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SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE MEDICINAL PRODUCT

Propofol-Lipuro 1 % (10 mg/ml)

emulsion for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Propofol-Lipuro 1 % (10 mg/ml) contains

	per 1 ml	per 20 ml ampoule or vial	per 50 ml vial	per 100 ml vial
Propofol	10 mg	200 mg	500 mg	1000 mg

Excipients with known effect:
1 ml emulsion for injection or infusion contains

Soya-bean oil refined	50 mg
Sodium	0.03 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection or infusion
White milky oil-in-water emulsion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Propofol-Lipuro 1 % (10 mg/ml) 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.

4.2 Posology and Method of Administration

General instructions

Propofol-Lipuro 1 % (10 mg/ml) 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-oximetry) and facilities for maintenance of patent airways, artificial ventilation, and other resuscitation facilities should be immediately available at all times. For sedation during surgical or diagnostic procedures Propofol-Lipuro 1 % (10 mg/ml) 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-Lipuro 1 % (10 mg/ml).

Posology

Propofol-Lipuro 1 % (10 mg/ml) 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-Lipuro 1 % (10 mg/ml) 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/kg body weight.

In patients over this age 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-Lipuro 1 % (10 mg/ml) may be reduced to a minimum of 1 mg/kg body weight. 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-Lipuro 1 % (10 mg/ml) either by continuous infusion or by repeat bolus injections. If a technique involving repeat bolus injections is used, increments of 25 mg (2.5 ml Propofol-Lipuro 1 % (10 mg/ml)) to 50 mg (5.0 ml Propofol-Lipuro 1 % (10 mg/ml)) 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 body weight/h.

In elderly patients, 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-Lipuro 1 % (10 mg/ml) should be slowly titrated 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 of age require approximately 2.5 mg/kg body weight of propofol 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-Lipuro 1 % (10 mg/ml) 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 section 4.4)

• Sedation of ventilated patients in the Intensive Care Unit

For sedation during intensive care it is advised that propofol should be administered by continuous infusion. The infusion rate should be determined by the desired depth of sedation. In most patients sufficient sedation can be obtained with a dosage of 0.3 – 4 mg/kg/h of propofol (see also section 4.4).

Propofol is not indicated for sedation in intensive care of patients of 16 years of age or younger (see section 4.3).

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/kg body weight over 1 to 5 minutes for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol-Lipuro 1 % (10 mg/ml) infusion to the desired level of sedation. Most patients will require 1.5 – 4.5 mg/kg body weight/h. The infusion may be supplemented by bolus administration of 10 – 20 mg (1 – 2 ml Propofol-Lipuro 1 % (10 mg/ml)) 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-Lipuro 1 % (10 mg/ml) 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 body weight of propofol for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol-Lipuro 1 % (10 mg/ml) 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 b.w. if a rapid increase of depth of sedation is required.

In ASA III and IV patients lower doses may be required.

Method and duration of administration

• Method of administration

Intravenous use

Propofol-Lipuro 1 % (10 mg/ml) 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 6.6). Containers should be shaken before use.

Before use, the neck of the ampoule or the surface of the rubber stopper of the vial should be cleaned with medicinal alcohol (spray or swabs). After use, tapped containers must be discarded.

Propofol-Lipuro 1 % (10 mg/ml) contains no antimicrobial preservatives and supports growth of microorganisms. Therefore, Propofol-Lipuro 1 % (10 mg/ml) is to be drawn up aseptically into a sterile syringe or an infusion set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol-Lipuro 1 % (10 mg/ml) and the infusion equipment throughout the infusion period.

Any medicinal products or fluids added to a running Propofol-Lipuro 1 % (10 mg/ml) infusion must be administered close to the cannula site.

Propofol-Lipuro 1 % (10 mg/ml) must not be administered via infusion sets with microbiological filters.

The contents of one ampoule or one vial of Propofol-Lipuro 1 % (10 mg/ml) and any syringe containing Propofol-Lipuro 1 % (10 mg/ml) are for **single use** in **one** patient.

Infusion of undiluted Propofol-Lipuro 1 % (10 mg/ml)

When administering Propofol-Lipuro 1 % (10 mg/ml) 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 Propofol-Lipuro 1 % (10 mg/ml) from **one** infusion system must not exceed 12 hours. The infusion line and the reservoir of Propofol-Lipuro 1 % (10 mg/ml) must be discarded and replaced after 12 hours at the latest. Any portion of Propofol-Lipuro 1 % (10 mg/ml) remaining after the end of infusion or after replacement of the infusion system must be discarded.

Infusion of diluted Propofol-Lipuro 1 % (10 mg/ml)

For administering infusion of diluted Propofol-Lipuro 1 % (10 mg/ml), 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 Propofol-Lipuro 1 % (10 mg/ml).

Propofol-Lipuro 1 % (10 mg/ml) diluted 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 (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, Propofol-Lipuro 1 % (10 mg/ml) may be mixed with preservative-free lidocaine injection 1 % (mix 20 parts of Propofol-Lipuro 1 % (10 mg/ml) with up to 1 part of lidocaine injection 1 %).

Before giving the muscle relaxants atracurium or mivacurium subsequent to Propofol-Lipuro 1 % (10 mg/ml) through the same intravenous line, it is recommended that the line be rinsed prior to administration.

Propofol may also be used by Target Controlled Infusion. Due to the different algorithms available on the market for dosage recommendations please refer to the instructions for use leaflet of the device manufacturer.

• Duration of administration

Propofol-Lipuro 1 % (10 mg/ml) can be administered for a maximum period of 7 days.

4.3 Contraindications

Propofol-Lipuro 1 % (10 mg/ml) is contraindicated in patients with a known hypersensitivity to propofol or to any of the excipients.

Propofol-Lipuro 1 % (10 mg/ml) contains soya-bean oil and should not be used in patients who are hypersensitive to peanut or soya.

Propofol-Lipuro 1 % (10 mg/ml) must not be used in patients of 16 years of age or younger for sedation for intensive care.

4.4 Special Warnings and Precautions for Use

Propofol should be given by those trained in anaesthesia (or, where appropriate, doctors trained in the care of patients in Intensive Care).

Patients should be constantly monitored and facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment and other resuscitative facilities should be readily available at all times. Propofol should not be administered by the person conducting the diagnostic or surgical procedure.

The abuse of propofol, predominantly by health care professionals, has been reported. As with other general anaesthetics, the administration of propofol without airway care may result in fatal respiratory complications.

When propofol is administered for conscious sedation, for surgical and diagnostic procedures, patients should be continually monitored for early signs of hypotension, airway obstruction and oxygen desaturation.

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.

An adequate period is needed prior to discharge of the patient to ensure full recovery after use of propofol. 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.)

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 that reduces cardiac output will also reduce propofol clearance.

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 vagal tone is likely to predominate or when propofol is used in conjunction with other agents likely to cause bradycardia.

When propofol ia administered to an epileptic patient, there may be a risk of convulsion.

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. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1.0 ml of Propofol-Lipuro 1 % (10 mg/ml) contains 0.1 g of fat.

The use of propofol is not recommended in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data (see section 5.2) indicate that clearance is considerably reduced in neonates and has a very high inter-individual variability. Relative overdose could result on administering doses recommended for older children and result in severe cardiovascular depression.

Advisory statements concerning Intensive Care Unit management

The safety and efficacy 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 (back-ground) 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 the intensive care unit.

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

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PACKAGE LEAFLET: INFORMATION FOR THE USER

Propofol-Lipuro 1 % (10 mg/ml)

emulsion for injection or infusion

Propofol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Propofol-Lipuro 1 % (10 mg/ml) is and what it is used for

Propofol-Lipuro 1 % (10 mg/ml) belongs to a group of medicines called general anaesthetics. General anaesthetics are used to cause unconsciousness (sleep) so that surgical operations or other procedures can be performed. They can also be used to sedate you (so that you are sleepy but not completely asleep).

Propofol-Lipuro 1 % (10 mg/ml) is used to:
- induce and maintain general anaesthesia in adults and children > 1 month
- sedate patients > 16 years of age receiving artificial respiration in intensive care
- sedate adults and children > 1 month during diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia.

2. What you need to know before you use Propofol-Lipuro 1 % (10 mg/ml)

Do not use Propofol-Lipuro 1 % (10 mg/ml):
- if you are allergic (hypersensitive) to propofol, soya, peanut or any of the other ingredients of this medicine (listed in section 6).

It must not be used in patients of 16 years of age or younger for sedation during intensive care.

Warnings and precautions

Special care has to be taken
- if you have a disorder in which your body does not handle fat properly,
- if you have any other health problems which require much caution in the use of fat emulsions,
- if your blood volume is too low (hypovolaemia),
- if you are very weak (debilitated) or have heart, kidney or liver problems,
- if you have high pressure within in the skull,
- if you have problems with your breathing,
- if you have epilepsy,
- if you are undergoing some procedures where spontaneous movements are particularly undesirable.

Please tell your doctor if you have one of these diseases or conditions.

If you are receiving other lipids by a drip into your vein at the same time your doctor will pay attention to your total daily fat intake.

Propofol will be administered to you by a physician trained in anaesthesia or intensive care. You will be constantly monitored during anaesthesia and waking-up time.

If you experience signs of the so called 'propofol infusion syndrome' (for a detailed list of the symptoms see section 4 'Possible side effects', a doctor must be called if the following happen?) your doctor will decrease the dosage of propofol or will switch to an alternative drug.

Please see also section 'Driving and using machines' for precautions to be taken after the use of propfol.

The use of Propofol-Lipuro is not recommended in newborn infants.

Other medicines and Propofol-Lipuro 1 % (10 mg/ml)

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Propofol has effectively been used with different regional anaesthesia techniques that only numb a part of your body (epidural and spinal anaesthesia).

Additionally, safe use has been demonstrated in combination with
- drugs you receive before surgery
- other medicines like muscle relaxing drugs
- anaesthetic drugs that can be inhaled
- pain killers.

However your physician may give you lower doses of propofol if general anaesthesia or sedation is needed as a supplement to regional anaesthesia techniques.

Propofol-Lipuro 1 % (10 mg/ml) and alcohol

Your doctor will advise you on the consumption of alcohol before and after the use of Propofol-Lipuro.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Propofol-Lipuro should not be used during pregnancy unless it is definitely needed. It crosses the placenta and may depress the vital functions of the newborn.

However, propofol may be used during an induced abortion.

If you are breast-feeding your child you should stop nursing and discard breast milk for 24 hours after you have received Propofol-Lipuro 1 % (10 mg/ml). Studies in breast-feeding women showed that propofol is excreted in small amounts into the milk.

Driving and using machines

You should not drive or operate machinery for a while after you have had an injection or infusion of Propofol-Lipuro 1 % (10 mg/ml)

Your doctor will advise you
- if you should be accompanied when you are leaving.
- when you can drive and use machinery again.
- on the use of other tranquillizing drugs (e.g. tranquillizers, strong pain killers, alcohol).

Propofol-Lipuro 1 % (10 mg/ml) contains sodium and soya-bean oil

This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, that is, it is essentially 'sodium free'.

Propofol-Lipuro contains soya-bean oil. If you are allergic to peanut or soya, do not use this medicine.

3. How to use Propofol-Lipuro 1 % (10 mg/ml)

Propofol-Lipuro 1 % (10 mg/ml) will only be given by anaesthetists or by specially trained doctors in an intensive care unit.

Dosage

The dose you are given will vary depending on your age, body weight and physical condition. The doctor will give the correct dose to start and to sustain anaesthesia or to achieve the required level of sedation, by carefully watching your responses and vital signs (pulse, blood pressure, breathing, etc).

The doctor will also observe limits of the time of application, if necessary.

Propofol-Lipuro 1 % (10 mg/ml) will usually be given by injection when used to induce general anaesthesia and by continuous infusion (a slower, longer injection) when used to maintain general anaesthesia. It may be given as an infusion either diluted or undiluted. When used as a sedative it will usually be given by infusion.

Propofol-Lipuro 1 % (10 mg/ml) will only be given for a maximum of 7 days.

Method of administration

You will receive Propofol-Lipuro 1 % (10 mg/ml) by intravenous injection or infusion, that is, through a needle or small tube placed in one of your veins.

Because Propofol-Lipuro 1 % (10 mg/ml) does not contain preservatives, an infusion from one vial of Propofol-Lipuro 1 % (10 mg/ml) will not last longer than 12 hours. An infusion from one container of diluted Propofol-Lipuro 1 % (10 mg/ml) will not last longer than 6 hours.

Your circulation and breathing will be constantly monitored while you are being given the injection or infusion.

If you received more Propofol-Lipuro 1 % (10 mg/ml) than you should

It is unlikely that this occurs because the doses you receive are very carefully controlled.

Yet if you accidentally got an overdose, this could lead to depression of heart function and breathing. In this case your doctor will employ any necessary treatment immediately.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

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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

Propofol-Lipuro 1 % (10 mg/ml) contains no antimicrobial preservatives and supports growth of micro-organisms.

When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the seal. Administration must commence without delay. Aseptis must be maintained for both propofol and infusion equipment throughout the infusion period. Any infusion fluids added to the propofol line must be administered close to the cannula site. Propofol must not be administered via a microbiological filter.

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.

This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, i.e. essentially 'sodium free'.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Propofol 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.

4.6 Pregnancy and lactation

Pregnancy

The safety of propofol during pregnancy has not been established. Propofol should not be given to pregnant women except when absolutely necessary. Propofol crosses the placenta and can cause neonatal depression. Propofol can, however, be used during an induced abortion.

Breast-feeding

Studies of breast-feeding mothers showed that small quantities of propofol are excreted in human milk. Women should therefore not breast-feed for 24 hours after administration of propofol. Milk produced during this period should be discarded.

4.7 Effects on the Ability to Drive and Use Machines

Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after use of propofol.

Propofol induced impairment is not generally detectable beyond 12 hours (please see section 4.4).

4.8 Undesirable Effects

Induction and maintenance of anaesthesia or sedation with propofol is generally smooth with minimal evidence of excitation. The most commonly reported ADRs are pharmacologically predictable side effects of an anaesthetic/sedative agent, such as hypotension. The nature, severity and incidence of adverse events observed in patients receiving propofol may be related to the condition of the recipients and the operative or therapeutic procedures being undertaken.

Table of Adverse Drug Reactions

System Organ Class	Frequency	Undesirable Effects
Immune system disorders:	Very rare (<1/10 000)	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
Metabolism and Nutritional disorder:	Frequency not known [9]	Metabolic acidosis [5], hyperkalaemia [5], hyperlipidaemia [5]
Psychiatric disorders:	Frequency not known [9]	Euphoric mood, drug abuse[8]
Nervous system disorders:	Common (>1/100, <1/10)	Headache during recovery phase
	Rare (>1/10 000, <1/1000)	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	Very rare (<1/10 000)	Postoperative unconsciousness
	Frequency not known [9]	Involuntary movements
Cardiac disorders:	Common (>1/100, <1/10)	Bradycardia [1]
	Very rare (<1/10 000)	Pulmonary oedema
	Frequency not known [9]	Cardiac arrhythmia [3], cardiac failure [5], [7]
Vascular disorders:	Common (>1/100, <1/10)	Hypotension [2]
	Uncommon (>1/1000, <1/100)	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders:	Common (>1/100, <1/10)	Transient apnoea during induction
Gastrointestinal disorders:	Common (>1/100, <1/10)	Nausea and vomiting during recovery phase
	Very rare (<1/10 000)	Pancreatitis
Hepatobiliary disorders	Frequency not known [9]	Hepatomegaly [5]
Musculoskeletal and connective tissue disorders:	Frequency not known [9]	Rhabdomyolysis [3], [5]
Renal and urinary disorders	Very rare (<1/10 000)	Discolouration of urine following prolonged administration
	Frequency not known [9]	Renal failure [5]
Reproductive system and breast	Very rare (<1/10 000)	Sexual disinhibition
General disorders and administration site conditions:	Very common (>1/10)	Local pain on induction [4]
Investigations	Frequency not known [9]	Brugada type ECG [5], [6]
Injury, poisoning and procedural complications:	Very rare (<1/10 000)	Postoperative fever

[1] Serious bradycardias are rare. There have been isolated reports of progression to asystole.
[2] Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of propofol.
[3] Very rare reports of rhabdomyolysis have been received where propofol has been given at doses greater than 4 mg/kg/hr for ICU sedation.
[4] May be minimised by using the larger veins of the forearm and antecubital fossa. With Propofol-Lipuro 1 % (10 mg/ml) local pain can also be minimised by the co-administration of lidocaine.
[5] Combinations of these events, reported as "Propofol infusion syndrome", may be seen in seriously ill patients who often have multiple risk factors for the development of the events, see section 4.4.
[6] Brugada-type ECG - elevated ST-segment and coved T-wave in ECG.
[7] Rapidly progressive cardiac failure (in some cases with fatal outcome) in adults. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment.
[8] Drug abuse, predominantly by health care professionals.
[9] Not known as it cannot be estimated from the available clinical trial data.

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmaco therapeutic group: other general anaesthetics, ATC-code: N01AX10.

Mechanism of action, pharmacodynamic effect

After intravenous injection of Propofol-Lipuro 1 % (10 mg/ml), 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.

Paediatric population

Limited studies on the duration of propofol based anaesthesia in children indicate safety and efficacy is unchanged up to duration of 4 hours. Literature evidence of use in children documents use for prolonged procedures without changes in safety or efficacy.

5.2 Pharmacokinetic Properties

Distribution

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.

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.

Biotransformation

Propofol is mainly metabolized in the liver to form glucuronides of propofol and glucuronides and sulphate conjugates of its corresponding quinol. All metabolites are inactive.

Elimination

Propofol is rapidly cleared from the body (total clearance approx. 2 l/min). Clearance occurs by metabolism, mainly in the liver, where it is blood flow dependent. Clearance is higher in children compared with adults. About 88 % of an administered dose is excreted in the form of metabolites in urine. Only 0.3 % is excreted unchanged in urine.

Paediatric population

After a single dose of 3 mg/kg intravenously, propofol clearance/kg body weight increased with age as follows: Median clearance was considerably lower in neonates < 1 month old (n = 25) (20 ml/kg/min) compared to older children (n = 36, age range 4 months – 7 years). Additionally inter-individual variability was considerable in neonates (range 3.7 – 78 ml/kg/min). Due to this limited trial data that indicates a large variability, no dose recommendations can be given for this age group.

Median propofol clearance in older aged children after a single 3 mg/kg bolus was 37.5 ml/min/kg (4–24 months) (n = 8), 38.7 ml/min/kg (11– 43 months) (n = 6), 48 ml/min/kg (1 – 3 years)(n = 12), 28.2 ml/min/kg (4 – 7 years)(n = 10) as compared with 23.6 ml/min/kg in adults (n = 6).

5.3 Preclinical Safety Data

Preclinical data reveal no specific 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 tool tolerance studies, intramuscular injection resulted in tissue damage around the injection site.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Soya-bean oil, refined,
medium-chain triglycerides,
glycerol,
egg lecithin,
sodium oleate,
water for injections.

6.2 Incompatibilities

This medicinal product must not be mixed with other products except those mentioned in section 6.6.

6.3 Shelf Life

2 years.

After first opening:
to be used immediately.

After dilution according to directions:
administration of dilution must commence immediately after preparation.

6.4 Special Precautions for Storage

Do not store above 25 °C.
Do not freeze.
Keep the ampoules and vials in the outer carton in order to protect from light.

6.5 Nature and Contents of Container

Colourless Type I glass ampoules containing 20 ml of emulsion.

Colourless Type II glass vials sealed with bromobutyl rubber stoppers containing 20 ml, 50 ml or 100 ml of emulsion.

Pack sizes:
glass ampoules: 5 x 20 ml
glass vials: 10 x 20 ml, 1 x 50 ml, 10 x 50 ml, 1 x 100 ml, 10 x 100 ml
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handlings

Any unused product or waste material should be disposed of in accordance with local requirements.

Containers should be shaken before use.

For single use only. Any portion of contents remaining after use must be discarded, see section 4.2.

If two layers can be seen after shaking the medicinal product should not be used.

Propofol-Lipuro 1 % (10 mg/ml) should only be mixed with the following products: glucose 50 mg/ml (5 % w/v) solution, sodium chloride 9 mg/ml (0.9 % w/v) solution, or sodium chloride 1.8 mg/ml (0.18%) and glucose 40 mg/ml (4% w/v) solution, and preservative-free lidocaine injection 10 mg/ml (1 %) (see section 4.2 "Method and duration of administration", "Infusion of diluted Propofol-Lipuro 1 % (10 mg/ml)")

Co-administration of Propofol-Lipuro 1 % (10 mg/ml) together with glucose 50 mg/ml (5 % w/v) solution or sodium chloride 9 mg/ml (0.9 % w/v) solution, or sodium chloride 1.8 mg/ml (0.18%) and glucose 40 mg/ml (4% w/v) solution via a Y-connector close to the injection site is possible.

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl-Braun-Strasse 1
34212 Melsungen, Germany

Postal address:
34209 Melsungen, Germany
Phone: +49-5661-71-0
Fax: +49-5661-71-4567

8 MARKETING AUTHORISATION NUMBER(S)

PA 736/18/01 (Ireland, 20 ml glass ampoule)
PA 736/18/02 (Ireland, 50 ml and 100 ml glass bottle)
PL 03551/0055 (United Kingdom)
MA 223/00601 (Malta)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

May 12, 2000 (Ireland)
May 26, 2000 (United Kingdom)
July 1, 2008 (Malta)

Date of last renewal:
May 05, 2009 (common renewal date)

10 DATE OF REVISION OF THE TEXT

10/2011

B. Braun Melsungen AG
34209 Melsungen, Germany

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

A doctor must be called immediately if the following happen

Common (may affect up to 1 in 10 people):
- Low blood pressure that might occasionally need infusion of fluids and reduction of the speed of administration of propofol.
- Too low heartbeat that might be serious in rare cases.

Rare (may affect up to 1 in 1,000 people):
- Convulsions like in epilepsy

Very rare (may affect up to 1 in 10,000 people):
- Allergic reactions including swelling of the face, tongue or throat, wheezing breath, skin redness and low blood pressure
- There have been cases of unconsciousness occurring after operations. You will therefore be carefully observed during the waking-up time.
- Water on lungs (lung oedema) after administration of propofol
- Inflammation of the pancreas.

Not known (frequency cannot be estimated from the available data):
- There have been reports of isolated cases of severe adverse reactions presenting as a combination of the following symptoms: breakdown of muscle tissue, accumulation of acidic (sour) substances in the blood, abnormally high blood potassium level, high blood fat levels, abnormalities in the electrocardiogram (Brugada-type ECG), liver enlargement, irregular heart-beat, kidney failure and heart failure. This has been called the **"propofol infusion syndrome"**. Some of the affected patients eventually died. These effects have only been seen in patients in intensive care with doses higher than 4 mg of propofol per kg body weight per hour. See also section 2, 'Warnings and precautions'.

Other side effects are:

Very common (affects more than 1 treated patient of 10):
- Pain at the injection site occurring during the first injection. The pain may be reduced by injecting propofol into larger veins of the forearm. Injection of lidocaine (a local anaesthetic) and propofol at the same time also helps to reduce the pain at the injection site.

Common (may affect up to 1 in 10 people):
- Short interruption of breathing
- Headache during the time of recovery
- Sickness or vomiting during the time of recovery

Uncommon (may affect up to 1 in 100 people):
- Blood clots in veins or inflammation of veins

Very rare (may affect up to 1 in 10,000 people):
- Loss of sexual control during the time of recovery
- Abnormal colour of urine after longer lasting administration of propofol
- Cases of fever after an operation

Not known (frequency cannot be estimated from the available data):
- Involuntary movements
- Abnormally good mood
- Drug abuse
- Failure of the heart
- Breakdown of muscle tissue has been reported very rarely in cases where propofol has been given at greater doses than recommended for sedation in intensive care units

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

5. How to store Propofol-Lipuro

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton after EXP. The expiry date refers to the last day of that month.

Keep ampoules and vials in the outer carton in order to protect from light.

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

Propofol-Lipuro 1 % (10 mg/ml) must be used immediately after opening the vial or ampoule.

Dilutions of Propofol-Lipuro 1 % (10 mg/ml) must be used immediately after preparation.

Do not use Propofol-Lipuro 1 % (10 mg/ml) if two separate layers can be seen after shaking the product.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Propofol-Lipuro 1 % (10 mg/ml) contains

- The active substance is propofol
  Each millilitre of Propofol-Lipuro 1 % (10 mg/ml) contains 10 mg of propofol.
  1 ampoule or vial with 20 ml contains 200 mg propofol.
  1 vial with 50 ml contains 500 mg propofol.
  1 vial with 100 ml contains 1000 mg propofol.

- The other ingredients are:
  Soya-bean oil refined,
  Medium-chain triglycerides,
  Egg lecithin,
  Glycerol,
  Sodium oleate,
  Water for injections

What Propofol-Lipuro 1 % (10 mg/ml) looks like and contents of the pack

It is an emulsion for injection or infusion.
It is a milky-white oil-in water emulsion.

It comes in:
- glass ampoules of 20 millilitres, available in packs of 5 ampoules
- glass vials of 20 millilitres, available in packs of 10 vials
- glass vials of 50 or 100 millilitres, available in packs of one or 10 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

B. Braun Melsungen AG
Carl-Braun-Straße 1
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Postal address:
34209 Melsungen, Germany

Phone: +49/5661/71-0
Fax: +49/5661/71-4567

This medicinal product is authorised in the Member States of the EEA under the following names:

Propofol-Lipuro 1 % (10 mg/ml):	Czech Republic, Ireland, Malta, Poland, Portugal, Slovakia, United Kingdom
Propofol B. Braun 1 % (10 mg/ml):	Italy
Propofol "B. Braun" 10 mg/ml:	Denmark
Propofol-Lipuro 10 mg/ml:	Austria, Estonia, Finland, France, Germany, Hungary, Latvia, Lithuania, Luxembourg, Netherlands, Slovenia, Spain, Sweden, Norway
Propofol-Lipuro 10 mg/ml:	Cyprus, Greece

This leaflet was last revised in [10/2011].

The following information is intended for healthcare professionals only:

The containers are for single use in one patient only.
Any unused emulsion must be thrown away at the end of administration.
The containers must be shaken before use.

B. Braun Melsungen AG
34209 Melsungen, Germany

598/12260486/1011

SUMMARY OF PRODUCT CHARACTERISTICS

B. Braun Melsungen AG · 34209 Melsungen, Germany

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Propofol-Lipuro 1 % (10 mg/ml) contains

	per 1 ml	per 20 ml ampoule or vial	per 50 ml vial	per 100 ml vial
Propofol	10 mg	200 mg	500 mg	1000 mg

Excipients with known effect:
1 ml emulsion for injection or infusion contains
Soya-bean oil refined 50 mg
Sodium 0.03 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection or infusion
White milky oil-in-water emulsion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Propofol-Lipuro 1 % (10 mg/ml) 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.

4.2 Posology and Method of Administration

General instructions

Propofol-Lipuro 1 % (10 mg/ml) 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-oximetery) and facilities for maintenance of patent airways, artificial ventilation, and other resuscitation facilities should be immediately available at all times. For sedation during surgical or diagnostic procedures Propofol-Lipuro 1 % (10 mg/ml) 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-Lipuro 1 % (10 mg/ml).

Posology

Propofol-Lipuro 1 % (10 mg/ml) 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-Lipuro 1 % (10 mg/ml) 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/kg body weight.

In patients over this age 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-Lipuro 1 % (10 mg/ml) may be reduced to a minimum of 1 mg/kg body weight. 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-Lipuro 1 % (10 mg/ml) either by continuous infusion or by repeat bolus injections. If a technique involving repeat bolus injections is used, increments of 25 mg (2.5 ml Propofol-Lipuro 1 % (10 mg/ml)) to 50 mg (5.0 ml Propofol-Lipuro 1 % (10 mg/ml)) 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 body weight/h.

In elderly patients, in patients of poorer 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-Lipuro 1 % (10 mg/ml) should be slowly titrated 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 of age require approximately 2.5 mg/kg body weight of propofol 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-Lipuro 1 % (10 mg/ml) 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 section 4.4)

• Sedation of ventilated patients in the Intensive Care Unit

For sedation during intensive care it is advised that propofol should be administered by continuous infusion. The infusion rate should be determined by the desired depth of sedation. In most patients sufficient sedation can be obtained with a dosage of 0.3 – 4 mg/kg/h of propofol (see also section 4.4).

Propofol is not indicated for sedation in intensive care of patients of 16 years of age or younger (see section 4.3).

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/kg body weight over 1 to 5 minutes for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol-Lipuro 1 % (10 mg/ml) infusion to the desired level of sedation. Most patients will require 1.5 – 4.5 mg/kg body weight/h. The infusion may be supplemented by bolus administration of 10 – 20 mg (1 – 2 ml Propofol-Lipuro 1 % (10 mg/ml)) 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-Lipuro 1 % (10 mg/ml) 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 body weight of propofol for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol-Lipuro 1 % (10 mg/ml) 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 b.w. if a rapid increase of depth of sedation is required.

In ASA III and IV patients lower doses may be required.

Method and duration of administration

• Method of administration

Intravenous use

Propofol-Lipuro 1 % (10 mg/ml) 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 6.6). Containers should be shaken before use.

Before use, the neck of the ampoule or the surface of the rubber stopper of the vial should be cleaned with medicinal alcohol (spray or swabs). After use, tapped containers must be discarded.

Propofol-Lipuro 1 % (10 mg/ml) contains no antimicrobial preservatives and supports growth of microorganisms. Therefore, Propofol-Lipuro 1 % (10 mg/ml) is to be drawn up aseptically into a sterile syringe or an infusion set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol-Lipuro 1 % (10 mg/ml) and the infusion equipment throughout the infusion period.

Any medicinal products or fluids added to a running Propofol-Lipuro 1 % (10 mg/ml) infusion must be administered close to the cannula site. Propofol-Lipuro 1 % (10 mg/ml) must not be administered via infusion sets with microbiological filters.

1. NAME OF THE MEDICINAL PRODUCT

Propofol-Lipuro 1 % (10 mg/ml)

emulsion for injection or infusion

The contents of one ampoule or one vial of Propofol-Lipuro 1 % (10 mg/ml) and any syringe containing Propofol-Lipuro 1 % (10 mg/ml) are for **single use** in **one** patient.

Infusion of undiluted Propofol-Lipuro 1 % (10 mg/ml)

When administering Propofol-Lipuro 1 % (10 mg/ml) 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 Propofol-Lipuro 1 % (10 mg/ml) from **one** infusion system must not exceed 12 hours. The infusion line and the reservoir of Propofol-Lipuro 1 % (10 mg/ml) must be discarded and replaced after 12 hours at the latest. Any portion of Propofol-Lipuro 1 % (10 mg/ml) remaining after the end of infusion or after replacement of the infusion system must be discarded.

Infusion of diluted Propofol-Lipuro 1 % (10 mg/ml)

For administering infusion of diluted Propofol-Lipuro 1 % (10 mg/ml), 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 Propofol-Lipuro 1 % (10 mg/ml).

The maximum dilution must not exceed 1 part of Propofol-Lipuro 1 % (10 mg/ml) 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, Propofol-Lipuro 1 % (10 mg/ml) may be mixed with preservative-free lidocaine injection 1 % (mix 20 parts of Propofol-Lipuro 1 % (10 mg/ml) with up to 1 part of lidocaine injection 1 %).

Before giving the muscle relaxants atracurium or mivacurium subsequent to Propofol-Lipuro 1 % (10 mg/ml) through the same intravenous line, it is recommended that the line be rinsed prior to administration.

Propofol may also be used by Target Controlled Infusion. Due to the different algorithms available on the market for dosage recommendations please refer to the instructions for use leaflet of the device manufacturer.

• Duration of administration

Propofol-Lipuro 1 % (10 mg/ml) can be administered for a maximum period of 7 days.

4.3 Contraindications

Propofol-Lipuro 1 % (10 mg/ml) is contraindicated in patients with a known hypersensitivity to propofol or to any of the excipients.

Propofol-Lipuro 1 % (10 mg/ml) contains soya-bean oil and should not be used in patients who are hypersensitive to peanut or soya.

Propofol-Lipuro 1 % (10 mg/ml) must not be used in patients of 16 years of age or younger for sedation for intensive care.

4.4 Special Warnings and Precautions for Use

Propofol should be given by those trained in anaesthesia (or, where appropriate, doctors trained in the care of patients in Intensive Care).

Patients should be constantly monitored and facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment and other resuscitative facilities should be readily available at all times. Propofol should not be administered by the person conducting the diagnostic or surgical procedure.

The abuse of propofol, predominantly by health care professionals, has been reported. As with other general anaesthetics, the administration of propofol without airway care may result in fatal respiratory complications.

When propofol is administered for conscious sedation, for surgical and diagnostic procedures, patients should be continually monitored for early signs of hypotension, airway obstruction and oxygen desaturation.

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.

An adequate period is needed prior to discharge of the patient to ensure full recovery after use of propofol. 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.)

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 that reduces cardiac output will also reduce propofol clearance.

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 vagal tone is likely to predominate or when propofol is used in conjunction with other agents likely to cause bradycardia.

When propofol ia administered to an epileptic patient, there may be a risk of convulsion.

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. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1.0 ml of Propofol-Lipuro 1 % (10 mg/ml) contains 0.1 g of fat.

The use of propofol is not recommended in newborn infants as this patient population has not been fully investigated. Pharmacokinetic data (see section 5.2) 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

The safety and efficacy 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 (back-ground) 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 the intensive care unit.

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

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PACKAGE LEAFLET: INFORMATION FOR THE USER

Propofol-Lipuro 1 % (10 mg/ml)

emulsion for injection or infusion

Propofol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Propofol-Lipuro 1 % (10 mg/ml) is and what it is used for

Propofol-Lipuro 1 % (10 mg/ml) belongs to a group of medicines called general anaesthetics. General anaesthetics are used to cause unconsciousness (sleep) so that surgical operations or other procedures can be performed. They can also be used to sedate you (so that you are sleepy but not completely asleep).

Propofol-Lipuro 1 % (10 mg/ml) is used to:
- induce and maintain general anaesthesia in adults and children > 1 month
- sedate patients > 16 years of age receiving artificial respiration in intensive care
- sedate adults and children > 1 month during diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia.

2. What you need to know before you use Propofol-Lipuro 1 % (10 mg/ml)

Do not use Propofol-Lipuro 1 % (10 mg/ml):
- if you are allergic (hypersensitive) to propofol, soya, peanut or any of the other ingredients of this medicine (listed in section 6).

It must not be used in patients of 16 years of age or younger for sedation during intensive care.

Warnings and precautions

Special care has to be taken
- if you have a disorder in which your body does not handle fat properly,
- if you have any other health problems which require much caution in the use of fat emulsions,
- if your blood volume is too low (hypovolaemia),
- if you are very weak (debilitated) or have heart, kidney or liver problems,
- if you have high pressure within in the skull,
- if you have problems with your breathing,
- if you have epilepsy,
- if you are undergoing some procedures where spontaneous movements are particularly undesirable.

Please tell your doctor if you have one of these diseases or conditions.

If you are receiving other lipids by a drip into your vein at the same time your doctor will pay attention to your total daily fat intake.

Propofol will be administered to you by a physician trained in anaesthesia or intensive care. You will be constantly monitored during anaesthesia and waking-up time.

If you experience signs of the so called 'propofol infusion syndrome' (for a detailed list of the symptoms see section 4 'Possible side effects', a doctor must be called if the following happen?) your doctor will decrease the dosage of propofol or will switch to an alternative drug.

Please see also section 'Driving and using machines' for precautions to be taken after the use of propfol.

The use of Propofol-Lipuro is not recommended in newborn infants.

Other medicines and Propofol-Lipuro 1 % (10 mg/ml)

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Propofol has effectively been used with different regional anaesthesia techniques that only numb a part of your body (epidural and spinal anaesthesia).

Additionally, safe use has been demonstrated in combination with
- drugs you receive before surgery
- other medicines like muscle relaxing drugs
- anaesthetic drugs that can be inhaled
- pain killers.

However your physician may give you lower doses of propofol if general anaesthesia or sedation is needed as a supplement to regional anaesthesia techniques.

Propofol-Lipuro 1 % (10 mg/ml) and alcohol

Your doctor will advise you on the consumption of alcohol before and after the use of Propofol-Lipuro.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Propofol-Lipuro should not be used during pregnancy unless it is definitely needed. It crosses the placenta and may depress the vital functions of the newborn.

However, propofol may be used during an induced abortion.

If you are breast-feeding your child you should stop nursing and discard breast milk for 24 hours after you have received Propofol-Lipuro 1 % (10 mg/ml). Studies in breast-feeding women showed that propofol is excreted in small amounts into the milk.

Driving and using machines

You should not drive or operate machinery for a while after you have had an injection or infusion of Propofol-Lipuro 1 % (10 mg/ml)

Your doctor will advise you
- if you should be accompanied when you are leaving.
- when you can drive and use machinery again.
- on the use of other tranquillizing drugs (e.g. tranquillizers, strong pain killers, alcohol).

Propofol-Lipuro 1 % (10 mg/ml) contains sodium and soya-bean oil

This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, that is, it is essentially 'sodium free'.

Propofol-Lipuro contains soya-bean oil. If you are allergic to peanut or soya, do not use this medicine.

3. How to use Propofol-Lipuro 1 % (10 mg/ml)

Propofol-Lipuro 1 % (10 mg/ml) will only be given by anaesthetists or by specially trained doctors in an intensive care unit.

Dosage

The dose you are given will vary depending on your age, body weight and physical condition. The doctor will give the correct dose to start and to sustain anaesthesia or to achieve the required level of sedation, by carefully watching your responses and vital signs (pulse, blood pressure, breathing, etc).

The doctor will also observe limits of the time of application, if necessary.

Propofol-Lipuro 1 % (10 mg/ml) will usually be given by injection when used to induce general anaesthesia and by continuous infusion (a slower, longer injection) when used to maintain general anaesthesia. It may be given as an infusion either diluted or undiluted. When used as a sedative it will usually be given by infusion.

Propofol-Lipuro 1 % (10 mg/ml) will only be given for a maximum of 7 days.

Method of administration

You will receive Propofol-Lipuro 1 % (10 mg/ml) by intravenous injection or infusion, that is, through a needle or small tube placed in one of your veins.

Because Propofol-Lipuro 1 % (10 mg/ml) does not contain preservatives, an infusion from one vial of Propofol-Lipuro 1 % (10 mg/ml) will not last longer than 12 hours. An infusion from one container of diluted Propofol-Lipuro 1 % (10 mg/ml) will not last longer than 6 hours.

Your circulation and breathing will be constantly monitored while you are being given the injection or infusion.

If you received more Propofol-Lipuro 1 % (10 mg/ml) than you should

It is unlikely that this occurs because the doses you receive are very carefully controlled.

Yet if you accidentally got an overdose, this could lead to depression of heart function and breathing. In this case your doctor will employ any necessary treatment immediately.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

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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

Propofol-Lipuro 1 % (10 mg/ml) contains no antimicrobial preservatives and supports growth of micro-organisms.

When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the seal. Administration must commence without delay. Aseptis must be maintained for both propofol and infusion equipment throughout the infusion period. Any infusion fluids added to the propofol line must be administered close to the cannula site. Propofol must not be administered via a microbiological filter.

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.

This medicinal product contains less than 1 mmol (23 mg) sodium in 100 ml, i.e. essentially 'sodium free'.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Propofol 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.

4.6 Pregnancy and lactation

Pregnancy

The safety of propofol during pregnancy has not been established. Propofol should not be given to pregnant women except when absolutely necessary. Propofol crosses the placenta and can cause neonatal depression. Propofol can, however, be used during an induced abortion.

Breast-feeding

Studies of breast-feeding mothers showed that small quantities of propofol are excreted in human milk. Women should therefore not breast-feed for 24 hours after administration of propofol. Milk produced during this period should be discarded.

4.7 Effects on the Ability to Drive and Use Machines

Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after use of propofol.

Propofol induced impairment is not generally detectable beyond 12 hours (please see section 4.4).

4.8 Undesirable Effects

Induction and maintenance of anaesthesia or sedation with propofol is generally smooth with minimal evidence of excitation. The most commonly reported ADRs are pharmacologically predictable side effects of an anaesthetic/sedative agent, such as hypotension. The nature, severity and incidence of adverse events observed in patients receiving propofol may be related to the condition of the recipients and the operative or therapeutic procedures being undertaken.

Table of Adverse Drug Reactions

System Organ Class	Frequency	Undesirable Effects
Immune system disorders:	Very rare (<1/10 000)	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
Metabolism and Nutritional disorder:	Frequency not known [9]	Metabolic acidosis [5], hyperkalaemia [5], hyperlipidaemia [5]
Psychiatric disorders:	Frequency not known [9]	Euphoric mood, drug abuse[8]
Nervous system disorders:	Common (>1/100, <1/10)	Headache during recovery phase
	Rare (>1/10 000, <1/1000)	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	Very rare (<1/10 000)	Postoperative unconsciousness
	Frequency not known [9]	Involuntary movements
Cardiac disorders:	Common (>1/100, <1/10)	Bradycardia [1]
	Very rare (<1/10 000)	Pulmonary oedema
	Frequency not known [9]	Cardiac arrhythmia [3], cardiac failure [5], [7]
Vascular disorders:	Common (>1/100, <1/10)	Hypotension [2]
	Uncommon (>1/1000, <1/100)	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders:	Common (>1/100, <1/10)	Transient apnoea during induction
Gastrointestinal disorders:	Common (>1/100, <1/10)	Nausea and vomiting during recovery phase
	Very rare (<1/10 000)	Pancreatitis
Hepatobiliary disorders	Frequency not known [9]	Hepatomegaly [5]
Musculoskeletal and connective tissue disorders:	Frequency not known [9]	Rhabdomyolysis [3], [5]
Renal and urinary disorders	Very rare (<1/10 000)	Discolouration of urine following prolonged administration
	Frequency not known [9]	Renal failure [5]
Reproductive system and breast	Very rare (<1/10 000)	Sexual disinhibition
General disorders and administration site conditions:	Very common (>1/10)	Local pain on induction [4]
Investigations	Frequency not known [9]	Brugada type ECG [5], [6]
Injury, poisoning and procedural complications:	Very rare (<1/10 000)	Postoperative fever

[1] Serious bradycardias are rare. There have been isolated reports of progression to asystole.
[2] Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of propofol.
[3] Very rare reports of rhabdomyolysis have been received where propofol has been given at doses greater than 4 mg/kg/hr for ICU sedation.
[4] May be minimised by using the larger veins of the forearm and antecubital fossa. With Propofol-Lipuro 1 % (10 mg/ml) local pain can also be minimised by the co-administration of lidocaine.
[5] Combinations of these events, reported as "Propofol infusion syndrome", may be seen in seriously ill patients who often have multiple risk factors for the development of the events, see section 4.4.
[6] Brugada-type ECG - elevated ST-segment and coved T-wave in ECG.
[7] Rapidly progressive cardiac failure (in some cases with fatal outcome) in adults. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment.
[8] Drug abuse, predominantly by health care professionals.
[9] Not known as it cannot be estimated from the available clinical trial data.

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmaco therapeutic group: other general anaesthetics, ATC-code: N01AX10.

Mechanism of action, pharmacodynamic effect

After intravenous injection of Propofol-Lipuro 1 % (10 mg/ml), 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.

Paediatric population

Limited studies on the duration of propofol based anaesthesia in children indicate safety and efficacy is unchanged up to duration of 4 hours. Literature evidence of use in children documents use for prolonged procedures without changes in safety or efficacy.

5.2 Pharmacokinetic Properties

Distribution

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.

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.

Biotransformation

Propofol is mainly metabolized in the liver to form glucuronides of propofol and glucuronides and sulphate conjugates of its corresponding quinol. All metabolites are inactive.

Elimination

Propofol is rapidly cleared from the body (total clearance approx. 2 l/min). Clearance occurs by metabolism, mainly in the liver, where it is blood flow dependent. Clearance is higher in children compared with adults. About 88 % of an administered dose is excreted in the form of metabolites in urine. Only 0.3 % is excreted unchanged in urine.

Paediatric population

After a single dose of 3 mg/kg intravenously, propofol clearance/kg body weight increased with age as follows: Median clearance was considerably lower in neonates < 1 month old (n = 25) (20 ml/kg/min) compared to older children (n = 36, age range 4 months – 7 years). Additionally inter-individual variability was considerable in neonates (range 3.7 – 78 ml/kg/min). Due to this limited trial data that indicates a large variability, no dose recommendations can be given for this age group.

Median propofol clearance in older aged children after a single 3 mg/kg bolus was 37.5 ml/min/kg (4–24 months) (n = 8), 38.7 ml/min/kg (11– 43 months) (n = 6), 48 ml/min/kg (1 – 3 years)(n = 12), 28.2 ml/min/kg (4 – 7 years)(n = 10) as compared with 23.6 ml/min/kg in adults (n = 6).

5.3 Preclinical Safety Data

Preclinical data reveal no specific 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 tool tolerance studies, intramuscular injection resulted in tissue damage around the injection site.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Soya-bean oil, refined,
medium-chain triglycerides,
glycerol,
egg lecithin,
sodium oleate,
water for injections.

6.2 Incompatibilities

This medicinal product must not be mixed with other products except those mentioned in section 6.6.

6.3 Shelf Life

2 years.

After first opening:
to be used immediately.

After dilution according to directions:
administration of dilution must commence immediately after preparation.

6.4 Special Precautions for Storage

Do not store above 25 °C.
Do not freeze.
Keep the ampoules and vials in the outer carton in order to protect from light.

6.5 Nature and Contents of Container

Colourless Type I glass ampoules containing 20 ml of emulsion.

Colourless Type II glass vials sealed with bromobutyl rubber stoppers containing 20 ml, 50 ml or 100 ml of emulsion.

Pack sizes:
glass ampoules: 5 x 20 ml
glass vials: 10 x 20 ml, 1 x 50 ml, 10 x 50 ml, 1 x 100 ml, 10 x 100 ml
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handlings

Any unused product or waste material should be disposed of in accordance with local requirements.

Containers should be shaken before use.

For single use only. Any portion of contents remaining after use must be discarded, see section 4.2.

If two layers can be seen after shaking the medicinal product should not be used.

Propofol-Lipuro 1 % (10 mg/ml) should only be mixed with the following products: glucose 50 mg/ml (5 % w/v) solution, sodium chloride 9 mg/ml (0.9 % w/v) solution, or sodium chloride 1.8 mg/ml (0.18%) and glucose 40 mg/ml (4% w/v) solution, and preservative-free lidocaine injection 10 mg/ml (1 %) (see section 4.2 "Method and duration of administration", "Infusion of diluted Propofol-Lipuro 1 % (10 mg/ml)")

Co-administration of Propofol-Lipuro 1 % (10 mg/ml) together with glucose 50 mg/ml (5 % w/v) solution or sodium chloride 9 mg/ml (0.9 % w/v) solution, or sodium chloride 1.8 mg/ml (0.18%) and glucose 40 mg/ml (4% w/v) solution via a Y-connector close to the injection site is possible.

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl-Braun-Strasse 1
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34209 Melsungen, Germany
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8 MARKETING AUTHORISATION NUMBER(S)

PA 736/18/01 (Ireland, 20 ml glass ampoule)
PA 736/18/02 (Ireland, 50 ml and 100 ml glass bottle)
PL 03551/0055 (United Kingdom)
MA 223/00601 (Malta)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

May 12, 2000 (Ireland)
May 26, 2000 (United Kingdom)
July 1, 2008 (Malta)

Date of last renewal:
May 05, 2009 (common renewal date)

10 DATE OF REVISION OF THE TEXT

10/2011

B. Braun Melsungen AG
34209 Melsungen, Germany

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

A doctor must be called immediately if the following happen

Common (may affect up to 1 in 10 people):
- Low blood pressure that might occasionally need infusion of fluids and reduction of the speed of administration of propofol.
- Too low heartbeat that might be serious in rare cases.

Rare (may affect up to 1 in 1,000 people):
- Convulsions like in epilepsy

Very rare (may affect up to 1 in 10,000 people):
- Allergic reactions including swelling of the face, tongue or throat, wheezing breath, skin redness and low blood pressure
- There have been cases of unconsciousness occurring after operations. You will therefore be carefully observed during the waking-up time.
- Water on lungs (lung oedema) after administration of propofol
- Inflammation of the pancreas.

Not known (frequency cannot be estimated from the available data):
- There have been reports of isolated cases of severe adverse reactions presenting as a combination of the following symptoms: breakdown of muscle tissue, accumulation of acidic (sour) substances in the blood, abnormally high blood potassium level, high blood fat levels, abnormalities in the electrocardiogram (Brugada-type ECG), liver enlargement, irregular heart-beat, kidney failure and heart failure. This has been called the **"propofol infusion syndrome"**. Some of the affected patients eventually died. These effects have only been seen in patients in intensive care with doses higher than 4 mg of propofol per kg body weight per hour. See also section 2, 'Warnings and precautions'.

Other side effects are:

Very common (affects more than 1 treated patient of 10):
- Pain at the injection site occurring during the first injection. The pain may be reduced by injecting propofol into larger veins of the forearm. Injection of lidocaine (a local anaesthetic) and propofol at the same time also helps to reduce the pain at the injection site.

Common (may affect up to 1 in 10 people):
- Short interruption of breathing
- Headache during the time of recovery
- Sickness or vomiting during the time of recovery

Uncommon (may affect up to 1 in 100 people):
- Blood clots in veins or inflammation of veins

Very rare (may affect up to 1 in 10,000 people):
- Loss of sexual control during the time of recovery
- Abnormal colour of urine after longer lasting administration of propofol
- Cases of fever after an operation

Not known (frequency cannot be estimated from the available data):
- Involuntary movements
- Abnormally good mood
- Drug abuse
- Failure of the heart
- Breakdown of muscle tissue has been reported very rarely in cases where propofol has been given at greater doses than recommended for sedation in intensive care units

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

5. How to store Propofol-Lipuro

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton after EXP. The expiry date refers to the last day of that month.

Keep ampoules and vials in the outer carton in order to protect from light.

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

Propofol-Lipuro 1 % (10 mg/ml) must be used immediately after opening the vial or ampoule.

Dilutions of Propofol-Lipuro 1 % (10 mg/ml) must be used immediately after preparation.

Do not use Propofol-Lipuro 1 % (10 mg/ml) if two separate layers can be seen after shaking the product.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Propofol-Lipuro 1 % (10 mg/ml) contains

- The active substance is propofol
  Each millilitre of Propofol-Lipuro 1 % (10 mg/ml) contains 10 mg of propofol.
  1 ampoule or vial with 20 ml contains 200 mg propofol.
  1 vial with 50 ml contains 500 mg propofol.
  1 vial with 100 ml contains 1000 mg propofol.

- The other ingredients are:
  Soya-bean oil refined,
  Medium-chain triglycerides,
  Egg lecithin,
  Glycerol,
  Sodium oleate,
  Water for injections

What Propofol-Lipuro 1 % (10 mg/ml) looks like and contents of the pack

It is an emulsion for injection or infusion.
It is a milky-white oil-in water emulsion.

It comes in:
- glass ampoules of 20 millilitres, available in packs of 5 ampoules
- glass vials of 20 millilitres, available in packs of 10 vials
- glass vials of 50 or 100 millilitres, available in packs of one or 10 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This medicinal product is authorised in the Member States of the EEA under the following names:

Propofol-Lipuro 1 % (10 mg/ml):	Czech Republic, Ireland, Malta, Poland, Portugal, Slovakia, United Kingdom
Propofol B. Braun 1 % (10 mg/ml):	Italy
Propofol "B. Braun" 10 mg/ml:	Denmark
Propofol-Lipuro 10 mg/ml:	Austria, Estonia, Finland, France, Germany, Hungary, Latvia, Lithuania, Luxembourg, Netherlands, Slovenia, Spain, Sweden, Norway
Propofol-Lipuro 10 mg/ml:	Cyprus, Greece

This leaflet was last revised in [10/2011].

The following information is intended for healthcare professionals only:

The containers are for single use in one patient only.
Any unused emulsion must be thrown away at the end of administration.
The containers must be shaken before use.

B. Braun Melsungen AG
34209 Melsungen, Germany