Drug Enforcement Administration
Office of Diversion Control
Drug & Chemical Evaluation Section

Fospropofol
(Lusedra ®)

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Introduction:

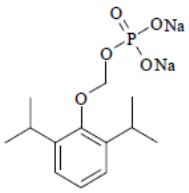
Fospropofol (2,6-diisopropopylphenoxymethyl phosphate disodium) is a short acting intravenous (i.v.) anesthetic approved (Lusedra®) in December 2008 for monitored anesthesia care sedation in adult patients. Fospropofol is a prodrug of propofol, a non-controlled short-acting anesthetic currently marketed under the brand name Diprivan®.

Licit Uses:

Fospropofol is a non-barbiturate sedative for use in medical facilities by trained medical professionals for the induction and maintenance of general anesthesia and for sedation of ventilated adult patients undergoing diagnostic or therapeutic procedures.

Chemistry:

Fospropofol or 2,6-diisopropopylphenoxymethyl phosphate disodium ($C_{13}H_{19}O_5PNa_2$, MW = 332.24 g/mol) is a simple molecule and its chemical structure is shown below.



Pharmacology:

Fospropofol is metabolized to propofol *in vivo* (in the body) and the pharmacological effects of fospropofol are attributed to propofol. Thus, fospropofol is a "prodrug of propofol."

The binding profile of fospropofol has been shown to be similar to that of propofol. The binding site of propofol is on the gamma-aminobutyric acid ($GABA_A$) receptor, acting as a modulator by potentiating the activity of GABA at the receptor. Various other classes of psychoactive drugs (e.g., barbiturates, benzodiazepines, and volatile anesthetics) also potentiate GABA at the $GABA_A$ receptors. Similar to barbiturates and benzodiazepines, propofol has reinforcing effects in animals and humans. In clinical studies, humans with history of recreational drug abuse reported increases in sedation and "liking" scores following propofol. Propofol at anesthetic doses is reported to cause dream incidence in 20% to 60% of the exposed population.

Propofol produces loss of consciousness rapidly within 40 seconds of an i.v. injection. Propofol's duration of action is short with a mean of 3 to 5 min following a single bolus dose of 2 to 2.5 mg/kg body weight. Fospropofol and propofol have short elimination half lives of 0.8 and 2 hours, respectively.

Propofol has a narrow window of safety. Prolonged high dose infusions of propofol for sedation in adults and children have been associated with cessation of breathing, breakdown of heart muscle, heart and kidney failure leading to death in some cases, a condition referred to as "Propofol Infusion Syndrome." Propofol abuse may also cause fluid retention in lungs, cardio-respiratory depression and death. There is no antagonist or reversal medication for propofol overdose.

In humans, the adverse events with fospropofol are similar to those experienced with other schedule IV sedative-hypnotics. In nine clinical studies with healthy volunteers (n=273), fospropofol administered i.v. produced paresthesia (75.8 percent), pruritus (21.6 percent), headache (7.7 percent), and dizziness (6.2 percent).

Illicit Uses:

Fospropofol's abuse potential is based on its metabolism to propofol. Case reports and surveys published in scientific literature indicate that propofol is abused for recreational purposes, mostly by anesthetists, practitioners, nurses and other healthcare staff. Some fatalities occurred from propofol abuse. Fospropofol, unlike propofol, upon oral ingestion is pharmacologically active. The oral activity of fospropofol increases the likelihood of its abuse by other routes of administration and its use to commit other crimes (e.g., date rape).

User Population:

Propofol, the metabolite of fospropofol, is mostly abused by healthcare staff including anesthetists, practitioners, nurses and technicians.

Control Status:

Effective November 5, 2009, fospropofol is a schedule IV substance under the Controlled Substances Act (CSA).

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section, Fax 202-353-1263, Phone 202-307-7183, or E-mail ODE@usdoj.gov.