PACKAGE INSERT - INSTRUCTIONS FOR USE - READ CAREFULLY!

Fresofol 1 %

emulsion for injection or infusion

12IP 0/8
(100.04)

Composition

1 ml emulsion contains 10 mg propofol,

soybean oil, purified egg phosphatide, glycerol, oleic acid, sodium hydroxide, water for injections

Pharmaceutical form

Emulsion for injection or infusion

Address of the pharmaceutical company

Fresenius Kabi Deutschland GmbH
61346 Bad Homburg v.d.H.
Germany

Manufacturer:

Fresenius Kabi Austria GmbH
Hafnerstraße 36
8055 Graz
Austria

Therapeutic indications

Induction and maintenance of general anaesthesia
Sedation of ventilated patients receiving intensive care

Contra-indications

Hypersensitivity to propofol or to one of the excipients.

Fresofol 1% must not be used during pregnancy, and obstetrics (except abortion).

Fresofol 1% must not be used for general anaesthesia in children less than 1 month of age and for sedation of children less than 16 years of age in the Intensive Care Unit.

Use during pregnancy and lactation:

Although animal studies showed no teratogenic effects, propofol is contraindicated during pregnancy. Propofol passes the placental barrier and may cause neonatal depression. Therefore, propofol is contraindicated for obstetric anaesthesia, including Caesarean section deliveries.
Studies in breast-feeding women showed that propofol is excreted in small amounts into the milk. Therefore, mothers should stop breast-feeding for 24 hours after administration of propofol.

Special warnings and precautions for use

In debilitated patients, elderly patients, patients with cardiac, respiratory, renal or hepatic impairment or in hypovolaemic or epileptic patients Fresofol 1% should be administered with caution and a reduced administration rate.

Cardiac, circulatory or pulmonary insufficiency and hypovolaemia should be compensated before administration of Fresofol 1%.

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 with Fresofol 1% should be considered, especially in situations where vagal tone is likely to predominate or when Fresofol 1% is used in conjunction with other agents likely to cause a bradycardia.

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 Fresofol 1% contains 0.1 gram of fat.

Lipids should be monitored in the ICU treatment after 3 days.

Fresofol 1% should not be administered in patients with advanced cardiac failure or other severe myocardial diseases 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 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.

To reduce pain on the injection site during induction of anaesthesia with Fresofol 1%, lidocaine can be injected prior to the Propofol emulsion. Before administration of lidocaine it should be noted that lidocaine must not be used in patients with hereditary porphyria.

Use of Fresofol 1% is not recommended with electroconvulsive therapy.

Fresofol 1% must only be given by physicians trained in anaesthesia or in care of patients in intensive care.

The usual equipment for resuscitation must be immediately available, because the maintenance of ventilation and adequate oxygenation must be preserved.
Fresofol 1% should not be administered by the persons conducting the diagnostic or surgical procedure.

Fresofol 1% is not advised for general anaesthesia in children younger than 1 month of age. The safety and efficacy of Fresofol 1% for (background) sedation in children younger than 16 years of age have not been demonstrated. Although no causal relationship has 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, hyperlipidemia, 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 ICU. 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 treated for more than 58 hours with dosages in excess of 5 mg/kg/hr. These exceed the maximum dosage of 4 mg/kg/hr currently advised for sedation in the ICU. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment. Prescribers are reminded - if possible - not to exceed the dosage of 4 mg/kg/hr which is usually sufficient for sedation of mechanically ventilated patients in the ICU situation (treatment durations in excess of 1 day). Prescribers should be alert to these possible undesirable effects and decrease the dosage or switch to an alternative sedative at the first sign of occurrence of symptoms.

Fresofol 1% contains soybean oil which might cause severe allergic reaction in rare cases.

Full recovery from general anaesthesia should be confirmed prior to discharge.

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

Fresofol 1% and any infusion equipment containing Fresofol 1% are for ***single administration*** in an ***individual patient.***

Effects on ability to drive and use machines:

After administration of Fresofol 1%, 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

Fresofol 1% 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 neostigmine.

As some of these drugs are reported to act hypotensive or to impair respiration concomitant use of Fresofol 1% may intensify 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 Fresofol 1% 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.

Posology and method of administration

Usual equipment must be available for the eventuality of incidents whilst under anaesthesia and facilities for resuscitation should be available immediately. Circulatory and respiratory functions should be monitored (e.g. ECG, pulse oxymetry). The dose of Fresofol 1% 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%.

Posology

- ***Anaesthesia in adults:***

Induction of anaesthesia:

For induction of anaesthesia Fresofol 1% should be titrated (approximately 20 - 40†mg 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, especially those with impaired cardiac function, the requirements will generally be less and induction should be performed more slowly. Lower rates of administration of Fresofol 1% should be used [approximately 2†ml (20†mg) every 10 seconds].

Maintenance of anaesthesia:

Anaesthesia can be maintained by administering Fresofol 1% either by continuous infusion or repeat bolus injections.

For maintenance of anaesthesia using continuous infusion, the dose and rate of administration must be individualised, generally 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 Fresofol 1% 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 Fresofol 1%) should be given.

- ***Anaesthesia in children over 1 month of age:***

Due to lack of experience Fresofol 1% must not be used in children under 1 month of age.

Induction of anaesthesia:

When used to induce anaesthesia, it is recommended that Fresofol 1% 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 requirements may be higher. The initial dose should be 3 mg propofol/kg body weight. If necessary, additional doses in steps of 1 mg propofol/kg body weight can be administered.

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

Maintenance of anaesthesia:

For maintenance of anaesthesia using continuous infusion doses of 9 to 15†mg propofol/kg body weight/h should be given.

Younger children, less than 3 years, may have higher dosage requirements, within the range of recommended dosages, when compared with older paediatric patients. Dosage should be adjusted individually and particular attention paid to the need for adequate analgesia.

A maximum duration of use of approximately 60 minutes should not be exceeded except where there is a specific indication for longer use e.g. malignant hyperthermia where volatile agents must be avoided.

- ***Sedation in adults during intensive care:***

The dose should be adjusted according to the depth of sedation required. Using continuous infusion doses of 0.3 to 4.0 mg propofol/kg body weight/h should be given. Rates of infusion greater than 4.0 mg/kg body weight/h are not recommended.

If the patient is receiving other intravenous lipids concurrently, the amount of fat infused as part of the Fresofol 1% formulation should be taken into account. 1.0 ml Fresofol 1% contains 0.1 gram of fat.

Fresofol 1% must not be used for sedation of children under 16 years of age.

Method of administration

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

Containers should be shaken before use.

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 swap dipped in alcohol.

Fresofol 1% is a lipid containing emulsion without antimicrobial preservatives and may support rapid growth of microorganisms.

The emulsion must be drawn aseptically into a ste-

rile 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 Fresofol 1% and infusion equipment throughout the infusion period. Co-administration of other drugs or fluids added to the Fresofol 1% infusion line must occur close to the cannula site. Fresofol 1% must not be administered via a microbiological filter.

Fresofol 1% and any infusion equipment containing Fresofol 1% are for ***single*** administration in an ***individual*** patient.

Infusion of undiluted Fresofol 1%:

When Fresofol 1% 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 emulsions, the infusion of Fresofol 1% via one infusion system must not exceed 12 hours. After 12 hours, the infusion system and reservoir of Fresofol 1% must be discarded or replaced if necessary.

Infusion of diluted Fresofol 1%:

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 Fresofol 1%. 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 Fresofol 1% and 4 parts 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.

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

To reduce pain on the injection site, Fresofol 1% may be mixed, immediately for use, with preservative free Lidocaine Injection 1% (20 parts of Fresofol 1% 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 Fresofol 1%.

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 position patient horizontal, 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 Fresofol 1% and/or fluid replacement therapy, if necessary vasoconstrictive drugs. Asystole and bradycardia have been reported.

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

During induction of anaesthesia minimal excitation may occur frequently. In single cases pulmonary oedema has been observed.

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 discolouration of urine following prolonged administration of propofol have been reported.

Rarely, clinical features of anaphylaxis, which may include Quincke¥s edema, bronchospasm, erythema and hypotension, occur following Fresofol 1% administration.

Very rarely pancreatitis has been reported following use of propofol, a causal relationship has not been established.

In very rare cases rhabdomyolysis, metabolic acidosis, hyperkalaemia or cardiac failure, sometimes with fatal outcome, have been observed when propofol was administered at dosages in excess of 4 mg/kg/hr for sedation in the ICU (see "Special warnings and precautions for use").

Thrombosis and phlebitis are rare.

The local pain which may occur during the injection of Fresofol 1% can be minimised by the co-administration of lidocaine and by the use of the larger veins of the forearm and antecubital fossa. After co-administration of lidocaine the following undesirable effects may occur: giddiness, vomiting, drowsiness, convulsions, bradycardia, cardiac arrhythmia and shock.

Following paravenous application severe tissue responses may occur in single cases.

Pharmaceutical precautions

Fresofol 1% should not be used after expiry date.

Administration of the emulsion must commence without delay after opening the ampoule or breaking the vial seal.

Administration systems with undiluted Fresofol 1% 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.

Do not store above 25 °C. Do not freeze.

Containers should be shaken before use.

Use only homogeneous preparations and undamaged containers.

Presentation

Packs containing 5 glass ampoules with 20 ml emulsion
Packs containing 1 glass vial with 50 or 100 ml emulsion

Fresenius Kabi