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FRONT

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DOSAGE AND ADMINISTRATION

Induction of General Anesthesia	**Healthy Adults Less Than 55 Years of Age:** 40 mg every 10 seconds until induction onset (2 to 2.5 mg/kg).
	Elderly, Debilitated, or ASA-PS III or IV Patients: 20 mg every 10 seconds until induction onset (1 to 1.5 mg/kg).
	Cardiac Anesthesia: 20 mg every 10 seconds until induction onset (0.5 to 1.5 mg/kg).
	Neurosurgical Patients: 20 mg every 10 seconds until induction onset (1 to 2 mg/kg)
	Pediatric Patients - healthy, from 3 years to 16 years of age: 2.5 to 3.5 mg/kg administered over 20-30 seconds.
Maintenance of General Anesthesia:	**Infusion**
	Healthy Adults Less Than 55 Years of Age: 100 to 200 mcg/kg/min (6 to 12 mg/kg/h).
	Elderly, Debilitated, ASA-PS III or IV Patients: 50 to 100 mcg/kg/min (3 to 6 mg/kg/h).
	Cardiac Anesthesia: Most patients require: Primary Propofol Injectable Emulsion with Secondary Opioid – 100 – 150 mcg/kg/min Low-Dose PROPOFOL Injectable Emulsion with Primary Opioid – 50 - 100 mcg/kg/min
	Neurosurgical Patients: 100 to 200 mcg/kg/min (6 to 12 mg/kg/h).
	Pediatric Patients - healthy, from 2 months of age to 16 years of age: 125 to 300 mcg/kg/min (7.5 to 18 mg/kg/h) Following the first half hour of maintenance, if clinical signs of light anesthesia are not present, the infusion rate should be decreased.
Maintenance of General Anesthesia:	**Intermittent Bolus**
	Healthy Adults Less Than 55 Years of Age: Increments of 20 to 50 mg as needed.
Initiation of MAC Sedation:	**Healthy Adults Less Than 55 Years of Age:** Slow infusion or slow injection techniques are recommended to avoid apnea or hypotension. Most patients require an infusion of 100 to 150 mcg/kg/min (6 to 9 mg/kg/h) for 3 to 5 minutes or a slow injection of 0.5 mg/kg over 3 to 5 minutes followed immediately by a maintenance infusion.
	Elderly, Debilitated, Neurosurgical, or ASA-PS III or IV Patients: Most patients require dosages similar to healthy adults. Rapid boluses are to be avoided.
Maintenance of MAC Sedation	**Healthy Adults Less Than 55 Years of Age:** A variable rate infusion technique is preferable over an intermittent bolus technique. Most patients require an infusion of 25 to 75 mcg/kg/min (1.5 to 4.5 mg/kg/h) or incremental bolus doses of 10 mg or 20 mg.
	In Elderly, Debilitated, Neurosurgical, or ASA-PS III or IV Patients: Most patients require 80% of the usual adult dose. A rapid (single or repeated) bolus dose should not be used.
Initiation and Maintenance of ICU Sedation in Intubated, Mechanically Ventilated	
	Adult Patients - Because of the residual effects of previous anesthetic or sedative agents, in most patients the initial infusion should be 5 µg/kg/min (0.3 mg/kg/h) for at least 5 minutes. Subsequent increments of 5 to 10 mcg/kg/min (0.3 to 0.6 mg/kg/h) over 5 to 10 minutes may be used until desired clinical effect is achieved. Maintenance rates of 5 to 50 mcg/kg/min (0.3 to 3 mg/kg/h) or higher may be required. Evaluation of clinical effect and assessment of CNS function should be carried out daily throughout maintenance to determine the minimum dose of PROPOFOL Injectable Emulsion required for sedation. The tubing and any unused portions of PROPOFOL Injectable Emulsion should be discarded after 12 hours because PROPOFOL Injectable Emulsion contains no preservatives and is capable of supporting growth of microorganisms

Dosage and administration rate should be individualized and titrated to the desired effect. Lower doses are usually required for elderly and debilitated or high risk surgical patient or those with circulatory disorders. The dosage of intravenously administered Propofol should be adjusted according to the type and amount of premeditation used.

Intensive Care Unit Sedation
Propofol Injectable Emulsion should be individualized according to the patient's condition and response, blood lipid profile and vital signs.

For incubated, mechanically ventilated adult patient, Intensive Care Unit sedation should be initiated slowly with a continuous infusion in order to titrate to desire clinical effect and minimize hypotension. When indicated initiation of sedation should begin at 5µ/kg/min (0.3mg/kg/h).The infusion rate should be increased by increment of 5 to 10µ/kg/min (0.3mg/kg/h) until the desired level of sedation is achieved. A minimum period of 5 to 10 minutes between adjustments should be allowed for onset of peak drug effect. Most adult patients require maintenance rate of a 5 to 50µ/kg/ min (0.3 to 3mg/kg/h) or higher. Dosage of Propofol injectable emulsion should be reduced in patients who have received large dose of narcotics. Conversely, adequate management of pain may reduce the Propofol injectable emulsion dosage requirement with analgesic agents.

Evalution of level of sedation and assessment of CNS function should be carried out daily throghout maintenance to determine the minimum dose of propofol injectable emulsion required for sedation.

Bolus administration of 10 or 20 mg should only be used to rapidly increase depth of sedation in patient where hypotension is not likely to occur. Patients with compromised myocardial function, intra vascular volume depletion, or abnormally low vascular tone (eg. sepsis) may be more susceptible to hypotension.
For children: - Propofol Injectable Emulsion is not recommended for use in children less than 3 year of age.

COMPATIBILITY AND STABILITY
Propofol injectable emulsion should not be mixed with other therapeutic agents prior to administration.

Dilution Prior to Administration: Propofol injectable emulsion is provided as a ready to use formulation. However, should dilution be necessary, it should only be diluted with 5% dextrose Injection, and it should not be diluted to a concentration less than 2 mg/ml because it is an Emulsion. In dilution form it has been shown to be more stable when in contact with glass than with plastic (95% potency after 2 hour of running infusion in plastic).

ADMINISTARTION
Compatibility of Propofol injectable emulsion with the co administration of blood/ serum / plasma has not been established.

Propofol injectable emulsion ha been shown to be compatible with the following intravenous Fluids.

- 5% Dextrose Injection (5D)
- Lactated Ringers Injection (RL)
- Lactated Ringers and 5% Dextrose Injection (5D with RL)
- 5% Dextrose and 0.45% Sodium Chloride Injection
- 5% Dextrose and 0.2% Sodium Chloride Injection

OVERDOSAGE
Overdosage is likely to cause cardio respiratory depression. Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression may require repositioning of the patient by raising the patient's legs, increasing the flow rates of intravenous fluids, and administering pressor agents and/or anticholinergic agents.
If overdosage occurs, Propofol Injectable Emulsion administration should be discontinued immediately.

Handling Procedures
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Clinical experience with the use of in-line filters and Propofol Injectable Emulsion during anesthesia or ICU/MAC sedation is limited. Propofol Injectable Emulsion should only be administered through a filter with a pore size of 5 mcm or greater unless it has been demonstrated that the filter does not restrict the flow of Propofol Injectable Emulsion and/or cause the breakdown of the emulsion. Filters should be used with caution and where clinically appropriate. Continuous monitoring is necessary due to the potential for restricted flow and/or breakdown of the emulsion.

Do not use if there is evidence of separation of the phases of the emulsion.

Guidelines for Aseptic Technique for General Anesthesia/MAC Sedation:
Propofol Injectable Emulsion should be prepared for single-patient use only. When Propofol Injectable Emulsion is administered directly from the vial, strict aseptic techniques must be followed. The vial rubber stopper should be disinfected using 70% isopropyl alcohol. A sterile vent spike and sterile tubing must be used for administration of Propofol Injectable Emulsion. As with other lipid emulsions, the number of IV line manipulations should be minimized. Administration should commence promptly and must be completed within 12 hours after the vial has been spiked.
Any unused portions of Propofol Injectable Emulsion, reservoirs, dedicated administration tubing and/or solutions containing Propofol Injectable Emulsion must be discarded at the end of the anesthetic procedure or at 12 hours, whichever occurs sooner. The IV line should be flushed every 12 hours and at the end of the anesthetic procedure to remove residual Propofol Injectable Emulsion.

PRESENTATION
Propofol Injectable Emulsion is available in ready to use 10 mL, 20 mL, 50 mL & 100 mL infusion vials containing 10 mg / ml Propofol .

10 mL Infusion vials, 20 mL Infusion vials, 50 mL Infusion vials, 100 mL bottle Propofol undergoes oxidative degradation, in the presence of oxygen, and is therefore packaged under nitrogen to eliminate this degradation path.

STORAGE
Store below 30°C. Do not freeze. Shake well before use.

ACULIFE®
Manufactured in India by:
Aculife Healthcare Pvt. Ltd.
Sachana, Gujarat 382150, India.
* TM Owners-Nirma Ltd.

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For the use of Registered Medical Practitioner or Hospital or a Laboratory only

Propofol Injection BP (1% w/v)

NIRFOL®* 1%

for I.V. administration

DESCRIPTION
Propofol Injectable Emulsion is a sterile, nonpyrogenic oil-in-water emulsion containing 10 mg / ml of Propofol suitable for intravenous administration.
It is chemically described as 2,6-diisopropylphenol and has a molecular weight of 178.27.
Propofol is highly soluble in water.
Propofol Injectable Emulsion is isotonic & pH of 7-8.5

COMPOSITION
Propofol Injection 1% each mL (of emulsion) contains:
Propofol BP 10 mg
Excipients
Soybean Oil USP
Glycerol BP
Egg Lecithin
Water for Injections BP q. s.

PHARMACOLOGY
PHARMACODYNAMIC:
Propofol is a short-acting general anaesthetic agent with a rapid onset of action of approximately 30 seconds. Recovery from anaesthesia is usually rapid. The mechanism of action, like all general anaesthetics, is poorly understood. However, Propofol is thought to produce its sedative/anaesthetic effects by the positive modulation of the inhibitory function of the neurotransmitter GABA through the ligand-gated GABAA receptors.

Pharmacodynamic properties of Propofol are dependent upon the therapeutic blood Propofol concentrations.

Undesirable side effects, such as cardiorespiratory depression, are likely to occur at higher blood concentrations which result from bolus dosing or rapid increases in infusion rates. An adequate interval (3 to 5 minutes) must be allowed between dose adjustments in order to assess clinical effects.

The hemodynamic effects of Propofol Injectable Emulsion during induction of anesthesia vary. If spontaneous ventilation is maintained, the major cardiovascular effect is arterial hypotension (sometimes greater than a 30% decrease) with little or no change in heart rate and no appreciable decrease in cardiac output. If ventilation is assisted or controlled (positive pressure ventilation),there is an increase in the incidence and the degree of depression of cardiac output.Addition of an opioid, used as a premedicant, further decreases cardiac output and respiratory drive.

Although ventilatory depression can occur following administration of Propofol injectable emulsion, any effects are qualitatively similar to those of other intravenous anaesthetic agents and are readily manageable in clinical practice. Induction of anesthesia with Propofol is frequently associated with apnea in both adults and pediatric patients.

Propofol injectable emulsion reduces cerebral blood flow, intracranial pressure and cerebral metabolism. The reduction in intracranial pressure is greater in patients with an elevated baseline intracranial pressure.

Recovery from anaesthesia is usually rapid and clear headed with a low incidence of headache and postoperative nausea and vomiting.

In general, there is less postoperative nausea and vomiting with Propofol injectable emulsion than with inhalational agents. There is evidence that this may be related to a reduced emetic potential of Propofol .

Propofol at the concentration of 1% does not inhibit the synthesis of adrenocortical hormones clinically.

Limited studies available on Propofol based anesthesia in children, which indicates safety and efficacy are unchanged up to duration of 4 years

PHARMACOKINETICS:
The decline in Propofol concentrations following a bolus dose or following the termination of an infusion can be described by a three compartment open model with very rapid distribution (half-life 2–4 minutes), rapid elimination (half-life 30–60 minutes), and a slower final phase, representative of redistribution of Propofol from poorly perfused tissue.

After Intravenous administration, about 98% Propofol is bound to plasma protein.

Propofol is extensively distributed and rapidly cleared from the body (total body clearance 1.5–2 litres/minute).-Clearance occurs by metabolic processes, mainly in the liver where it is blood flow dependent, to form inactive conjugates of Propofol and its corresponding quinol Which are excreted in urine. About 88 % of an administered dose is excreted in the form of metabolites in urine, only 0.3% of the administered dose is excreted unchanged in urine.

When Propofol injectable emulsion is used to maintain anaesthesia, blood concentrations asymptotically approach the steady-state value for the given administration rate. The pharmacokinetics are linear over the recommended range of infusion rates of Propofol injectable emulsion.

After a single dose of 3 mg/kg intravenously, Propofol clearance/kg body weight increased with age as follows: Median clearance was considerably lower in neonates <1 month old (n=25) (20 ml/kg/min) compared to older children (n= 36, age range 4 months–7 years). Additionally inter-individual variability was considerable in neonates (range 3.7–78 ml/kg/min). Due to limited trial data suggest a large variability, no dose recommendations can be given for this age group.

Adults: Propofol clearance ranges from 23-50 mL/kg/min (1.6 to 3.4 L/min in 70 kg adults)

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Pediatrics: The Distribution and clearance of Propofol in children is similar to adults

Geriatrics: With increasing patient age, the dose of Propofol needed to achieve a defined anesthetic end point (dose-requirement) decreases.

Organ failure: The pharmacokinetic of Propofol does not appear to be different in people with chronic hepatic cirrhosis or chronic renal impairment compared to adults with normal hepatic and renal function.

INDICATIONS

	Approved Patient
Initiation and maintenance of Monitored Anesthesia Care (MAC) sedation	Adults only
Combined sedation and regional anesthesia	Adults only
Induction of General Anesthesia	Patients ≥ 3 years of age
Mainenance of General Anesthesia	Patients ≥ 2 months of age
Intensive Care Unit (ICU) sedation of intubated, mechanically ventilated patients	Adults only

Propofol Injectable Emulsion is not recommended in
- Paediatric ICU sedation & MAC Sedation as Safety, effectiveness and dosing guidelines for Propofol Injectable Emulsion have not been established.
- Propofol injectable emulsion is not recommended for induction of anesthesia below the age of 3 years or for maintenance of anesthesia below the age of 2 months because its safety and effectiveness have not been established in those populations.
- Obstetrics, including cesarean section deliveries as it crosses placental barrier & may be associated with neonatal depression
- Nursing mother as it is excreted in human milk & the effects of oral absorption of small amount of Propofol is not known

CONTRAINDICATIONS
Propofol injectable emulsion is contraindicated in patients with a known Hypersensitivity to Propofol or its components Or when general anesthesia or sedation is contraindicated.

Propofol injectable emulsionis contraindicated in patients with allergies to eggs, egg products, soybeans or soy products

WARNINGS
Propofol Injectable emulsion should be administrated only by person trained in the administration of general anesthesia and not involved in the conduct of the surgical / diagnostic procedure. Sedative Patients should be continuously monitored and facilities for maintenance of a patient airway, artificial ventilation and oxygen enrichment and circulatory resuscitation must be immediately available.

For sedation of intubated, mechanically ventilated patients in the Intensive Care Unit (ICU), Propofol Injectable Emulsion should be administered only by persons skilled in management of critically ill patients and trained in cardiovascular resuscitation and airway management.

Patient should be continuously monitored for early signs of hypotension, apnea, airway obstruction, and/or oxygen desaturation. These cardio respiratory effects are more likely to occur following rapid bolus administration, especially in the elderly, debilitated ASA III /IV patients.

Use of Propofol Injectable Emulsion infusions for both adult and pediatric ICU sedation has been associated with a constellation of metabolic derangements and organ system failures, referred to as Propofol Infusion Syndrome, that have resulted in death.The syndrome is characterized by severe metabolic acidosis, hyperkalemia, lipemia, rhabdomyolysis, hepatomegaly, cardiac and renal failure. The syndrome is most often associated with prolonged, high-dose infusions (> 5 mg/kg/h for > 48h) but has also been reported following large-dose, short-term infusions during surgical anesthesia. In the setting of prolonged need for sedation, increasing Propofol dose requirements to maintain a constant level of sedation, or onset of metabolic acidosis during administration of a Propofol infusion, consideration should be given to using alternative means of sedation.

Abrupt discontinuation of Propofol injectable emulsion prior to weaning or for daily evaluation of sedation levels should be avoided. This may result in rapid awakening with associated anxiety, agitation, and resistance to mechanical ventilation. Infusions of Propofol emulsion should be adjusted to maintain a light level of sedation through the weaning process or evaluation of sedation level.

Propofol Injectable Emulsion should not be co-administered through the same IV catheter with blood or plasma because compatibility has not been established.

Strict aseptic technique must always be maintained during handling.
As per the literature reviewed, failure to use aseptic technique when handling Propofol Injectable Emulsion is associated with microbial contamination of the product and with fever, infection, sepsis, other life-threatening illness, and death. Do not use if contamination is suspected. Discard unused portions as directed within the required time limits

PRECAUTIONS
General
Adult patients: A lower induction dose and a slower maintenance rate of administration should be used in elderly, debilitated or ASA III/ IV patients. Patients should be continuously monitored for early signs of elevation of lower extremities, use of pressor agents, or administration of atropine. Apnea often occurs during induction and may persist for more than 60 seconds. Propofol Injectable Emulsion use requires caution when administered to patients with disorders of lipid metabolism such as primary hyperlipoproteinemia, diabetic hyperlipemia, and pancreatitis. Ventilator support may be required. Very rarely the use of Propofol may be associated with the development of a period of postoperative unconsciousness, which may be accomplished by an increase in muscle tone.
When Propofol Injectable Emulsion is administered to an epileptic patient, there may be risk of seizure during the recovery phase.

Attention should be paid to minimize pain on administration of Propofol Injectable Emulsion. Transient local pain can be minimized if the larger veins of the forearm or antecubital fossa are used. Pain during intravenous injection may also be reduced by prior injection of IV lidocaine (1 ml of a 1% solution).

If smaller vein is used for injection, pain on injection for pediatric is high.With pretreatment of lidocaine and in case of use of an antecubital veins, pain can be minimized

As per the literature reviewed, the addition of lidocaine to Propofol in quantities greater than 20 mg lidocaine/200 mg Propofol results in instability of the emulsion which is associated with increases in globule sizes over time and (in rat studies) a reduction in anesthetic potency. Therefore, it is recommended that lidocaine be administered prior to Propofol administration or that it be added to Propofol immediately before administration and in quantities not exceeding 20 mg lidocaine/200 mg Propofol .

Rare adverse events including angioedema, bronchospasm, erythema, hypotension, pulmonary edema, Post operative pancreatitis may occur with Propofol Injectable Emulsion administration.

Perioperative myoclonia, rarely including convulsions and opisthotonos may occur in association with Propofol Injectable Emulsion administration.

Intensive Care Unit Sedation
The administration of Propofol Injectable Emulsion should be initiated as a continuous infusion and changes in the rate of administration made slowly (>5 min) in order to minimize hypotension and avoid acute overdosage.

Patients should be monitored for early signs of significant hypotension and/or cardiovascular depression, which may profound. These effects are responsive to discontinuation of Propofol Injection, IV fluid administration, and/or vasopressin therapy. As with other sedative medications, there is wide inter patient variability in Propofol Injectable Emulsion dosage requirements, and these requirements may change with time.

Failure to reduce the infusion rate in patients receiving Propofol Injectable Emulsion for extended periods may result in excessively high blood concentrations of the drug. Thus, titration to clinical response and daily evaluation of sedation levels are important during use of Propofol Injectable Emulsion infusion for ICU sedation, especially when it is used for long durations.

Opioids and paralytic agents should be discontinued and respiratory function optimized prior to weaning patients from mechanical ventilation.

Since Propofol Injectable Emulsion is formulated in an oil-in-water emulsion, elevations in serum triglycerides may occur when Propofol Injectable Emulsion is administered for extended periods of time. Patients at risk of hyperlipidemia should be monitored for increases in serum triglycerides or serum turbidity.

The long-term administration of Propofol Injectable Emulsion to patients with renal failure and/or hepatic insufficiency has not been evaluated.

Neuro surgical Anesthesia: When Propofol Injectable Emulsion is used in patients with increased intra cranial pressure or impaired cerebral circulation, significant decrease in mean arterial pressure should be avoided because of the resultant decrease in cerebral perfusion pressure. To avoid significant hypotension and decreases in cerebral perfusion pressure. an infusion or slow bolus of approximately 20 mg every 10 seconds should be utilized instead of rapid, more frequent, and/or larger boluses of Propofol Injectable Emulsion. When increased ICP is suspected, hyperventilation and hypocarbia should accompany the administration of Propofol Injectable Emulsion.

Cardiac Anesthesia: Slower rates of administration should be utilized in pre-medicated patients, geriatric patients, patients with recent fluid shifts, or patients who are hemodynemically unstable. Any fluid deficit should be corrected prior to administration of Propofol Injectable Emulsion. In those patients where additional fluid therapy may be contraindicated, other measures, e.g., elevation of lower extremities, or use of pressor agents,may be useful to offset the hypotension which is associated with the induction of anesthesia with Propofol Injectable Emulsion.

DRUG INTERACTIONS
This induction dose requirements of Propofol Injectable Emulsion may be reduced in patients with intra muscular or intravenous pre-medication, particularly with narcotics (e.g., Benzodiazepines, barbiturates, chloral hydrate, droperidol, etc). These agents may increase the anesthetic or sedative effects of Propofol Injectable Emulsion and may also results in more pronounced decrease in systolic, diastolic and mean arterial pressures and cardiac output.

During maintenance of anesthesia or sedation, the rate of Propofol Injectable Emulsion administration should be adjusted according to the desired level of anesthesia or sedation and may be reduce in the presence of supplemental analgesic agents (e.g. nitrous oxides or opioids). The concurrent administration of potent inhalational agents (e.g.isoflurane, enflurane and halothane) during maintenance with Propofol Injectable Emulsion has not been extensively evaluated. These inhalational agents can also be expected to increase the anesthetic or sedative and cardio respiratory effects of Propofol Injectable Emulsion.

Propofol Injectable Emulsion does not cause a clinically significant change in onset, intensity of duration of action of the commonly used neuromuscular blocking agents (e.g. succinylcholine and non depolarizing muscle relaxants).

No significant adverse interactions with commonly used pre-medications or drugs used during anesthesia or sedation (including a range of muscle relaxants, inhalational agents, analgesic agents and local anesthetic agents) have been observed in adults.

Pediatric patients
In pediatric patients, administration of fentanyl concomitantly with Propofol may result in serious bradycardia
Serious adverse events and death may occur in pediatric patients with upper respiratory tract infections receiving Propofol Injectable Emulsion for ICU sedation.

In pediatric patients, abrupt discontinuation following prolonged infusion may result in flushing of the hands and feet, agitation, tremulousness and hyperirritability. Increased incidences of bradycardia (5%), agitation (4%), and jitteriness (9%) may occur

Geriatrics
A lower induction dose and a slower maintenance rate of administration of Propofol Injectable Emulsion should be used in elderly patients. In this group of patients, rapid (single or repeated) bolus administration should not be used in order to minimize undesirable cardiorespiratory depression including hypotension, apnea, airway obstruction, and/or oxygen desaturation. All dosing should be titrated according to patient condition and response.

Carcinogenesis, mutagenesis, impairment of fertility
Carcinogenesis: Long-term studies in animals have not been performed to evaluate the carcinogenic potential of Propofol .

Mutagenesis: Propofol is not mutagenic in the in vitro bacterial reverse mutation assay(Ames test) using Salmonella typhimurium
Propofol is not mutagenic in either the gene mutation/gene conversion test using Saccharomyces cerevisiae.

Impairment of fertility: As per the Literature reviewed, Impairment of fertility is not observed in male/female species.

Teratogenic effects: No adequate and well-controlled studies have done in pregnant women. Because animal reproduction studies are not always predictive of human responses, this drug should be used during pregnancy only if clearly needed

ADVERSE REACTIONS

System Organ Class	Frequency	Undesirable effects
Immune System Disorders	Very rare (<1/10000)	Anaphylaxis - may include angioedema, bronchospasm, erythema and hypotension
Metabolism and nutritional disorder	Frequency not known (9)	Metabolic acidosis (5), hyperkalaemia (5), hyperlipidaemia (5)
Psychiatric disorders	Frequency not known (9)	Euphoric mood, drug abuse(8)
Nervous system disorders	Common(>1/100, <1/10)	Headache during recovery phase
	Rare (>1/10 000, <1/1000)	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	Very rare (<1/10 000)	Postoperative unconsciousness
	Frequency not known (9)	Involuntary movements
Cardiac disorders:	Common (>1/100, <1/10)	Bradycardia (1)
	Very rare (<1/10 000)	Pulmonary oedema
	Frequency not known (9)	Cardiac arrhythmia (5),cardiac failure (5), (7)
Vascular disorders:	Common (>1/100, <1/10)	Hypotension (2)
	Uncommon (>1/1000, <1/100)	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders:	Common (>1/100, <1/10)	Transient apnoea during induction
Gastrointestinal disorders:	Common (>1/100, <1/10)	Nausea and vomiting during recovery phase
	Very rare (<1/10 000)	Pancreatitis
Hepatobiliary disorders	Frequency not known (9)	Hepatomegaly (5)
Musculoskeletal and connective tissue disorders:	Frequency not known (9)	Rhabdomyolysis (3), (5)
Renal and urinary disorders	Very rare (<1/10 000)	Discolouration of urine following prolonged administration
	Frequency not known (9)	Renal failure(5)
Reproductive system and breast	Very rare (<1/10 000)	Sexual disinhibition
General disorders and administration site conditions:	Very common (>1/10)	Local pain on induction (4)
Investigations	Frequency not known (9)	Brugada type ECG (5), (6)
Injury, poisoning and procedural complications:	Very rare (<1/10 000)	Postoperative fever

(1) Serious bradycardias are rare.
(2) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of Propofol.
(3) Rhabdomyolysis rarely occur where Propofol has been given at doses greater than 4 mg/kg/hr for ICU sedation.
(4) May be minimised by using the larger veins of the forearm and antecubital fossa. With Propofol 1% local pain can also be minimised by the co-administration of lidocaine.
(5) Combinations of these events, reported as "Propofol Infusion Syndrome" may be seen in seriously ill patients who often have multiple risk factors for the development of the events
(6) Brugada-type ECG - elevated ST-segment and coved T-wave in ECG.
(7) Rapidly progressive cardiac failure (in some cases with fatal outcome) in adults. The cardiac failure in such cases is usually unresponsive to inotropic supportive treatment.
(8) Drug abuse, predominantly by health care professionals.
(9) Not known as it cannot be estimated from the available clinical trial data.
Dystonia/dyskinesia may occur

General
There are insufficient data to support an accurate estimate of their incidence rates. Most adverse events are mild and transient.

Anesthesia and MAC Sedation in Adults
During MAC sedation, significant respiratory events included cough, upper airway obstruction, apnea, and hypoventilation and dyspnea