

RESEARCH MONOGRAPH . COMPOUND PROFILE

Buprenorphine

A semi-synthetic mu-opioid partial agonist with kappa-opioid antagonism; the primary medication-assisted treatment for opioid use disorder.

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COMPOUND CLASS	Mu-opioid partial agonist + kappa-opioid antagonist

RESEARCH USE ONLY

ABSTRACT

Buprenorphine ((2S,6R,7R,14S)-17-cyclopropylmethyl-7-[(S)-1-hydroxy-1,2,2-trimethylpropyl]-6-methoxy-4,5-epoxy-6,14-ethano-morphinan-3-ol; CAS 52485-79-7; molecular formula C₂₉H₄₁NO₄; molecular weight 467.65) is a semi-synthetic thebaine-derived mu-opioid partial agonist with concurrent kappa-opioid antagonist and ORL1 (nociceptin receptor) partial agonist activity. Originally approved by the FDA in 1981 as an analgesic; reformulated and approved in 2002 (Subutex, Suboxone) for opioid use disorder. Mu-opioid affinity is high (K_i approximately 0.2 nM) with intrinsic activity approximately 30 percent (partial agonism); the partial agonism produces a ceiling effect on respiratory depression and euphoria, distinguishing buprenorphine safety profile from full agonists like fentanyl or morphine. Long plasma half-life (24 to 60 hours) supports once-daily or less-frequent dosing. Suboxone formulation includes naloxone (a mu antagonist with poor sublingual bioavailability) to deter intravenous misuse. Approved for opioid use disorder and chronic pain (transdermal Butrans). The kappa-opioid antagonism is being investigated for treatment-resistant depression. Used as the canonical mu-opioid partial agonist in addiction medicine.

1. Compound Identification

Buprenorphine is described as mu-opioid partial agonist + kappa-opioid antagonist. A semi-synthetic mu-opioid partial agonist with kappa-opioid antagonism; the primary medication-assisted treatment for opioid use disorder.

1.1 Class summary

Mu-opioid partial agonist + kappa-opioid antagonist

1.2 Subtitle

A semi-synthetic mu-opioid partial agonist with kappa-opioid antagonism; the primary medication-assisted treatment for opioid use disorder.

2. Abstract

Buprenorphine ((2S,6R,7R,14S)-17-cyclopropylmethyl-7-[(S)-1-hydroxy-1,2,2-trimethylpropyl]-6-methoxy-4,5-epoxy-6,14-ethano-morphinan-3-ol; CAS 52485-79-7; molecular formula C₂₉H₄₁NO₄; molecular weight 467.65) is a semi-synthetic thebaine-derived mu-opioid partial agonist with concurrent kappa-opioid antagonist and ORL1 (nociceptin receptor) partial agonist activity. Originally approved by the FDA in 1981 as an analgesic; reformulated and approved in 2002 (Subutex, Suboxone) for opioid use disorder. Mu-opioid affinity is high (K_i approximately 0.2 nM) with intrinsic activity approximately 30 percent (partial agonism); the partial agonism produces a ceiling effect on respiratory depression and euphoria, distinguishing buprenorphine safety profile from full agonists like fentanyl or morphine. Long plasma half-life (24 to 60 hours) supports once-daily or less-frequent dosing. Suboxone formulation includes naloxone (a mu antagonist with poor sublingual bioavailability) to deter intravenous misuse. Approved for opioid use disorder and chronic pain (transdermal Butrans). The kappa-opioid antagonism is being investigated for treatment-resistant depression. Used as the canonical mu-opioid partial agonist in addiction medicine.

3. Mechanism of Action

High-affinity mu-opioid partial agonist (~30 percent intrinsic activity; ceiling effect on respiratory depression); kappa-opioid antagonist; ORL1 partial agonist. Long plasma half-life.

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 OUD 4 to 24 mg sublingual daily; analgesia 0.3 to 0.6 mg IV every 6 to 8 hours or 5 to 20 mcg/hour transdermal.

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. Walsh SL, et al. Clinical pharmacology of buprenorphine: ceiling effects at high doses. Clin Pharmacol Ther 1994.
2. Ling W, et al. Buprenorphine maintenance treatment for opioid use disorder. Lancet 2003.
3. Fava M, et al. Opioid system modulation with buprenorphine/samidorphan combination for major depressive disorder. Mol Psychiatry 2020.

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