSTRACT

Cetirizine (2-[2-[4-[(R/S)-(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl]ethoxy]acetic acid; CAS 83881-51-0; molecular formula C₂₁H₂₅ClN₂O₃; molecular weight 388.89) is a second-generation H₁ antihistamine developed at UCB and approved by the FDA in 1995 (Zyrtec). The compound is the principal active carboxylic acid metabolite of hydroxyzine; the addition of the carboxyl group eliminates blood-brain barrier penetration, producing peripheral H₁ antagonism without the central sedating effects of hydroxyzine. H₁ selectivity is high; minimal anticholinergic activity. Plasma half-life is approximately 8 hours; minimal hepatic metabolism (excreted largely unchanged renally). The compound has minor sedating effect in approximately 10 to 15 percent of users (slightly more than fexofenadine or loratadine), reflecting some BBB penetration. Approved indications: allergic rhinitis, urticaria, allergic conjunctivitis. Used as the canonical second-generation peripheral H₁ antagonist in research.

1. Compound Identification

Cetirizine is described as second-generation h1 antihistamine (peripheral). A second-generation peripheral H1 antihistamine; the principal active metabolite of hydroxyzine without CNS penetration.

1.1 Class summary

Second-generation H1 antihistamine (peripheral)

1.2 Subtitle

A second-generation peripheral H1 antihistamine; the principal active metabolite of hydroxyzine without CNS penetration.

2. Abstract

Cetirizine (2-[2-[4-[(R/S)-(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl]ethoxy]acetic acid; CAS 83881-51-0; molecular formula C₂₁H₂₅ClN₂O₃; molecular weight 388.89) is a second-generation H₁ antihistamine developed at UCB and approved by the FDA in 1995 (Zyrtec). The compound is the principal active carboxylic acid metabolite of hydroxyzine; the addition of the carboxyl group eliminates blood-brain barrier penetration, producing peripheral H₁ antagonism without the central sedating effects of hydroxyzine. H₁ selectivity is high; minimal anticholinergic activity. Plasma half-life is approximately 8 hours; minimal hepatic metabolism (excreted largely unchanged renally). The compound has minor sedating effect in approximately 10 to 15 percent of users (slightly more than fexofenadine or loratadine), reflecting some BBB penetration. Approved indications: allergic rhinitis, urticaria, allergic conjunctivitis. Used as the canonical second-generation peripheral H₁ antagonist in research.

3. Mechanism of Action

Second-generation H1 antagonist with peripheral selectivity (carboxyl group prevents BBB penetration). Minimal anticholinergic and sedating activity.

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 10 mg per oral administration daily.

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. Spencer CM, et al. Cetirizine: a reappraisal. *Drugs* 1993.
2. Snowman AM, Snyder SH. Cetirizine: actions on neurotransmitter receptors. *J Allergy Clin Immunol* 1990.
3. Simons FE. Comparative pharmacology of H1 antihistamines: clinical relevance. *Am J Med* 2002.

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.