

RESEARCH MONOGRAPH . COMPOUND PROFILE

Etomidate

An imidazole intravenous induction anesthetic; cardiovascular stable but causes adrenocortical suppression.

DOCUMENT	KDC-MN-345
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	GABA-A receptor positive allosteric modulator (intravenous anesthetic)

RESEARCH USE ONLY

ABSTRACT

Etomidate ((R)-1-(1-phenylethyl)-1H-imidazole-5-carboxylic acid ethyl ester; CAS 33125-97-2; molecular formula C₁₄H₁₆N₂O₂; molecular weight 244.29) is an imidazole intravenous induction anesthetic developed at Janssen and approved by the FDA in 1972 (Amidate). The compound is a GABA-A receptor positive allosteric modulator with a binding site at the beta-2 and beta-3 subunits that produces preferential activity at extrasynaptic and synaptic GABA-A receptors. Distinct among IV anesthetics by minimal cardiovascular effects (preserved blood pressure and heart rate), making it preferred for patients with hemodynamic instability. The principal limitation is dose-dependent inhibition of 11-beta-hydroxylase (CYP11B1), the final enzyme in cortisol biosynthesis; even a single induction dose suppresses cortisol for 4 to 6 hours, with potential clinical consequence in critically ill patients. Plasma half-life is approximately 2 to 5 hours. Used as a reference IV anesthetic with cardiovascular stability and adrenocortical suppression.

1. Compound Identification

Etomidate is described as gaba-a receptor positive allosteric modulator (intravenous anesthetic). An imidazole intravenous induction anesthetic; cardiovascular stable but causes adrenocortical suppression.

1.1 Class summary

GABA-A receptor positive allosteric modulator (intravenous anesthetic)

1.2 Subtitle

An imidazole intravenous induction anesthetic; cardiovascular stable but causes adrenocortical suppression.

2. Abstract

Etomidate ((R)-1-(1-phenylethyl)-1H-imidazole-5-carboxylic acid ethyl ester; CAS 33125-97-2; molecular formula C₁₄H₁₆N₂O₂; molecular weight 244.29) is an imidazole intravenous induction anesthetic developed at Janssen and approved by the FDA in 1972 (Amidate). The compound is a GABA-A receptor positive allosteric modulator with a binding site at the beta-2 and beta-3 subunits that produces preferential activity at extrasynaptic and synaptic GABA-A receptors. Distinct among IV anesthetics by minimal cardiovascular effects (preserved blood pressure and heart rate), making it preferred for patients with hemodynamic instability. The principal limitation is dose-dependent inhibition of 11-beta-hydroxylase (CYP11B1), the final enzyme in cortisol biosynthesis; even a single induction dose suppresses cortisol for 4 to 6 hours, with potential clinical consequence in critically ill patients. Plasma half-life is approximately 2 to 5 hours. Used as a reference IV anesthetic with cardiovascular stability and adrenocortical suppression.

3. Mechanism of Action

GABA-A receptor positive allosteric modulator at beta-2/3 subunit binding site. Cardiovascular stable. Inhibits 11-beta-hydroxylase, suppressing cortisol synthesis.

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 induction 0.2 to 0.6 mg/kg IV.

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. Forman SA. Clinical and molecular pharmacology of etomidate. Anesthesiology 2011.
2. Cuthbertson BH, et al. The effects of etomidate on adrenal responsiveness and mortality in patients with septic shock. Intensive Care Med 2009.
3. Vanlersberghe C, Camu F. Etomidate and other non-barbiturates. Handb Exp Pharmacol 2008.

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.