

PRODUCT INFORMATION

PROPOFOL SANDOZ 200MG/20ML, 500MG/50ML, 1000MG/100ML EMULSION FOR INJECTION VIAL

NAME OF THE MEDICINE

Propofol Sandoz is composed of:-

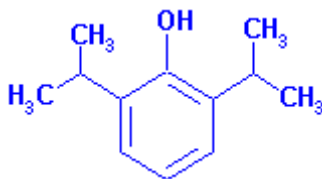
Active: Propofol (10 mg/mL).

Excipients: Soya oil (100 mg/mL), glycerol (22.5 mg/mL), egg lecithin (12 mg/mL), sodium oleate (0.3 mg/mL).

DESCRIPTION

Chemical name: 2,6-diisopropylphenol.

Chemical structure:



CAS: 2078-54-8.

Molecular formula: C₁₂H₁₈O

Molecular Weight: 178

Propofol Sandoz is a white, oil in water emulsion in a clear glass vial.

PHARMACOLOGY

Pharmacodynamics: 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, as for other general anaesthetics, is poorly understood. The majority of pharmacodynamic properties exhibited by propofol are proportional to the dose or concentration in the blood. These dose or dose rate dependent properties include the desired therapeutic effects of mild sedation through to anaesthesia, but also include the increasing incidence of cardiac and respiratory depression seen with increasing dose.

The cardiovascular effects of propofol range from a minimal reduction in blood pressure through to arterial hypotension, and a decrease in heart rate. However, the

haemodynamic parameters normally remain relatively stable during maintenance and the incidence of untoward haemodynamic changes is low.

Although ventilatory depression can occur following administration of propofol, any effects are qualitatively similar to those of other intravenous anaesthetic agents and are readily manageable in clinical practice.

It has been reported that in patients with normal intraocular pressure that propofol anaesthesia produces a decrease in intraocular pressure, which may be associated with a concomitant decrease in systemic vascular resistance.

In combination with hypocarbia, propofol increases cerebrovascular resistance, decreases cerebral blood flow, cerebral metabolic oxygen consumption and intracranial pressure, but does not affect cerebrovascular reactivity to changes in arterial carbon dioxide tension.

It has been stated that limited experience in susceptible patients does not indicate any propensity of propofol to induce malignant hyperthermia.

Propofol does not suppress the adrenal response to adrenocorticotrophic hormone (ACTH).

Pharmacokinetics: The pharmacokinetics of propofol show a three compartment open model with compartments representing the plasma, rapidly equilibrating tissues, and slowly equilibrating tissues. Following an intravenous bolus dose, there is rapid equilibration between the plasma and the highly perfused tissue of the brain, thus accounting for the rapid onset of anaesthesia. Plasma levels initially decline rapidly as a result of both distribution and metabolic clearance. The initial (distribution) half-life is between two and four minutes, followed by a rapid elimination phase with a half-life of 30 to 60 minutes and followed by a slower final phase, representative of redistribution of propofol from poorly perfused tissue. Accumulation may occur if higher than necessary infusion rates are used.

In the adult, propofol clearance ranges from 1.5 to 2 L/minute (21 to 29 mL/kg/minute). Propofol is primarily metabolised by the liver to predominantly glucuronide conjugates and their corresponding quinols, which are inactive. These are excreted via the kidney. The pharmacokinetics of propofol are linear over the recommended range of infusion rates of the product. Moderate hepatic or renal impairment do not alter these pharmacokinetics. Patients with severe hepatic or renal impairment have not been adequately studied.

In children, the distribution and clearance down to the age of three years are similar to those of adults.

In older patients for a given dose, a higher peak plasma concentration is observed. The VD (volume of distribution) and clearance are also decreased; which may explain the decreasing dose requirement with increasing age and the sensitivity of older patients to the other dose related effects of propofol.

Discontinuation of propofol after the maintenance of anaesthesia for approximately one hour, or of Intensive Care Unit (ICU) sedation for one day, results in a prompt decrease in blood propofol concentrations and rapid awakening, usually within five minutes. Longer infusions (ten days of ICU sedation) result in accumulation of significant tissue stores of propofol, such that the reduction in circulating propofol is slowed and the time to awakening may be increased by up to 15 minutes.

INDICATIONS

Short acting intravenous anaesthetic agent suitable for induction and maintenance of general anaesthesia in adults and in children aged three years and older. Propofol Sandoz has no analgesic properties.

Although the safety and efficacy of propofol in paediatric day surgery have not been demonstrated, it may be a useful agent in this setting and its use should not be precluded.

Propofol Sandoz may also be used in adults for sedation of ventilated patients receiving intensive care.

Propofol Sandoz may also be used in adults for monitored conscious sedation for surgical and diagnostic procedures.

CONTRAINDICATIONS

Known allergy to propofol or any of the other ingredients contained in Propofol Sandoz (see NAME OF THE MEDICINE).

Propofol Sandoz is contraindicated in children 16 years of age or younger for sedation during intensive care and for monitored conscious sedation for surgical and diagnostic procedures.

PRECAUTIONS

Monitoring and facilities: As with all anaesthetic procedures, Propofol Sandoz should be given by those trained in anaesthesia (or where appropriate, doctors trained in the care of patients in intensive care). Patients should be continuously monitored and facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment and other resuscitation facilities should be readily available at all times. Propofol Sandoz should not be administered by the person conducting the diagnostic or surgical procedure.

When Propofol Sandoz is administered as a sedative for surgical or diagnostic procedures, patients should be continuously monitored by persons not involved in the

conduct of the surgical/ diagnostic procedures. When propofol is used for sedation during operative procedures, involuntary patient movements may occur. During procedures requiring immobility these movements may be hazardous to the operative site. Oxygen supplementation should be immediately available and provided when clinically indicated; oxygen saturation should be monitored in all patients. Patients should be continuously monitored for early signs of hypotension, apnoea, airway obstruction and/or oxygen desaturation. These cardiorespiratory effects are more likely to occur following rapid initiation (loading) bolus doses or during supplemental maintenance bolus doses, especially in the elderly, debilitated and American Society of Anesthesiologists (ASA) grade III or IV patients, and with coadministration of other sedatives and opioid agents. Monitoring during the procedure and during the recovery period should be in accordance with the needs of the patient.

Premedication: During induction of anaesthesia, hypotension and apnoea, similar to effects with other intravenous anaesthetic agents, commonly occur and may be influenced by the rate of administration, the use of premedication and other agents including benzodiazepines.

Propofol lacks vagolytic activity and has been associated with reports of bradycardia (occasionally profound) and also asystole. The intravenous administration of an anticholinergic agent before induction or during maintenance of anaesthesia should be considered, especially in situations where vagal tone is likely to predominate or when Propofol Sandoz is used in conjunction with other agents likely to cause bradycardia (see also INTERACTIONS WITH OTHER MEDICINES).

Induction, maintenance and recovery: Occasionally hypotension may require use of intravenous fluids and reduction in the rate of administration of Propofol Sandoz during the period of anaesthetic maintenance. Ventilatory depression can occur following administration of propofol. Propofol reduces cerebral blood flow, intracranial pressure and cerebral metabolism. This reduction in intracranial pressure is greater in patients with an elevated baseline intracranial pressure. An adequate period is needed prior to discharge of the patient to ensure full recovery after general anaesthesia. Very rarely the use of propofol may be associated with the development of unconsciousness after the period when recovery from anaesthesia should have occurred. This may be accompanied by an increase in muscle tone and may or may not be preceded by a period of wakefulness. Although recovery is spontaneous, appropriate care of an unconscious patient should be administered.

Concomitant disease states: As with other intravenous anaesthetic agents, caution should be applied in patients with cardiac, respiratory, renal or hepatic impairment, or in hypovolaemic or debilitated patients.

Elevation of serum triglycerides: Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. As Propofol Sandoz is formulated as an oil-in-water emulsion, elevations in serum triglycerides may occur when the product is administered for extended periods of time. Patients at risk of hyperlipidaemia should be monitored for increases in serum triglycerides or serum turbidity. Administration of Propofol

Sandoz should be adjusted if lipids are being cleared inadequately from the body. A reduction in the quantity of concurrently administered lipids is indicated to compensate for the amount of lipid infused as part of the Propofol Sandoz formulation. 1.0 mL of Propofol Sandoz contains approximately 0.1 g of fat. The calorific value of Propofol Sandoz is similar to that of Intralipid 10%. That is, 1.0 mL of Propofol Sandoz provides 1.1 kcals.

Caution should be taken when treating patients with mitochondrial disease. These patients may be susceptible to exacerbations of their disorder when undergoing anaesthesia, surgery and ICU care. Maintenance of normothermia, provision of carbohydrates and good hydration are recommended for such patients. The early presentations of mitochondrial disease exacerbation and of the 'propofol infusion syndrome' may be similar.

Epilepsy: Propofol has been found to have no effect on electroshock seizure threshold in animals. When propofol is administered to an epileptic patient, there may be a risk of seizure during the recovery phase. Perioperative myoclonia, less frequently including convulsions and opisthotonus, has occurred in temporal relationship to cases in which propofol has been administered.

As with thiopentone, *in vitro* studies have shown that propofol is much less potent than etomidate in the inhibition of synthesis of adrenocortical hormones. At concentrations of propofol likely to be encountered in anaesthetic practice, no clinically significant effect on adrenocortical hormones has been noted in studies to date.

Anaphylactoid reactions: Propofol has been reported to occasionally cause clinical anaphylactic/ anaphylactoid type of reactions with angioedema, bronchospasm, erythema and hypotension. These reactions have been reported to respond to adrenaline.

Use for sedation during intensive care: Life-threatening adverse events, occurring together or in combinations, of cardiac failure, arrhythmias, metabolic acidosis, rhabdomyolysis and renal failure associated with propofol when used for sedation during intensive care.

There have been very rare reports of metabolic acidosis, rhabdomyolysis, hyperkalaemia, and/or rapidly progressive cardiac failure (in some cases with a fatal outcome) in adults treated for more than 58 hours with propofol infusions in excess of 5 mg/kg/hour. These reports have mainly (but not exclusively) been in patients with serious head injuries associated with raised intracranial pressure. The following appear to be major risk factors for the development of these events: decreased oxygen delivery to tissues; serious neurological injury and/or sepsis; high dosages of one or more of the following pharmacological agents: vasoconstrictors, steroids, inotropes and/or propofol. If these adverse events occur unexpectedly in the presence of high infusion rates of propofol, or hypertriglyceridemia/lipidemia is detected, consideration should be given to decreasing the propofol dosage or switching to an alternative sedative. In the event of propofol dosage modification patients with raised intracranial

pressure should continue to be monitored and treated appropriately as should patients with metabolic, respiratory and/or haemodynamic disturbances. The risk of these life-threatening events occurring may be increased in the presence of persistent low cardiac output. The maximum dose of propofol for adult sedation during intensive care should not exceed 4.0 mg/kg/hour [see DOSAGE and ADMINISTRATION]. The use of propofol for sedation in children 16 years of age and younger during intensive care and for monitored conscious sedation for surgical and diagnostic procedures is contraindicated [see CONTRAINDICATIONS].

Disodium edetate is a chelator of metal ions, including zinc. Calcium disodium edetate has been used in gram quantities to treat heavy metal toxicity. When used in this manner, it is possible that as much as 10 mg of elemental zinc can be lost per day via this mechanism. Although with propofol there are no reports of decreased zinc levels or zinc deficiency-related adverse events, propofol should not be infused for longer than 5 days without providing a drug holiday to safely replace estimated or measured urine zinc losses.

The need for supplemental zinc should be considered during prolonged administration of propofol, particularly in patients who are predisposed to zinc deficiency, such as those with burns, diarrhoea and/or major sepsis.

Paediatric Use: There are no clinical trials to support the use of propofol for the sedation of children with croup or epiglottitis receiving intensive care.

Use in neonates: Propofol is not recommended for induction and maintenance of anaesthesia in neonates. There are no data to support the use of propofol for the sedation of premature neonates receiving intensive care.

Aseptic technique: (See also Pharmaceutical precautions, below.) Strict aseptic technique must always be maintained during handling. Propofol Sandoz is for single use in one patient only. Propofol Sandoz can support the growth of microorganisms as it is not an antimicrobially preserved product. There have been reports in which failure to use aseptic technique when handling propofol injection was associated with microbial contamination of the product and with fever, infection/sepsis, other life-threatening illness, and/or death. Accordingly, strict aseptic technique must be adhered to. Do not use if contamination is suspected. Discard unused portions as directed within the required time limits (see below). When Propofol Sandoz is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after breaking the vial seal. To reduce microbiological hazard, use as soon as practicable after reconstitution. If storage is required, hold at 2-8°C for not more than 12 hours. Asepsis must be maintained for both Propofol Sandoz and the infusion equipment throughout the infusion period. Any drugs or fluids added to the Propofol Sandoz line must be administered close to the cannula site. Propofol Sandoz must not be administered via a microbial filter. Containers of Propofol Sandoz and any syringe containing Propofol Sandoz are for single use in an individual patient. In accordance with established guidelines for other lipid emulsions, a single infusion of Propofol Sandoz must not exceed 12 hours. At the end of the procedure or at 12 hours,

whichever is the sooner, both the reservoir of Propofol Sandoz and the infusion line must be discarded and replaced as appropriate.

Pharmaceutical precautions: (See also Aseptic technique, above.)

Storage precautions - The emulsion should be stored between 2 and 30°C; it must not be frozen.

In use precautions - Each vial should be shaken before use. Do not use if the emulsion is separated or discoloured. Any portion of the contents remaining after use should be discarded. The emulsion should not be mixed prior to administration with other therapeutic agents or infusion fluids other than Glucose 5% Intravenous Infusion BP. The final concentration of propofol should not be less than 2mg/mL to preserve the emulsion base.

The neuromuscular blocking agents atracurium and mivacurium should not be given through the same intravenous line as Propofol Sandoz without prior flushing.

Carcinogenesis, mutagenesis, impairment of fertility: Animal carcinogenicity studies have not been performed with propofol. Propofol was not genotoxic in a series of assays for gene mutation (*Salmonella typhimurium*, *Saccharomyces cerevisiae*), chromosomal damage (dominant lethal, micronucleus and cytogenetics assays) and other genotoxic effects (*Saccharomyces cerevisiae* gene conversion).

Studies in female rats at intravenous doses up to 15 mg/kg/day for two weeks before pregnancy to day 7 of gestation did not show impaired fertility. Male fertility in rats was not affected in a dominant lethal study at intravenous doses up to 15 mg/kg/day for five days.

Use in pregnancy: (Category C)

All general anaesthetics cross the placenta and carry the potential to produce central nervous system and respiratory depression in the newborn infant. In routine practice this does not appear to be a problem; however, in the compromised fetus, careful consideration should be given to this potential depression, and to the selection of anaesthetic drugs, doses and techniques.

Propofol Sandoz should not be used in pregnancy. Teratology studies with propofol in rats and rabbits show some evidence of delayed ossification or abnormal cranial ossification with an increase in the incidence of subcutaneous haematomas. Reproductive studies in rats suggest that administration of propofol to the dam adversely affects perinatal survival of the offspring.

Obstetrics: Propofol Sandoz should not be used for obstetric anaesthesia as propofol crosses the placenta and may be associated with neonatal depression.

Use in lactation: Propofol Sandoz is not recommended for use in women who are breastfeeding because propofol has been reported to be excreted in human milk and the effects of oral absorption of small amounts of propofol are unknown.

Effect on ability to drive or operate machinery: Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after general anaesthesia.

INTERACTIONS WITH OTHER MEDICINES

As with other intravenous sedative agents, when propofol is given with central nervous system depressants, such as potent analgesics, the sedative effect may be intensified and the possibility of severe respiratory or cardiovascular depression should be considered. The induction dose requirements of Propofol Sandoz may be reduced in patients with intramuscular or intravenous premedication (see PRECAUTIONS, Premedication), particularly with narcotics (e.g. morphine, meperidine and fentanyl, etc.) and combinations of opioids and sedatives (e.g. benzodiazepines, barbiturates, chloral hydrate, droperidol, etc.). These agents may increase the anaesthetic or sedative effects of propofol and may also result in more pronounced decreases in systolic, diastolic and mean arterial pressures and cardiac output. Decreased oxygen saturation has been reported when propofol is administered with fentanyl; and for this reason, oxygen supplementation should be used. During maintenance of anaesthesia or sedation, the rate of Propofol Sandoz administration should be adjusted according to the desired level of anaesthesia or sedation and may be reduced in the presence of supplemental analgesic agents (e.g. nitrous oxide or opioids). The concurrent administration of potent inhalational agents (e.g. isoflurane, enflurane and halothane) during maintenance with propofol has not been extensively evaluated. These inhalational agents can also be expected to increase the anaesthetic or sedative and cardiorespiratory effects of Propofol Sandoz.

Profound hypotension has been reported following anaesthetic induction with propofol in patients treated with rifampicin.

Propofol does not cause a clinically significant change in onset, intensity or duration of action of the commonly used neuromuscular blocking agents (e.g. suxamethonium and nondepolarising muscle relaxants).

No significant adverse interactions with commonly used premedications or drugs used during anaesthesia or sedation (including a range of muscle relaxants, inhalational agents, analgesic agents and local anaesthetic agents) have been observed.

Lower doses of Propofol Sandoz may be required where general anaesthesia is used as an adjunct to regional anaesthetic techniques.

ADVERSE EFFECTS

It has been reported that during induction in clinical trials hypotension and transient apnoea occurred in up to 75% of patients. Excitatory phenomena such as involuntary movements, twitches, tremors, hypertonus and hiccup occurred in 14% of patients. Bradycardia responsive to atropine has been reported.

During the recovery phase vomiting, headache and shivering occurred in about 2% of the patients, with nausea occurring more frequently.

Very Common

- Body as a whole: Pain during injection (burning, tingling/ stinging)

Common

- Body as a whole: elation/ euphoria, headache, shivering.
- Cardiovascular: Hypotension, hypertension, brachycardia.
- Gastrointestinal: Nausea, vomiting.
- Respiratory: Transient apnoea, cough.
- Skin: Flush/ rash.

Uncommon

- Cardiovascular: Arrhythmias, tachycardia, extrasystole.
- Blood: Thrombosis, phlebitis.

Rare

- Body as a whole: Fever.
- Central nervous system: Convulsions and seizures of the epileptic type.
- Urogenital: Discolouration of the urine on prolonged use.
- Other: Anaphylactoid reactions, in some cases with angioedema, bronchospasm, erythema and hypotension. (These reactions have been reported to respond to adrenaline.)

Very rare

- Musculoskeletal and connective tissue- Rhabdomyolysis (when propofol has been administered at doses greater than 4 mg/kg/hour for ICU sedation).
- Gastrointestinal: Pancreatitis, abdominal cramps.
- CNS: Pulmonary oedema, post operative unconsciousness
- Other: Hiccup, post operative fever .

Very rare reports of cardiac failure, metabolic acidosis, renal failure and hyperkalaemia have been reported.

Occasionally, hypotension may require use of intravenous fluids and reduction of the rate of administration of Propofol Sandoz during the period of anaesthetic maintenance or sedation.

Epileptiform movements, including convulsions and opisthotonus, have occurred. As with other anaesthetic agents, depression of cardiac output may occur. As with other anaesthetics, sexual disinhibition may occur during recovery. Depression, crying, confusion, restlessness, bronchospasm or laryngospasm were also observed.

Following abrupt discontinuation of propofol in children receiving intensive care, withdrawal symptoms and flushing have been noted. Cardio-respiratory depression

may occur in neonates if paediatric dosage regimen is used for induction of anaesthesia.

Accidental clinical extravasation and animal studies showed minimal tissue reaction.

Intra-arterial injection in animals did not induce local tissue effects.

Other reported adverse effects include:

Psychiatric disorders

Not known: drug abuse and drug dependence.

Respiratory, thoracic and mediastinal disorders

Not known: Respiratory depression (dose dependent).

General disorders and administration site conditions

Very Rare: Tissue necrosis following accidental extravascular administration.

Not known: Local pain, swelling, following accidental extravascular administration.

Injury, poisoning and procedural complications

Necrosis has been reported where tissue viability has been impaired.

DOSAGE AND ADMINISTRATION

Aseptic technique (refer also to PRECAUTIONS): Strict aseptic technique must always be maintained during the handling of Propofol Sandoz. Propofol Sandoz is for single use in one patient only. Propofol Sandoz can support the growth of microorganisms as it is not an antimicrobially preserved product. Accordingly, strict aseptic technique must still be adhered to. Do not use if contamination is suspected. Discard unused portions as directed within the required time limits (see PRECAUTIONS, Aseptic technique). There have been reports in which failure to use aseptic technique when handling propofol products was associated with microbial contamination of the product and with fever, infection/ sepsis, other life-threatening illness, and/or death.

Adults - Induction of general anaesthesia: Propofol Sandoz may be used to induce anaesthesia by slow bolus injection or infusion. In unpremedicated and in premedicated patients, it is recommended that Propofol Sandoz should be titrated (approximately 4 mL (40 mg) every ten seconds in an average healthy adult) against the response of the patient until the clinical signs show the onset of anaesthesia. Most adult patients aged less than 55 years are likely to require Propofol Sandoz at 2.0 to 2.5 mg/kg. In elderly patients, requirements will be generally less (see Elderly patients, below). In general, slower rates of infusion at induction results in a lower induction dose requirement and greater haemodynamic stability. In patients of ASA grades III and IV, lower rates of administration should be used (approximately 2 mL (20 mg) every ten seconds).

Recovery from induction doses usually occurs within five to ten minutes.

Maintenance of general anaesthesia: Anaesthesia can be maintained by administering Propofol Sandoz either by continuous infusion or by repeat bolus injections to maintain the depth of anaesthesia required. Experience in procedures lasting more than one hour is reported to be limited.

Continuous infusion - The required rate of administration varies considerably between patients, but rates in the region of 0.067 to 0.2 mg/kg/minute (4 to 12 mg/kg/hour) usually maintain satisfactory anaesthesia.

Repeat bolus injections - If a technique involving repeat bolus injections is used, increments of 25 mg (2.5 mL) to 50 mg (5 mL) may be given according to clinical need.

Sedation during intensive care: When used to provide sedation for ventilated adult patients undergoing intensive care, it is recommended that Propofol Sandoz be given by continuous infusion. The infusion rate should be adjusted according to the depth of sedation required but rates in the region of 1.0 to 3.0 mg/kg/hour should achieve satisfactory sedation. Infusion rates greater than 4.0 mg/kg/hour are not recommended.

Propofol Sandoz is contraindicated for sedation in children as safety and efficacy have not been demonstrated. Although no causal relationship has been established, serious adverse events (including fatalities) have been observed from spontaneous reports of unregistered use. These events were seen more frequently in children with respiratory tract infections (including croup) given doses in excess of those recommended for adults. Lipaemia and an evolving metabolic acidosis may be precursors of fatal outcomes.

Monitored conscious sedation for surgical and diagnostic procedures: Propofol Sandoz is contraindicated for sedation in children as safety and efficacy have not been demonstrated.

To provide sedation for surgical and diagnostic procedures in adult patients, rates of administration should be individualised and titrated to clinical response.

Most patients will require 0.5 to 1 mg/kg over one to five minutes for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol Sandoz infusion to the desired level of sedation; most patients will require 1.5 to 3.0 mg/kg/hour. In addition to the infusion, bolus administration of 10 to 20 mg may be used if a rapid increase in the depth of sedation is required. In patients in ASA grades III or IV (according to the classification of the American Society of Anaesthesiologists) and in the elderly, the rate of administration and dosage may need to be reduced. Patients should not be discharged for at least three hours after the procedure. Monitored conscious sedation in patients should be continuously monitored by persons not involved in the conduct of the surgical or diagnostic procedure. Oxygen supplementation should be immediately available and provided where clinically indicated; oxygen saturation should be monitored in all patients. Patients should be

continuously monitored for early signs of hypotension, apnoea, airway obstruction and/or oxygen desaturation. These cardiorespiratory effects are more likely to occur following rapid initiation (loading) boluses or during supplemental maintenance boluses, especially in the elderly, debilitated or ASA grade III or IV patients. Patients should be monitored during sedation and recovered according to the standards of the Australian and New Zealand College of Anaesthetists.

Use in the elderly: In elderly patients the dose requirement for induction of anaesthesia with Propofol Sandoz is reduced. The reduction should take account of the physical status and age of the patient. The reduced dose should be given at a slower rate and titrated against the response. Induction infusion rates of 300 mL/hour (50 mg/minute) are associated with less hypotension and apnoea in elderly patients. Where Propofol Sandoz is used for maintenance of anaesthesia or sedation the rate of infusion or target concentration should also be reduced. Patients of ASA grades III and IV will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in the elderly unventilated patient as this may lead to apnoea. A rapid bolus may also depress cardiac function.

Paediatric usage - Induction of general anaesthesia: Propofol Sandoz is not recommended for use in children less than three years of age. When used to induce anaesthesia in children, it is recommended that Propofol Sandoz be given slowly until the clinical signs show the onset of anaesthesia. The dose should be adjusted for age and/or weight. Most patients over eight years of age are likely to require approximately 2.5 mg/kg Propofol Sandoz for induction of anaesthesia. Under this age the requirement may be more. Lower dosage is recommended for children of ASA grades III or IV.

Maintenance of general anaesthesia: Propofol Sandoz is not recommended for use in children less than three years of age. Anaesthesia can be maintained by administering Propofol Sandoz by infusion or repeat bolus injection to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients but rates in the region of 9 to 15 mg/kg/hour usually achieve satisfactory anaesthesia.

Sedation during intensive care: Propofol Sandoz is contraindicated for sedation in children as safety and efficacy have not been demonstrated. Although no causal relationship has been established, serious adverse events (including fatalities) have been observed from spontaneous reports of unregistered use. These events were seen more frequently in children with respiratory tract infections (including croup) given doses in excess of those recommended for adults. Lipaemia and an evolving metabolic acidosis may be precursors of fatal outcomes.

Monitored conscious sedation for surgical and diagnostic procedures: Propofol Sandoz is contraindicated for sedation in children as safety and efficacy have not been demonstrated.

Administration: See also Precautions, Pharmaceutical precautions.

Propofol Sandoz can be infused undiluted from plastic syringes or glass infusion bottles. It can be diluted with Glucose 5% Intravenous Infusion BP only, and used from glass or PVC infusion bags/bottles. Dilutions should be prepared aseptically immediately before administration and must be used within six hours of preparation. Such dilutions must not be more dilute than one volume of Propofol Sandoz to four volumes of diluent (propofol 2 mg/mL). It is recommended that in order to prepare diluted Propofol Sandoz, the volume of Glucose 5% Intravenous Infusion BP removed from the infusion bag during the dilution process be totally replaced in volume by Propofol Sandoz emulsion. The dilution may be used with a variety of infusion control techniques but a giving set used alone will not avoid the risk of accidental, uncontrolled infusion of large volumes of diluted Propofol Sandoz. A burette, drop counter or volumetric pump must be included in the infusion line. The risk of uncontrolled infusion must be taken into account when deciding the maximum amount of dilution in the burette.

When Propofol Sandoz is used undiluted to maintain anaesthesia, it is recommended that drop counters, syringe pumps or volumetric infusion pumps should always be used to control infusion rates.

Changes to the haemodynamic parameters such as systolic arterial pressure, diastolic arterial pressure, cardiac output and systemic vascular resistance appear to be independent of changes to the rate of infusion of propofol.

Propofol Sandoz may be administered via a Y-piece close to the injection site, into infusions of Glucose 5% Intravenous Infusion BP, Sodium Chloride 0.9% Intravenous Infusion BP, or Glucose 4% with Sodium Chloride 0.18% Intravenous Infusion BP. Propofol Sandoz should not be mixed prior to administration with other therapeutic agents or infusion fluids other than Glucose 5% Intravenous Infusion BP.

OVERDOSAGE

Accidental overdosage is likely to cause cardiorespiratory depression.

Treatment: Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression would require lowering of the patient's head and, if severe, use of plasma expanders and pressor agents.

PRESENTATION AND STORAGE CONDITIONS

Injection, emulsion for (intravenous infusion)

- Propofol Sandoz in a glass vial containing propofol 1% in a clear glass vial with a grey butyl rubber closure and aluminium and plastic violet flip-off seal.

Propofol Sandoz is available in 20mL, 50mL and 100mL vials.

Propofol Sandoz in unopened containers should be stored below 30°C. Do not freeze.
Keep in carton until use to protect contents from light.

NAME AND ADDRESS OF THE SPONSOR

Sandoz Pty Ltd
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54 Waterloo Road
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Australia
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POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG): 16/06/2008

DATE OF MOST RECENT AMENDMENT: 09/02/2016