Propofol Injectable Emulsion USP

(1% p/v)

For intravenous use

Composition:

Each ml (of emulsion) contains:

Propofol USP	10 mg
Soybean oil USP	100 mg
Egg lecithin	13 mg
Glycerin BP	22.5 mg
Disodium edetate BP	0.05 mg
Monothioglycerol USP	0.4 mg
Sodium hydroxide BP	1 mg
Water for injections BP	q.s.

Pharmacodynamic properties

Pharmacotherapeutic group: General anesthetics; Other general anesthetics,

ATC code N01AX10.

Following intravenous injection of Propofol, the onset of the hypnotic effect is rapid. Depending on the injection rate, the time to induction of anesthesia is between 30 and 40 seconds. The duration of action following a single bolus administration is short due to rapid metabolism and excretion (4–6 minutes).

With the recommended dosage regimen, no clinically relevant accumulation of propofol has been observed following repeated bolus injections or infusion. Patients regain consciousness rapidly.

Bradycardia and hypotension occasionally occur during induction of anesthesia, likely due to a lack of vagolytic activity. Cardiocirculatory status usually normalizes during the maintenance of anesthesia.

Pediatric population

Limited studies on the duration of propofol-based anesthesia in children indicate that safety and efficacy remain unchanged for durations of up to 4 hours. Evidence from the literature regarding use in children documents its use for prolonged procedures without changes in safety or efficacy.

Pharmacokinetic properties

Following intravenous administration, approximately 98% of propofol binds to plasma proteins. Following a single intravenous dose of 3 mg/kg, propofol clearance per kg of body weight increased with age, as follows: median clearance was considerably lower in newborns < 1 month of age (n=25) (20 mL/kg/min) compared to older children (n=36, age range 4 months to 7 years). Furthermore, inter-individual variability was considerable in newborns (range 3.7–78 mL/kg/min). Due to these limited study data indicating high variability, no dosage recommendation can be made for this age group.

After intravenous bolus administration, the initial blood level of propofol decreases rapidly due to rapid distribution into different compartments (α-phase). The distribution half-life was calculated to be 2–4 minutes.

During elimination, the decline in blood levels is slower. The elimination half-life during the β-phase is in the range of 30 to 60 minutes. Subsequently, a third, deep compartment becomes apparent, representing the redistribution of propofol from poorly perfused tissues.

Clearance is higher in children compared to adults.

The central volume of distribution is in the range of 0.2–0.79 L/kg of body weight; the steady-state volume of distribution is in the range of 1.8–5.3 L/kg of body weight. Propofol is widely distributed and rapidly eliminated from the body (total clearance of 1.5 to 2 L/minute). Clearance occurs via metabolic processes, primarily in the liver—where it is blood-flow dependent—to form propofol glucuronide and the glucuronide and sulfate conjugates of its corresponding quinol. All metabolites are inactive. Approximately 88% of an administered dose is excreted in the urine as metabolites. Only 0.3% of the administered dose is excreted unchanged in the urine.

Therapeutic indications

Propofol 10 mg/ml is a short-acting intravenous general anesthetic agent for:

- Induction and maintenance of general anesthesia in adults and children > 1 month of age
- Sedation for diagnostic and surgical procedures, alone or in combination with local or regional anesthesia, in adults and children > 1 month of age
- Sedation of ventilated patients > 16 years of age in the intensive care unit.

Contraindications

Propofol must not be used:

- in patients with known hypersensitivity to propofol or to any of the emulsion's excipients
- in patients allergic to peanuts or soya
- in patients aged 16 years or younger for intensive care sedation.

Special warnings and precautions

Propofol should be administered with caution and at a reduced rate in patients with cardiac, respiratory, renal, or hepatic impairment; in elderly, debilitated, hypovolemic, or epileptic patients; and in patients with impaired consciousness. Propofol clearance is blood-flow dependent; therefore, concomitant medication that reduces cardiac output will also reduce propofol clearance.

Cardiac, circulatory, or pulmonary insufficiency and hypovolemia should be compensated for prior to Propofol administration.

Before anesthetizing an epileptic patient, it should be verified that the patient has received antiepileptic treatment. Although several studies have demonstrated efficacy in treating status epilepticus, propofol administration in epileptic patients may also increase the risk of seizures.

Propofol should not be administered to patients with advanced heart failure or other severe myocardial disease, except with extreme caution and intensive monitoring.

The risk of relative vagotonia may be increased because propofol lacks vagolytic activity. It has been associated with reports of bradycardia (occasionally profound) and asystole. Intravenous administration of an anticholinergic agent prior to induction or during maintenance of anesthesia should be considered, especially in situations where vagal tone may predominate or when Propofol is used in conjunction with other agents that may cause bradycardia.

Use with electroconvulsive therapy is not recommended. As with other sedative agents, involuntary patient movements may occur when Propofol is used for sedation during surgical procedures. During procedures requiring immobility, these movements can pose a risk to the surgical site.

Special care should be taken with patients suffering from disorders of fat metabolism and in other conditions where lipid emulsions must be used with caution. If patients are receiving parenteral nutrition, the lipid content of the Propofol formulation must be taken into account: 1.0 ml of Propofol contains 0.1 gram of fat.

Lipid levels should be monitored in the intensive care unit after 2 days.

Interaction with other medicinal products and other forms of interaction

Propofol may be used in conjunction with other anesthetic agents (premedication, volatile anesthetics, analgesics, muscle relaxants, local anesthetics). No serious interactions with these drugs have been reported to date. Some of these centrally acting drugs may exert a circulatory and respiratory depressant effect, thereby enhancing the effects when used concomitantly with Propofol.

Lower doses may be required when general anesthesia is performed in conjunction with regional anesthesia.

Concomitant use of benzodiazepines, parasympatholytic agents, or inhalational anesthetics has been reported to prolong anesthesia and reduce respiratory rate.

Fertility, pregnancy, and lactation

Pregnancy: The safety of Propofol 10 mg/ml during pregnancy has not been established. Therefore, Propofol 10 mg/ml should not be used in pregnant women unless clearly necessary. Propofol crosses the placenta and may be associated with neonatal depression. High doses (exceeding 2.5 mg/kg of body weight for induction or 6 mg of Propofol/kg of body weight/h for maintenance of anesthesia) should be avoided. Animal studies have shown reproductive toxicity.

Breastfeeding: Studies in breastfeeding women have shown that propofol is excreted in small amounts in breast milk. Therefore, mothers should stop breastfeeding and discard breast milk for 24 hours after propofol administration.

Overdose

Overdose may cause cardiovascular and respiratory depression. Respiratory depression is treated with artificial ventilation. Cardiovascular depression may require lowering the patient's head and administering plasma volume expanders and vasopressors.

Storage:

Store below 30°C. Do not freeze.

Keep medicines out of the reach of children.

Shake before use.

Código N° : HFW-H(DRUGS)2016-17

Presentation: Pack containing a 20 ml vial.

Manufactured in India:

US Pharma®

(INDIA) Private Limited

Pioneering Excellence, Redefining Quality.

www.uspharma.in