**Propofol Injection IP 1%**

(Fresofol® 1% MCT/LCT)

Emulsion for Injection or Infusion

*For use of Hospital, Registered Medical practitioners Only*

**Composition**

1 ml contains: Propofol IP 10 mg, Soybean oil IP 50 mg, Triglycerides medium-chain IP 50 mg, Purified egg phosphatides 12 mg, Glycerol IP 22.5 mg, Oleic acid IP 0.6 mg, Sodium hydroxide IP 0.08 mg, Water for injections to 1 ml.

**Pharmaceutical form**

Emulsion for injection or infusion

**Theoretical Indications**

Fresofol 1% MCT/LCT is a short-acting intravenous general anaesthetic agent for:
- induction and maintenance of general anaesthesia
- sedation of artificially ventilated patients in the Intensive Care Unit (ICU)
- Sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia

**Contraindications**

Fresofol 1% MCT/LCT must not be used:
- in patients with a known hypersensitivity to propofol or to any of the excipients of the emulsion
- in patients who are allergic to soya or peanut
- for sedation in children 16 years of age and younger (see section "Special warnings and precautions for use")

**Use during pregnancy and lactation:**

The safety of propofol during pregnancy has not been established. Therefore, propofol should not be used in pregnant women unless clearly necessary. Propofol crosses the placenta and may be associated with neonatal depression. High doses (more than 2.5 mg propofol/kg body weight for induction or 6 mg propofol/kg body weight/h for maintenance of anaesthesia) should be avoided.

Studies in breast-feeding women showed that propofol is excreted in small amounts into the milk. Therefore, mothers should stop breast-feeding and discard breast milk for 24 hours after administration of propofol.

**Special warnings and precautions for use**

In patients with cardiac, respiratory, renal or hepatic impairment or in elderly, debilitated, hypovolaemic or epileptic patients or patients with disorders of lipid metabolism, the risk of serious undesirable effects may be increased.

To reduce pain on the injection site during induction of anaesthesia with Fresofol 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 porphyrias.

Propofol is not advised for general anaesthesia in children younger than 1 month of age. The safety of propofol for (background) sedation in children younger than 16 years of age have not been demonstrated.

Although a causal relationship has not been established. Serious undesirable effects with (background) sedation in patients younger than 16 years of age (including cases with fatal outcome) have been reported during unlicensed use. In particular these effects concerned occurrence of metabolic acidosis, hyperlipidaemia, rhabdomyolysis and/or cardiac failure. These effects were most frequently seen in children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit. Similarly very rare reports have been received of occurrence of metabolic acidosis, rhabdomyolysis, hyperkalaemia and/or rapidly progressive cardiac failure (in some cases with fatal outcome) in adults who were treated for more than 58 hours with dosages in excess of 5 mg propofol/kg body weight/h. This exceeds the maximum dosage of 4 mg propofol/kg body weight/h currently advised for sedation in the intensive care unit. The patients affected were mainly (but not only) seriously head-injured patients with increased intracranial pressure (ICP). The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment. Treating physicians are reminded if possible not to exceed the dosage of 4 mg propofol/kg body weight/h.

Prescribers should be alert to these possible undesirable effects and consider decreasing the propofol dosage to an alternative sedative at the first sign of occurrence of symptoms. Patients with raised ICP should be given appropriate treatment to support the cerebral perfusion pressure during these treatment modifications.

Special care should be exercised when propofol is used for anaesthesia in infants and children up to 3 years of age although currently available data do not suggest significant differences in terms of safety compared with children older than 3 years.

In isolated cases there may be a phase of postoperative unconsciousness that may be accompanied by an increased muscle tone. The occurrence of such an event is not related to whether the patient was awake or not. Although consciousness returns spontaneously, unconscious patients should be kept under close observation.

Fresofol 1% MCT/LCT contains soybean oil, which might cause severe allergic reaction in rare cases.
Cardiac, circulatory or pulmonary insufficiency and hypovolemia should be compensated before administration of Fresolf 1% MCT/LCT.

Before anaesthesia of an epileptic patient, it should be checked that the patient has received the antiepileptic treatment. Although several studies have demonstrated efficacy in treating status epilepticus, administration of propofol in epileptic patients may also increase the risk of seizure.

Fresolf 1% MCT/LCT should not be administered in patients with advanced cardiac failure or other severe myocardial disease except with extreme caution and intensive monitoring.

The risk of relative vagotonia may be increased because propofol 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 Fresolf 1% MCT/LCT is used in conjunction with other agents likely to cause a bradycardia.

Use is not recommended with electroconvulsive therapy.

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.

Special care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used with caution. If patients receive parenteral nutrition it is necessary to take account of the amount of lipid infusion as part of the Fresolf 1% MCT/LCT formulation: 1.0 ml Fresolf 1% MCT/LCT contains 0.1 gram of fat. Lipids should be monitored in the Intensive Care Unit treatment after 3 days.

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

Effects on ability to drive and use machines:

After administration of Fresolf 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:

Fresolf 1% MCT/LCT can be used in combination with other medicinal products for anaesthesia (premedications, volatile anaesthetics, analgesics, muscle relaxants, local anaesthetics). Severe interactions with these medicinal products have been reported. Some of these centrally acting medicinal products may exhibit a circulatory and respiratory depressive effect, thus leading to increased effects when used together with Fresolf 1% MCT/LCT.

Lower doses may be required when general anaesthesia is carried out in conjunction with regional anaesthesia.

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

After additional premedication with opioids, the sedative effects of propofol may be intensified and prolonged, and there may be a higher incidence and longer duration of apnoea.

It should be taken into consideration that concomitant use of propofol and medicinal products for 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 intensification of their sedative effects. When Fresolf 1% MCT/LCT is combined with centrally depressant agents administered parenterally, severe respiratory and cardiovascular depression may occur.

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

Bradyarhythmia and cardiac arrest may occur after treatment with suxamethonium or neostigmin. Leuconecephalopathy has been reported with administration of lipid emulsions such as propofol in patients receiving cyclosporine.
Incompatibilities: Fresofol 1% MCT/LCT should not be mixed prior to administration with injection or infusion solutions other than 5% w/v glucose solution or 0.9% w/v sodium chloride solution or 1% lidocaine injection solution (see section “Posology and method of administration”). Final propofol concentration must be below 2 mg/ml.

Posology and method of administration

Fresofol 1% MCT/LCT must only be given 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 patient airways, artificial ventilation, and other resuscitation facilities should be immediately available at all times.

For sedation during surgical and diagnostic procedures Fresofol 1% MCT/LCT should not be administered by the same person conducting the surgical or diagnostic procedure.

The dose of Fresofol 1% MCT/LCT emulsion should be individualised based on the response of the patient and premedications used.

Supplementary analgesic agents are generally required in addition to Fresofol 1% MCT/LCT.

Posology

- General anaesthesia in adults:

Induction of anaesthesia:

For induction of anaesthesia Fresofol 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.

In patients over this age, and in patients of ASA grades III and IV, especially those with impaired cardiac functions, the requirements will generally be less and the total dose of Fresofol 1% MCT/LCT may be reduced to a minimum of 1 mg propofol/kg body weight. Lower rates of administration of Fresofol 1% MCT/LCT should be used (approximately 2 ml (20 mg propofol) every 10 seconds).

Maintenance of anaesthesia:

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

For maintenance of anaesthesia generally doses of 4 to 12 mg propofol/kg body weight/h should be given.
mg propofol/kg body weight/h may be sufficient during less stressful surgical procedures such as minimal invasive surgery.

In elderly patients, patients with unstable general conditions, patients with impaired cardiac function or hypovolaemic patients and patients of ASA grades III and IV, the dosage of Fresofol 1% MCT/LCT may be reduced further depending on the severity of the patient's condition and on the performed anaesthetic technique.

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

Rapid bolus administration (single or repeated) should not be used in the elderly as this may lead to cardiopulmonary depression.

- General anaesthesia in children under 1 month of age:

Fresofol 1% MCT/LCT is not advised for general anaesthesia in children younger than 1 month of age.

Induction of anaesthesia:

When used to induce anaesthesia, it is recommended that Fresofol 1% MCT/LCT should be titrated slowly until the clinical signs show the onset of anaesthesia.

The dose should be adjusted for age and/or body weight. Children over 8 years of age are likely to require approximately 2.5 mg propofol/kg body weight for induction of anaesthesia. Under this age the dose requirement may be higher.

Storage:

Do not store above 25 ºC. Do not freeze.

Keep out of reach of children.

Containers should be shaken before use.

Use only if the emulsion is homogeneous and the container undamaged.

Presentation:

Packs containing 1 glass vial with 50 ml emulsion

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Fresenius Kabi India Pvt. Ltd.
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