

RESEARCH MONOGRAPH . COMPOUND PROFILE

Remimazolam

A soft drug benzodiazepine designed for ester hydrolysis by tissue esterases, FDA-approved 2020 for procedural sedation with the kinetics of propofol but the safety reversibility of midazolam.

DOCUMENT	KDC-MN-1322
ISSUED	2026-05-10
REVISION	1.0
AUTHOR	Kodiac biolabs Research
COMPOUND CLASS	Ultrashort-acting benzodiazepine intravenous sedative

ABSTRACT

Remimazolam besylate (CAS 308242-62-8 free base; molecular formula $C_{21}H_{19}BrN_4O_2$ free base, molecular weight 439.31) is an ultrashort-acting benzodiazepine designed as a soft drug analog of midazolam, with an ester linkage on the 1-position imidazole substituent that is hydrolyzed by tissue carboxylesterases to the inactive carboxylic acid metabolite CNS7054. The compound was developed at Glaxo Group Research, advanced through Phase 3 by Cosmo Pharmaceuticals and PAION, and approved by the FDA in July 2020 (Byfavo) for procedural sedation. Mechanism is positive allosteric modulation of GABA-A receptors at the benzodiazepine site (alpha-1 subunit-containing receptors), identical to midazolam and other clinical benzodiazepines, with reversibility by flumazenil. Pharmacokinetics distinguish remimazolam from other benzodiazepines: the context-sensitive half-time after a 4-hour infusion is approximately 7 to 8 minutes (versus over 2 hours for midazolam), driven by tissue esterase hydrolysis that does not depend on hepatic CYP3A4 metabolism (the dominant midazolam pathway). The clinical effect is a sedation kinetic similar to propofol (rapid onset within 1 to 3 minutes, brief duration with minimal accumulation in extended infusions) combined with the favorable cardiovascular and respiratory profile of benzodiazepines (less hypotension, less respiratory depression than equipotent propofol) and the safety advantage of reversibility by flumazenil for any inadvertent oversedation. Approved indications are procedural sedation for upper endoscopy, colonoscopy, and bronchoscopy in adults at induction doses of 5 mg followed by 2.5 mg supplemental boluses to clinical effect. ICU sedation indications are under regulatory review in multiple

jurisdictions; Japan and South Korea approved general anesthesia indications in 2020. Cost is currently substantially higher than midazolam.

1. Compound Identification

Remimazolam is described as ultrashort-acting benzodiazepine intravenous sedative. A soft drug benzodiazepine designed for ester hydrolysis by tissue esterases, FDA-approved 2020 for procedural sedation with the kinetics of propofol but the safety reversibility of midazolam.

1.1 Class summary

Ultrashort-acting benzodiazepine intravenous sedative

1.2 Subtitle

A soft drug benzodiazepine designed for ester hydrolysis by tissue esterases, FDA-approved 2020 for procedural sedation with the kinetics of propofol but the safety reversibility of midazolam.

2. Abstract

Remimazolam besylate (CAS 308242-62-8 free base; molecular formula $C_{21}H_{19}BrN_4O_2$ free base, molecular weight 439.31) is an ultrashort-acting benzodiazepine designed as a soft drug analog of midazolam, with an ester linkage on the 1-position imidazole substituent that is hydrolyzed by tissue carboxylesterases to the inactive carboxylic acid metabolite CNS7054. The compound was developed at Glaxo Group Research, advanced through Phase 3 by Cosmo Pharmaceuticals and PAION, and approved by the FDA in July 2020 (Byfavo) for procedural sedation. Mechanism is positive allosteric modulation of GABA-A receptors at the benzodiazepine site (alpha-1 subunit-containing receptors), identical to midazolam and other clinical benzodiazepines, with reversibility by flumazenil. Pharmacokinetics distinguish remimazolam from other benzodiazepines: the context-sensitive half-time after a 4-hour infusion is approximately 7 to 8 minutes (versus over 2 hours for midazolam), driven by tissue esterase hydrolysis that does not depend on hepatic CYP3A4 metabolism (the dominant midazolam pathway). The clinical effect is a sedation kinetic similar to propofol (rapid onset within 1 to 3 minutes, brief duration with minimal accumulation in extended infusions) combined with the favorable cardiovascular and respiratory profile of benzodiazepines (less hypotension, less respiratory depression than equipotent propofol) and the safety advantage of reversibility by flumazenil for any inadvertent oversedation. Approved indications are procedural sedation for upper endoscopy, colonoscopy, and bronchoscopy in adults at induction doses of 5 mg followed by 2.5 mg supplemental boluses to clinical effect. ICU sedation indications are under regulatory review in multiple jurisdictions; Japan and South Korea approved general anesthesia indications in 2020. Cost is currently substantially higher than midazolam.

3. Mechanism of Action

GABA-A positive allosteric modulation at the benzodiazepine site (alpha-1 selective). Tissue esterase hydrolysis to inactive CNS7054 drives ultrashort context-sensitive half-time. Flumazenil-reversible.

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

Procedural sedation 5 mg IV induction then 2.5 mg supplemental boluses.
Continuous infusion 0.1 to 0.4 mg/kg/h in non-US approvals.

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. Kilpatrick GJ, et al. CNS 7056: a novel ultra-short-acting benzodiazepine. *Anesthesiology* 2007.
2. Antonik LJ, et al. Phase I single ascending-dose study of remimazolam. *Anesth Analg* 2012.
3. Pastis NJ, et al. Remimazolam for moderate sedation during bronchoscopy. *Chest* 2019.

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.