

RESEARCH MONOGRAPH . COMPOUND PROFILE

Lisdexamfetamine

L-lysine-d-amphetamine conjugate; a prodrug providing slow conversion to active d-amphetamine, with reduced abuse potential.

DOCUMENT	KDC-MN-379
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Prodrug d-amphetamine (lysine conjugate)

ABSTRACT

Lisdexamfetamine ((2S)-2,6-diamino-N-[(2S)-1-phenylpropan-2-yl]hexanamide; CAS 608137-32-2; molecular formula $C_{15}H_{25}N_3O$; molecular weight 263.38) is a prodrug of d-amphetamine in which the amphetamine amino group is conjugated with L-lysine via a peptide bond. Approved by the FDA in 2007 (Vyvanse). Mechanism: the prodrug is biologically inactive; following oral absorption, red blood cell cytosolic enzymes hydrolyze the lysine-amphetamine bond, releasing free d-amphetamine over several hours. The slow, sustained release produces a flatter plasma curve than IR amphetamine and reduces the rate of dopamine increase that drives abuse liability. The lysine conjugation also means parenteral routes (IV, snorted) do not produce a faster onset, since the cleavage requires enzymatic activity. Approved indications: ADHD and binge eating disorder. Plasma half-life of the released d-amphetamine is approximately 11 hours. Schedule II. Used as the canonical abuse-deterrent stimulant prodrug.

1. Compound Identification

Lisdexamfetamine is described as prodrug d-amphetamine (lysine conjugate). L-lysine-d-amphetamine conjugate; a prodrug providing slow conversion to active d-amphetamine, with reduced abuse potential.

1.1 Class summary

Prodrug d-amphetamine (lysine conjugate)

1.2 Subtitle

L-lysine-d-amphetamine conjugate; a prodrug providing slow conversion to active d-amphetamine, with reduced abuse potential.

2. Abstract

Lisdexamfetamine ((2S)-2,6-diamino-N-[(2S)-1-phenylpropan-2-yl]hexanamide; CAS 608137-32-2; molecular formula C₁₅H₂₅N₃O; molecular weight 263.38) is a prodrug of d-amphetamine in which the amphetamine amino group is conjugated with L-lysine via a peptide bond. Approved by the FDA in 2007 (Vyvanse). Mechanism: the prodrug is biologically inactive; following oral absorption, red blood cell cytosolic enzymes hydrolyze the lysine-amphetamine bond, releasing free d-amphetamine over several hours. The slow, sustained release produces a flatter plasma curve than IR amphetamine and reduces the rate of dopamine increase that drives abuse liability. The lysine conjugation also means parenteral routes (IV, snorted) do not produce a faster onset, since the cleavage requires enzymatic activity. Approved indications: ADHD and binge eating disorder. Plasma half-life of the released d-amphetamine is approximately 11 hours. Schedule II. Used as the canonical abuse-deterrent stimulant prodrug.

3. Mechanism of Action

Inactive prodrug; red blood cell enzymes cleave lysine to release d-amphetamine slowly. Reduced abuse liability via slowed pharmacokinetics.

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 30 to 70 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. Pennick M. Absorption of lisdexamfetamine dimesylate and its enzymatic conversion to d-amphetamine. *Neuropsychiatr Dis Treat* 2010.
2. Biederman J, et al. Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in children with ADHD. *Clin Ther* 2007.
3. McElroy SL, et al. Lisdexamfetamine dimesylate for adults with moderate to severe binge eating disorder. *JAMA Psychiatry* 2015.

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.