World Health Organization

Pre-Review Report:

Etomidate

Expert Committee on Drug Dependence

This report contains the views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization

Contents

Executive Summary

Etomidate is a potent non-benzodiazepine sedative-hypnotic which acts as a positive allosteric modulator of the GABA receptor, a major inhibitor neurotransmitter in the central nervous system. Etomidate is an intravenous anesthetic with notably selective action on the $GABA_A$ receptor. Etomidate also acts as an agonist at α2-adrenoceptors, which may account for its relative lack of effect on cardiovascular function.

Etomidate was first introduced into clinical use in 1972 and is now marketed world-wide as an intravenous anesthetic. Trade names include Amidate, Hypnomidate, and Tomvi. Therapeutic advantages of etomidate include rapid onset of action, short duration of action, and limited effect on hemodynamic function. These characteristics led to its widespread use as a short-term anesthetic for medical procedures such as endotracheal intubation and endoscopy, especially in critically ill or hemodynamically compromised patients. The estimated value of the global market for etomidate in 2025 ranges from US$85.7 million to US$2.3 billion, a range that cannot be explained without access to the proprietary underlying data and methodology. Other short-acting intravenous anesthetics, such as propofol and ketamine, have replaced etomidate as a first-line choice in many clinical situations but etomidate is still recommended by some medical specialty society clinical guidelines and expert reviews.

Etomidate is also recommended as immediate treatment for patients with severe, acute Cushing's disease (excess of adrenocorticosteroids) who are unable or unwilling to take oral medication. Etomidate is effective for this condition because it is an inhibitor of 11β-hydroxylase, a key enzyme in the pathway of adrenocortical steroid synthesis. A single bolus dose of etomidate reduces adrenocorticosteroid levels for 6-8 hours, although the clinical consequences of this reduction are unclear. Etomidate is no longer used as a long-term infusion to maintain surgical anesthesia because of concern over etomidate-induced adrenocorticoid steroid suppression. Etomidate is not on the WHO list of essential medications, but is on the essential medications list of several African and Asian nations.

Etomidate has poor water solubility so is marketed for intravenous use as a 0.2% solution in 35% propylene glycol or as a lipid emulsion. Etomidate is rapidly taken up into highly vascularized tissue and readily crosses the blood-brain barrier due to its high lipid solubility. Etomidate is metabolized by hepatic esterases into the inactive metabolite etomidate acid, which is excreted largely in the urine, with a small amount in the bile. Only 2% of administered etomidate is excreted unchanged. The elimination half-life of etomidate is 2-5 hours in adults.

The typical intravenous dose of etomidate for anesthesia induction is 0.2-0.3 mg/kg. Initial hypnotic effects are seen within 2 minutes; loss of consciousness occurs within 6 minutes. Etomidate does not possess intrinsic analgesic effects. Etomidate, at recommended doses, does not have clinically significant effects on cardiovascular function.

The commonest adverse reactions with therapeutic use of intravenous etomidate are myoclonus (up to 80% of cases), pain at the injection site (50-70% of cases), nausea and vomiting (20-30% of cases), dyskinesia. Myoclonus can vary from brief, mild muscle fasciculations or tremor to

involuntary jerky limb movements to tonic-clonic muscle contractions throughout the body, which sometimes mimic a seizure.

Non-medical (recreational) use of etomidate is almost exclusively by inhalation, either by smoking tobacco cigarettes to which etomidate powder or, more commonly, by inhaling e-cigarette cartridges containing etomidate. Etomidate-containing e-cigarettes are commonly termed K-pods (which may contain etomidate, pharmacologically active etomidate analogues [metomidate, propoxate, isopropoxate], ketamine, or a combination of these substance), space oil, dizzy smoke, dizzy e-cigarette, zombie cigarettes, or zombie juice ("zombie" comes from the involuntary jerky movements often associated with etomidate use. Non-medical etomidate use is largely confined to East and Southeast Asia. It was first identified in Korea in 2011, after propofol was made a controlled substance. Similar non-medical use of etomidate was first reported in China after stricter controls were placed on synthetic cannabinoids in 2021. Non-medical use of vaporized etomidate first appeared in Hong Kong and Taiwan in 2023; in Cambodia, Indonesia, Malaysia, Singapore, and Thailand in 2024; in Japan and New Zealand in 2025; and in Vietnam in 2026.

There are no population-based data on the prevalence of non-medical use of etomidate. Low-quality information comes from counts of cases that come to medical or law enforcement attention. This information suggests that the majority of cases occur in East or Southeast Asia. There are 712 reports involving etomidate received by the UNODC tox-portal from 2019-2025: 700 from Singapore (98 in 2024, 602 in 2025), 5 from the United States (1 in 2024, 4 in 2025), 4 from the Republic of Korea (all 2024), and 3 from the Hong Special Administrative Region of China (all 2025). The Peoples Republic of China reported 29,000 cases of etomidate "misuse" in the fourth quarter of 2023, with 21,000 being new users. The Hong Kong Central Registry of Drug Abuse recorded 1,106 people who use etomidate nonmedically from 2024 through the first quarter of 2026; almost two-thirds (62%) were younger than 21 years The Health Sciences Authority of the Singapore Ministry of Health issued about 7,000 fines for possession or use of e-vaporizers containing etomidate in 2023 and more than 14,000 such fines in 2024 (Singapore Ministry of Health, 2025).

In contrast to East and Southeast Asia, there are few reports of non-medical etomidate use from the rest of the world. In North America, there are few reports of non-medical use of etomidate over the past six years. The UNODC tox-portal received 5 etomidate-related reports from the US in 2024-2025 and none from Canada or Mexico. The US National Forensic Laboratory Information System received eight drug case reports mentioning etomidate from 2020-2025: (out of about 1 million cases annually). Health Canada's Drug Analysis Service received 21 reports of etomidate in samples from January 2023 through June 2025. In the UK, the National Crime Agency reported five seizures of etomidate powder (either alone or with heroin) in 2023 and 11 seizures in 2024, either in powder form (sometimes with heroin) or in tablet form (sometimes with bromazolam).

No human pharmacological (pharmacokinetic or pharmacodynamic) studies using inhaled etomidate, which is the primary route of administration for non-medical use, were identified. Available information comes from retrospective case reports of individuals who came to medical or law enforcement and thus are probably not representative of the full spectrum of users. In addition, users typically do not know what they are inhaling, as illicit e-cigarette cartridges or pods

(K-pods) are not accurately labeled or marketed and may contain etomidate, etomidate analogues, ketamine, methamphetamine, or a combination of these substances. This uncertainty complicates the attribution of observed effects to a specific chemical. A chemical analysis of 496 e-liquid samples seized by law enforcement agencies in eastern Taiwan between January and July 2025 found that 401 (80.8%) samples contained at least one psychoactive substance. Among these 401 positive samples, 349 (87%) were positive for etomidate. Among the 349 etomidate-positive samples, 251 (72%) were positive for etomidate only and 98 (28%) were also positive for one or more other psychoactive substances. Among the 98 samples containing multiple substances, 56 (57%) contained etomidate plus one or two pharmacologically active etomidate analogues (39 etomidate + isopropoxate, 10 etomidate + propoxate, 7 etomidate + isopropoxate + metomidate), 25 (26%) contained etomidate + ketamine, 10 (10%) etomidate + methamphetamine, and 7 (7%) etomidate + isopropoxate + methamphetamine.

Limited information about typical dosages of non-medical etomidate use was identified. Among a case series of 103 inpatients admitted to the Hunan Kangda Voluntary Drug Rehabilitation Center, Hunan, China and diagnosed with etomidate dependence syndrome between March and July 2023, the number of e-cigarette cartridges used varied from 3-4 times per week to five cartridges daily.

No controlled studies evaluating the abuse or dependence potential of etomidate in humans were identified. Available information about dependence comes from retrospective reports of patients, with the majority from China. The largest case series was 560 people voluntarily admitted as inpatients to the Hunan Kangda Voluntary Drug Rehabilitation Center, Hunan, China between March and July 2023 who used only etomidate (by inhalation) and had no history of other “drug abuse” for the prior 3 years. Almost one-fifth (18.4%) of patients met ICD-10 criteria for etomidate dependence, as assessed by clinical staff. All met criteria for tolerance and increasing quantity/frequency of use. Four-fifths (81.6%) of patients had harmful use of etomidate by ICD-10 criteria. Etomidate-associated harms included injuries from falls and motor vehicle accidents (26.8%), hypokalemia (15.54%), menstrual disorders (51.7% of female patients), aggressive or impulsive behavior (10.2%), weight loss of more than 5 kg (5.5%), and darkened skin (3.6%). A small number (not specified) had memory impairment, irritability, or apathy. No patient had hallucinations or delusions. A case series of 11 male patients were treated at Guangzhou Huayou Hospital, Guangzhou, China from May 1 to July 31, 2022 for effects from using etomidate “smoke powder”, with the duration of etomidate use ranging from 3 to 12 months. All 11 patients met ICD-10 criteria for etomidate dependence syndrome (no specific diagnostic criteria mentioned). Etomidate-associated harms included irritability and aggressiveness (all 11 patients), drowsiness (all 11 patients), anxiety (6), fall injuries (6), burns (2), repeated vomiting (2), and paranoia (1). Within one week after stopping etomidate use, six patients experienced mild to moderate anxiety. No patients experienced physical withdrawal symptoms.

No studies evaluating the dependence potential of etomidate in animals were identified. Two studies evaluating the abuse potential were identified. Both studies found that intraperitoneal administration of etomidate promoted conditioned place preference (CPP) in rodents; one study found that intraperitoneal etomidate sustained self-administration in rats. Both the CPP test and

drug self-administration are validated, widely used methods for evaluating the abuse potential of substances in animals.

No controlled studies of adverse reactions to inhaled etomidate in humans were identified. Case reports suggest that inhaled etomidate can cause muscle tremors, unsteady gait, bradykinesia, blurred vision, dizziness, nausea, and vertigo. Among the 712 etomidate cases reported to the UNODC tox-portal from 2019-2025, “common manifestations” included drowsiness or lethargy, confusion, anxiety, depression, emotional instability, psychotic symptoms (e.g., hallucinations), suicidality, aggression, agitation or restlessness, tremors or shaking, abnormal movements, unsteady gait, and slurred speech. “Clinically significant” medical effects were less common and included seizures, cardiac arrest, hypertension, tachycardia, bradycardia, syncope, injury from falls or traffic accidents (including head injury), and adrenal insufficiency. At least 8 deaths from etomidate ingestion have been reported in the published literature: 4 from China, 2 from the United States, and one each from Poland and South Korea. One case involved unintended iatrogenic administration of etomidate (United States) and one involved diazepam and morphine (Poland), so the attribution to etomidate is unclear. The UNODC tox-portal recorded 32 deaths associated with (not necessarily caused by) etomidate: 4 from the United States and 28 from Singapore.

No information was identified regarding industrial use of etomidate, the illicit manufacture of etomidate or ease of converting to a controlled substance.

Etomidate is not currently under international control nor has it previously been considered for control by the WHO ECDD. Six countries in East and Southeast Asia (China, Indonesia, Japan, South Korea, Taiwan, Thailand), as well as Hong Kong and New Zealand, have placed etomidate under strict control over the past 3 years because of increasing levels of non-medical use.

1. Substance identification

A. International Nonproprietary Name (INN)

Etomidate

B. Chemical Abstract Service (CAS) Registry Number

33125-97-2 (R enantiomer racemate)
56649-47-9 (S enantiomer)
15301-65-2 (racemate)

C. Other Chemical Names

- 1H-Imidazole-5-carboxylic acid, 1-(1-phenylethyl)-, ethyl ester, (R)-
- Imidazole-5-carboxylic acid, 1-(α-methylbenzyl)-, ethyl ester, (R)-(+)
- (+)-Etomidate
- (R)-Ethyl 1-(1-phenylethyl)-1H-imidazole-5-carboxylate
- Ethyl 1-[(1R)-1-phenylethyl]-1H-imidazole-5-carboxylate
- 1H-Imidazole-5-carboxylic acid, 1-[(1R)-1-phenylethyl]-, ethyl ester
- D-Etomidate
- d-Etomidate
- R-(+)-Etomidate

D. Trade Names

Etomidate has been marketed under several trade names in different countries and formulations. Amidate is a well-established trade name in the United States for an injectable formulation containing etomidate 2 mg/mL (DailyMed, 2026a). Hypnomidate is another established trade name for etomidate 2 mg/mL injection and has been marketed in several European countries, including the United Kingdom (Electronic Medicines Compendium, 2024). The spelling Hypnomidat also occurs in the European clinical literature as a trade name for etomidate (Christensen et al., 1986). Tomvi is a Canadian trade name for an injectable etomidate product containing 2 mg/mL (DIN 02498650) (Health Canada, n.d.). Etomidate is also available as a lipid-emulsion formulation under the trade name Etomidate-Lipuro, with corresponding national variants including Etomidato-Lipuro and Etomidaat-Lipuro (Agencia Española de Medicamentos y Productos Sanitarios, n.d.). Radenarcon is a historical trade name for etomidate documented in European clinical literature (Hohlfeld, 1987). In addition, Propiscin is an etomidate-containing formulation used as a veterinary anaesthetic in aquaculture and should therefore be distinguished from pharmaceutical products intended for human use (Rożyński et al., 2018).

E. Street Names

Etomidate-containing illicit vaping products are marketed under several regional street names, particularly in East and Southeast Asia. Reported names include Kpod/K-pod (Singapore: Lian et al., 2026; Ministry of Health Singapore, 2025); space oil/space oil drug

and headrush e-cigarette (Hong Kong: Narcotics Division, Security Bureau, Hong Kong Special Administrative Region Government, 2025; United Nations Office on Drugs and Crime [UNODC], 2025a); space vape (Australia: Victoria Department of Health, 2026); dizzy smoke/dizzy e-cigarette (mainland China: Wang et al., 2025); zombie cigarette (Thailand: Advisory Council on the Misuse of Drugs [ACMD], 2026); and zombie vape, zombie vape pod/cartridge, and zombie vape juice (Taiwan: Taiwan High Prosecutors Office, Ministry of Justice, 2026; Workforce Development Agency, Ministry of Labor, Taiwan, 2026).
Additional local terms reported by Taiwanese authorities include sleep vape pod/cartridge, anaesthetic vape pod/cartridge, one-puff dizzy, sleep-aid vape pod, etomidate vape pod, and headrush smoke (Taiwan High Prosecutors Office, Ministry of Justice, 2026).

F. Physical Appearance

Pure etomidate is a white or almost white powder, as specified in the European Pharmacopoeia (European Pharmacopoeia, n.d.).
In the non-medical drug market, etomidate is most commonly encountered in e-liquids and vape cartridges intended for use in electronic vaporisers, particularly in East and Southeast Asia (UNODC, 2025a; UNODC, 2026a). In a forensic study of 70 seized e-liquid samples from 12 cases, etomidate-containing products were described as colourless or tawny liquids packaged in cartridges (Li et al., 2024).
Less frequently, etomidate has also been reported in solid forms, including tablets, powders and crystalline materials (UNODC, 2025a; UNODC, 2026a).

G. WHO Review History

Etomidate has not been considered by the WHO Expert Committee on Drug Dependence for international control.

2. Chemistry

A. Chemical Name

Racemate

IUPAC Name: ethyl 3-[1-phenylethyl]imidazole-4-carboxylate
CA Index Name: 1H-Imidazole-5-carboxylic acid, 1-(1-phenylethyl)-, ethyl ester
Canonical SMILES: CCOC(=O)C1=CN=CN1C(C)C2=CC=CC=C
InChI: InChI=1S/C14H16N2O2/c1-3-18-14(17)13-9-15-10-16(13)11(2)12-7-5-4-6-8-12/h4-11H,3H2,1-2H3
InChIKey: NPUKDXXFDDZOKR-UHFFFAOYSA-N

R enantiomer

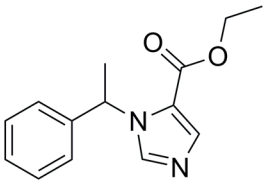
IUPAC Name: ethyl 1-[(1R)-1-phenylethyl]-1H-imidazole-5-carboxylate
CA Index Name: 1H-Imidazole-5-carboxylic acid, 1-[(1R)-1-phenylethyl]-, ethyl ester

Canonical SMILES: CCOC(=O)C1=CN=CN1[C@H](C)C2=CC=CC=C2
InChI: InChI=1S/C14H16N2O2/c1-3-18-14(17)13-9-15-10-16(13)11(2)12-7-5-4-6-8-12/h4-11H,3H2,1-2H3/t11-/m1/s1
InChIKey: NPUKDXXFDDZOKR-LLVKDONJSA-N

S enantiomer

IUPAC Name: ethyl 1-[(1S)-1-phenylethyl]-1H-imidazole-5-carboxylate
CA Index Name: 1H-Imidazole-5-carboxylic acid, 1-[(1S)-1-phenylethyl]-, ethyl ester
Canonical SMILES: CCOC(=O)C1=CN=CN1[C@@H](C)C2=CC=CC=C2
InChI: InChI=1S/C14H16N2O2/c1-3-18-14(17)13-9-15-10-16(13)11(2)12-7-5-4-6-8-12/h4-11H,3H2,1-2H3/t11-/m0/s1
InChIKey: NPUKDXXFDDZOKR-NSHDSACASA-N

B. Chemical Structure

Free base: 

Molecular Formula: $C_{14}H_{16}N_2O_2$
Molecular Weight: 244.289 g/mol

C. Stereoisomers

Etomidate contains a single stereogenic centre in the 1-phenylethyl moiety and can therefore exist as two enantiomers, R-(+)-etomidate and S-(−)-etomidate. The etomidate used for medicinal purposes is the R-enantiomer as it is pharmacologically more potent than the S-(−)-enantiomer (Tomlin et al., 1998; Valk and Struys, 2021). The European Pharmacopoeia (n.d.) defines etomidate as ethyl 1-[(1R)-1-phenylethyl]-1H-imidazole-5-carboxylate.

Etomidate is a fully synthetic imidazole derivative. The original route, developed by Janssen in the 1960s, involved a multistep synthesis of the imidazole-5-carboxylate scaffold from a 1-phenylethylamine derivative and initially afforded racemic material containing both R- and S-enantiomers (Godefroi et al., 1965; Godefroi and Van der Eycken, 1964; Vega Alanis et al., 2020). Because the clinically relevant form is the more active R-(+)-enantiomer, subsequent work focused first on resolution of the racemate and later on stereocontrolled synthetic approaches that allowed preparation of highly enantiomerically enriched material (Heykants et al., 1975; Roevens et al., 1977; Vega Alanis et al., 2020; Zolle et al., 2008). More recent routes have introduced alternative oxidation steps, preformed imidazole scaffolds and chiral starting materials, demonstrating that etomidate can be

prepared through several distinct synthetic strategies (A synthetic method of etomidate, 2024; Vega Alanis et al., 2020).

Etomidate found on the illicit market may originate either from diversion of legitimate pharmaceutical products or active pharmaceutical ingredient, or from illicit manufacture. UNODC has reported evidence suggesting that at least part of the etomidate circulating in East and Southeast Asia is illegally produced rather than solely diverted from legal sources (2025a). In December 2024, Thai authorities seized approximately 2,200 L and 250 kg of chemicals, together with production equipment, from a Bangkok facility reportedly capable of supporting the manufacture of about 200 kg of etomidate; the case was subsequently cited by the UK ACMD as evidence of large-scale illicit synthesis (ACMD, 2026; UNODC, 2025a).

Despite the availability of several published synthetic routes, etomidate cannot be considered a simple drug to manufacture. Its preparation requires multiple synthetic and purification steps, and production of material comparable with pharmaceutical etomidate additionally requires control of both chemical and stereochemical purity (Godefroi et al., 1965; Godefroi and Van Der Eycken, 1964; Heykants et al., 1975 Roevens et al., 1977; Vega Alanis et al., 2020; Zolle et al., 2008). Nevertheless, the identification of clandestine production facilities demonstrates that manufacture is technically feasible for organised illicit laboratories with suitable precursors, equipment and synthetic expertise (UNODC, 2025a; UNODC, 2026a).

D. Chemical Properties

Melting point: 67 °C (153 °F)

Boiling point: 392 °C (738 °F)

Solubility: Etomidate is a weak base (pKa = 4.5), and is therefore hydrophobic at physiological pH (7.4) and very poorly soluble in water (Valk and Struys, 2021). Commercially available etomidate for approved medical use is available as a 0.2% solution in 35% propylene glycol or as a lipid emulsion (Valk and Struys., 2021).
According to the European Pharmacopoeia (n.d.), etomidate is very slightly soluble in water and freely soluble in ethanol (96%) and methylene chloride.

E. Identification and Analysis

Analytical methods for etomidate depend on the matrix examined. Chromatographic techniques coupled with mass spectrometry represent the principal confirmatory approaches, although etomidate is not routinely included in all toxicological screening panels and targeted analysis may therefore be required (ACMD, 2026).

Pharmaceutical substances

For pharmaceutical-grade etomidate, the European Pharmacopoeia specifies identification by infrared spectroscopy, a specific optical rotation of +67 to +70, liquid chromatography

with UV detection at 235 nm for related substances, and non-aqueous titration for assay (European Pharmacopoeia, n.d.). Because medicinal etomidate is the R-enantiomer, stereochemical purity is also relevant; a validated dual-cyclodextrin capillary electrophoresis method permits determination of S-etomidate at approximately 0.05% (w/w), corresponding to the reported quantification level for this enantiomer (Hammitzsch et al., 2006).

Seized materials

For seized materials, particularly e-liquids and vape cartridges, GC-MS and rapid mass-spectrometric techniques are widely used.

Thermal Desorption–Electrospray Ionization Tandem Mass Spectrometry (TD-ESI-MS/MS) can analyse etomidate, metomidate and isopropoxate with no sample pretreatment in approximately 1 min and was successfully applied to 70 seized e-liquid samples from 12 cases, with qualitative results fully concordant with confirmatory GC-MS (Li et al., 2024). The method was developed primarily for qualitative screening and reported a detection limit of 3 ng/mL rather than a formal LOQ (Li et al., 2024).

Probe Electrospray Ionization–Quadrupole Time-of-Flight Mass Spectrometry (PESI-QTOF-MS) permits qualitative and quantitative analysis in approximately 0.3 min and was applied to 38 authentic positive e-liquid samples; the reported LOD and LOQ were 20 and 50 ng/mL, respectively, for the investigated compounds (Lin et al., 2025).
Full-scan GC-MS has also been used for large-scale surveillance of 496 seized e-liquids (Lin, 2026).

LC-Q-Orbitrap-MS/MS, GC-QTOF-MS and NMR have been used to characterise eight etomidate analogues, including previously unreported compounds (Fan et al., 2025), while SERS has been investigated as a rapid preliminary screening method for e-liquids with a reported detection limit of approximately 17 ppb, although no formal validated LOQ was provided (Mo et al., 2024).

Biological specimens

In biological specimens, LC-MS/MS and UHPLC-MS/MS are the principal analytical approaches. Both etomidate and its major hydrolysis metabolite, etomidate acid, should preferably be monitored.

A validated UHPLC-MS/MS method was applied to blood and urine from 62 authentic forensic cases (Zhou et al., 2024). The reported LOQs were 1 ng/mL for etomidate and 5 ng/mL for etomidate acid in blood, and 2 ng/mL and 5 ng/mL, respectively, in urine (Zhou et al., 2024). Another UPLC-MS/MS method simultaneously determined etomidate, etomidate acid, metomidate, propoxate and isopropoxate in blood from six authentic forensic cases (Qian et al., 2025). For this method, the LOQ was 0.1 ng/mL for etomidate, metomidate, propoxate and isopropoxate, and 1 ng/mL for etomidate acid (Qian et al., 2025).

A more recent urine method covered etomidate and 12 structural analogues, including separation of structural isomers, and was applied to 37 authentic urine samples; reported LOQs ranged from 1 to 10 ng/mL depending on the analyte (Qian et al., 2026).

Etomidate acid is particularly important in urine because it may occur at substantially higher concentrations than the parent drug (Jung et al., 2019; Zhou et al., 2024). In the dilute-and-shoot LC-MS/MS method of Jung et al. (2019), the LOQs were 0.4 ng/mL for etomidate and 1.0 ng/mL for etomidate acid.

Hair analysis provides a longer retrospective detection window. A validated UHPLC-MS/MS method for etomidate, etomidate acid, metomidate, propoxate and isopropoxate identified 56 positive authentic hair samples (Pei et al., 2024). Depending on the analyte, reported LOQs ranged from approximately 5 to 20 pg/mg of hair (Pei et al., 2024).

Chiral analysis may provide additional forensic information. A chiral UHPLC-MS/MS method applied to 98 authentic hair specimens separately quantified R- and S-etomidate and R- and S-metomidate. The reported LOQ was 10 pg/mg for the individual enantiomers (Zhang et al., 2026). Etomidate enantiomeric fractions ranged from 0.40 to 1.00, and S-etomidate was detected together with R-etomidate in 8 samples, findings considered compatible with exposure to racemic or incompletely refined material (Zhang et al., 2026). However, enantiomeric composition alone cannot establish the origin or synthetic route of a seized product.

Rapid screening approaches are also emerging. Ambient flame ionisation mass spectrometry can analyse urine in less than 0.2 min without sample preparation and was applied to 116 authentic urine samples, 75 of which were positive (Lin et al., 2026). Because this method was developed primarily as a rapid targeted/non-targeted screening procedure, a conventional quantitative LOQ was not reported (Lin et al., 2026). A fluorescent microsphere-based lateral-flow immunoassay provides results for etomidate and metomidate in approximately 10 min (Liu et al., 2025), although the study reported quantitative working ranges and visual cut-off values rather than a conventional analytical LOQ (Liu et al., 2025). An Aggregation-Induced Emission Enzyme-Linked Immunosorbent Assay (AIE-ELISA) has achieved a reported LOD of 3.52 ng/mL in artificial urine and saliva (Liu et al., 2025). These techniques are promising for preliminary screening, whereas chromatographic separation coupled with mass spectrometric detection remains the more established approach for definitive forensic identification and quantification.

3. Ease of Convertibility into Controlled Substances

No information was found regarding convertibility of etomidate into controlled substances.

4. General Pharmacology

A. Routes of administration and dosage

Etomidate is approved for medical use as a liquid for intravenous administration, either dissolved in 35% polyethylene glycol or as a lipid emulsion (Valk and Struys, 2021). The typical intravenous dose for anesthesia induction is 0.2-0.3 mg/kg (Valk and Struys, 2021). Etomidate is also readily absorbed through the oral and rectal mucosa but is not used clinically via this route (ACMD, 2026).

Etomidate for non-medical (recreational) use is self-administered via inhalation, either by adding etomidate powder to tobacco cigarettes, which are then smoked, or by adding etomidate to the oil used in e-cigarette pods, which are vaporized for inhalation (Wenfu et al., 2024). Almost all (98%) of the 712 cases of non-medical etomidate use reported to the UNODC tox-portal from 2019 to 2025 used etomidate via inhalation (UNODC, 2026b). Users typically do not know what they are inhaling, as illicit e-cigarette cartridges or pods (K-pods) are not accurately labeled or marketed and may contain etomidate, etomidate analogues, ketamine, methamphetamine, or a combination. This uncertainty complicates the attribution of observed effects to a specific chemical.

A chemical analysis of 70 e-cigarette cartridges (from 12 cases) seized by police in Fuzhou, China (dates not given) found that 46 (66%) contained etomidate only, 13 (19%) contained isopropoxate (pharmacologically active etomidate analogue), and 11 (16%) contained etomidate plus metomidate (pharmacologically active etomidate analogue) (Li et al., 2024). A chemical analysis of 496 e-liquid samples seized by law enforcement agencies in eastern Taiwan between January and July 2025 found that 401 (80.8%) samples contained at least one psychoactive substance (Lin, 2026). Among these 401 positive samples, 349 (87%) were positive for etomidate. Among the 349 etomidate-positive samples, 251 (72%) were positive for etomidate only and 98 (28%) were also positive for one or more other psychoactive substances. Among the 98 samples containing multiple substances, 56 (57%) contained etomidate plus one or two pharmacologically active etomidate analogues (39 etomidate + isopropoxate, 10 etomidate + propoxate, 7 etomidate + isopropoxate + metomidate), 25 (26%) contained etomidate + ketamine, 10 (10%) etomidate + methamphetamine, and 7 (7%) etomidate + isopropoxate + methamphetamine.

Limited information about typical dosages of non-medical etomidate use was found. Among a case series of 103 inpatients admitted to the Hunan Kangda Voluntary Drug Rehabilitation Center, Hunan, China and diagnosed with etomidate dependence syndrome between March and July 2023, the number of e-cigarette cartridges used varied from 3-4 times per week to five cartridges daily (Wenfu et al., 2024).

B. Pharmacokinetics

Etomidate is well absorbed via intravenous, oral transmucosal and rectal routes of administration (Valk and Struys, 2021). All published human pharmacokinetic studies are

based on intravenous administration to patients. No human pharmacokinetic studies using inhalation of vaporized etomidate, which is the primary route of administration for non-medicinal (recreational) use, were identified.

Etomidate is 75% protein-bound in plasma, almost exclusively to albumin (Valk et al., 2021). It is rapidly taken up into highly vascularized tissue and readily crosses the blood-brain barrier due to its high lipid solubility (Zheng et al., 2025). Etomidate then more slowly redistributes into other tissues, especially muscle (Zheng et al., 2025). Etomidate has a relatively large volume of distribution (4.7 L/kg in one study) due to its high lipid solubility (Valk and Struys, 2021). The volume of distribution may vary with body weight.

Etomidate is metabolized by hepatic esterases into etomidate acid, an inactive, hydrophilic carboxylic acid metabolite which is excreted largely in the urine, with a small amount in the bile (Valk et al., 2021). Only 2% of administered etomidate is excreted unchanged. The plasma clearance rate is 15-20 ml/kg/min (Zheng et al., 2025). The elimination half-life of etomidate is 2-5 hours in adults (Valk and Struys, 2021). Older adults have a smaller initial volume of distribution and delayed clearance (due to reduced protein binding) of etomidate, making them more sensitive to standard doses. Etomidate probably crosses the placenta and is excreted in breast milk (ACMD, 2026).

C. Pharmacodynamics

Etomidate's primary action is as a selective positive allosteric modulator of the gamma-aminobutyric acid type A ($GABA_A$) receptor, influencing only receptors containing β2 or β3 subunits (Valk and Struys, 2021). This positive allosteric modulation enhances the effect of the neurotransmitter GABA on the receptor. The $GABA_A$ receptor is the major inhibitory neurotransmitter receptor in the mammalian central nervous system (CNS). By enhancing the intrinsic activity (efficacy) of GABA at this receptor, etomidate enhances CNS inhibition. Etomidate is the only major intravenous anesthetic that has such selective action on the $GABA_A$ receptor (Valk and Struys, 2021). Etomidate has relatively limited cardiovascular effects compared with many other intravenous anesthetics (see below).

All published studies of the human pharmacodynamics of etomidate used the intravenous route of administration. No human pharmacodynamic studies using inhalation of vaporized etomidate, which is the primary route of administration for non-medical (recreational) use, were identified.

The typical intravenous dose for anesthesia induction is 0.2-0.3 mg/kg (Valk and Struys, 2021). Initial hypnotic effects are seen within 2 minutes; with one study reporting a loss of consciousness occurs within 6 minutes. Etomidate does not possess intrinsic analgesic effects (Valk and Struys, 2021). Etomidate, at recommended doses, does not have clinically significant effects on cardiovascular function (Valk and Struys, 2021). Etomidate does not cause hypotension or inhibit myocardial contractility, sympathetic tone or autonomic reflexes such as the baroreflex. Etomidate does not significantly alter major hemodynamic parameters such as heart rate, central venous pressure, pulmonary artery pressure,

cardiac index, and systemic vascular resistance. These characteristics give etomidate a significant clinical advantage over other rapidly acting intravenous anesthetics (e.g., propofol) for use in seriously ill patients, such as those with sepsis, coronary artery disease, or valvular heart disease.

5. Toxicology

A major toxic effect of etomidate is inhibition of enzymes involved in corticosteroid and mineralocorticoid synthesis, which may result in adrenocorticoid insufficiency and hypokalemia (low blood potassium concentration) (Valk and Struys, 2021). Blockage of corticosterioid synthesis may increase androgen secretion, resulting in androgenic signs and symptoms (Lau et al., 2024).

Etomidate inhibits 11β-hydroxylase, a key enzyme in the pathway of adrenocortical steroid synthesis. Inhibition of adrenocortical steroid synthesis can lead to adrenal insufficiency (Valk and Struys, 2021). A single bolus dose of etomidate may cause measurable adrenocortical suppression for 6-8 hours (Lundy et al., 2007), although the clinically significance of these effects is unclear (Valk and Struys, 2021). Enzyme inhibition occurs at etomidate doses lower than those that produce anesthesia. Continuous etomidate infusion may result in adrenocortical suppression lasting more than 24 hours. This effect is used therapeutically for acute treatment of severe Cushing's syndrome (i.e., over-secretion of adrenocorticoids) (Araujo-Castro et al., 2026; Muthukuda et al., 2025; Pence et al., 2022).

Adrenal insufficiency occurs in non-medical users of etomidate. Twenty patients (50% women, ages 18-54 years) at the Princess Margaret Hospital, Hong Kong, China with a spot urine toxicology sample that tested positive for etomidate or propoxate (etomidate analogue) were randomly selected from a pool of 37 such patients to have urine steroid profiling (Cheung et al., 2025). Seven of these patients inhaled etomidate via e-cigarettes; the route of administration for the other 13 patients was unknown. All 20 patients using etomidate had a pattern of urinary steroid excretion similar to that seen in patients with congenital adrenal hyperplasia, i.e., marked increase in the excretion of tetrahydro-11-deoxycortisol (THS) and tetrahydrodeoxycorticosterone (THDOC), which are the metabolites of 11-deoxycortisol and 11-deoxycorticosterone, respectively. THC and THDOC are substrates of 11β-hydroxylase. As expected, excretion of metabolites proximal to THS and THDOC in the steroidogenesis pathway, such as pregnanetriol and pregnanediol, was also significantly increased.

At least 10 other cases of etomidate-induced adrenal insufficiency in non-medical users have been reported in the published literature. Ten cases occurred in individuals (7 men, 3 women, ages 16-38 years, 5 from Hong Kong, 4 from China, 1 from Singapore) who inhaled etomidate via e-cigarettes and came to medical attention because of medical or psychiatric symptoms (Tng et al., 2026). All 10 patients had serum hormone concentrations consistent with adrenal insufficiency, i.e., low cortisol and elevated ACTH concentrations. No other causes of adrenal insufficiency were identified by medical evaluation. In 6 patients with some follow-up, one resolved after 8 months of abstinence from etomidate, 4 cases

resolved after unknown periods, and 1 case persisted over 5 months (with etomidate use status not reported).

Non-medical use of etomidate is associated with increased androgen excretion along with adrenal insufficiency. A 35-year-old woman with a previously normal obstetrical and gynecological history presented to a Hong Kong hospital with dysfunctional uterine bleeding, secondary amenorrhea, and virilization (increased facial hair requiring shaving, acne vulgaris, male-pattern alopecia, and deepening of voice) (Lau et al., 2024). The patient had been inhaling etomidate via e-cigarettes (one-half capsule daily) for the prior 4 months. The presence of etomidate in her urine and e-cigarette oil was confirmed by toxicological testing. No other cause for her androgen syndrome was identified. Her androgenic symptoms persisted over 8 months of follow-up, as did her etomidate use. In a case series of 20 adults whose urine samples tested positive for etomidate at the Princess Margaret Hospital, Hong Kong from December 2023 through July 2024, the median urine concentrations of adrenal androgens (e.g., dehydroepiandrosterone (DHEA), etiocholanone, androsterone, androstenediol) were 5-13-fold greater than normal (Cheung et al., 2025). No evaluation for signs of virilization was reported. All patients had urine steroid profiles consistent with adrenal insufficiency.

Non-medical use of etomidate is associated with hypokalemia, presumably due to disruption of mineralocorticoid synthesis (e.g., aldosterone). Among 45 cases reporting non-medical etomidate use presenting to Hong Kong hospital emergency departments between May-December 2024, 62% had hypokalemia (Wong et al., 2025). Two young adults (29, 32 years old) came to medical attention in Wuhan, China because of sudden onset of muscle weakness with difficulty standing and walking (Wu et al., 2024). Both patients had significant hypokalemia and blood steroid concentrations consistent with adrenal insufficiency (low cortisol, elevated ACTH). Both patients had been inhaling etomidate via e-cigarettes for the past 2 to 4 months. No other cause for the hypokalemia or muscle weakness was identified.

6. Adverse Reactions in Humans

Most information about adverse reactions from etomidate comes from studies of its medical use as an intravenous anesthetic. The commonest adverse reaction is myoclonus, which occurs in up to 80% of cases (Zheng et al., 2025). Myoclonus can vary from brief, mild muscle fasciculations or tremor to involuntary jerky limb movements to tonic-clonic muscle contractions throughout the body, which can sometimes mimic a seizure (Ball and Westhorpe, 2002; Van Keulen and Burton, 2003). Myoclonus occurs 30-60 seconds after bolus intravenous injection of etomidate. Pain at the site of etomidate injection occurs in 50-70% of cases (Zheng et al., 2025). Nausea and vomiting occur in 20-30% of cases (Zheng et al., 2025). Dyskinesia and hypotension are also common (ACMD, 2026).

The US Food and Drug Administration (FDA) Adverse Event Monitoring System (AEMS) has received 18 reports of adverse events associated with etomidate since 2002, including 6

since 2022 (Food and Drug Administration [FDA], 2026). The type of adverse event was not mentioned, nor was the route of administration.

No controlled studies of adverse reactions to inhaled etomidate in humans were identified. Available information comes from case reports of individuals inhaling etomidate who came to medical or law enforcement attention, and those are probably not representative of the full spectrum of individuals using etomidate. The case reports suggest that etomidate can cause muscle tremors and bradykinesia in the hands and arms, blurred vision, and vertigo (Zheng et al., 2025). Among the 712 etomidate cases reported to the UNODC tox-portal from 2019-2025, "common manifestations" (numbers or proportions not provided) included drowsiness or lethargy, confusion, anxiety, depression, emotional instability, psychotic symptoms (e.g., hallucinations), suicidality, aggression, agitation or restlessness, tremors or shaking, abnormal movements, unsteady gait, and slurred speech (UNODC, 2026b). "Clinically significant" medical effects were less common and included seizures, cardiac arrest, hypertension, tachycardia, bradycardia, syncope, injury from falls or traffic accidents (including head injury), and adrenal insufficiency.

A case series of 62 patients seen in the emergency departments of 3 Taiwan hospitals between June and November 2024 had urine toxicology prompted by altered mental status (e.g., drowsiness (27%), delirium (53%)) and tested positive for etomidate or etomidate analogues such as metomidate (Weng et al., 2025). There was poor concordance between self-reported etomidate use and the results of urine toxicology testing. Fifteen patients tested positive for etomidate (2 [15%]) or metomidate (13) and for no other illicit psychoactive drugs. Forty-seven patients tested positive for etomidate (2 [4%]) or an etomidate analogue (metomidate in 57% of these cases) and one or more other illicit psychoactive substance (methamphetamine 66%, synthetic cathinones 38%, ketamine 36%) (Weng et al., 2025). The etomidate or etomidate analogue only group and the etomidate or etomidate analogue plus another psychoactive substance group were similar in clinical characteristics, except that the etomidate or etomidate analogue only group was significantly younger: mean age 21 years (range 19-31 years) vs. 33 years (23-37 years). The two groups were 53% and 66% male, respectively. The initial clinical presentations were delirium (53% and 36%, respectively), drowsiness (27% and 11%, respectively), self-harm/suicide (20% and 36%, respectively), traffic accident (20% and 12%, respectively), violent behavior (13% and 21%, respectively), vomiting (7% and 2%, respectively), and tremor 7% and 2%, respectively). None of the etomidate or etomidate analogue only patients were hospitalized; 11 (23%) of the patients who used etomidate or an etomidate analogue in combination with another illicit psychoactive substance were hospitalized. Of the 11 hospitalized patients, four were admitted to a regular ward and seven to the intensive care unit (ICU): five with altered mental status and two with major trauma due to falls while in a drug-induced delirium. No data were presented separately for the etomidate vs etomidate analogue patients.

Among 20 patients (50% women, ages 18-54 years) at the Princess Margaret Hospital, Hong Kong, China with a spot urine toxicology sample who tested positive for etomidate or propoxate [pharmacologically active etomidate analogue] (randomly selected from a pool

of 37 such patients), the reasons for toxicology testing included substance misuse (7), low mood (4), unstable emotion (2), and one patient each with automobile crash, cellulitis, chest pain, confusion, convulsion, fall injury, and thyroid storm (BP 205/120) (Cheung et al., 2025). No data were presented separately for the etomidate vs. propoxate patients.

A case series of 22 self-reported users of inhaled K-pods (containing either etomidate or ketamine) was identified by searching social media platforms (Google, Instagram, TikTok, YouTube, Reddit, X) from 18 to 23 July 2023 (Lian et al., 2026). The researchers were in Singapore; the locations of the people who used etomidate was not given. Cases ranged in age from 18 to 58 years old. Common self-reported features of K-pod use included unsteady gait (36%), uncontrolled movements (32%), emotional dysregulation (e.g., depression, agitation) (32%), suicidal ideation or self-harm (18%), and nausea and vomiting (9%).

In four motor vehicle collisions in China associated with etomidate use (confirmed by blood toxicology), the driver's acute intoxication was associated with agitation, anxiety, and impaired cognition (Qian et al., 2025).

Police reports from Hainan and elsewhere in China state that individuals who inhale etomidate via e-cigarettes quickly experience dizziness, muscle tremors (especially of hands and arms), nausea, unfocused vision, and unsteady gait (Yu, 2023). Higher doses were associated with anxiety, agitation, irritability, and paranoia.

At least 8 deaths from etomidate ingestion have been reported in the published literature: 4 from China, 2 from the United States, and one each from Poland and South Korea (He et al, 2024; Lo et al., 2025). One case involved unintended iatrogenic administration of etomidate (United States) and one also involved diazepam and morphine (Poland), so the attribution to etomidate is unclear. The UNODC tox-portal recorded 32 deaths associated with (not necessarily caused by) etomidate: 4 from the United States and 28 from Singapore (UNODC, 2026b). Three deaths associated with K-pod use (containing either etomidate or ketamine) were identified in a search of social media platforms from 18 to 23 July 2023 (Lian et al., 2026); these deaths could not be independently confirmed.

7. Dependence Potential

A. Animal Studies

No studies evaluating the dependence potential (i.e., tolerance, withdrawal) of etomidate in animals were identified.

B. Human Studies

No controlled studies evaluating the dependence potential (i.e., tolerance, withdrawal) of etomidate in humans were identified. Information about dependence in humans comes from retrospective reports of patients who come to medical attention because of non-

medical (recreational) use of etomidate. All such reports involve inhalational use via e-cigarettes; the majority come from China.

The largest case series was 560 patients voluntarily admitted as inpatients to the Hunan Kangda Voluntary Drug Rehabilitation Center, Hunan, China between March and July 2023 who used only etomidate (by smoking tobacco cigarettes to which etomidate powder was added or by inhaling e-cigarettes [vapes]) and had no history of other "drug abuse" for the prior 3 years (Wenfu et al., 2024). Patients came from two sources: referral by local police after a qualitative urine toxicology test positive for etomidate and self-referral or referral by relatives. The youngest patient was 13 years old; 15.7% of patients were younger than 18 years old, 73.7% male, 83% unmarried, 51.2% unemployed, and 90% with no more than a high school education. Most (90.7%) reported no previous drug use. All patients inhaled etomidate via e-cigarettes; 32% had started by smoking tobacco cigarettes to which they added etomidate powder. Motivations for etomidate use varied and overlapped: 95% believed that etomidate was harmless because it was a medicine, 91% blamed "temptation," 64.2% peer pressure, and 39.3% curiosity. The majority (61.3%) of patients had been using etomidate less than one month; only 5.4% had been using more than six months, with the longest period of use being three years. Almost one-fifth (18.4%) of patients met ICD-10 criteria for etomidate dependence, as assessed by clinical staff. All met criteria for tolerance and increasing quantity/frequency of use.

A case series of 11 patients (all male) were treated at Guangzhou Huayou Hospital, Guangzhou, China from May 1 to July 31, 2022 for effects from using etomidate "smoke powder", with the duration of etomidate use ranging from 3 to 12 months (Che et al., 2023). Their ages ranged from 16 to 40 years, six were married, none had more than a junior high school education, and all were unemployed (Che et al., 2023). All patients attributed their initial etomidate use to environmental stimuli and peer temptation. The authors state that all 11 patients met ICD-10 criteria for etomidate dependence but the paper provides no information about specific diagnostic criteria. Etomidate-associated harms included irritability and aggressiveness (all 11 patients), drowsiness (all 11 patients), anxiety (6), fall injuries (6), burns (2), repeated vomiting (2), and paranoia (1). Within one week after stopping etomidate use, six patients experienced mild to moderate anxiety. No patients experienced physical withdrawal symptoms.

One case involving etomidate dependence was reported from Taiwan (Lin and Lin, 2024). A 21-year-old woman with dependence on benzodiazepines starting at age 20 years developed etomidate dependence after using one e-cigarette cartridge every 3 days for insomnia, increasing to 3-5 cartridges per day within 2 months (Lin and Lin, 2024). On stopping etomidate use, she developed anxiety, irritability, visual hallucinations, severe mood swings, suicidal ideation and a strong craving for etomidate. She was admitted to a psychiatric ward for a 3-day detoxification treatment, including oxazepam (90 mg/day) and aripiprazole (20 mg/day). Her urine toxicology test showed etomidate acid (major metabolite of etomidate, which is pharmacologically inactive). After discharge, she remained abstinent from etomidate for two weeks under family supervision.

8. Abuse Potential

A. Animal Studies

Two studies evaluating the abuse potential of etomidate in animals were identified. Both studies found that etomidate promoted conditioned place preference (CPP) in rodents; one study found that etomidate sustained self-administration in rats. Both the CPP test and drug self-administration are validated, widely used methods for evaluating the abuse potential of substances in animals.

A study of male rodents evaluated reward using the conditioned place preference (CPP) test and reinforcement using intravenous self-administration (Kuai et al., 2025). Etomidate at 3 mg/kg and 6 mg/kg i.p. produced significant dose-dependent CPP in ICR mice. The lowest dose of 1 mg/kg i.p. had no significant effect; the highest dose of 10 mg/kg i.p. also had no significant effect, likely because it significantly inhibited spontaneous locomotor activity in the open field test. The ED_{50} for inhibition of spontaneous locomotor activity was 2.4 mg/kg. The ED_{50} for loss of righting reflex (a measure of anesthetic action) was 9.2 mg/kg. In the self-administration paradigm, Sprague-Dawley rats could receive an etomidate infusion by poking their nose into a hole. Etomidate sustained significant self-administration (20-30 responses per 4-hour session) at doses of 0.05, 0.075, and 0.10 mg/kg). The lowest dose (0.025 mg/kg) and highest dose (0.125 mg/kg) produced response rates similar to vehicle (0.5% ethanol + Tween80 solution) (5 responses per session). These findings suggest that etomidate has rewarding and reinforcing effects in rodents at doses lower than those that produce sedation or anesthesia.

A study of adult male C57BL/6 J mice found that etomidate—3 mg/kg intraperitoneally daily for 14 days produced a 50% increase in CPP; 1 mg/kg had no significant effect (Ding et al., 2024). The lower etomidate dose decreased open field locomotion by about 25%; the higher etomidate dose decreased open field locomotion by about 80%. There was a significant decrease of the etomidate effect over the 14 days of treatment, suggesting some tolerance to the effect.

In adult Wistar-Kyoto rats subjected to forebrain ischemia for 10 minutes, an etomidate infusion (0.6 mg/kg/min for 10 minutes) reduced extracellular levels in the corpus striatum of dopamine by 30% and of the dopamine metabolites 3,4-dihydroxy-phenylacetic acid (DOPAC) and homovanillic acid (HVA) by 30% and 50%, respectively (Lesser et al., 1999). This finding may be more reflective of a neuroprotective effect of etomidate against ischemic effects than of an action on neuronal dopamine release.

B. Human Studies

No controlled studies of the abuse potential of etomidate in humans were identified. Information about abuse potential in humans comes from retrospective reports of patients who come to medical attention because of non-medical (recreational) use of etomidate. All such reports involve inhalational use via e-cigarettes; the majority come from China.

The largest case series was 560 patients voluntarily admitted as inpatients to the Hunan Kangda Voluntary Drug Rehabilitation Center, Hunan, China between March and July 2023 who used only etomidate (via tobacco cigarettes or e-cigarettes) and had no history of other "drug abuse" for the prior 3 years (Wenfu et al., 2024). See section 7.B. above for more details about this patient cohort. Four-fifths (81.6%) of patients had harmful use of etomidate by ICD-10 criteria (Wenfu et al., 2024). Etomidate-associated harms included injuries from falls and motor vehicle accidents (26.8%), hypokalemia (15.54%), menstrual disorders (51.7% of female patients), aggressive or impulsive behavior (10.2%), weight loss of more than 5 kg (5.5%), and darkened skin (3.6%). A small number (not specified) had memory impairment, irritability, or apathy. No patient had hallucinations or delusions. Psychosocial treatment methods included cognitive behavioral therapy, motivational interviewing, and education about addiction. Medications targeted specific symptoms: antipsychotics for cognitive impairment and insomnia, mood stabilizers, sertraline for depression, buspirone or benzodiazepine for anxiety. Almost two-thirds (63.6%) of patients had been discharged by June, 2023: 91.6% "clinically cured" (stable, good insight into their etomidate abuse, intent not to resume use) and 8.4% improved (reasonably stable, some insight, would make effort not to resume use). Telephone follow-up one month after discharge reached 77.3% of patients: 98.6% were in self-reported remission (abstaining from etomidate use, returned to work or school), 1.4% had resumed etomidate use and re-entered treatment.

9. Therapeutic Applications and Extent of Therapeutic Use and Epidemiology of Medical Use

Etomidate is a non-barbiturate, non-benzodiazepine ultra-short-acting hypnotic that is used intravenously as a quick-onset, short-acting agent for induction of general anesthesia and to provide short-term anesthesia during medical procedures such as endotracheal intubation, endoscopy, bronchoscopy, arthroscopy, dental procedures, and cardiac catheterization (ACMD, 2026; Erdoes et al., 2014). Etomidate is no longer used as a long-term infusion for the maintenance of anesthesia because it suppresses production of adrenocortical hormones, resulting in clinically significant adrenal insufficiency (Valk and Struys, 2021) (see Toxicology above). This action was thought to be associated with increased mortality observed in seriously ill patients receiving etomidate anesthesia in some studies, compared with other anesthetics (Erdoes et al., 2014).

Etomidate was developed in 1964 by Janssen Pharmaceuticals and introduced into clinical use in Europe in 1972, making it the first available non-barbiturate intravenous anesthetic (Valk and Struys, 2021). Etomidate entered the US market in 1983.

Only limited quantitative data on the extent of therapeutic use of etomidate was identified. A prospective survey of 2380 consecutive patients undergoing endotracheal intubation and treated with a neuromuscular blocking agent in the emergency department of 22 hospitals (20 United States, 1 Canada, 1 Asia) from 1997-1999 found that 62% of the rapid sequence intubations used etomidate was the anesthetic agent (Sivilloti et al., 2003).

Other anesthetic agents used included benzodiazepines (18%), barbiturates (7.6%), ketamine (3.1%), and other medications (1.9%). A national, cross-sectional survey of 246 Pakistani anesthesiologists from 196 hospitals that was conducted January to June 2021 found that etomidate was widely used for induction of general anesthesia and during emergency procedures (Malik and Khan, 2023). Almost two-thirds (61.1%) of respondents reported experiencing shortages of etomidate in their practice.

Etomidate is used as a short-term anesthetic agent for medical procedures, especially in patients who are critically ill or hemodynamically unstable. Two medical specialty society clinical practice guidelines recommend etomidate for such use in select patients, although not necessarily as a first-line medication. The Society for Critical Care Medicine gives a conditional recommendation for the use of etomidate during rapid sequence intubation of critically ill adult patients, based on moderate-quality evidence (Acquisito et al., 2023). This recommendation is based on the absence of hemodynamic disturbance with etomidate use, etomidate's low cost and wide availability, and the poor quality of the data suggesting that etomidate increases mortality in critically ill patients. The American College of Emergency Physicians clinical policy on sedation for procedures performed in the emergency department gives a Level B recommendation for use of etomidate in adults (after propofol, a Level A recommendation) and a Level C recommendation for use of etomidate in children (after ketamine, Level A recommendation) (Goodwin et al., 2014). The internal clinical practice guidelines of some hospitals may also mention etomidate as a short-term option for anesthesia during rapid sequence intubation. As an example, the Vanderbilt University Medical Center Guidelines for Rapid Sequence Intubation mention etomidate among four intravenous induction agents (ketamine, propofol, midazolam) that could be used (Dennis, et al. 2020). Etodimate's advantage over other medications is that it causes minimal hemodynamic change.

Etomidate infusion is used as initial treatment for severe Cushing's syndrome (i.e., over-secretion of adrenocorticoids) until definitive treatment (such as surgical removal of an ACTH-secreting tumor) can be undertaken, although it is not approved for this indication by any national regulatory authority (Araujo-Castro et al., 2026; Muthukuda et al., 2025; Pence et al., 2022). Etomidate has an advantage over other available anti-corticosteroid medications in that it is the only one that can be administered intravenously and has a relatively rapid onset of therapeutic effect. Some experts recommend etomidate infusion as first-line treatment of severe Cushing's syndrome in patients who are unable or unwilling to take oral medication or who need prompt reduction in corticosteroid levels (Araujo-Castro et al., 2026; Pence et al., 2022).

Etomidate is occasionally used as the anesthetic for electroconvulsive shock therapy (ECT), although other intravenous anesthetics, such as propofol, methohexital, thiopental, and ketamine, are used more often (Kellner and Bryson, 2014). Etomidate anesthesia is associated with significantly longer seizure duration, although it is unclear whether this provides a significant efficacy advantage (Gurel et al., 2022; Singh et al., 2015; Yoon et al., 2023).

10. Listing on the WHO Model List of Essential Medicines

Etomidate does not appear on the WHO Model List of Essential Medicines for adults (24th edition, September, 2025) or for children (10th edition, September, 2025).

Etomidate appears on the list of essential medications for several Asian and African nations, e.g., Seychelles (Seychelles, 2023), South Africa (National Department of Health, 2019), and Tanzania (The National Essential Medications List [NEMLIT], 2026).

Etomidate appears on the list of essential medications for emergency care (anesthetic for endotracheal intubation) in Africa (Broccoli et al., 2018). This list was developed by consensus among 83 clinicians (61% emergency medicine specialists, 10% non-emergency medicine physicians, 11% emergency nurses, 8% mid-level providers [note that total does not equal 100%]) from 25 countries.

11. Marketing Authorizations (as a Medicinal Product)

Etomidate is approved for medical use by national regulatory authorities in North America, the European Union, and most countries in Asia, Africa, and Latin America.
Etomidate is not approved for medical use in Japan.

12. Industrial Use

No industrial use of etomidate was identified.

13. Non-Medical Use, Abuse and Dependence

Non-medical use of etomidate by inhalation from e-cigarettes was first identified in Korea in 2011, after propofol was made a controlled substance (ACMD, 2026). Similar non-medical use of etomidate was first reported in China after stricter controls were placed on synthetic cannabinoids in 2021 (UNODC, 2025b). Non-medical use of vaporized etomidate first appeared in Hong Kong and Taiwan in 2023; in Cambodia, Indonesia, Malaysia, Singapore, and Thailand in 2024; in Japan (UNODC, 2026c) and in New Zealand in 2025 (High Alert, 2025); and in Vietnam in 2026 (UNODC, 2026c).

14. Nature and Magnitude of Public Health Problems Related to Misuse, Abuse and Dependence

No population-based data on the prevalence of non-medical use of etomidate were identified. Questions about etomidate use are not included in large epidemiological surveys of psychoactive substance use at the national or international levels. Low-quality information about the prevalence of etomidate use comes from counts of cases that come to medical or law enforcement attention. This information suggests that the majority of cases (at least those with some severity) occur in East or Southeast Asia, with few or no cases elsewhere in the world. The largest case series is the 712 reports involving etomidate received by the UNODC tox-portal from 2019-2025: 700 from Singapore (98 in 2024, 602 in 2025), 5 from the United States (1 in 2024, 4 in 2025), 4 from the Republic of Korea (all 2024), and 3 from the Hong Special Administrative Region of China (all 2025) (UNODC, 2026b). These cases were 23.4% female and 76.6% male (109 cases had unknown sex).

Ages ranged from 13-17 years old (11.1%) to 60-79 years old (0.9%) (155 cases had unknown age). Almost half (47.8%) of cases were 25-39 years old; one-fifth were 18-24 years old (20.4%) and 40-59 years old (19.8%).

The Peoples Republic of China reported 29,000 cases of etomidate "misuse" in the fourth quarter of 2023, with 21,000 being new users (Office of National Narcotics Control Commission,China, 2024). Assay of 245 intake samples collected from 31 wastewater treatment plants (WWTP) throughout China from 29 September to 6 October 2023 found that 13 samples from 3 WWTPs tested positive for etomidate (Yuan et al., 2024). One WWTP with etomidate-positive samples mainly treated medical wastewater from hospitals, so the detected etomidate may have been from medical use. The other two WWTPs with etomidate-positive samples mainly treated domestic wastewater from entertainment venues such as bars and dance halls, so the detected etomidate may have come from recreational use.

The Hong Kong Central Registry of Drug Abuse recorded 1,106 people who use etomidate from 2024 through the first quarter of 2026; more than half (58%) were men and almost two-thirds (62%) were younger than 21 years (Hong Kong Government, 2026). There were 232 new cases of etomidate use in 2024 (12.7% of all new cases of psychotropic drug use), 370 new cases in 2025 (21.6% of all new case psychotropic drug use), and 86 new cases in the first quarter of 2026 (19.9% of all new cases of psychotropic drug use). The comparable data for previously known etomidate use was 77 in 2024 (2.4% of all previously known cases of psychotropic drug use), 245 in 2025 (7.9% of previously known cases of psychotropic drug use), and 96 in the first quarter of 2026 (8.9% of previously known cases of psychotropic drug use). The Health Sciences Authority of the Singapore Ministry of Health issued about 7,000 fines for possession or use of e-vaporizers containing etomidate in 2023 and more than 14,000 such fines in 2024 (Singapore Ministry of Health, 2025). The proportion of vape cartridges seized and analyzed in Singapore that contained etomidate was 63.6% in 2024 and 63.8% in 2025 (UNODC, 2026c). Etomidate use accounted for about 5% of all 'drug abuse' cases in Taiwan in 2024 (Thomson, 2024). In 2025, Malaysia found etomidate in 90 analyzed samples and Indonesia in 75 (UNODC, 2026c).

In contrast to East and Southeast Asia, there are few reports of non-medical etomidate use elsewhere in the world. These reports do not provide any information about the number of people using etomidate or the mode of use. In North America, there are few reports of non-medical use of etomidate in the US and Canada over the past 6 years. The UNODC tox-portal received 5 etomidate-related reports from the US in 2024-2025 and none from Canada or Mexico (UNODC, 2026b). In the US, the National Forensic Laboratory Information System (NFLIS) received eight drug case reports mentioning etomidate from 2020-2025: 1 case in 2020, none in 2021-2022, 3 in 2023, 2 in 2024, and 2 in 2025 (NFLIS, 2026). The NFLIS receives about one million drug cases annually. Post-marketing surveillance of 2,496 patients receiving etomidate for medical purposes in the US (presumably for intravenous anesthesia) identified no cases of etomidate abuse (eHealthME, 2026). The US National Drug Early Warning System (NDEWS) web monitoring team found Reddit posts mentioning etomidate from May through September, 2023 (1-2

per month) and from December 2023 through March 2024 (2-7 per month) (National Drug Early Warning System [NDEWS] (2024). Most online commenters did not recommend etomidate for recreational use due to its very short duration of effects. A small number of Reddit users reported the presence of etomidate as an adulterant in heroin supplies. The Philadelphia (Pennsylvania, US) Department of Public Health (PDPH) Surveillance Drug Checking Program detected etomidate in Philadelphia's drug supply in June 2024, in combination with fentanyl and medetomidine (Philadelphia Department of Public Health [PDPH], 2024). This was considered the first detection of illicit etomidate in Philadelphia and possibly the first in the US. The Philadelphia Medical Examiner's Office identified at least one drug overdose fatality that involved etomidate. In Canada, Health Canada's Drug Analysis Service received 21 reports of etomidate in samples from January 2023 through June 2025, all from Ontario and British Columbia (Health Canada, 2026a). Health Canada's Canadian Drug and Substance Watch system of web monitoring detected 27 mentions of etomidate from January 2023 through June 2025 (Health Canada, 2026a). Health Canada's National Wastewater Drug Surveillance initiative identified one sample containing etomidate (from Ontario) from April 2024 through January 2026 (Health Canada, 2026b).

Regarding the European Union, etomidate is not mentioned as an emerging novel psychoactive substance in either the 2025 (European Union Drugs Agency, 2025) or 2026 European Drug Reports (European Union Drugs Agency, 2026). In the UK, the National Crime Agency reported five seizures of etomidate powder (either alone or with heroin) in 2023 and 11 seizures in 2024, either in powder form (sometimes with heroin) or in tablet form (sometimes with bromazolam) (ACDM, 2026). The UK Local Drug Information System reported seizure in June 2023 of 60 green tablets in the East Midlands containing etomidate, bromazolam (a potent benzodiazepine), and protonitazene (a potent synthetic opioid) (ACDM, 2026). The Scottish Prison Service - Leverhulme Research Centre for Forensic Science/Public Health Scotland - Rapid Action Drug Alerts & Response (PHS-RADAR) reported two detections of etomidate powder in 2023 (ACDM, 2026). The Scottish Police Authority reported one detection of etomidate powder in 2023 and one detection of an etomidate vape pen in 2024 (ACDM, 2026). The Public Health Wales WEDINOS drug testing service analyzes anonymous samples submitted by the public. Among the 7744 samples analyzed by WEDINOS from April 2022-March 2023, four contained etomidate (one also contained protonitazene) (ACDM, 2026). Among the 8466 samples analyzed by WEDINOS April 2023-March 2024, five contained etomidate (four also contained protonitazene). No etomidate samples were identified between January, 2024 and January 2026 (ACDM, 2026).

In Oceania, there are single reports of etomidate e-cigarettes identified in New Zealand in 2025 (High Alert, 2025) and of an e-cigarette pod containing etomidate found in Melbourne, Australia in June 2026 (Victoria Department of Health, 2026). The National Drug and Alcohol Research Center of Australia has no reports of non-medical use of etomidate for the past several years (National Drug and Alcohol Research Centre, 2026).

Non-medical use of etomidate is commonly accompanied by use of other psychoactive substances. Among the 712 cases of etomidate use reported to the UNODC tox-portal

from 2019 to 2025, almost three-quarters (71.8%) involved use of at least one other psychoactive substance: methamphetamine (56.9%), ketamine (9.2%), nimetazepam (7.4%), cannabis (7.0%), MDMA (6.6%), heroin (3.1%), 4-MMC (2.5%), 5F-MDMB-PINACA (2.3%), MDMB-4en-PINACA (2.2%) or cocaine (0;8%) (UNODC, 2026b).

15. Licit Production, Consumption and International Trade

Etomidate for medical use is made or distributed by about a dozen pharmaceutical companies, largely in the US, Germany, China, Czech Republic, and India (DailyMed, 2026b).

The estimated value of the global market for etomidate in 2025 ranges from US$85.7 million (ReAnIn, 2026) to US$2.3 billion (Allied Market Research, 2026). This wide difference in estimates cannot be readily explained because the underlying data and methodologies used to generate these estimates are not publicly available. A study freely available on the internet valued the 2025 global etomidate market at US$279 million in 2025, estimated to reach US$464.6 million by 2034, a compound annual growth rate of 5.8% (Sharma, 2026). In 2025, the market was 38.5% in North America, 28.2% in Europe, 15.4% in Asia-Pacific, 11.2% in Latin America, and 6.7% in Middle East-Africa.

Etomidate is sold in the global market for injection use, primarily in vials (58.7%) and ampoules (35.4%); a small amount (5.9%) is sold as pre-filled syringes or specialized infusion preparations (Sharma, 2026). Almost half (42.3%) of etomidate use is for induction of general anesthesia; another third (31.7%) is for sedation during medical procedures such as endoscopy, bronchoscopy, arthroscopy, dental procedures, and cardiac catheterization. Other uses include in emergency medicine (e.g., for rapid intubation) (19.2%) and miscellaneous uses such as sedation in the intensive care unit (ICU) and during electrophysiological testing (6.8%).

More than three-quarters of the global etomidate supply is used by hospitals (64.2%) and ambulatory surgical centers (21.5%); the remainder is used by specialty clinics and diagnostic centers (10.1%) and by military field hospitals and disaster response units (4.2%) (Sharma, 2026). Etomidate is distributed primarily by hospital pharmacies (72.3%), with the remainder distributed by retail pharmacies (15.8%), online pharmacies and directly to the provider (8.7%), and government procurement (3.2%).

16. Illicit Manufacture and Traffic and Related Information

Little is known about the manufacture and traffic in illicit etomidate. Some etomidate is diverted from legal medical channels in Korea and the United States (ACMD, 2026), but much of it appears to be manufactured or formulated illicitly. Jakarta, Indonesia and Bangkok, Thailand are major centers of illicit manufacture, based on law enforcement seizures of large quantities of bulk etomidate and drug making equipment (Lassi and Jiang, 2026) (UNODC, 2025b). Illicit etomidate is also manufactured in China and Vietnam (UNODC, 2026c). A large illicit production center in Bangkok, Thailand used precursor chemicals imported from China (including phenylethylamine, ethyl chloroacetate,

triethylamine, ethyl formate, formic acid, benzene, and potassium thiocyanate) sufficient to produce 200 kg of etomidate (UNODC, 2025b). Etomidate from Indonesia and Thailand has been found in Singapore and Japan (Okinawa) (Lassi and Jiang, 2026). Thailand is also a transshipment point for illicit etomidate manufactured in India to other Asian countries (Thai PBS World, 2026). Cartridge packaging operations for etomidate-containing e-cigarettes have been seized in Hong Kong, China, Taiwan, and Singapore (UNODC, 2025b).

17. Current International Controls and Their Impact

Etomidate is not currently listed under the UN international drug conventions (ACMD, 2026).

18. Current and Past National Controls

Several countries in East and Southeast Asia have placed etomidate under strict control over the past 3 years because of increasing misuse via e-cigarettes. China classified etomidate as a class II psychotropic drug on Oct. 1, 2023 (Zheng et al., 2025). Hong Kong classified etomidate as a dangerous drug on 14 Feb. 2025 (UNODC, 2025b). Japan designated etomidate as a "designated drug" in May 2024 (Japan Today, 2025). New Zealand placed etomidate in schedule 3 of the Misuse of Drugs Act on 9 Dec. 2025 (New Zealand Gazette, 2025). Singapore classified etomidate as a class C controlled drug on 1 Sept. 2025 (UNODC, 2025b). South Korea designated etomidate as a narcotic on 13 Feb. 2026 (Straits Times, 2026). Taiwan classified etomidate as a category 2 narcotic in 2024; proposed as category 1 narcotic in June 2026 (Focus Taiwan, 2026). Thailand classified etomidate as a category 2 controlled substance in July 2025 (Thai PBS World, 2026).

19. Other Medical and Scientific Matters Relevant for a Recommendation on the Scheduling of the Substance

This review has several information gaps that limit the ability to draw firm conclusions about the prevalence, pharmacology, and abuse potential of non-medical (inhaled) use of etomidate. First, no controlled studies of the pharmacology of inhaled (smoked or vaporized) etomidate in animals or humans, including studies of abuse potential, intoxication, tolerance, and withdrawal, were identified. Inhalation is the route of administration for non-medical (recreational) use of etomidate. All available information about the human pharmacology of inhaled etomidate comes from retrospective case reports of individuals who come to medical or law enforcement attention. Second, the prevalence of etomidate non-medical use or abuse is unknown. Large-scale and population-based epidemiological surveys do not commonly include questions about etomidate. Information about prevalence comes only from counts of cases that come to medical or law enforcement attention. China, the country with a large number of etomidate abuse cases, keeps comprehensive case registries, but these are not readily accessible. Third, China conducts the only current clinical research on nonmedical use of etomidate, but almost all of this information is available only in Chinese (e.g., Chinese Biomedical Literature Database, which includes more than 2500 journals, of which only

about 6% are included in Medline [Cohen et al., 2015]) and is not identifiable or accessible via non-Chinese electronic databases.

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