

RESEARCH MONOGRAPH . COMPOUND PROFILE

# Brivaracetam

*A propyl-substituted levetiracetam analog with 15-fold higher SV2A affinity, FDA-approved 2016 as Briviact for partial-onset seizures.*

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| DOCUMENT       | KDC-MN-034                                                   |
| ISSUED         | 2026-05-09                                                   |
| REVISION       | 1.0                                                          |
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| COMPOUND CLASS | Propyl-substituted pyrrolidinone (high-affinity SV2A ligand) |

RESEARCH USE ONLY

## ABSTRACT

Brivaracetam (Briviact; UCB-34714; (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]butanamide; CAS 357336-20-0; molecular formula C<sub>11</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>; molecular weight 212.29) is a propyl-substituted levetiracetam analog developed at UCB Pharma and approved by the FDA in February 2016 as adjunctive therapy for partial-onset seizures. Brivaracetam binds SV2A with approximately 15-fold higher affinity than levetiracetam (K<sub>d</sub> 0.06 microM versus 1 microM) and shows higher selectivity for SV2A over other potential targets. The clinical consequence is improved seizure protection at lower doses with a flatter pharmacokinetic-pharmacodynamic relationship. Compared with levetiracetam, brivaracetam shows lower rates of behavioral and psychiatric adverse effects (irritability, depression), which are dose-limiting for some levetiracetam patients. Pharmacokinetics: plasma half-life 9 hours; oral bioavailability essentially complete; metabolism is hepatic via amide hydrolysis and CYP2C19. Approved doses are 50 to 200 mg per day in two divided administrations. Schedule V in the United States.

# 1. Compound Identification

**Brivaracetam** is described as propyl-substituted pyrrolidinone (high-affinity sv2a ligand). A propyl-substituted levetiracetam analog with 15-fold higher SV2A affinity, FDA-approved 2016 as Briviact for partial-onset seizures.

## 1.1 Class summary

Propyl-substituted pyrrolidinone (high-affinity SV2A ligand)

## 1.2 Subtitle

A propyl-substituted levetiracetam analog with 15-fold higher SV2A affinity, FDA-approved 2016 as Briviact for partial-onset seizures.

## 2. Abstract

Brivaracetam (Briviact; UCB-34714; (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]butanamide; CAS 357336-20-0; molecular formula C<sub>11</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>; molecular weight 212.29) is a propyl-substituted levetiracetam analog developed at UCB Pharma and approved by the FDA in February 2016 as adjunctive therapy for partial-onset seizures. Brivaracetam binds SV2A with approximately 15-fold higher affinity than levetiracetam (K<sub>d</sub> 0.06 µM versus 1 µM) and shows higher selectivity for SV2A over other potential targets. The clinical consequence is improved seizure protection at lower doses with a flatter pharmacokinetic-pharmacodynamic relationship. Compared with levetiracetam, brivaracetam shows lower rates of behavioral and psychiatric adverse effects (irritability, depression), which are dose-limiting for some levetiracetam patients. Pharmacokinetics: plasma half-life 9 hours; oral bioavailability essentially complete; metabolism is hepatic via amide hydrolysis and CYP2C19. Approved doses are 50 to 200 mg per day in two divided administrations. Schedule V in the United States.

### 3. Mechanism of Action

SV2A high-affinity ligand (15-fold higher affinity than levetiracetam). Same mechanism class as levetiracetam, refined.

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

50 to 200 mg per day in two divided doses.

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. Klitgaard H, et al. Brivaracetam: rationale for discovery and preclinical profile. *Epilepsia* 2016.
2. Klein P, et al. A randomized double-blind placebo-controlled multicenter dose-ranging study of brivaracetam as adjunctive treatment in adults with refractory partial-onset seizures. *Epilepsia* 2015.

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