For further copies of this leaflet, visit emc.medicines.org.uk or call Aspen on +44 (0)1 748 828 391.

Package leaflet: Information for the user

Propofol 10mg/ml (1%) emulsion for injection or infusion
propofol

Read all of this leaflet carefully before you start having 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 or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Propofol 1% is and what it is used for

Propofol 1% contains a medicine called propofol. This 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 1% will be given to you as an injection by a doctor.

In adults and children over 1 month of age it is used to:
- Help put you to sleep **before** an operation or other procedure.
- Keep you asleep **during** an operation or other procedure.
- Sedate you during diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia.

In people over 16 years of age it is also used to:
- Sedate you when receiving artificial respiration in an Intensive Care Unit (ICU).

2. What you need to know before you use Propofol 1%

Do not use Propofol 1%:
- If you are allergic to propofol or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to peanut or soya. This is because Propofol 1% contains soya oil.
- If you are 16 years of age or younger for sedation in intensive care.

If any of the above apply to you, do not have Propofol 1% and tell your doctor, anaesthetist or nurse. If you are not sure, talk to one of these people before having Propofol 1%.

Warnings and precautions
The use of Propofol 1% is not recommended in newborn infants.
Talk to your doctor, anaesthetist or nurse before using Propofol 1%.

Before you have this medicine, tell your doctor, anaesthetist or nurse
- If you have ever had a fit or convulsion.

- If you have ever been told that you have very high levels of fat in your blood.
- If you have ever been told that your body has problems using fat.
- If your body has lost lots of water (you are dehydrated).
- If you have any other health problems, such as problems with your heart, breathing, kidneys or liver.
- If you have been generally unwell for some time.
- If you have mitochondrial disease.

Studies in young animals and clinical data suggest that repeated or lengthy use of general anaesthetics or sedation drugs in children younger than 3 years or in pregnant women during their third trimester may have negative effects on the development of the child's brain. Parents and caregivers should discuss the benefits, risks, timing and length of surgery or procedures requiring anaesthetics or sedation with your doctor.
If you are not sure if any of the above apply to you, talk to your doctor or nurse before having Propofol 1%.

Other medicines and Propofol 1%
Tell your doctor if you are taking or have recently taken or might take any other medicines. This includes medicines that you buy without a prescription and herbal medicines.

In particular, tell your doctor, anaesthetist or nurse if you are taking any of the following medicines:
- Rifampicin (for tuberculosis - TB)
- Midazolam (used to induce sedation - a very relaxed state of calm, drowsiness or sleep - and to relieve anxiety and muscle tension)

Pregnancy and breast-feeding
Do not have Propofol 1% if you are pregnant unless absolutely necessary.

Studies have shown that small amounts of propofol can pass into breast milk. Therefore, you should not breastfeed your baby for 24 hours after taking propofol.

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

Driving and using machines
After having propofol, you may still feel sleepy for some time. Do not drive or use any tools or machines until you are sure the effects have worn off.
- If you are able to go home shortly after having Propofol 1%, do not drive a car or use any tools or machines.
- Ask your doctor when you can start doing these activities again and when you can go back to work.

Propofol 1% contains sodium, soya oil and disodium edetate
Propofol 1% contains sodium. If you are on a sodium controlled diet, you will need to take this into account.

Propofol 1% contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

Propofol 1% contains disodium edetate. During prolonged use of Propofol 1% for intensive care, you may
need to be given a zinc (a mineral) supplement.

3. How to use Propofol 1%

You will be given Propofol 1% by a doctor. It will be given to you as an injection into a vein. This is usually in the back of your hand or in your forearm.

- The doctor will give you the injection using a needle or through a fine plastic tube called a 'cannula'.
- The doctor can also use an electric pump to control how fast the injection is given. This may be done if you are having a long operation or if you are in an Intensive Care Unit.

The dose of Propofol 1% varies from one patient to another. The amount of propofol that you need depends on your age, size, physical fitness and the level of sleepiness or sleep that you need. The doctor will give you 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.).

You may need several different medicines to keep you asleep or sleepy, free from pain, breathing in a healthy way and to keep your blood pressure steady. The doctor will decide which medicines you need and when you need them.

4. Possible side effects

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

Side effects that can happen during anaesthesia

The following side effects can happen during anaesthesia (while the injection is being given to you or when you are sleepy or asleep). Your doctor will be looking out for these. If they happen, your doctor will give you appropriate treatment.

Very common (may affect more than 1 in 10 people)

- A feeling of pain at the site of the injection (while the injection is being given, before you fall asleep).

Common (may affect up to 1 in 10 people)

- Low blood pressure.
- Changes in your breathing pattern.
- Slow heart beat.

Rare (may affect up to 1 in 1,000 people)

- Twitching and shaking of your body, or a fit (may also happen when you wake up).
- Unusual colour of urine (may also happen when you wake up).

Very rare (may affect up to 1 in 10,000 people)

- Allergic reactions.
- Stopping of your heart beat.
- Build up of fluid in the lungs which can make you very breathless (may also happen when you wake up).

Not known: frequency cannot be estimated from the available data

- Shallow breathing.
- Prolonged, often painful erection (priapism).

Side effects that can happen after anaesthesia

The following side effects can happen after anaesthesia (when you are waking up or after you have woken up).

Common (may affect up to 1 in 10 people)

- Feeling sick (nausea).
- Being sick (vomiting).
- Headache.

Uncommon (may affect up to 1 in 100 people)

- Swelling and redness along a vein or blood clots.

Very rare (may affect up to 1 in 10,000 people)

- Feeling sexually aroused.

- High temperature (fever).
- Redness or soreness where the injection was given.
- Being unconscious after the operation. (When this has happened, the patients have recovered without problems.)
- Tissue damage.

Not known: frequency cannot be estimated from the available data

- A feeling of pain at the site of the injection.
- Swelling at the site of injection.
- Prolonged, often painful erection (priapism).

Other possible side effects

The following side effects have been seen when propofol is used in intensive care at higher doses than recommended.

Very rare (may affect up to1 in 10,000 people)

- Heart failure.
- Inflamed pancreas (pancreatitis) which causes severe stomach pain.
- Too much acid in your blood. This may make you breathe more quickly.
- Increased amount of potassium in your blood.
- High blood level of a type of fat called lipids.
- Abnormal heart beat.
- Enlargement of the liver.
- Kidney failure.

The following side effects have been seen in children in intensive care when propofol has been stopped suddenly.

Common (may affect up to 1 in 10 people)

- 'Withdrawal symptoms'. These include unusual behaviour, sweating, shaking and feeling anxious.
- Flushing of the skin.

Do not be concerned by this list of possible side effects. You may not get any of them.

Not known: frequency cannot be estimated from the available data

- Euphoric mood.
- Involuntary movements.
- Drug abuse and dependence on propofol, mostly by healthcare professionals.
- Abnormal ECG.
- Breakdown of muscle cells (rhabdomyolysis).

If you think you have a side effect or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Propofol 1%

- Keep this medicine out of the sight and reach of children.
- The doctor and hospital pharmacist are responsible for storing, using and disposing of Propofol 1% correctly.
- Store Propofol 1% between 2°C and 25°C. Do not freeze.

- Do not use Propofol 1% after the expiry date which is stated on the carton after EXP.

6. Contents of the pack and other information

What Propofol 1% contains
The active substance is propofol. There is 10 mg of propofol in each millilitre.
The other ingredients are glycerol, purified egg phosphatide, sodium hydroxide, soya bean oil, water for injections, nitrogen and disodium edetate.

What Propofol 1% looks like and contents of the pack
Propofol 1% is a milky, white liquid. It comes in glass ampoules of 20 ml, glass vials of 50 ml or 100 ml, or pre-filled syringes of 20 ml or 50 ml.

Marketing Authorisation Holder and Manufacturer
The Marketing Authorisation for Propofol 1% is held by Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
Tel: +44 (0)1 748 828 391
Propofol 1% is manufactured by
Corden Pharma S.P.A, Viale dell' Industria 3, 20867 Caponago, Italy
or
AstraZeneca UK Ltd, Silk Road Business Park, Macclesfield, Cheshire, SK10 2NA, UK.

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge: 0800 198 5000 (UK only)
Please be ready to give the following information:
Product name **Propofol 10mg/ml (1%) emulsion for injection or infusion**
Reference number 39699/0074
This is a service provided by the Royal National Institute of the Blind.

This leaflet was last revised in November 2023.

Medical Information Leaflet
Propofol 10mg/ml (1%) emulsion for injection or infusion
(Issued to the Medical Professions Only)

1. Trade Name of the Medicinal Product

Propofol 10mg/ml (1%) emulsion for injection or infusion

2. Qualitative and Quantitative Composition

Propofol 10 mg/ml

Excipient(s) with known effect:
Soya-bean Oil, Refined Ph Eur

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Emulsion for injection or infusion.
White aqueous isotonic oil-in-water emulsion.

4. Clinical Particulars

4.1 Therapeutic indications

Propofol 1% is a short-acting intravenous general anaesthetic for:

- Induction and maintenance of general anaesthesia in adults and children >1 month.
- Sedation for diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia in adults and children >1 month.
- Sedation of ventilated patients >16 years of age in the intensive care unit.

4.2 Posology and method of administration

For specific guidance relating to the administration of Propofol 1% with a target controlled infusion (TCI) device, which incorporates Diprifusor TCI software, (see Section 4.2.5). Such use is restricted to induction and maintenance of anaesthesia in adults. The Diprifusor TCI system is not recommended for use in ICU sedation or sedation for surgical and diagnostic procedures, or in children.

- Posology

Induction of general anaesthesia

Adults
In unpremedicated and premedicated patients, it is recommended that Propofol 1% should be titrated (approximately 4 ml [40 mg] every 10 seconds in an average healthy adult by bolus injection or infusion) against the response of the patient until the clinical signs show the onset of anaesthesia. Most adult patients aged less than 55 years are likely to require 1.5–2.5 mg/kg of Propofol 1%. The total dose required can be reduced by lower rates of administration (2–5 ml/min [20–50 mg/min]). Over this

age, the requirement will generally be less. In patients of ASA Grades 3 and 4, lower rates of administration should be used (approximately 2 ml [20 mg] every 10 seconds).
Elderly
In older people the dose requirement for induction of anaesthesia with Propofol 1% is reduced. The reduction should take into account the physical status and age of the patient. The reduced dose should be given at a slower rate and titrated against the response.

Paediatric population
Propofol 1% is not recommended for induction of anaesthesia in children aged less than 1 month. For induction of anaesthesia in children over 1 month of age, Propofol 1% should be titrated slowly until clinical signs show the onset of anaesthesia. The dose 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 1% 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).

For ASA 3 and 4 patients lower doses are recommended (see also Section 4.4).
Administration of Propofol 1% by a Diprifusor TCI system is not recommended for induction of general anaesthesia in children.

Maintenance of general anaesthesia

Adults
Anaesthesia can be maintained by administering Propofol 1% either by continuous infusion or by repeat bolus injections to prevent the clinical signs of light anaesthesia. Recovery from anaesthesia is typically rapid and it is therefore important to maintain Propofol 1% administration until the end of the procedure.

- Continuous infusion

The required rate of administration varies considerably between patients, but rates in the region of 4–12 mg/kg/h usually maintain satisfactory anaesthesia.

- Repeat bolus injections

If a technique involving repeat bolus injections is used, increments of 25 mg (2.5 ml) to 50 mg (5 ml) may be given according to clinical need.

Elderly
When Propofol 1% is used for maintenance of anaesthesia the rate of infusion or 'target concentration' should also be reduced. Patients of ASA grades 3 and 4 will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in older people as this may lead to cardiorespiratory depression.

Paediatric population
Propofol 1% is not recommended for maintenance of anaesthesia in children aged less than 1 month.Anaesthesia can be maintained in children over 1 month of age by administering Propofol 1% by infusion or repeated bolus injection to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients, but rates in the region of 9–15 mg/kg/h usually achieve satisfactory anaesthesia. In younger children, especially between the age of 1 month and 3 years, dose requirements may be higher.

For ASA 3 and 4 patients lower doses are recommended (see also Section 4.4).Administration of Propofol 1% by a Diprifusor TCI system is not recommended for maintenance of general anaesthesia in children.

Sedation during intensive care

Adults
For sedation during intensive care it is advised that Propofol 1% 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 1% (see 4.4 Special warnings and special precautions for use). Propofol 1% is not indicated for sedation in intensive care

of patients of 16 years of age or younger (see 4.3 Contraindications). Administration of Propofol 1% by Diprifusor TCI system is not advised for sedation in the intensive care unit.
Propofol 1% may be diluted with 5% Dextrose (see Dilution and Co-administration table below).
It is recommended that blood lipid levels be monitored should Propofol 1% be administered to patients thought to be at particular risk of fat overload. Administration of Propofol 1% 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 1% formulation; 1 ml of Propofol 1% contains approximately 0.1 g of fat.
If the duration of sedation is in excess of 3 days, lipids should be monitored in all patients.

Elderly
When Propofol 1% is used for sedation the rate of infusion should also be reduced. Patients of ASA grades 3 and 4 will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in older people as this may lead to cardiorespiratory depression.

Paediatric population
Propofol 1% is contraindicated for the sedation of ventilated children aged 16 years or younger receiving intensive care.

Sedation for surgical and diagnostic procedures

Adults
To provide sedation for surgical and diagnostic procedures, rates of administration should be individualised and titrated to clinical response.
Most patients will require 0.5–1 mg/kg over 1–5 minutes for onset of sedation.

Maintenance of sedation may be accomplished by titrating Propofol 1% infusion to the desired level of sedation – most patients will require 1.5–4.5 mg/kg/h. In addition to the infusion, bolus administration of 10–20 mg may be used if a rapid increase in the depth of sedation is required. In patients of ASA Grades 3 and 4 the rate of administration and dosage may need to be reduced.

Administration of Propofol 1% by a Diprifusor TCI system is not recommended for sedation for surgical and diagnostic procedures.

Elderly people
When Propofol 1% is used for sedation the rate of infusion or 'target concentration' should also be reduced. Patients of ASA grades 3 and 4 will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in older people as this may lead to cardiorespiratory depression.

Paediatric population
Propofol 1% is not recommended for surgical and diagnostic procedures in children aged less than 1 month.

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 1% for onset of sedation. Maintenance of sedation may be accomplished by titrating Propofol 1% infusion to the desired level of sedation. Most patients require 1.5–9 mg/kg/h Propofol 1%. The infusion may be supplemented by bolus administration of up to 1 mg/kg body weight if a rapid increase of depth of sedation is required.

In ASA 3 and 4 patients lower doses may be required.

Method of administration
Propofol 1% has no analgesic properties and therefore supplementary analgesic agents are generally required in addition to Propofol 1%.

Propofol 1% can be used for infusion undiluted from glass containers, plastic syringes or Propofol 1% pre-filled syringes or diluted with 5% Dextrose (Intravenous Infusion BP) only, in PVC infusion bags or glass infusion bottles. Dilutions, which must not exceed 1 in 5 (2 mg propofol per ml) should be prepared aseptically immediately before administration and must be used within 6 hours of preparation.

It is recommended that, when using diluted Propofol 1%, the volume of 5% Dextrose removed from the infusion bag during the dilution process is totally replaced in volume by Propofol 1% emulsion (see Dilution and co-administration table below).

The dilution may be used with a variety of infusion control techniques, but a giving set used alone will not avoid the risk of accidental uncontrolled infusion of large volumes of diluted Propofol 1%. A burette, drop counter or volumetric pump must be included in the infusion line. The risk of uncontrolled infusion must be taken into account when deciding the maximum amount of Propofol 1% in the burette.

When Propofol 1% is used undiluted to maintain anaesthesia, it is recommended that equipment such as syringe pumps or volumetric infusion pumps should always be used to control infusion rates.

Propofol 1% may be administered via a Y-piece close to the injection site into infusions of the following:

- Dextrose 5% Intravenous Infusion B.P.
- Sodium Chloride 0.9% Intravenous Infusion B.P.
- Dextrose 4% with Sodium Chloride 0.18% Intravenous Infusion B.P.

The glass pre-filled syringe (PFS) has a lower frictional resistance than plastic disposable syringes and operates more easily. Therefore, if Propofol 1% is administered using a hand held pre-filled syringe, the line between the syringe and the patient must not be left open if unattended.

When the pre-filled syringe presentation is used in a syringe pump appropriate compatibility should be ensured. In particular, the pump should be designed to prevent siphoning and should have an occlusion alarm set no greater than 1000 mm Hg. If using a programmable or equivalent pump that offers options for use of different syringes then choose only the B-D 50/60 ml PLASTIPAK setting when using the Propofol 1% pre-filled syringe.

Propofol 1% may be premixed with alfentanil injection containing 500 microgram/ml alfentanil in the ratio of 20:1 to 50:1 v/v. Mixtures should be prepared using sterile technique and used within 6 hours of preparation.

In order to reduce pain on initial injection, Propofol 1% may be mixed with preservative-free Lidocaine Injection 0.5% or 1% (see Dilution and Co-administration table below).

<u>Target Controlled Infusion – Administration of Propofol 1% by a Diprifusor TCI System in adults</u>
Administration of Propofol 1% by a Diprifusor TCI system is restricted to induction and maintenance of general anaesthesia in adults. It is not recommended for use in ICU sedation or sedation for surgical and diagnostic procedures, or in children.

Propofol 1% may be administered by TCI only with a Diprifusor TCI system incorporating Diprifusor TCI software. Such systems will operate only on recognition of electronically tagged pre-filled syringes containing Propofol 1% or 2% Injection. The Diprifusor TCI system will automatically adjust the infusion rate for the concentration of propofol recognised. Users must be familiar with the infusion pump users' manual, and with the administration of Propofol 1% by TCI and with the correct use of the syringe identification system.

The Diprifusor allows the anaesthetist to achieve and control a desired speed of induction and depth of anaesthesia by setting and adjusting target (predicted) blood concentrations of propofol. An alternative effect-site mode of administration may be accessible on some Diprifusors, but its safety and efficacy have not yet been established.

The Diprifusor TCI system assumes that the initial blood propofol concentration in the patient is zero. Therefore, in patients who have received prior propofol, there may be a need to select a lower initial target concentration when commencing Diprifusor TCI. Similarly, the immediate recommencement of Diprifusor TCI is not recommended if the pump has been switched off.

Guidance on propofol target concentrations is given below. In view of interpatient variability in propofol pharmacokinetics and pharmacodynamics, in both premedicated and unpremedicated patients the target propofol concentration should be titrated against the response of the patient in order to achieve the depth of anaesthesia required.

Induction and maintenance of general anaesthesia

In adult patients under 55 years of age anaesthesia can usually be induced with target propofol concentrations in the region of 4–8 microgram/ml. An initial target of 4 microgram/ml is recommended in premedicated patients and in unpremedicated patients an initial target of 6 microgram/ml is advised. Induction time with these targets is generally within the range of 60–120 seconds. Higher targets will allow more rapid induction of anaesthesia but may be associated with more pronounced haemodynamic and respiratory depression.

A lower initial target concentration should be used in patients over the age of about 55 years and in patients of ASA grades 3 and 4. The target concentration can then be increased in steps of 0.5–1 microgram/ml at intervals of 1 minute to achieve a gradual induction of anaesthesia.

Supplementary analgesia will generally be required and the extent to which target concentrations for maintenance of anaesthesia can be reduced will be influenced by the amount of concomitant analgesia administered. Target propofol concentrations in the region of 3–6 microgram/ml usually maintain satisfactory anaesthesia.

The predicted propofol concentration on waking is generally in the region of 1–2 microgram/ml and will be influenced by the amount of analgesia given during maintenance.

Dilution and co-administration of Propofol 1% with other drugs or infusion fluids (see also Additional precautions section)

Co-administration Technique	**Additive or Diluent**	**Preparation**	**Precautions**
Pre-mixing	Dextrose 5% intravenous infusion	Mix 1 part of Propofol 1% with up to 4 parts of dextrose 5% intravenous infusion in either PVC infusion bags or glass infusion bottles. When diluted in PVC bags it is recommended that the bag should be full and that the dilution be prepared by withdrawing a volume of infusion fluid and replacing it with an equal volume of Propofol 1%	Prepare aseptically immediately before administration. The mixture is stable for up to 6 hours
	Lidocaine hydrochloride injection (0.5% or 1% without preservatives)	Mix 20 parts of Propofol 1% with up to 1 part of either 0.5% or 1% lidocaine hydrochloride injection	Prepare mixture aseptically immediately prior to administration. Use for induction only

Co-administration Technique	Additive or Diluent	Preparation	Precautions
	Alfentanil injection (500 microgram/ml)	Mix Propofol 1% with alfentanil injection in a ratio of 20:1 to 50:1 v/v	Prepare mixture aseptically; use within 6 hours of preparation
Co-administration via a Y-piece connector	Dextrose 5% intravenous infusion	Co-administer via a Y-piece connector	Place the Y-piece connector close to the injection site
	Sodium chloride 0.9% intravenous infusion	As above	As above
	Dextrose 4% with sodium chloride 0.18% intravenous infusion	As above	As above

This leaflet was last revised in November 2023.