Fresenius Propoven 2%

Emulsion for Injection or Infusion
Propofol

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fresenius Propoven 2%, emulsion for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml emulsion contains 20 mg propofol.
Each 50 ml vial contains 1000 mg propofol.
For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection or infusion
Isotonic, white oil-in-water emulsion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fresenius Propoven 2% 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)

4.2 Posology and method of administration

Fresenius Propoven 2% 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.

The dose of Fresenius Propoven 2% emulsion should be individualised based on the response of the patient and premedications used.
Supplementary analgesic agents are generally required in addition to Fresenius Propoven 2%.

Posology

- General anaesthesia in adults:

Induction of anaesthesia:

For induction of anaesthesia Fresenius Propoven 2% 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 function, the requirements will generally be less and the total dose of Fresenius Propoven 2% may be reduced to a minimum of 1 mg propofol/kg body weight. Lower rates of administration of Fresenius Propoven 2% should be used (approximately 1 ml (20 mg propofol) every 10 seconds).

Maintenance of anaesthesia:

Anaesthesia can be maintained by administering Fresenius Propoven 2% by continuous infusion.

For maintenance of anaesthesia 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, patients with impaired cardiac function or hypovolaemic patients and patients of ASA grades III and IV, the dosage of Fresenius Propoven 2% may be reduced further depending on the severity of the patient's condition and on the performed anaesthetic technique.

- General anaesthesia in children over 3 years of age:

Fresenius Propoven 2% is not advised for general anaesthesia in children between 1 month and 3 years of age since the 2% strength is difficult to be titrated in small children due to the extremely small volumes needed. The use of Propofol 1% (10 mg/1 ml) MCT Fresenius should be considered in children between 1 month and 3 years of age if a dose less than e.g. 100 mg/h is expected.
Propofol (both 1% and 2%) is not advised in children younger than 1 month of age.

Induction of anaesthesia:

When used to induce anaesthesia, it is recommended that Fresenius Propoven 2% 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. 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.

Lower dosages are recommended for young patients at increased risk (ASA grades III and IV).

Administration of propofol by a Target Controlled Infusion (TCI) system is not advised for induction of general anaesthesia in children.

Maintenance of anaesthesia:

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

There is no data on maintenance of anaesthesia with repeated injections of propofol in children.

Dosage should be adjusted individually and particular attention paid to the need for adequate analgesia.

Administration of propofol by a Target Controlled Infusion (TCI) system is not advised for maintenance of general anaesthesia in children.

- Sedation in adults during intensive care:

When used to provide sedation for ventilated patients under intensive care conditions, it is recommended that Fresenius Propoven 2% 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 body weight/h. Rates of infusion greater than 4.0 mg propofol/kg body weight/h are not recommended (see section 4.4 Special warnings and precautions for use).

Propofol must not be used for sedation in intensive care of patients of 16 years of age or younger (see 4.3 Contraindications).

Administration of Fresenius Propoven 2% by a Target Controlled Infusion (TCI) system is not advised for sedation in the Intensive Care Unit.

Method of administration

For intravenous use.

Fresenius Propoven 2% is administered undiluted intravenously by continuous infusion. Fresenius Propoven 2% should not be given by repeat bolus injection for maintenance of anaesthesia.

When Fresenius Propoven 2% is infused, it is recommended that equipment such as burettes, drop counter, syringe pumps or volumetric infusion pumps should always be used to control infusion rates.

Containers should be shaken before use.
Use only homogeneous preparations and undamaged containers.

Prior to use, the rubber membrane should be cleaned using an alcohol spray or a swab dipped in alcohol. After use, tapped containers must be discarded.

Fresenius Propoven 2% is a lipid containing emulsion without antimicrobial preservatives and may support rapid growth of microorganisms.

The emulsion must be drawn aseptically into a sterile syringe or giving set immediately after breaking the vial seal. Administration must commence without delay.

Asepsis must be maintained for both Fresenius Propoven 2% and infusion equipment throughout the infusion period. Co-administration of other medicinal products or fluids added to the Fresenius Propoven 2% infusion line must occur close to the cannula site using a Y-piece connector or a three-way valve.

Fresenius Propoven 2% must not be mixed with other solutions for infusion or injection. But 5% w/v glucose solution, 0.9% w/v sodium chloride solution or 0.18% w/v sodium chloride and 4% w/v glucose solution may be administered via suitable appendages at the cannula site.

Fresenius Propoven 2% must not be administered via a microbiological filter.

Fresenius Propoven 2% and any infusion equipment containing Fresenius Propoven 2% are for **single** administration in an **individual** patient. After use remaining solution of Fresenius Propoven 2% has to be discarded.

As usual for fat emulsions, the infusion of Fresenius Propoven 2% via one infusion system must not exceed 12 hours. After 12 hours, the infusion system and reservoir of Fresenius Propoven 2% must be discarded or replaced if necessary.

To reduce pain on the injection site, Fresenius Propoven 2% should be administered in a larger vein or lidocaine injection solution may be administered before induction of anaesthesia with Fresenius Propoven 2%.
Muscle relaxants like atracurium and mivacurium should only be administered after flush of the same infusion site used for Fresenius Propoven 2%.

Duration of administration

The duration of administration must not exceed 7 days.

4.3 Contraindications

Fresenius Propoven 2% 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 4.4 Special warnings and precautions for use)

4.4 Special warning 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 consciousness Fresenius Propoven 2% should be administered with caution and a reduced administration rate (see section 4.2 Posology and method of administration).

Cardiac, circulatory or pulmonary insufficiency and hypovolaemia should be compensated before administration of Fresenius Propoven 2%.

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.

Fresenius Propoven 2% 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

Fresenius Propoven 2% 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 Fresenius Propoven 2% formulation: 1.0 ml Fresenius Propoven 2% 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 recognised 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 Fresenius Propoven 2% lidocaine can be injected prior to the propofol emulsion.

Dilutions with lidocaine solution must not be used in patients with hereditary acute porphyria.

Fresenius Propoven 2% is not advised for general anaesthesia in children younger than 3 years of age since the 2% strength is difficult to be titrated in small children due to the extremely small volumes needed. The use of Fresenius Propoven 1% should be considered in children between 1 month and 3 years of age if a dose less than e.g. 100 mg/h is expected. Propofol is not advised for general anaesthesia in children younger than 1 month of age.
In any case, 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.

The safety of propofol 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, 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 or switching 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.

Patient Information Leaflet

Fresenius Propoven 2%

Emulsion for Injection or Infusion
Propofol

What you should know about Propofol

- Keep this leaflet with you while you are receiving Propofol. You may want to read it later.
- Please read this leaflet carefully as it contains a summary of information about your medicine.
- If you are not sure about anything, please ask your doctor, hospital pharmacist or a member of the nursing staff.
- Propofol can only be prescribed by a doctor, who will be trained in anaesthesia or in the care of patents in intensive care.

What is in your medicine?

Propofol is a milky white liquid, containing 20 mg Propofol in each millilitre. It is supplied in glass vials containing 50 ml of solution. The product also contains the following inactive ingredients soybean oil refined, triglycerides medium chain, purified egg phosphatide, glycerol, oleic acid, sodium hydroxide and water for injections. Propofol belongs to a group of medicines called general anaesthetics. This means that it causes you to become unconscious (asleep). It can also be used in some circumstances to sedate you (make you feel sleepy without sending you to sleep).

Who has made your medicine?

The marketing authorisation holder is Fresenius Kabi Limited, Cestrian Court, Eastgate Way, Manor Park, Runcorn, Cheshire, WA7 1NT, U.K.
Fresenius Propoven 2% is manufactured on behalf of Fresenius Kabi Ltd. by Fresenius Kabi Austria GmbH, Hafnerstrasse 36, A-8055 Graz, Austria and Fresenius Kabi AB, Rapsgatan 7, S-75174 Uppsala, Sweden.

What is your medicine for?

Propofol is used either to make you unconscious (asleep) or to sedate you (make you sleepy), while you are undergoing intensive care.

When should Propofol not be used.

You should not be given Propofol if:

- You have ever received Propofol before and have experienced an allergic reaction to it or to any of the inactive ingredients
- You are allergic to soya or peanuts.

Propofol must not be used for sedation in children 16 years of age and younger.

What precautions should be taken with Fresenius Propoven 2%?

If any of the following apply, propofol may not be suitable for you or your doctor may need to take special precautions:

- You have problems with your heart, breathing, kidneys or liver
- Your blood pressure is to high or low
- You have epilepsy
- You have been told that you have very high fat levels in your blood or your body has problems being able to handle and use fat.
- You have had a stroke or a head injury
- You have a rare condition called hereditary acute porphyria.
- You are elderly or debilitated, or severely overweight
- You are pregnant or think that you may be pregnant, or are breast-feeding.

Before receiving propofol tell you doctor if you think any of these may apply to you.

You should be sure that your doctor is aware if you are taking any other medicines, including any that don't require a prescription. Propofol can react badly with some other medicines.

After receiving Propofol your ability to drive a car or operate machinery may be affected for some time. Therefore, if you are able to go home shortly after receiving propofol you should avoid alcohol and not drive a car. Your doctor should not let you go home unaccompanied. Ask your doctor when you can return to work, particularly if you use machinery or heavy equipment.

Receiving your medicine

Propofol will be given by, or under the direct supervision of, your anaesthetist or intensive care doctor, who will closely control the amount of Propofol given to you. Dosage will be adjusted to the individual's requirements so that adequate anaesthesia or sedation is obtained. The dose of Propofol you require may vary according to other medicines, including premedications that you have received, and on your age, size, and the level of sleepiness required. Your condition will be continuously monitored and your doctor may need to use several different medicines to keep you asleep or sedated.

For induction of anaesthesia most adult patients aged less than 55 years are likely to require 1.5 to 2.5 mg/propofol/kg body weight. For maintenance of anaesthesia generally doses of 4 to 12 mg /propofol/kg body weight/h are given.

For sedation of 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 are typically given. Rates of infusion greater than 4.0 mg/propofol/kg body weight/h are not recommended.

Dose requirements may be higher for children and lower for elderly patients.

Your medicine will be given to you as an injection into a vein, usually in the back of the hand or in the forearm through a needle, or a fine plastic tube called a cannula.

For maintenance of anaesthesia or sedation, your medicine may be given as an intravenous infusion (or IV drip) using an electric pump which will automatically control the rate at which the infusion is given.

M092553/03 GB

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.

Fresenius Propoven 2% contains soybean oil, which might cause severe allergic reaction in rare cases.

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

4.5 Interaction with other medicinal products and other forms of interaction

Fresenius Propoven 2% 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 Fresenius Propoven 2%.

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 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 Fresenius Propoven 2% 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.

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

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

4.6 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 (see also section 5.3 Preclinical safety data). 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.

4.7 Effects on ability to drive and use machines

After administration of Fresenius Propoven 2%, 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.

4.8 Undesirable effects

Commonly observed side effects of propofol are hypotension and respiratory depression. These effects depend on the propofol dose administered but also on the type of premedication and other concomitant medication. Specifically, the following side effects have been observed:

Immune system disorders:

Rare (< 1:1000, ≥ 1:10 000):
Clinical features of anaphylaxis, which may include Quincke's oedema, bronchospasm, erythema and hypotension.

Psychiatric disorders:
Rare (< 1:1000, ≥ 1:10 000):
Euphoria and sexual disinhibition during the recovery period.

Nervous system disorders:
Common (< 1:10, ≥ 1:100):
During induction of anaesthesia spontaneous movements and myocloni, minimal excitation.

Rare (< 1:1000, ≥ 1:10 000):
Headache, vertigo, shivering and sensations of cold during the recovery period.
Epileptiform movements including convulsions and opisthotonus.

Very rare (< 1:10 000):
Delayed epileptiform attacks, the delay period ranging from a few hours to several days.
Risk of convulsions in epileptic patients after administration of propofol.
Cases of postoperative unconsciousness (see section 4.4 Special warnings and precautions for use).
Cardiac disorders / Vascular disorders:

Common (< 1:10, ≥ 1:100):
During induction of anaesthesia, hypotension, bradycardia, tachycardia, hot flushes.

Uncommon (< 1:100, ≥ 1:1000):
Marked hypotension. This may require a lowering of the administration rate of Fresenius Propoven 2% and/or fluid replacement therapy, if necessary vasoconstrictive medicinal products.

Account should be taken of the possibility of a severe drop in blood pressure in patients with impaired coronary or cerebral perfusion or those with hypovolaemia.
Bradycardia during general anaesthesia with progressive severity (asystole). The intravenous administration of an anticholinergic medicinal product prior to induction or during maintenance of anaesthesia should be considered (see also section 4.4. Special warnings and precautions for use).

Rare (< 1:1000, ≥ 1:10 000):
Arrhythmia during the recovery period.
Thrombosis and phlebitis.

Respiratory, thoracic and mediastinal disorders:
Common (< 1:10, ≥ 1:100):
During induction of anaesthesia hyperventilation, transient apnoea, coughing, singultus.

Uncommon (< 1:100, ≥ 1:1000):
Coughing during maintenance of anaesthesia.

Rare (< 1:1000, ≥ 1:10 000):
Coughing during the recovery period.

Very rare (< 1:10 000):
Pulmonary oedema.

Gastrointestinal disorders:
Rare (< 1:1000, ≥ 1:10 000):
Nausea or vomiting during the recovery period.

Very rare (< 1:10 000):
Pancreatitis has been reported after administration of propofol. A causal relationship, however, could not be established.

Skin and subcutaneous tissue disorders:
Very rare (< 1:10 000):
Severe tissue responses after accidental paravenous application.

Renal and urinary disorders:
Rare (< 1:1000, ≥ 1:10 000):
Cases of discoloration of urine following prolonged administration of propofol.
General disorders and administration site conditions:
Very common (> 1:10):
Local pain occurring during the initial injection. Prophylaxis or treatment see below.

The local pain which may occur during the initial injection of Fresenius Propoven 2% can be minimised by the administration of lidocaine prior to the propofol emulsion and by the use of larger veins of the forearm and antecubital fossa (see section 4.2 Method of administration). Upon administration of lidocaine the following undesirable effects may occur rarely (< 1:1000, ≥ 1:10 000): giddiness, vomiting, drowsiness, convulsions, bradycardia, cardiac arrhythmia and shock.

Rare (< 1:1000, ≥ 1:10 000):
Cases of post-operative fever

Very rare (< 1:10 000):
There have been reports of isolated cases of severe undesirable effects presenting as a complex of symptoms including: rhabdomyolysis, metabolic acidosis, hyperkalaemia, and cardiac failure, sometimes with fatal outcome. Most of these effects have been observed in patients in intensive care with doses exceeding 4 mg/kg body weight/h. For more detail, see section 4.4 Special warnings and precautions for use.

4.9 Overdose

Overdose is likely to cause cardiovascular and respiratory depression. Respiratory depression is treated with artificial ventilation. Cardiovascular depression may require lowering the patient's head and administering plasma volume substitutes and vasopressive agents.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other general anaesthetics
ATC-Code: NO1AX10

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.

5.2 Pharmacokinetic properties

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

After intravenous bolus administration the initial blood level of propofol declines rapidly due to rapid distribution into different compartments (α-phase). The distribution half-life has been calculated as 2 - 4 minutes.

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

The central volume of distribution is in the range of 0.2 - 0.79 l/kg body weight, the steady-state volume of distribution in the range of 1.8 - 5.3 l/kg body weight. Propofol is rapidly cleared from the body (total clearance 1.5 to 2 litres/minute). Clearance occurs by metabolic processes, mainly in the liver, to form glucuronides of propofol and glucuronides and sulphate conjugates of its corresponding quinol. All metabolites are inactive. About 88 % of an administered dose is excreted in the form of metabolites in urine. Only 0.3 % of the administered dose is excreted unchanged in urine.

5.3 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. Reproductive toxicity studies have shown effects related to pharmacodynamic properties of propofol only at high doses. 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Soya-bean oil, refined
Triglycerides medium-chain
Purified egg phosphatides
Glycerol
Oleic acid
Sodium hydroxide
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

The shelf life of the medicinal product in its original package is 3 years.

The infusion of Fresenius Propoven 2% via one infusion system must not exceed 12 hours.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Colourless glass vial (type II) of 50 ml with a bromobutyl rubber closure, packs of 1 unit and 10 and 15 units
Not all pack sizes may be marketed.

6.6 Instructions for use and handling

For single use. Any unused emulsion must be discarded.

Containers should be shaken before use.
If two layers can be seen after shaking the emulsion should not be used.
Use only homogeneous preparations and undamaged containers.

Prior to use, the rubber membrane should be cleaned using an alcohol spray or a swab dipped in alcohol. After use, tapped containers must be discarded.

7. MARKETING AUTHORISATION HOLDER

Fresenius Kabi Limited,
Cestrian Court, Eastgate Way,
Manor Park, Runcorn, Cheshire,
WA7 1NT, U.K.

8. MARKETING AUTHORISATION NUMBER

PL 08828/0168 UK
PA 566/36/3 Ireland

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/4/05 Ireland
8/6/05 UK

10. DATE OF REVISION OF THE TEXT

November 2006

What undesirable events may be associated with this medicine

As with all medicines, propofol can cause undesirable side effects:

Very common (occurring in more than 10% of patients)

The initial injection of Propofol may cause some local discomfort or pain while the injection is given.

Common (occurring between one in ten and one in a hundred patients).

As with other anaesthetic agents, you may have a fall in your blood pressure, an increase or decrease in the rate of your heart, hot flushes, changes in your breathing pattern, coughing and hiccups. Your doctor can deal with these if they happen.
During induction of anaesthesia muscular spasms and excitation may be observed. These do not normally cause any problems.

Uncommon (occurring between one in a hundred and one in a thousand patients)

Uncommonly patients have a significant fall in blood pressure or slowing of the heart rate, requiring intervention by the anaesthetist.
Coughing during maintenance of anaesthesia is reported uncommonly.

Rare (occurring between one in a thousand and one in ten thousand patients)

Severe allergic reactions (e.g. swelling of the throat, difficulty breathing, reddening of the skin or low blood pressure).
Redness or soreness or a blood clot in the vein where the propofol was injected.
During the recovery period coughing, being sick or feeling sick, headache, vertigo, shivering or feeling cold, fever, epileptic movements or spasms, irregular heartbeat, euphoria and sexual disinhibition are reported rarely.
Discolouration of urine may occur rarely following prolonged administration of propofol.

Very rare (occurring in less than one in ten thousand patients)

There have been very rare reports of:
Inflammation of the pancreas (pancreatitis)
Too much fluid in the lungs.
Post-operative unconsciousness have also been observed.
Delayed epileptic convulsions (fits).
Severe tissue damage after accidental misplacement of the injection outside the vein.

Muscle damage has been reported very rarely, resulting in too much acid or too much potassium in your blood, and very rarely heart failure. Most of these severe reactions have followed prolonged administration during Intensive Care.

Do not be alarmed by this list of possible events. You may not have any of them. But if you think you experience any side effects please tell your doctor or nursing staff immediately.

What should be done in case of overdose

Your doctor will ensure that you receive the right amount of propofol for you and for the procedure you are undergoing. However different people need different doses and if you do receive too much for you, your anaesthetist may need to take measures to make sure your heart and breathing are adequately supported. This is why anaesthetic drugs are only administered by doctors trained in anaesthesia or in the care of patents in intensive care

Storing Propofol

The shelf life if the product in its original package is 3 years.
It should not be used after the expiry date shown on the container label.
Containers should be shaken before use.
If two layers can be seen after shaking, the emulsion should not be used.
Use only homogeneous preparations in undamaged containers.
Do not store above 25°C. Do not freeze.
Keep out of the reach and sight of children.
For single use. Any unused emulsion must be discarded.
Your doctor and hospital pharmacist are responsible for the correct storage, use and disposal of Propofol

Date of Preparation: February 2007.

Fresenius Kabi