Professional Information for Human Medicine

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

Propofol 2 % (20 mg/ml) B. Braun emulsion for intravenous injection or infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml emulsion for injection or infusion contains 20 mg propofol.

One vial of 50 ml contains 1000 mg propofol.

Excipients with known effect:

1 ml of emulsion contains:

Soya bean oil refined	50 mg
Sodium	0,030 mg

For the full list if excipients, see section 6.1

3. PHARMACEUTICAL FORM

Emulsion for injection or infusion.

White milky oil-in-water emulsion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Propofol B. Braun is indicated for:

- Induction and maintenance of general anaesthesia as part of a balanced anaesthetic technique
- Sedation of ventilated adult patients receiving intensive care for a period of up to 72 hours.

4.2 Posology and method of administration

Posology

Propofol should be given by those trained in anaesthesia (or, where appropriate, doctors trained in the care of patients in Intensive Care).

Patients should be constantly monitored and facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment and other resuscitative facilities should be readily available at all times. Propofol should not be administered by the person conducting the diagnostic or surgical procedure.

Supplementary analgesic medicines are required in addition to Propofol B. Braun, where analgesia is required.

Propofol B. Braun has been used in association with spinal and epidural anaesthesia and with commonly used premedication, neuromuscular blocking medicines, inhalation and analgesic medicines; no pharmacological incompatibility has been encountered.

Dosage adjustment may be necessary when used together with the above medicines, particularly the narcotics (e.g. morphine, meperidine and fentanyl), combinations of opioids and sedatives (e.g. benzodiazepines, barbiturates, droperidol etc.), supplementary analgesic medicines (e.g. nitrous oxide or opioids) and the potent inhalation medicines (e.g. isoflurane, enflurane and halothane).

Where general anaesthesia with Propofol B. Braun is used simultaneously with a regional anaesthetic technique, lower doses of Propofol B. Braun may be required.

A. ADULTS

Induction of general anaesthesia:

Propofol B. Braun should be used to induce anaesthesia by infusion and only in those patients who will receive Propofol B. Braun for maintenance of anaesthesia.

In unpremedicated and premedicated patients:

Most adult patients aged less than 55 years are likely to require 1,5 to 2,5 mg/kg (0,075 - 0,125 mL/kg) of Propofol B. Braun, (approximately 40 mg every 10 seconds in an average healthy adult) by infusion titrated against the response of the patient until clinical signs show onset of anaesthesia. The total dose required can be reduced by lower rates of administration (20-50 mg/min [1-2,5 mL/min]). Over the age of 55 years the requirement will generally be less. In patients of ASA Grades 3 and 4, lower rates of administration should be used (approximately 20 mg [1 mL] every 10 seconds).

Maintenance of general anaesthesia:

Anaesthesia can be maintained by administering Propofol B. Braun by continuous infusion to prevent the clinical signs of light anaesthesia.

Infusion:

The average rate of administration varies between patients, but rates in the region of 4 to 12 mg/kg/hr (0,2 -0,6 ml/kg/hr) usually maintain satisfactory anaesthesia.

Slightly higher rates of administration may be required for 10 to 20 minutes after induction of anaesthesia.

Sedation during intensive care:

To provide sedation for ventilated adult patients undergoing intensive care, it is recommended that Propofol B. Braun be given by continuous infusion, for up to 72

hours. Adjust infusion rate according to the depth of sedation required. Rates of 0,3-4,0 mg/kg/hr should achieve satisfactory sedation. Rates above 4,0 mg/kg/hr are not recommended.

B. ELDERLY PATIENTS

In elderly patients the dose requirement for induction of anaesthesia with Propofol B. Braun 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. Where Propofol B. Braun is used for maintenance of anaesthesia or sedation the rate of infusion or "target concentration" should also be reduced. Patients of ASA Grades 3 and 4 will require further reductions in dose and dose rate.

C. CHILDREN

Induction of general anaesthesia:

Propofol B. Braun is not recommended for use in children less than 3 years of age (see Section 4.3, 4.4 and 4.8).

It is recommended that Propofol B. Braun be given slowly until the clinical signs show the onset of anaesthesia. Adjust dose for age and/or weight. Most patients over 8 years of age are likely to require approximately 2,5 mg/kg (0,125 ml/kg) of Propofol B. Braun for induction. Between the ages of 3 and 8 years the requirement may be more. Lower dosage is recommended for children of ASA Grades 3 and 4.

Maintenance of general anaesthesia:

Propofol B. Braun is not recommended for use in children less than 3 years of age.

Administer Propofol B. Braun by infusion to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients. 9 to 15 mg/kg/hr (0,45 - 0,75 ml/kg/hr) usually achieves satisfactory anaesthesia.

Sedation during intensive care:

Propofol B. Braun is not recommended 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 unlicensed use and these events were seen most often in children with respiratory tract infections, given doses in excess of those recommended for adults. Associated findings include metabolic acidosis, lipaemia, rhabdomyolysis, cardiac irregularities and renal failure.

The duration of administration must not exceed 72 hours

Method of administration

Administration of Propofol B. Braun by bolus injection is not recommended.

Propofol B. Braun must be used undiluted. It is recommended that equipment such as drop counters, syringe pumps or volumetric infusion pumps should always be used to control infusion rates. Propofol B. Braun can be used for infusion undiluted from glass infusion bottles, plastic syringes, or Propofol B. Braun pre-filled syringes.

Propofol B. Braun may be administered via a Y-piece close to the injection site, into intravenous infusions of dextrose 5 % or sodium chloride 0,9 %.
It is recommended that blood lipid levels be monitored routinely should Propofol B. Braun be administered to patients thought to be at particular risk of fat overload. Administration of Propofol B. Braun should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to

take account of the amount of lipid infused as part of the Propofol B. Braun formulation; 1,0 mL of Propofol B. Braun contains 0,1 g of fat.

Patients with hypovolaemia should have fluid-volume deficits corrected prior to administration of Propofol B. Braun.

General anaesthesia:
In accordance with established guidelines for other lipid emulsions a single infusion of Propofol B. Braun must not exceed 6 hours. The syringe or giving set and any unused portion of Propofol B. Braun or solution containing Propofol B. Braun must be discarded at the end of the surgical procedure, or at 6 hours, whichever is the sooner, and replaced as appropriate.

Intensive care sedation:
Administration should commence promptly and must be completed within 12 hours after the vial has been spiked. The tubing and any unused portions of Propofol B. Braun must be discarded after 12 hours.

If Propofol B. Braun is transferred to a syringe or other container prior to administration, the handling procedures for "General anaesthesia" (above) should be followed and the product should be discarded and administration lines changed after 6 hours.

4.3 Contraindications

- Hypersensitivity to the active substance propofol or to any of the excipients of Propofol B. Braun listed in section 6.1
- Propofol B. Braun is not for use in children under the age of 3 years

- Propofol B. Braun contains soya-bean oil and should not be used in patients who are hypersensitive to peanut or soya
- Propofol B. Braun must not be used in patients of 16 years of age or younger for sedation for intensive care
- Sedation of children of all ages with croup or epiglottitis receiving intensive care.

4.4 Special warnings and precautions for use

Respiration will be depressed and must be monitored to ensure adequate gas exchange. Special care should be exercised when used with other respiratory depressants.

A generalised systemic reaction which may be anaphylactic in nature (including angioedema, bronchospasm, erythema and hypotension) may occur following propofol administration - estimated as 1 in 15 000.

The abuse of and dependence on propofol, predominantly by health care professionals, have been reported. As with other general anaesthetics, the administration of propofol without airway care may result in fatal respiratory complications.
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.

An adequate period is needed prior to discharge of the patient to ensure full recovery after use of propofol. The use of propofol may be associated with the development of a period of post-operative unconsciousness, which may be accompanied by an increase in muscle tone. This may or may not be preceded by a period of wakefulness. Although

recovery is spontaneous, appropriate care of an unconscious patient should be administered.

Propofol induced impairment is not generally detectable beyond 12 hours. The effects of propofol, the procedure, concomitant medications, the age and the condition of the patient should be considered when advising patients on:

- The advisability of being accompanied on leaving the place of administration
- The timing of recommencement of skilled or hazardous tasks such as driving
- The use of other medicines that may sedate (e.g. benzodiazepines, opiates, alcohol).

Interference with daily activities may continue for up to 24 hours and no legal/contractual decisions should be entered into for 24 hours after receiving anaesthetic/conscious sedation. Alcohol use should also be avoided for the same time period.

Caution should be applied in patients with cardiac, respiratory, renal or hepatic impairment or in hypovolaemic or debilitated patients.

The pharmacokinetics of propofol may be prolonged in people with chronic hepatic cirrhosis or chronic renal impairment. Recovery times may double as a result. The effects of acute hepatic or renal failure on the pharmacokinetics of propofol have not been studied.

Propofol clearance is blood flow dependent, therefore, concomitant medication that reduces cardiac output will also reduce propofol clearance.

Propofol lacks vagolytic activity and has been associated with reports of bradycardia (occasionally profound) and also asystole. The intravenous administration of an anticholinergic medicine before induction or during maintenance of anaesthesia should

be considered, especially in situations where vagal tone is likely to predominate or when propofol is used in conjunction with other medicines likely to cause bradycardia. When propofol is administered to an epileptic patient, there may be a risk of convulsion.

Paediatric population

The use of propofol is contraindicated in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data indicate that clearance is considerably reduced in neonates and has a very high inter-individual variability. Relative overdose could occur on administering doses recommended for older children and result in severe cardiovascular depression.
Propofol must not be used in patients of 16 years of age or younger for sedation for intensive care as the safety and efficacy of propofol for sedation in this age group have not been demonstrated (see section 4.3)

Propofol B. Braun is contraindicated for use in children < 3 years of age due to difficulty in titrating small volumes.
Reports from off-label use of propofol for induction of anaesthesia in neonates indicates that cardio respiratory depression may occur if the dose regimen recommended for children 3 years and over is applied (see 4.2 Posology and method of administration).

Advisory statements concerning Intensive Care Unit management

Use of propofol for ICU sedation has been associated with a constellation of metabolic disturbances and organ system failures that may result in death. Reports have been received of combinations of the following: metabolic acidosis, rhabdomyolysis, hyperkalaemia, hepatomegaly, renal failure, hyperlipidaemia, cardiac dysrhythmia,

Brugada-type ECG (elevated ST-segment and coved T-wave) and rapidly progressive cardiac failure usually unresponsive to inotropic supportive treatment. Combinations of these events have been referred to as the **Propofol infusion syndrome**. These events were mostly seen in patients with serious head injuries and children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit.

The following appear to be the 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 medicines - vasoconstrictors, steroids, inotropes and/ or propofol (usually at dose rates greater than 4 mg/kg/h for more than 48 hours).

Prescribers should be alert to these events in patients with the above risk factors and immediately discontinue Propofol B. Braun when the above signs develop. All sedative and therapeutic medicine used in the intensive care unit (ICU) should be titrated to maintain optimal oxygen delivery and haemodynamic parameters. Patients with raised intra-cranial pressure (ICP) should be given appropriate treatment to support the cerebral perfusion pressure during these treatment modifications. Medicinal practitioners are reminded if possible not to exceed the dosage of 4 mg/kg/h. Appropriate care should be applied in patients with disorders of fat metabolism, patient predisposed to fat embolism and in other conditions where lipid emulsions must be used cautiously.

Fat metabolism may be disturbed in conditions such as renal insufficiency, uncompensated diabetes mellitus, certain forms of liver insufficiency, metabolic disorders, severe trauma including long-bone and multiple fractures, and sepsis

It is recommended that blood lipid levels should be monitored if propofol is administered to patients thought to be at particular risk of fat overload. Administration of propofol should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1,0 mL of Propofol B. Braun contains 0,1 g of fat.

Additional precautions

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.

Propofol B. Braun contains no antimicrobial preservatives and supports growth of micro-organisms.

When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both propofol and infusion equipment throughout the infusion period. Any infusion fluids added to the propofol line must be administered close to the cannula site. Propofol B. Braun must not be administered via a microbiological filter. If infusion sets with filters are to be used, these must be lipid-permeable.

Propofol and any syringe containing propofol are for single use in an individual patient. In accordance with established guidelines for other lipid emulsions, a single infusion of propofol must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner, both the reservoir of propofol and the infusion line must be discarded and replaced as appropriate.

Special warnings/precautions regarding excipients

This medicine contains less than 1 mmoL sodium (23 mg) in 100 mL that is to say essentially ‘sodium free’.

Propofol B. Braun contains soybean oil, which may cause severe allergic reaction in some cases. Propofol B. Braun should not be used in patients with an allergy to peanuts, eggs, or soya protein (see section 4.3).

4.5 Interaction with other medicines and other forms of interaction

Propofol has been used in association with spinal and epidural anaesthesia and with commonly used premedicants, neuromuscular blocking medicines, inhalational medicines and analgesic medicines; no pharmacological incompatibility has been encountered. Lower doses of Propofol B. Braun may be required where general anaesthesia or sedation is used as an adjunct to regional anaesthetic techniques.

The concurrent administration of other CNS depressants such as pre-medication medicines, inhalation medicine, and analgesic medicine may add to the sedative, anaesthetic and cardiorespiratory depressant effects of Propofol B. Braun. It is recommended that Propofol B. Braun is given after the administration of opioids so that the dose of Propofol B. Braun can be carefully titrated against the response. The dosage Propofol B. Braun should be reduced if used with nitrous oxide or halogenated

anaesthetics. Although propofol does not potentiate the effects of neuromuscular blockers, bradycardia and asystole have occurred after use of propofol with atracurium or suxamethonium.

Neuromuscular blocking medicines, atracurium and mivacurium should not be given through the same intravenous line as Propofol B. Braun without prior flushing (see section 6.2).

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

A need for lower propofol doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of propofol may be considered.

Benzodiazepines: Propofol and midazolam have been reported to act synergistically (see section 4.4).

Gastrointestinal medicines: The dose of propofol required for induction, is reduced in patients given metoclopramide.

General anaesthetics: The use of halothane or isoflurane has been reported to increase serum concentrations of propofol. Synergy has been reported between propofol and etomidate.

Local anaesthetics: A reduction in the amount of propofol required to provide adequate hypnosis or sedation has been reported after bupivacaine or lidocaine. However, lidocaine is often added to propofol emulsions to reduce pain at the site of injection**.**

Opioids: Concentrations of propofol were higher in patients pre-treated with fentanyl compared to patients maintained only on nitrous oxide (see section 4.4)

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of Propofol B. Braun during pregnancy has not been established. Studies in animals have shown reproductive toxicity.

Propofol B. Braun should not be given to pregnant women. Propofol crosses the placenta and has been associated with neonatal depression. Propofol B. Braun can, however, be used during termination of pregnancy in the first trimester.

Breastfeeding

Studies of breast-feeding mothers showed that small quantities of propofol are excreted in human milk. Safety to the neonates has not been established. Women should therefore not breastfeed for 24 hours after administration of Propofol B. Braun. Milk produced during this period should be discarded.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after use of Propofol B. Braun. After administration of Propofol B. Braun, the patient should be kept under observation for an appropriate period of time. The patient should not be allowed to go home unaccompanied and should be instructed to avoid consumption of alcohol.

Propofol B. Braun induced impairment is not generally detectable beyond 12 hours (See section 4.4).

4.8 Undesirable effects

Induction and maintenance of anaesthesia or sedation with propofol is generally smooth with minimal evidence of excitation. The most commonly reported adverse reactions are pharmacologically predictable side effects of an anaesthetic/sedative medicine, such as hypotension and apnoea. These effects depend on the propofol dose administered but also on the type of premedication and other concomitant medication.

The nature, severity and incidence of adverse events observed in patients receiving Propofol B. Braun may be related to the condition of the recipients and the operative or therapeutic procedures being undertaken.

Table of Adverse Drug Reactions

Undesirable effects are listed according to their frequencies as follows:

System Organ Class	**Frequency**	**Undesirable Effects**
Immune system disorders:	Less Frequent	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
Metabolism and nutritional disorders:	Frequency not known (9)	Metabolic acidosis (5), hyperkalaemia (5), hyperlipidaemia (5)
Psychiatric disorders:	Less frequent	Sexual disinhibition

	Frequency not known (9)	Euphoric mood, drug abuse and drug dependence (8)
Nervous system disorders:	Frequent	Headache during recovery phase
	Less Frequent	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery. Postoperative unconsciousness, syncope
	Frequency not known (9)	Involuntary movements
Cardiac disorders:	Frequent	Bradycardia (1)
	Less Frequent	Pulmonary oedema, excitation. Tachycardia, premature ventricular contractions, premature atrial contractions, abnormal ECG and segment depression.
	Frequency not known (9)	Cardiac dysrhythmia (5), cardiac failure (5), (7)
Vascular disorders:	Frequent	Hypotension (2), hypertension
Respiratory, thoracic and mediastinal disorders:	Frequent	Transient apnoea during induction
	Frequency not known (9)	Respiratory depression (dose-dependent)
Gastrointestinal disorders:	Frequent	Nausea and vomiting during recovery phase
	Less frequent	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	Less frequent	Discolouration of urine following prolonged administration
	Frequency not known (9)	Renal failure (5)
General disorders and administration site conditions:	Frequent	Local pain on induction (4)
	Less frequent	Injection site thrombosis and injection site phlebitis Tissue necrosis (10) following accidental extravascular administration (11)
	Frequency not known (9)	Local pain and swelling, following accidental extravascular administration (11)
Investigations	Frequency not known (9)	Brugada type ECG (5), (6)
Injury, poisoning and procedural complications:	Less frequent	Postoperative fever

(1) Serious bradycardias are less frequent. There have been isolated reports of progression to asystole.

(2) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of propofol.

(3) Reports of rhabdomyolysis have been received 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 local pain can also be minimised by the co-administration of lidocaine (lignocaine).

(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 was usually unresponsive to inotropic supportive treatment.

(8) Abuse of and drug dependence on propofol, predominantly by health care professionals.

(9) Not known as it cannot be estimated from the available clinical trial data.

(10) Necrosis has been reported where tissue viability has been impaired.

(11) Treatment is symptomatic and may include immobilisation and, if possible, elevation of affected limb, cooling, close observation, consultation of surgeon if necessary.

Reporting of side effects

Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report and suspected adverse reactions to SAHPRA via “**6.04 Adverse Drug Reaction Reporting Form**”, found online under SAHPRAs publications: https://primaryreporting.who-umc.org/ZA. By reporting side effects, you can help provide more information on the safety of Propofol B. Braun.

4.9 Overdose

Symptoms

Accidental overdosage is likely to cause cardiorespiratory depression.

Treatment

Respiratory depression should be treated by artificial ventilation with oxygen.

Cardiovascular depression may require lowering of the patient's head and, if severe, administering plasma expanders and pressor medicines.

5. PHARMOCOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Category and pharmacological classification: A.2.1 Anaesthetics.

Pharmacotherapeutic group: other general anaesthetics, ATC-code N01AX10.

Mechanism of action

After intravenous injection of propofol, onset of the hypnotic effect is rapid. Depending on the rate of injection, the time to induction of anaesthesia is between 30 and 40 seconds.

Pharmacodynamic effect

With the recommended dosage schedule, clinically relevant accumulation of propofol after repeated bolus injection or after infusion has not been observed.

Patients recover consciousness rapidly.

Bradycardia and hypotension occasionally occur during induction of anaesthesia probably due to the lack of vagolytic activity. The cardio-circulatory situation usually normalises during maintenance of anaesthesia.

Falls in mean arterial blood pressure and changes in heartrate are observed when propofol is administered.

Ventilatory depression can occur following administration of propofol.

Propofol reduces cerebral blood flow, intracranial pressure and cerebral metabolism.

Recovery from anaesthesia is usually rapid and clear-headed. Propofol has an anti-emetic effect.

Studies have shown that propofol at concentrations likely to occur clinically, does not inhibit the synthesis of adrenocortical hormones.

The formulation of propofol in a mixed medium- and long-chain triglyceride emulsion leads to lower concentrations of free propofol in the aqueous phase compared to pure long-chain triglyceride emulsions.

Paediatric population

Limited studies on the duration of propofol based anaesthesia in children indicate safety and efficacy is unchanged up to duration of 4 hours. Literature evidence of use in children documents use for prolonged procedures without changes in safety or efficacy.

5.2 Pharmacokinetic properties

Distribution

After intravenous administration about 98 % of propofol is bound to plasma protein.
After intravenous bolus administration the initial blood level of propofol declines rapidly due to rapid distribution into different compartments (α-phase). The distribution half-life has been calculated as 2 – 4 minutes.
During elimination the decline of blood levels is slower. The elimination half-life during the ß-phase is in the range of 30 to 60 minutes. Subsequently a third deep compartment becomes apparent, representing the re-distribution of propofol from weakly perfused tissue.

The central volume of distribution is in the range of 0,2 – 0,79 L/ kg body weight, the steady-state volume of distribution in the range of 1,8 – 5,3 L/ kg body weight.

Biotransformation

Propofol is mainly metabolised in the liver to form glucuronides of propofol and glucuronides and sulphate conjugates of its corresponding quinol. All metabolites are inactive.

Elimination

Propofol is rapidly cleared from the body (total clearance approx. 2 L/ min). Clearance occurs by metabolism, mainly in the liver, where it is blood flow dependent. Clearance is higher in paediatric patients compared with adults. About 88 % of an administered dose is excreted in the form of metabolites in urine. Only 0,3 % is excreted unchanged in the urine.

Paediatric population

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 this limited trial data that indicates a large variability, no dose recommendations can be given for this age group.

Median propofol clearance in older aged children after a single 3 mg/kg bolus was 37,5 mL/ min/ kg (4 – 24 months) (n = 8), 38,7 mL/ min/ kg (11 – 43 months) (n = 6), 48 mL/ min/ kg
(1 – 3 years) (n = 12), 28,2 mL/ min/ kg (4 – 7 years) (n = 10) as compared with 23,6 mL/min/kg in adults (n = 6).

5.3 Preclinical safety data

Preclinical data reveal no specific hazard for humans based on conventional studies on repeated dose toxicity or genotoxicity. Carcinogenicity studies have not been conducted.

Published studies in animals (including primates) at doses resulting in light to moderate anaesthesia demonstrate that the use of anaesthetic medicine during the period of rapid brain growth or synaptogenesis results in cell loss in the developing brain that can be associated with prolonged cognitive deficiencies. The clinical significance of the nonclinical findings is not known.

In local tolerance studies, intramuscular injection resulted in tissue damage around the injection site.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Soya-bean oil, refined

Medium-chain triglycerides

Glycerol

Egg phospholipids for injection

Sodium oleate

Water for injections.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Incompatibilities:

Propofol B. Braun should not be mixed prior to administration with injections or infusion fluids.

The neuromuscular blocking medicine, atracurium and mivacurium should not be given through the same intravenous line as Propofol B. Braun without prior flushing.

6.3 Shelf-life

Unopened

2 years at or below 25 ºC.

After first opening:

Use immediately.

6.4 Special precautions for storage

Store at or below 25 ºC. Do not freeze.

6.5 Nature and contents of container

The bottles are made of colourless glass (type II Ph. Eur.) sealed with with bromobutyl rubber closure and aluminium caps, containing 50 ml of emulsion. It is milky –white oil-in-water emulsion. It is available in packs of 1 x 50 mL, 10 x 50 mL.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

Containers should be shaken before use.

For single use in a single patient only. Any portion of contents remaining after first use must be discarded.

If two layers can be seen after shaking, the medicinal product should not be used.

Propofol B. Braun must not be mixed with other solutions for injection or infusion. However, co-administration of Propofol B. Braun together with glucose 50 mg/ mL solution or sodium chloride 9 mg/ mL (0,9 % w/v) solution via Y-connector close to the injection site is possible.

In-use precautions:

General:

Containers should be gently shaken before use. Propofol B. Braun should be inspected for particulate matter and discolouration before administration. Do not use if there is evidence of separation of the phases of the emulsion.
Propofol B. Braun contains no antimicrobial preservatives and the vehicle supports growth of microorganisms.

When Propofol B. Braun is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol B. Braun and infusion equipment throughout the infusion period. Any infusion fluids added to the Propofol B. Braun line must be administered close to the cannula site. Propofol B. Braun must not be administered via a microbiological filter.

7. HOLDER OF CERTIFICATE OF REGISTRATION

B. Braun Medical (Pty) Ltd
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8. REGISTRATION NUMBER(S):

47/2.1/1220

9: DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

12 July 2022

10. DATE OF REVISION OF THE TEXT

14 December 2023