For the use of an Anaesthesiologist attached to Hospital institutions and Nursing homes only.

Propofol Injection BP (1% w/v) with MCT-LCT

Propofol MCT-LCT 1% Baxter

Composition

Each mL (of emulsion) contains:

Propofol	Ph. Eur.	10 mg
Water for Injections	Ph. Eur.	q.s.

Excipients

Soyabean Oil USP
Medium chain triglycerides Ph. Eur.
Glycerol USP
Egg Lecithin
Sodium Oleate
Sodium Hydroxide Ph. Eur.

Pharmaceutical form

Emulsion for Injection or Infusion

Product description

A white milky emulsion, practically free from extraneous particulate contamination and large oil droplets. pH between 6.0 and 8.5.

Therapeutic Indications

- maintenance of general anaesthesia in adults and children > 3 years of age
- induction of general anaesthesia in adults and children > 1 month of age
- sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia in adults and children > 16 years
- sedation of ventilated patients >16 years of age in the intensive care unit.

Contraindications

Hypersensitivity to Propofol or to one of the excipients. Propofol 1 % MCT/LCT must not be used during pregnancy, breast- feeding and obstetrics (except abortion).

For sedation of children less than 16 years of age in the Intensive Care Unit.

Special warnings and precautions for use

Propofol1% MCT/LCT must only be given in hospitals or in other 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-oxymeter) and facilities for maintenance of patent airways, artificial ventilation and resuscitation facilities should be immediately available at all times. For sedation during surgical or diagnostic procedures, Propofol 1% MCT/LCT should not be given by the same person that carries out the surgical or diagnostic procedure.

Supplementary analgesic medicinal products are generally required in addition to Propofol 1% MCT/LCT.

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 which reduces cardiac output will also reduce propofol clearance.

In debilitated patients, patients with cardiac, respiratory, renal or hepatic Impairment or in hypovolaemic or epileptic patients, Propofol 1% MCT/LCT should be administered with a reduced administration rate. Cardiac, circulatory or pulmonary insufficiency and hypovolaemia should be compensated before administration of Propofol 1% MCT/ LCT.

Special care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used with caution.1.0 ml Propofol 1 % MCT/LCT contains 0.1 gram of fat.

Propofol 1 % MCT/LCT should not be administered in patients with advanced cardiac failure except with extreme caution and intensive monitoring.

Due to a higher dosage in patients with severe overweight the risk of haemodynamic effects on the cardiovascular system should be taken in consideration.

Special care should be recognized in patients with a high intracranial pressure and a low mean arterial pressure as there is a risk of a significant decrease of the intracerebral perfusion pressure. To reduce pain on the injection site during induction of anaesthesia with Propofol 1% MCT/ LCT, lidocaine can be injected prior to the Propofol emulsion. Dilutions with Lidocaine solution must not be used in patients with hereditary acute porphyria.

For sedation in adult patients Propofol 1% MCT/LCT, must be given only by those physicians trained in anaesthesia or intensive care.

Propofol 1% MCT/LCT should not be administered by the persons conducting the diagnostic or surgical procedure.

Although no causal relationship has been established, use of propofol for sedation in children has led to serious and sometimes fatal adverse events. These events observed from spontaneous reports of unlicensed use were seen most often in children with respiratory tract infections given doses in excess of those recommended for adults.

The use of Propofol 1% MCT/LCT is not recommended for newborn infants as this patient population has not been fully investigated.

Pharmacokinetic data indicate that clearance is considerably reduced in neonates with a very high inter-individual variability. Relative overdose could occur administering doses recommended for older children resulting in severe cardiovascular depression.

Some published studies in children have observed cognitive deficits after repeated or prolonged exposures to anaesthetic/sedative agents early in life. These studies have substantial limitations, and it is not clear if the observed effects are due to the anaesthetic/sedation drug administration or other factors such as the surgery or underlying illness.

Asepsis must be maintained for both Propofol 1% MCT/ LCT and infusion equipment throughout the infusion period. Co-administration of other drugs or fluids added to the Propofol 1% MCT/LCT Infusion line must occur close to the cannula site. Propofol 1% MCT/LCT must not be administered via a microbiological filter.

Propofol 1% MCT/LCT and any infusion equipment containing Propofol 1% MCT/LCT are for single administration in individual patient.

Effects on ability to drive and use machines

After administration of Propofol 1% MCT/LCT, the patient should be kept under observation for an appropriate period of time. The patient should be instructed not to drive, operate machinery, or work in potentially hazardous situations. The patient should not be allowed to go home unaccompanied, and should be instructed to avoid consumption of alcohol.

Interactions with other medications

Propofol 1% MCT/LCT has been used with commonly used premedicants, inhalational anaesthetics, analgesic agents, muscle relaxants or local anaesthetics. No Pharmacological incompatibility has been encountered.

Lower doses may be required when general anaesthesia is carried out in conjunction with regional anaesthesia. Concomitant use of benzodiazepines, parasympatholytic agents or inhalational anaesthetics has been reported to prolong the anaesthesia and to reduce the respiratory rate.

After supplementary premedication of opiate, apnoea may occur with increasing frequency and over a prolonged period.

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

As some of these drugs are reported to act hypotensive or to impair respiration, concomitant use of Propofol 1 % MCT/LCT may intensity these effects.

It should be taken into consideration that concomitant use of propofol and premedication, inhalation agents or analgesic agents may potentiate anaesthesia and cardiovascular side effects. Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics will result in accentuation of their sedative effects. When Propofol 1% MCT/LCT is combined with centrally depressant drugs administered parenterally, severe respiratory and cardiovascular depression may occur.

After administration of fentanyl, the blood level of propofol may be temporarily increased.

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

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

Posology and method of administration

Usual equipment must be available for the eventuality of incidents whilst under anaesthesia. The cardiovascular system must be monitored (e.g. ECG, pulse oxymetry).

The dose of Propofol 1% MCT/LCT emulsion should be individualized based on the response of the patient and premedications used. Supplementary analgesic agents are generally required in addition to Propofol 1% MCT/LCT.

Posology

Anaesthesia in adults

Induction of anaesthesia:

For induction of anaesthesia Propofol 1% MCT/LCT should be titrated (approximately 20 - 40 mg Propofol every 10 seconds) against the response of the patient until clinical signs show the onset of anaesthesia.

Most adult patients aged less than 55 years are likely to require 1.5 to 2.5 mg propofol/kg body weight.

Over this age, the requirement will be generally less. In patients of ASA grades III and IV the requirements will generally be less and induction should be performed more slowly. Lower rates of administration of Propofol 1 % MCT/LCT should be used (approximately 2ml (20mg) propofol every 10 seconds).

Maintenance of anaesthesia:

Anaesthesia can be maintained by administering Propofol 1 % MCT/ LCT either by continuous infusion or repeat bolus injections.

For maintenance of anaesthesia using continuous infusion, doses of 4 to 12 mg propofol/kg body weight/h should be given. A reduced maintenance dose of approximately 4 mg propofol/kg body weight/h may be sufficient during less stressful surgical procedures such as minimal invasive surgery.

In elderly patients, patients in unstable general conditions or hypovolaemic patients and patients of ASA grades III and IV, a reduction of the dosage of Propofol 1% MCT/LCT to 4 mg propofol/kg body weight/h is recommended.

For maintenance of anaesthesia using repeat bolus injections, dose increments of 25 to 50 mg propofol (=2.5 - 5 ml Propofol 1% MCT/ LCT) should be given.

General anaesthesia in children

Induction of anaesthesia:

For induction of anaesthesia Propofol 1% MCT/LCT should be titrated slowly until clinical signs show the onset of anaesthesia.

The dose should be adjusted according to age and/ or bodyweight. Most patients over 8 years of age require approximately 2.5 mg/ kg body weight Propofol MCT/LCT for induction of anaesthesia. In younger children, especially between the age of 1 month and 3 years, dose requirements may be higher (2.5 - 4 mg/kg body weight).

Maintenance of general anaesthesia:

Anaesthesia can be maintained by administering Propofol 1% MCT/LCT by infusion or repeated bolus injection to maintain the depth of anaesthesia required.

The required rate of administration varies considerably between patients but rates in the region of 9-15 mg/kg/h usually achieve satisfactory anaesthesia.

Due to the lack of clinical experience, lower dosages are recommended for young patients at increased risk (ASA grades III and IV).

Propofol 1% MCT/LCT should not be used in children < 3 years of age for the maintenance of general anaesthesia.

Sedation for diagnostic and surgical procedures in adult patients

To provide sedation during surgical and diagnostic procedures, doses and administration rates should be adjusted according to the clinical response. Most patients will require 0.5-1 mg propofol/kg bodyweight over 1 to 5 minutes for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol 1 % MCT/LCT infusion to the desired level of sedation.

Most patients will require 1.5-4.5 mg propofol/kg bodyweight/h. The infusion may be supplemented by bolus administration of 10 - 20 mg Propofol (1 - 2 ml Propofol 1% (10 mg/1 ml) MCT/LCT) if a rapid increase of the depth of sedation is required.

In patients, older than 55 years and in patients of ASA grades III and IV, lower doses of Propofol 1 % MCT/LCT may be required and the rate of administration may need to be reduced.

Propofol 1% MCT/LCT must not be used for sedation for diagnostic and surgical procedures in patients of 16 years of age or younger.

Sedation in patients over 16 years of age in the intensive care unit

When used to provide sedation for ventilated patients under intensive care conditions, it is recommended that Propofol 1% MCT/LCT should be given by continuous infusion. The dose should be adjusted according to the depth of sedation required. Usually satisfactory sedation is achieved with administration rates in the range of 0.3 to 4.0 mg propofol/kg bodyweight/h. Rates of infusion greater than 4.0 mg propofol/kg bodyweight/h are not recommended (see section Special warnings and precautions for use).

Administration of Propofol MCT/LCT by a target-controlled infusion (TCI) system is not advised for sedation in the intensive care unit (ICU).

Advisory statements concerning intensive care unit management

Use of propofol emulsion infusion for ICU sedation has been associated with 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, Hyperlipidemia, Cardiac arrhythmia, Brugada-type ECG (Elevated ST-segment and covered 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 factor 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, steroid, 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 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.

Method of administration

Propofol 1% MCT/LCT can be used for infusion undiluted or diluted with Dextrose 5% intravenous infusion solution or Sodium chloride 0.9 % intravenous infusion only, in glass infusion bottles.

Containers should be shaken before use.

Propofol 1% MCT/LCT is a lipid containing emulsion without antimicrobial preservatives and may support rapid growth of micro-organisms.

Use only homogeneous preparations and undamaged containers. Prior to use, the ampoule neck or rubber membrane should be cleaned using an alcohol spray or a swab dipped in alcohol. After use, tapped containers must be discarded.

The emulsion 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 1% MCT/LCT and infusion equipment throughout the infusion period. Co-administration of other drugs or fluid added to the Propofol 1% MCT/LCT infusion line must occur close to the cannula site. Propofol 1% MCT/LCT must not be administered via a microbiological filter.

Propofol 1% MCT/LCT and any infusion equipment containing Propofol 1 % MCT/LCT are for *single administration in an individual patient.*

Infusion of undiluted Propofol 1% MCT/LCT

When Propofol 1% MCT/LCT is infused undiluted, it is recommended that equipment such as drop counter, syringe pumps or volumetric infusion pumps should always be used to control infusion rates.

As usual for fat emulsion, the infusion of Propofol 1% MCT/LCT via one infusion system must not exceed 12 hours. After 12 hours, the infusion system and reservoir of Propofol 1% MCT/LCT must be discarded or replaced if necessary.

Infusion of diluted Propofol 1% MCT/LCT

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 1% MCT/LCT. A burette, drop counter or volumetric pump must be included in the infusion line.

The risk must be taken into account when deciding the maximum dilution in the burette.

Dilutions, which must not exceed 1 part of Propofol 1% MCT/LCT and 4 part of Dextrose 5% intravenous infusion solution or Sodium Chloride 0.9% intravenous infusion solution (at least 2 mg Propofol per ml) should be prepared aseptically immediately before administration and must be administered within 6 hours after preparation.

Incompatibilities

Propofol 1% MCT/LCT must not be diluted with other solution for infusion or injection. Co-administration of a Dextrose 5%, Sodium Chloride 0.9 % or Dextrose/Sodium chloride intravenous infusion solution with Propofol 1% MCT/LCT is permitted via a Y-piece connector close to the injection site.

To reduce pain on the injection site, Propofol 1% MCT/LCT may be mixed, immediately for use, with preservative free Lidocaine injection 1% (20 parts of Propofol 1% MCT/LCT with up to 1 part of 1% Lidocaine Injection Solution).

Muscle relaxants like atracurium and mivacurium should only be administered after flush of the same infusion site used for Propofol 1% MCT/LCT.

Duration of administration

The duration of administration must not exceed 7 days.

Overdosage

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

Undesirable effects

Hypotension and transient apnoea may occur depending on the dose and use of premedicants and other agents.

Occasionally, hypotension requires a lowering of the administration rate of Propofol 1% MCT/LCT and/or fluid replacement therapy, if necessary vasoconstrictive drugs.

Changes in cardiovascular parameter may be important in patients with impaired myocardial oxygen delivery capacity, cerebral circulatory disturbances and hypovolemia.

The risk of relative vagal over-activity may be increased because Propofol 1% MCT/LCT lacks vagolytic activity. It 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 1% MCT/LCT is used in conjunction with other agents likely to cause a bradycardia.

During induction of anaesthesia, minimal excitation may occur frequently.

During maintenance of anaesthesia, coughing is occasionally observed.

During the recovery phase, nausea, vomiting, headache, shivering or sensations of cold, euphoria and sexual disinhibition may occur rarely.

Epileptiform movements, including convulsions and opisthotonus have been reported rarely, in single cases delayed by some hours up to several days, in individual cases, there is a risk of convulsions when Propofol is given to epileptic patients.

Rarely, post-operative fever and discoloration of urine following prolonged administration of Propofol 1% MCT/LCT have been reported.

Rarely, clinical features of anaphylaxis, which may include Quincke's edema, bronchospasm, erythema and hypotension, occur following Propofol 1% MCT/LCT administration.

The local pain which may occur during the injection of the Propofol 1% MCT/LCT can be minimized by the co-administration of lidocaine and by the use of the larger veins of the forearms and antecubital fossa. Thrombosis and phlebitis are rare. Following paravenous application on severe tissue responses may occur in single cases. After co-administration of lidocaine, the following undesirable effects may occur: giddiness, vomiting, drowsiness, convulsions, bradycardia, cardiac arrhythmia, and shock.

In single cases pulmonary oedema has been observed.

Statement on usage during pregnancy

Propofol 1% MCT/LCT must not be used during pregnancy, breast-feeding and obstetrics (except abortion).

Studies in animals have shown reproduction toxicity (see section Preclinical safety data)

Preclinical safety data

Preclinical 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. In local tolerance studies, intramuscular injection resulted in tissue damage around the injection site, paravenous and subcutaneous injection induced histological reactions marked by inflammatory infiltration and focal fibrosis.

Published animal studies of some anaesthetic/sedation drugs have reported adverse effect on brain development in early life and late pregnancy. These studies have demonstrated that anaesthetic and sedation drugs that block N-methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity during the period of rapid brain growth or synaptogenesis may result in neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis when used for longer than 3 hours. The clinical significance of these non-clinical findings is yet to be determined. However, based on comparisons across species, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester through the first several months of life, but may extend out to approximately 3 years of age in humans.

Pharmaceutical precautions

Propofol 1% MCT/LCT should not be used after expiry date.

The administration of the emulsion must commence without delay after opening or breaking the vial seal.

Administration systems with undiluted Propofol 1% MCT/LCT should be replaced 12 hours after opening of the ampoule or vial.

Dilutions with Dextrose 5% intravenous infusion solution or Sodium chloride 0.9 % intravenous infusion solution should be prepared aseptically immediately before administration and administration should be completed within 6 hours after dilution.

Any portion of the contents remaining after first use should be discarded.

Store below 30°C. Do not freeze.

Containers should be shaken before use.

Use only homogenous preparations and undamaged containers.

Presentation

Propofol MCT-LCT 1% Baxter is available as

- 20 ml Glass Vial (Pack of 5 vials and 10 vials) SIN000000, and
- 50 ml Glass vial (Pack of 1 vial) SIN000000.

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