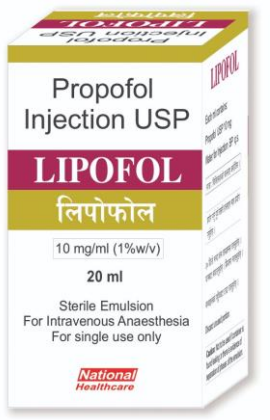
For the use of Anaesthesiologist in hospitals, institutions and Nursing homes only.

Propofol Injection USP
LIPOFOL
10 mg/mL (1%) in 20 ml
Sterile Emulsion for Intravenous Anaesthesia
For Single use only

Composition:
Each ml of emulsion contains:
Propofol USP 10 mg



In vehicle containing

Purified soybean oil
MCT Oil
Egg Phospholipids
Glycerine
Di-sodium EDTA
Sodium Hydroxide
Water for Injection

Pharmaceutical form:
White oil-in-water emulsion for injection or infusion with MCT-LCT technology.

Indications:
Propofol 10 mg/mL (1%) is a short-acting intravenous general anaesthetic for:
- induction and maintenance of general anaesthesia in adults and children > 1 month
- sedation of ventilated patients >16 years of age in the intensive care unit
- sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia in adults and children > 1 month.

Contraindications:
Propofol 10 mg/mL (1%) must not be used:
- in patients with known hypersensitivity to Propofol, soya, coconut or peanut
- in children younger than 1 month for induction and maintenance of anaesthesia,
- in patients of 16 years of age or younger for sedation in intensive care.

Special warnings and precautions for use:
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.)

Propofol clearance is blood flow dependent, therefore, concomitant medication which reduces cardiac output will also reduce Propofol clearance.
When Propofol is administered to an epileptic patient, there may be a risk of convulsion.
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 the vagal tone is likely to predominate or when Propofol is used in conjunction with other agents likely to cause bradycardia.
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.
The use of Propofol 10 mg/mL (1%) is not recommended in new- born 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.

Advisory statements concerning Intensive Care Unit management:
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 (in some cases with fatal outcome) in adults. Combinations of these events have been referred to as the **Propofol infusion syndrome.**
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 following extended dosing at dose rates greater than 4 mg/kg/h).
Prescribers should be alert to these events and consider decreasing the Propofol dosage or switching to an alternative sedative at the first sign of occurrence of symptoms. All sedative and therapeutic agents used in the intensive care unit (ICU), including Propofol, 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.

Additional precautions:
Lipofol contains no antimicrobial preservatives.

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.

Interactions:
Propofol 10 mg/mL (1%) has been used in association with spinal and epidural anaesthesia and with commonly used premedicants, neuromuscular blocking drugs, 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.

Incompatibilities
Propofol 10 mg/mL (1%) must not be mixed with other medicinal products except those mentioned in sections "**Dosage, *Method of administration***" and "**Instructions for storage / use / handling**".

Pregnancy and lactation
Pregnancy
Propofol should not be used in pregnancy.
Obstetrics:
Propofol should not be used for obstetric anaesthesia as Propofol crosses the placenta and may be associated with neonatal depression.
Breast-feeding
Propofol 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.

Dosage
General instructions
Propofol 10 mg/mL (1%) is given intravenously. The dosage is adjusted individually according to the patient's response.

General anaesthesia in adults
Induction of anaesthesia
For induction of anaesthesia Propofol 10 mg/mL (1%) should be titrated (20 – 40 mg of Propofol every 10 seconds) against the patient's response until the clinical signs show the onset of anaesthesia. Most adult patients younger than 55 years are likely to require 1.5 to 2.5 mg of Propofol/kg body weight (BW).
In older patients and in patients of ASA grades III and IV, especially those with impaired cardiac function, the dosage requirements will be less and the total dose of Propofol 10 mg/mL (1%) may be reduced to 1 mg of Propofol/kg BW or less. In these patients lower rates of administration should be applied (approximately 2 ml, corresponding to 20 mg, every 10 seconds).

Maintenance of anaesthesia

Anaesthesia can be maintained by administering Propofol 10 mg/ mL (1%) either by continuous infusion or by repeat bolus injections. If a technique involving repeat bolus injections is used, increments of 25 – 50 mg of Propofol (2.5 – 5.0 mL Propofol 10 mg/mL (1%) may be given according to clinical requirements. For maintenance of anaesthesia by continuous infusion the dosage requirements usually are in the range of 4 – 12 mg/kg BW/h.
In the elderly, in patients of poor general condition, in patients of ASA grades III and IV and in hypovolaemic patients the dosage may be reduced further depending on the severity of the patient's condition and on the performed anaesthetic technique.

General anaesthesia in children over 1 month of age

Induction of anaesthesia

For induction of anaesthesia Propofol 10 mg/mL (1%) should be titrated slowly against the patient's response until the clinical signs show the onset of anaesthesia. The dosage should be adjusted according to age and/or body weight.

Most patients over 8 years require approximately 2.5 mg of Propofol/kg BW 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 of Propofol/kg BW).

Maintenance of general anaesthesia:

Anaesthesia can be maintained by administering Propofol 10 mg/ mL (1%) 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. In younger children, especially between the age of 1 month and 3 years, dose requirements may be higher.
For ASA III and IV patients lower doses are recommended (see also **"Special warnings and precautions for use"**).

Sedation of ventilated patients in the intensive care unit

For sedation during intensive care it is advised that Propofol 10 mg/mL (1%) be given by continuous infusion. The infusion rate should be determined by the required depth of sedation.
In most patients sufficient sedation can be obtained with a dosage of 0.3 – 4.0 mg of Propofol/kg BW/h (see also section "Special warnings and precautions for use").
Propofol is not indicated for sedation in intensive care of patients of 16 years of age or younger (see **"Contraindications"**).
Administration of Propofol by Target Controlled Infusion (TCI) system is not advised for sedation in the intensive care unit.

Sedation for diagnostic and surgical procedures in adults

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 of Propofol/kg BW over 1 to 5 minutes for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol 10 mg/mL (1%) infusion to the desired level of sedation. Most patients will require 1.5 – 4.5 mg of Propofol/kg BW/h. The infusion may be supplemented by bolus administration of 10 – 20 mg of Propofol (1 – 2 mL Propofol 10 mg/mL

(1%)) if a rapid increase of the depth of sedation is required.
In patients older than 55 years and in patients of ASA grade III and IV lower doses of Propofol 10 mg/mL (1%) may be required and the rate of administration may need to be reduced.

Sedation for diagnostic and surgical procedures in children over 1 month 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 BW of Propofol for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol 10 mg/mL (1%) as infusion to the desired level of sedation. Most patients require 1.5 – 9 mg/kg/h of Propofol. The infusion may be supplemented by bolus administration of up to 1 mg/kg BW if a rapid increase of depth of sedation is required. In ASA III and IV patients, lower doses may be required.

Method of administration
Intravenous use.
Propofol 10 mg/mL (1%) is administered intravenously by injection or continuous infusion either undiluted or diluted with 5% w/v glucose solution or 0.9% w/v sodium chloride solution as well as in a 0.18% w/v sodium chloride and 4% w/v glucose solution (see also section **"Instructions for storage / use / handling"**).

Containers should be shaken before use.
Infusion of undiluted Lipofol
When administering Lipofol by continuous infusion, it is recommended that burettes, drop counters, syringe pumps or volumetric infusion pumps, should always be used to control the infusion rates. As established for the parenteral administration of all kinds of fat emulsions, the duration of continuous infusion of Lipofol from one infusion system must not exceed 12 hours. The infusion line and the reservoir of Lipofol must be discarded and replaced after 12 hours at the latest. Any portion of Lipofol remaining after the end of infusion or after re- placement of the infusion system must be discarded.
Infusion of diluted Lipofol
For administering infusion of diluted Lipofol, burettes, drop counters, syringe pumps, or volumetric infusion pumps should always be used to control infusion rates and to avoid the risk of accidentally uncontrolled infusion of large volumes of diluted Lipofol.
The maximum dilution must not exceed 1 part of Lipofol with 4 parts of 5% w/v glucose solution or 0.9% w/v sodium chloride solution, or 0.18% w/v sodium chloride and 4 % w/v glucose solution (minimum concentration 2 mg Propofol/mL). The mixture should be prepared aseptically immediately prior to administration and must be used within 6 hours of preparation.
In order to reduce pain on initial Injection, Lipofol may be mixed with preservative-free lidocaine injection 1% (mix 20 parts of Propofol 10 mg/mL (1%) with up to 1 part of lidocaine injection 1%).
Before giving the muscle relaxants atracurium or mivacurium subsequent to Lipofol through the same intravenous line, it is recommended that the line be rinsed prior to administration.

Duration of use
Propofol 10 mg/mL (1%) can be administered for a maximum period of 7 days.

Overdose

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

Undesirable effects

General:

Induction of anaesthesia is generally smooth with minimal evidence of excitation. During induction of anaesthesia, hypotension and transient apnoea may occur depending on the dose and use of premedicants and other agents. Burning in throat, wheezing, cough, hiccups have been reported.

During the recovery phase, nausea, vomiting and headache occur in only a small proportion of patients. Convulsions, including myoclonus and opisthotonos, have been reported rarely and usually after termination of product.

Rarely, clinical features of anaphylaxis, which may include angioedema, bronchospasm, erythema and hypotension, occur following Propofol 1% administration. Pulmonary edema has been observed. There have been reports of post operative fever.

Rarely, discoloration of urine has been reported following prolonged administration.

Local:

The local pain which may occur during the induction phase can be minimized by the use of larger veins of the forearm and antecubital fossa. With Propofol 1% the local pain can also be minimised by the co-administration of lignocaine. Thrombosis and phlebitis are rare.

Instructions for storage / use / handling

Store below 30°C. Do not freeze. For single use only. Any unused product or waste material should be disposed. Containers should be shaken before use. If two layers can be seen after shaking, the product should not be used. Propofol 10 mg/mL (1%) should only be mixed with the following products: 5% w/v glucose solution, 0.9% w/v sodium chloride solution, or 0.18% sodium chloride and 4% w/v glucose solution, and preservative-free lidocaine injection 1% (see section "**Dosage** / *Method of administration* / Infusion of diluted Propofol 10 mg/mL (1%)")

Co-administration of Propofol 10 mg/mL (1%) together with 5% w/v glucose solution or 0.9% w/v sodium chloride solution, or 0.18% w/v sodium chloride and 4% w/v glucose solution via a Y-connector close to the injection site is possible.

Availability of the product: 20 ml glass vial

Ref: https://www.medicines.org.uk/emc/product/11294/smpc#gref
https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019627s062lbl.pdf

National Healthcare

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