Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section

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PROPOFOL
(Trade Name: Diprivan®)

Introduction:

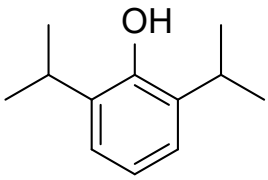
Propofol (U.S. Patent 4,447,657) is a prescription medication that was approved by the United States Food and Drug Administration (FDA) for use as a short-acting intravenous anesthetic. This drug is currently marketed as Diprivan (AstraZeneca) and is a sterile emulsion for use in human and veterinary medicine. Propofol is commonly referred to as the "milk of amnesia."

Licit Uses:

Propofol is a non-barbiturate sedative that is used in hospital settings by trained anesthetists for the induction and maintenance of general anesthesia, as well as sedation of ventilated adults receiving intensive care, for a period of up to 72 hours. According to the IQVIA National Prescription Audit™, total prescriptions dispensed for propofol in the United States were 1,063 in 2019, 911 in 2021, and 665 in 2024.

Chemistry:

Propofol is chemically known as 2,6-diisopropylphenol. Propofol has a molecular formula of $C_{12}H_{18}O$ and a molecular weight of 178.271 g/mol. Propofol is a simple molecule with the chemical structure shown below:



Pharmacology:

Propofol is a central nervous system (CNS) depressant. Propofol's primary mechanism of action is by enhancing the inhibitory effects of gamma-aminobutyric acid (GABA) through potentiation of $GABA_A$ receptors. Propofol, similar to barbiturates and benzodiazepines, produces rewarding and reinforcing effects in animals. In rats, subanesthetic and anesthetic doses of propofol have been shown to increase dopamine concentrations in the nucleus accumbens—a central part of the brain reward system.

Propofol has a fast onset of action and quickly penetrates the blood-brain barrier due to its high lipid solubility. Propofol produces rapid (within 40 seconds) loss of consciousness after an intravenous injection and, following a single bolus dose (2–2.5 mg/kg of body weight), has a short duration of action averaging 3–5 minutes. This short duration of action is due to the rapid distribution from the CNS to other tissues. Approximately 70% of the dose is excreted in the urine within 24 hours, and 90% is excreted within 5 days of administration.

Studies on the recovery profile of propofol reported that patients who were anesthetized with propofol wake up feeling "elated," "euphoric," and "talkative." Fifty percent of participating subjects reported "liking" on the Visual Analog Scale and showed preference for propofol over placebo. In addition, subanesthetic doses of propofol are reported to produce feelings of "being high," light-headedness, spacing out, and sedation. Anesthetic doses of propofol are reported to cause dream incidence in 20–60% of the exposed population.

Propofol has a narrow window of safety. In some adults and children, induction of anesthesia with propofol is associated with cessation of breathing. Additionally, prolonged high-dose infusions of propofol for sedation have been associated with cessation of breathing, breakdown of heart muscle, and heart and kidney failure; in some cases, this has led to death and is referred to as "Propofol Infusion Syndrome." In cases of abuse, propofol abuse may cause accumulation of fluid in the lungs, cardiorespiratory depression, and death. Currently, no antagonist or reversal medication for propofol toxicity is available.

Illicit Uses:

Propofol is abused for recreational purposes, evidenced by case reports and surveys published in scientific literature, and abuse of this substance has led to some fatalities. Propofol is primarily abused by anesthetists, practitioners, nurses, and other health care staff.

In 2007, a survey of propofol abuse in academic anesthesia programs revealed that 23 out of 126 (18%) anesthesiology departments in the United States experienced one or more individuals abusing propofol in the previous 10 years (between 1996 to mid-2006), and 2 departments had more than one incidence of abuse. Among all anesthesia personnel, the incidence of propofol abuse was 0.10%. Among anesthesiologists abusing propofol, the mortality rate was 28% (7 deaths in 25). Among anesthesiology staff, the incidence of propofol abuse increased in comparison to reports from the previous survey in 2002.

In 2019, another survey of propofol abuse across 147 accredited anesthesiology residency programs revealed that propofol was the second most commonly abused substance (20.3%) among residents between 2007–2017.

User Population:

Propofol is primarily abused by health care staff, including anesthetists, practitioners, nurses, and technicians.

Illicit Distribution

Propofol is not frequently encountered by law enforcement personnel or submitted to forensic laboratories for analysis, which may be partially due to its non-control status.

The Drug Enforcement Administration's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug received 96 reports of propofol since 1999. The annual number of reports has remained fairly stable, with propofol identified in 4 reports in 2020, 3 in 2021, 6 in 2022, 2 in 2023, and 8 in 2024 (reports still pending).

Control Status:

Propofol is not controlled under the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.