

RESEARCH MONOGRAPH . COMPOUND PROFILE

CX-516 (Ampalex)

The first ampakine to enter human clinical trials, developed at Cortex Pharmaceuticals as a mechanism prototype with limited efficacy.

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ABSTRACT

CX-516 (Ampalex; 1-(quinoxalin-6-ylcarbonyl)piperidine; CAS 154235-83-3; molecular formula C₁₄H₁₅N₃O; molecular weight 241.29) was the first ampakine compound to enter human clinical trials, developed at Cortex Pharmaceuticals (now RespireRx Pharmaceuticals) under license from Gary Lynch and Gary Rogers at the University of California, Irvine. The compound is a benzoylpyrrolidine class AMPA receptor positive allosteric modulator. CX-516 advanced through Phase 2 trials in mild cognitive impairment, schizophrenia (cognitive symptoms), and fragile X syndrome, with mixed results that did not support advancement to Phase 3. The compound has poor pharmacokinetic properties (very short plasma half-life, approximately 1 to 2 hours, and low oral bioavailability) which limit its clinical utility despite mechanistic interest. CX-516 retains research utility as an AMPA potentiator probe but is largely superseded by later-generation compounds (CX-546, CX-614, and others). Doses in clinical trials ranged from 200 to 1200 mg per administration, three to four times daily. The compound is sold as a research chemical in jurisdictions where it is not scheduled.

1. Compound Identification

CX-516 (Ampalex) is described as benzoylpyrrolidine ampakine. The first ampakine to enter human clinical trials, developed at Cortex Pharmaceuticals as a mechanism prototype with limited efficacy.

1.1 Class summary

Benzoylpyrrolidine ampakine

1.2 Subtitle

The first ampakine to enter human clinical trials, developed at Cortex Pharmaceuticals as a mechanism prototype with limited efficacy.

2. Abstract

CX-516 (Ampalex; 1-(quinoxalin-6-ylcarbonyl)piperidine; CAS 154235-83-3; molecular formula C₁₄H₁₅N₃O; molecular weight 241.29) was the first ampakine compound to enter human clinical trials, developed at Cortex Pharmaceuticals (now RespireRx Pharmaceuticals) under license from Gary Lynch and Gary Rogers at the University of California, Irvine. The compound is a benzoylpyrrolidine class AMPA receptor positive allosteric modulator. CX-516 advanced through Phase 2 trials in mild cognitive impairment, schizophrenia (cognitive symptoms), and fragile X syndrome, with mixed results that did not support advancement to Phase 3. The compound has poor pharmacokinetic properties (very short plasma half-life, approximately 1 to 2 hours, and low oral bioavailability) which limit its clinical utility despite mechanistic interest. CX-516 retains research utility as an AMPA potentiator probe but is largely superseded by later-generation compounds (CX-546, CX-614, and others). Doses in clinical trials ranged from 200 to 1200 mg per administration, three to four times daily. The compound is sold as a research chemical in jurisdictions where it is not scheduled.

3. Mechanism of Action

AMPA receptor positive allosteric modulator (benzoylpyrrolidine class). First-in-class clinical compound.

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

200 to 1200 mg per administration, 3-4 times daily (clinical trials).

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. Arai AC, et al. A centrally active drug that modulates AMPA receptor gated currents. Brain Res 1996.
2. Berry-Kravis E, et al. Open-label treatment trial of lithium to target the underlying defect in fragile X syndrome. Cogn Behav Neurol 2008.

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