SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Propofol 20mg/ml (2%) emulsion for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml emulsion for injection/infusion contains 20 mg of propofol.
Each 50 ml vial contains 1000 mg of propofol.

Excipients with known effect:

Each ml emulsion for injection/infusion contains 100 mg of soya-bean oil, refined

Each 50 ml vial contains 5 g of soya-bean oil, refined.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for injection/infusion.
White aqueous isotonic oil-in-water emulsion.
Osmolality: 285 to 320 mOsm/Kg
pH is in the range of 6.0 – 8.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Propofol is a short-acting intravenous general anaesthetic for:

- Induction and maintenance of general anaesthesia in adults and children > 3 years
- Sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia in adults and children > 3 years
- Sedation of ventilated patients > 16 years of age in the intensive care unit

4.2 Posology and method of administration

Propofol must only be administered in hospitals or adequately equipped day therapy units by physicians trained in anaesthesia or in the care of patients in intensive care.

Circulatory and respiratory functions should be constantly monitored (e.g. ECG, pulse oxymetry) and facilities for maintenance of a patient airways, artificial ventilation, and other resuscitation facilities should be immediately available at all times.

For sedation during surgical and diagnostic procedures Propofol should not be administered by the same person conducting the surgical or diagnostic procedure.

Propofol has no analgesic properties and therefore supplementary analgesic agents are generally required in addition to Propofol.

Posology

The dose of Propofol should be individually adapted according to the patient's response.

Rapid bolus administration (single or repeated) should not be used in older people as this may lead to cardiorespiratory depression.

Propofol should not be used for bolus injection as this may lead to cardiorespiratory depression.

General anaesthesia in adults

Induction of anaesthesia

For induction of anaesthesia Propofol must be titrated (20-40 mg propofol every 10 seconds) against the response of the patient until clinical signs show the onset of anaesthesia.

Usually an adult patient below 55 years will require 1.5 to 2.5 mg/kg body weight.

In patients over 55 years and in patients of ASA (American Society of Anaesthesiologists) classification III and IV, especially in those with impaired cardiac function the requirements will generally be less and the total dose of Propofol may be reduced to a minimum of 1 mg propofol/kg bodyweight. These patients also need lower rates of administration (approximately 2 ml corresponding to 20 mg propofol every 10 seconds).

Maintenance of anaesthesia

Anaesthesia can be maintained by administering Propofol either by continuous infusion or repeat bolus injections (Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion only).

Continuous Infusion:

When using a continuous infusion for maintenance of anaesthesia generally doses of 4 to 12 mg/kg/h should be given. In older people, patients in unstable general conditions, patients with impaired cardiac function or hypovolaemic patients and patients of ASA grades III and IV, the dosage of Propofol may be further reduced depending on the patient's condition and on the applied anaesthetic method.

Repeat Bolus Injection:
For maintenance of anaesthesia using repeat bolus injections dosages of 25 mg up to 50 mg (=2.5 up to 5 ml Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion) should be administered depending on the clinical requirements.

Sedation of mechanically ventilated patients during intensive care

Adults and adolescents (≥ 16 years of age)
When used to provide sedation for mechanically ventilated patients under intensive care conditions, the administration of Propofol as continuous infusion it is recommended. The rate of administration has to be adapted to the level of sedation required.

A satisfactory level of sedation can generally be achieved with a dosage of 0.3–4.0 mg/kg body weight/h (see section 4.4).

Administering Propofol through a TCI-system for sedation in intensive care is not recommended.

It is recommended that blood lipid levels be monitored should Propofol be 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 contains approximately 0.1g of fat.

If the duration of sedation is in excess of 3 days, lipids should be monitored in all patients.

Sedation for diagnostic and surgical procedures in adult patients

To provide sedation during surgical and diagnostic procedures, doses and administration rates need to be adapted to the clinical response.

Most patients will require 0.5 to 1.0 mg/kg body weight over 1 to 5 minutes for induction of sedation.

For maintenance of sedation the Propofol infusion should be titrated until the desired level of sedation is achieved. Generally 1.5 to 4.5 mg/kg body weight/h will be required.

The infusion may be supplemented by bolus injections of 10 to 20 mg (1 to 2 ml Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion) if a deeper level of sedation is rapidly required.

In patients older than 55 years and in patients of ASA classification III and IV the rate of administration and dosage may need to be reduced.

If lower doses are needed, Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion can be used as an alternative.

Paediatric population

General anaesthesia in children over 3 years of age

Propofol is not recommended for induction and maintenance of anaesthesia in paediatric patients between 1 month and 3 years old, because the 20 mg/ml strength is difficult to titrate in paediatric patients because of the very small volumes that are necessary (see section 4.4).

In these patients the use of Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion is recommended.

Induction of anaesthesia
For induction of anaesthesia Propofol should be titrated slowly until clinical signs show the onset of anaesthesia. The dose should be adjusted according to age and/or body weight. Most patients over 8 years of age require approximately 2.5 mg/kg body weight Propofol for induction of anaesthesia.

In younger children, dose requirements may be higher (2.5 – 4 mg/kg body weight).

Maintenance of general anaesthesia

Anaesthesia can be maintained by administering Propofol by infusion to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients but rates in the region of 9 – 15 mg/kg/h usually achieve satisfactory anaesthesia.

In younger children, dose requirements may be higher.

For ASA III and IV patients lower doses are recommended (see also section 4.4)

Sedation of ventilated paediatric patients during intensive care

Propofol is contraindicated in paediatric patients of 16 years of age or younger in the indication for sedation in intensive care (see section 4.3).

Sedation for diagnostic and surgical procedures in children over 3 years of age

Doses and administration rates should be adjusted according to the required depth of sedation and the clinical response. Most paediatric patients require 1 – 2 mg/kg body weight Propofol for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol infusion to the desired level of sedation. Most patients require 1.5-9 mg/kg/h Propofol.

In ASA III and IV patients lower doses may be required.

Method of administration

Containers should be shaken before use. If two layers can be seen after shaking, the emulsion should not be used.

Propofol is administered intravenously as an injection or as a continuous infusion, undiluted.

Prior to use, the rubber stopper should be disinfected using a medicinal alcohol (spray or dipped swab). After use, any remaining contents must be discarded (see section 6.6).

Propofol does not contain antimicrobial preservatives and is capable of supporting the growth of microorganisms. The emulsion must be drawn aseptically into a sterile syringe or infusion system immediately after spiking the vial.

Administration must commence without delay. During infusion sterility of Propofol as well as the infusion system must be maintained.

Medicinal products or liquids that are added to a running Propofol infusion should be added close to the cannula.

Propofol must not be administered via infusion systems that are provided with a microbiological filter.

The contents of one vial of Propofol and any infusion equipment are intended for **single** use in **one** patient.

Any remainder must be discarded immediately after use.

Propofol must not be diluted.

Infusion of Propofol
When Propofol is administered as a continuous infusion, it is recommended that equipment such as burettes, drop counter, syringe pumps or volumetric infusion pumps should always be used to control infusion rates.

As applies to parenteral administration of all kinds of fat emulsions, the duration of use for **one** infusion system for a continuous infusion of Propofol must not exceed 12 hours. The infusion system and the container must be discarded and replaced after a maximum of 12 hours.

The simultaneous administration of Propofol together with an infusion solution of glucose 50 mg/ml (5%), sodium chloride 9 mg/ml (0.9%) intravenous infusion solution or a combination solution of glucose 40 mg/ml (4%) and sodium chloride 1.8 mg/ml (0.18%) close to the Y-connector near the place of injection, is possible.

Any Propofol remaining at the end of the infusion period or after changing the system needs to be discarded and destroyed.

To reduce pain on the injection site lidocaine may be injected immediately before the use of Propofol. For the specific risks of lidocaine see sections 4.4 and 4.8.

The infusion system should be rinsed before administration of muscle relaxants like atracurium and mivacurium when using the same infusion system for Propofol.

Duration of administration
Propofol can be administered for a maximum of 7 days.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Propofol contains soya oil and should not be used in patients who are hypersensitive to soya or peanut
- Propofol must not be used in patients of 16 years of age or younger for sedation in intensive care (see section 4.4)

4.4 Special warnings and precautions for use

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.

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 administered for conscious sedation, for surgical and diagnostic procedures, patients should be continually monitored for early signs of hypotension, airway obstruction and oxygen desaturation.

During induction of anaesthesia, hypotension and transient apnoea may occur depending on the dose and use of premedications and other agents.

As with other sedative agents, 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. Very rarely 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 agents that may sedate (e.g, benzodiazepines, opiates, alcohol.)

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. 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 agent 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 agents likely to cause a bradycardia.

When Propofol is administered to an epileptic patient, there may be a risk of convulsion.

Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously.

Use of Propofol is not recommended with electroconvulsive therapy.

Paediatric population

The use of Propofol is not recommended in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data (see section 5.2) 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 20 mg/ml (2%) Emulsion for Injection/Infusion is not recommended for use in children < 3 years of age due to difficulty in titrating small volumes.

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).

Advisory statements concerning Intensive Care Unit management

Use of propofol emulsion infusions for ICU sedation has been associated with a constellation of metabolic derangements 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 arrhythmia, 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 pharmacological agents - vasoconstrictors, steroids, inotropes and/or Propofol (usually at dose rates greater than 4mg/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 when the above signs develop. All sedative and therapeutic agents 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. Treating physicians 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 and in other conditions where lipid emulsions must be used cautiously.

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 contains approximately 0.1 g of fat.

This medicinal product contains less than 1 mmol sodium (23 mg) per 100 ml, i.e. essentially 'sodium- free'.

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

EDTA chelates metal ions, including zinc, and reduces microbial growth rates. 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.

When Propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or 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 must not be administered via a microbiological filter.

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.

Dilutions of Propofol 10 mg/ml (1%) emulsion for injection/infusion with lidocaine solution must not be used in patients with hereditary predisposition to acute porphyria.

4.5 Interaction with other medicinal products and other forms of interaction

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

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

Concomitant use of benzodiazepines, parasympatholytic agents or volatile anaesthetics has been reported to prolong the anaesthesia and to reduce the respiratory rate.

When used in addition to local anaesthesia the dosage of Propofol may need to be reduced.

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

After additional premedication with opioids there may be a higher incidence and longer duration of apnoea.

Bradycardia and cardiac arrest may occur after treatment with suxamethonium or neostigmine.

It should be taken into consideration that concomitant use of propofol and active substances for premedication, volatile agents or analgesic agents may potentiate anaesthesia and cardiovascular side effects. Concomitant use of central nervous depressants e. g. alcohol, general anaesthetics, narcotic analgesics will result in intensification of their sedative effects.

After administration of fentanyl, the blood level of propofol may be temporarily increased with an increase in the rate of apnoea.

Leucoencephalopathy has been reported with administration of lipid emulsions such as propofol in patients receiving ciclosporin.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of propofol during pregnancy has not been established. Studies in animals have shown reproductive toxicity (see section 5.3). Propofol should

not be given to pregnant women except when absolutely necessary. Propofol crosses the placenta and can cause neonatal depression. Propofol can, however, be used during an induced abortion.

Studies in animals have shown reproductive toxicity (see section 5.3).

Breastfeeding
Studies of breastfeeding mothers showed that small quantities of propofol are excreted in human milk. Women should therefore not breastfeed for 24 hours after administration of Propofol. Milk produced during this period should be discarded.

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 general anaesthesia. Propofol 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 ADRs are pharmacologically predictable side effects of an anaesthetic/sedative agent, such as hypotension. The nature, severity and incidence of adverse events observed in patients receiving Propofol may be related to the condition of the recipients and the operative or therapeutic procedures being undertaken.
Specifically, the following side effects have been observed. The frequency categories are defined as follows:

Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1,000 to <1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)
Not known	(cannot be estimated from the available data)

Frequencies **System Organ Class**	*Very common*	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*

Frequencies **_____** **System Organ Class**	*Very common*	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
Immune system disorders					anaphylaxis – may include angiooedema, bronchospasm, erythema and hypotension	
Metabolism and nutritional disorders						metabolic acidosis hyperkalaem (5), hyperlipidae (5)
Psychiatric disorders						Euphoric mo drug abuse drug dependance (
Nervous system disorders		Excitation, headache during recovery period		Epileptiform movements including convulsions and opisthotonus during induction, maintenance and recovery, vertigo, shivering and sensations of cold during recovery period	Postoperative unconsciousness	Involuntary movements
Cardiac disorders		Bradycardia (1)			Pulmonary oedema	Cardiac arrhythmia cardiac fai (5), (7)

Frequencies **_____** **System Organ Class**	*Very common*	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
Vascular disorders		Hypotension (2)	Thrombosis and phlebitis			
Respiratory, thoracic and mediastinal disorders		Transient apnoea during induction, hyperventilation and, coughing during induction	Coughing during maintenance	Coughing during recoveryperiod		Respiratory depression (dose dependent)
Gastrointestinal disorders		Singultus during induction of anaesthesia, nausea and vomiting during recovery period			Pancreatitis	
Hepatobiliary disorders						Hepatomegal (5), hepat acute hep failure (10)
Musculoskeletal and connective tissue disorders						Rhabdomyol s (3), (5)
Renal and urinary disorders					Discolouration of urine following prolonged administration	Renal fail (5)
Reproductive system and breast					Sexual disinhibition	
General disorders	Local pain on	Hot flushes during			Tissue necrosis (9)	Local p swelling,

Frequencies **_____** **System Organ Class**	*Very common*	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
and administration site conditions	induction (4)	induction			following accidental extravascular administration	following accidental extravascular administratio
Investigations					Brugada type ECG (5), (6)	
Injury, poisoning and procedural complications					postoperative fever	

(1) Serious bradycardias are rare. 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) Very rare 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.
(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 (see section 4.4).
(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) Necrosis has been reported where tissue viability has been impaired.
(10) After both long- and short-term treatment and in patients without underlying risk factors

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme ().

4.9 Overdose

Accidental overdosage is likely to cause cardiorespiratory depression. Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression may require lowering of the patient's head and, if severe, use of plasma expanders and pressor agents.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, general; other general anaesthetics, ATC code: N01AX10
After intravenous injection of propofol, onset of the hypnotic effect occurs rapidly. Depending on the rate of injection, the time to induction of anaesthesia is between 30 and 40 seconds. The duration of action after a single bolus administration is short due to the rapid metabolism and excretion (4 - 6 minutes).
With the recommended dosage schedule a 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 a lack of vagolytic activity. The cardio-circulatory situation usually normalises during maintenance of anaesthesia.
Paediatric population
Limited studies on the duration of propofol based anaesthesia in children indicate safety and efficacy is unchanged up to a 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

After intravenous administration about 98 % of propofol is bound to plasma protein.

Propofol is extensively distributed and rapidly cleared from the body (total body clearance: 1.5-2 l/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 metabolite quinol, which are excreted in urine.

During elimination the decline of blood levels is slower. The elimination half-life during the □-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.

Clearance is higher in children compared with adults.

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

Non-clinical data reveal no special hazard for humans based on conventional studies on repeated dose toxicity or genotoxicity.

Carcinogenicity studies have not been conducted.

Teratogenic effects have not been observed.

Published studies in animals (including primates) at doses resulting in light to moderate anaesthesia demonstrate that the use of anaesthetic agents 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 these nonclinical findings in 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
Egg phospholipids
Glycerol
Sodium hydroxide (for pH-adjustment)

Water for injections

6.2 Incompatibilities

This medicinal product must not be diluted with injection or infusion solutions.

The neuromuscular blocking agents, atracurium and mivacurium should not be given through the same infusion system as Propofol without prior flushing.

6.3 Shelf life

Shelf life before opening
Vials: 2 years

Shelf life after first opening/dilution
To be used immediately.

Must not be diluted.

Chemical and physical in-use stability of the medicinal product has been demonstrated for 24 hours at 25ºC.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Store below 30ºC.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and contents of container

50ml emulsion for injection/infusion in colourless Type I glass vials with bromobutyl rubber stopper in the pack size of 1 vial and 5 times 1 vial.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

The simultaneous administration of Propofol together with an intravenous infusion solution of glucose 50 mg/ml (5%) or sodium chloride 9 mg/ml (0.9%) intravenous infusion solution or a combination solution of glucose 40 mg/ml (4%) and sodium chloride 1.8 mg/ml (0.18%) close to the Y-connector near the place of injection, is possible.

For single use only.

Parenteral products should be inspected visually for particulate matter prior to administration. If particulate matter is evident emulsion should not be used.

Containers should be shaken before use. If two layers can be seen after shaking, the emulsion should not be used.

Prior to use, the ampoule neck and rubber stopper should be disinfected using a medicinal alcohol (spray or dipped swab).

Any remaining contents after use should be discarded.

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

7 MARKETING AUTHORISATION HOLDER

Sandoz Limited
Frimley Business Park
Frimley
Camberley
Surrey
GU16 7SR
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 04416/1317

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/11/2025

10 DATE OF REVISION OF THE TEXT

04/11/2025