

RESEARCH MONOGRAPH . COMPOUND PROFILE

Naloxone

A short-acting mu-opioid antagonist; the standard reversal agent for opioid overdose.

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COMPOUND CLASS	Mu-opioid antagonist (short-acting)

ABSTRACT

Naloxone ((5 α)-4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one; CAS 465-65-6; molecular formula C₁₉H₂₁NO₄; molecular weight 327.37) is a short-acting mu-opioid antagonist approved by the FDA in 1971 (Narcan). The compound is a competitive antagonist at mu, kappa, and delta opioid receptors with preferential mu affinity (K_i approximately 1 nM). Unlike naltrexone, oral bioavailability is poor (less than 5 percent), restricting use to parenteral or intranasal administration. Plasma half-life is approximately 1 to 2 hours, shorter than most opioid agonists, requiring multiple doses or infusion in opioid overdose reversal where the half-life of the offending opioid exceeds naloxone's. The intranasal formulation (Narcan nasal spray, 4 mg) is widely available and has driven the modern public health response to the opioid overdose epidemic. Approved indications: opioid overdose reversal, postoperative opioid reversal, opioid-induced constipation (IV form alvimopan, methylnaltrexone for that latter). Used as the canonical mu-opioid antagonist in research.

1. Compound Identification

Naloxone is described as mu-opioid antagonist (short-acting). A short-acting mu-opioid antagonist; the standard reversal agent for opioid overdose.

1.1 Class summary

Mu-opioid antagonist (short-acting)

1.2 Subtitle

A short-acting mu-opioid antagonist; the standard reversal agent for opioid overdose.

2. Abstract

Naloxone ((5alpha)-4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one; CAS 465-65-6; molecular formula C₁₉H₂₁NO₄; molecular weight 327.37) is a short-acting mu-opioid antagonist approved by the FDA in 1971 (Narcan). The compound is a competitive antagonist at mu, kappa, and delta opioid receptors with preferential mu affinity (K_i approximately 1 nM). Unlike naltrexone, oral bioavailability is poor (less than 5 percent), restricting use to parenteral or intranasal administration. Plasma half-life is approximately 1 to 2 hours, shorter than most opioid agonists, requiring multiple doses or infusion in opioid overdose reversal where the half-life of the offending opioid exceeds naloxone's. The intranasal formulation (Narcan nasal spray, 4 mg) is widely available and has driven the modern public health response to the opioid overdose epidemic. Approved indications: opioid overdose reversal, postoperative opioid reversal, opioid-induced constipation (IV form alvimopan, methylnaltrexone for that latter). Used as the canonical mu-opioid antagonist in research.

3. Mechanism of Action

Competitive mu-opioid receptor antagonist ($K_i \sim 1$ nM); reversal of opioid overdose. Short half-life requires repeated dosing for long-acting opioids.

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 IV 0.4 to 2 mg every 2 to 3 minutes as needed; intranasal 4 mg one nostril, repeat every 2 to 3 minutes.

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. Boyer EW. Management of opioid analgesic overdose. N Engl J Med 2012.
2. Doe-Simkins M, et al. Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose. Am J Public Health 2009.
3. Faul M, et al. Disparity in naloxone administration by emergency medical service providers. Am J Public Health 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.