Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Propofol Hospira 1% w/v emulsion for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of emulsion for injection/infusion contains 10 mg of propofol.

Each 20 ml vial contains 200 mg of propofol.

Each 50 ml vial contains 500 mg of propofol.

Each 100 ml vial contains 1000 mg of propofol.

Excipient with known effect:

Each ml of emulsion for injection/infusion contains 100 mg of soya-bean oil and approximately 0.016 mmol (0.4 mg) of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Emulsion for Injection /Infusion.

White or slightly off-white emulsion, having a milk-like appearance with no evidence of oiling-out of the emulsion and free from visible particulate.

pH: 6.0 - 8.5
Osmolality: 300-330 mOsm/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Propofol Hospira 1% w/v is a short-acting intravenous general anaesthetic for:

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

4.2 Posology and method of administration

Lower doses of propofol may be necessary when general anaesthesia is used in addition to regional anaesthesia.

Posology

Adults

Induction of General Anaesthesia

In un-premedicated and premedicated patients, it is recommended that propofol 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. 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 III and IV, lower rates of administration should be used (approximately 2 ml [20 mg] every 10 seconds).

Maintenance of General Anaesthesia

Anaesthesia can be maintained by administering propofol 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 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 (5.0 ml) may be given according to clinical need.

Sedation During Intensive Care

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 4.4 Special warnings and precautions for use).

Sedation For Surgical And Diagnostic Procedures

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 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 III and IV the rate of administration and dosage may need to be reduced.

Elderly Patients

In elderly patients the dose requirement for induction of anaesthesia 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. When propofol is used for maintenance of anaesthesia or sedation the rate of infusion or 'target concentration' should also be reduced. Patients of ASA Grades III and IV will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in the elderly as this may lead to cardio-respiratory depression.

Paediatric Population

Induction of General Anaesthesia

Propofol should not be used for induction of anaesthesia in children aged less than 1 month.

For induction of anaesthesia in children over 1 month of age, propofol 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 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).

Due to lack of clinical experience, lower dosages are recommended for young patients at increased risk i.e. for ASA

Grades III and IV patients lower doses are recommended (see also section 4.4).

Maintenance of General Anaesthesia

Propofol should not be used 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 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 Grades III and IV patients lower doses are recommended (see also section 4.4).

Sedation During Intensive Care

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

Sedation For Surgical And Diagnostic Procedures

Propofol should not be used 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 for onset of sedation. Maintenance of sedation may be accomplished by titrating propofol infusion to the desired level of sedation. Most patients require 1.5–9 mg/kg/h propofol. 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 Grades III and IV patients lower doses may be required.

Method of administration

Propofol Hospira 1% w/v may be used as a slow bolus injection or infusion.

Propofol has no analgesic properties and therefore supplementary analgesic agents are generally required in addition to Propofol Hospira 1% w/v.

Containers should be shaken before use. If two layers can be seen after shaking, the emulsion should not be used. All contents that may be left over after a single use must be destroyed (see section 6.6).

Prior to use, the rubber stopper should be disinfected using a medicinal alcohol (spray or dipped swab).

Propofol Hospira 1% w/v contains no antimicrobial preservatives and supports growth of micro-organisms.

When Propofol Hospira 1% w/v is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol Hospira 1% w/v and infusion equipment throughout the infusion period. Any infusion fluids added to the Propofol Hospira 1% w/v line must be administered close to the cannula site. Propofol Hospira 1% w/v must not be administered via a microbiological filter.

Propofol Hospira 1% w/v is 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.

Propofol can be used for infusion undiluted from glass containers or diluted with 5% Dextrose (Intravenous Infusion BP) only, in 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.

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 in the burette.

When Propofol Hospira 1% w/v 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 Hospira 1% w/v 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.

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

In order to reduce pain on initial injection, Propofol Hospira 1% w/v may be mixed with preservative-free Lidocaine Injection 0.5 % or 1 %; (see section 6.6 for "Dilution and Co-administration" table).

The infusion system should be rinsed before administration of muscle relaxants like atracurium and mivacurium when using the same infusion system for Propofol Hospira 1% w/v.

For instructions on reconstitution and dilution of Propofol Hospira 1% w/v before administration, see section 6.6.

4.3 Contraindications

Propofol is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Propofol Hospira 1% w/v contains soya oil, and it must therefore not be used in patients with hypersensitivity to soya or groundnuts (peanuts).

Propofol must not be used in children aged 16 years or under for sedation in intensive care (see section 4.4).

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.

There have been reports of abuse and dependence on propofol, predominantly by health care professionals. As with other general anaesthesia, administration of propofol without airway care may lead to fatal complications.

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

As with other sedatives, involuntary movements may occur in the patient when propofol is used during surgical procedures. These movements may constitute a risk at the operation site during procedures that require immobility.

Sufficient time is required prior to discharge of the patient to ensure that the patient is fully conscious after administration.

Very rarely the use of propofol may be associated with the development of a period of postoperative unconsciousness, which may be accompanied by an increase in muscle tone. This may or may not be preceded by a conscious period. Although recovery is spontaneous, appropriate care of an unconscious patient should be administered.

Impairment of function caused by propofol generally cannot be detected after 12 hours. The effect of propofol, the procedure, concomitant medication, the patient's age and general condition, should be included in the considerations when patients are told:

- To have a companion when they leave the place of administration.
- To postpone dangerous tasks or those requiring concentration, such as driving
- The use of other substances may have a sedative effect (including benzodiazepines, opiates, alcohol.)

As with other intravenous anaesthetic agents, caution must be exercised in patients with impaired cardiac, respiratory, renal or hepatic function and to hypovolaemic or debilitated patients. Clearance of propofol depends on blood flow, and so concomitant treatment with medicinal products that reduces cardiac output will also reduce clearance of propofol.

Propofol lacks vagolytic activity and has been associated with cases of bradycardia (at times severe) and asystole. Intravenous administration of an anticholinergic for induction, or during maintenance of anaesthesia should be considered, especially in situations in which vagal tone is predominant, or in which propofol is used in conjunction with other medicinal products that may cause bradycardia.

Propofol may lead to seizures in patients with epilepsy.

Special attention should be paid to patients with disorders of lipid metabolism or other conditions in which lipid emulsions should be used with caution.

Paediatric Population

The use of propofol is not recommended in neonates as this patient population has not been studied sufficiently. Pharmacokinetic data (see section 5.2) indicate that clearance is significantly reduced in neonates but with very great inter-individual variability. Relative overdose may occur in the administration of doses recommended for older children, and may lead to severe cardiovascular depression.

Propofol must not be used in patients of 16 years of age or younger for sedation for intensive care as the safety and efficacy of propofol for sedation in this age group have not been demonstrated (see section 4.3).

Advice for intensive care units:

Use of propofol emulsion infusions for ICU sedation has been associated with a constellation of metabolic derangements and organ system failures that may result in death. There have been reports of combinations of the following: metabolic acidosis, rhabdomyolysis, hyperkalaemia, hepatomegaly, renal failure, hyperlipidaemia, cardiac arrhythmia, Brugada-type ECG (elevated ST-segment and T-wave inversion) and rapidly increasing heart failure, which generally does not respond to supportive treatment with inotropics. The combination of these events has been called propofol infusion syndrome. These events were mostly seen in patients with serious head injuries and children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit.

The following appear to increase the risk of developing these undesirable effects: reduced oxygen supply to tissue; severe neurological damage and/or sepsis; high dose of one or more of the following pharmacological substances - vasoconstrictors, steroids, inotropes and/or propofol (generally after an increase in the dose with doses higher than 4 mg/kg/h for more than 48 hours).

The prescriber must be aware of these undesirable effects in patients with the above risk factors and promptly consider a lower dose or stopping the use of propofol when the above signs develop. All sedatives and therapeutic medicinal products used in the intensive care unit (ICU) must be titrated to maintain optimal oxygen supply and haemodynamic parameters. Patients with increased intra-cranial pressure (ICP) should be treated with regard to maintaining cerebral

perfusion pressure in a change of treatment. The responsible doctor is reminded not to exceed the dosage of 4 mg/kg/h as far as possible

Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously.

If propofol is used in patients at particular risk of lipid overload, monitoring of the serum lipid level is recommended. If there are signs of insufficient elimination of fat, the administration of propofol may be adjusted If the patient is receiving another intravenous lipid concurrently, the total fat intake must be reduced to take account of the lipids that are administered intravenously as part of the formulation of propofol; 1.0 mL of Propofol Hospira 1 % w/v contains approximately 0.1 g of fat.

Further precautions

Caution should be taken when treating patients with mitochondrial disease. These patients may be susceptible to exacerbations of their disorder when undergoing anaesthesia, surgery and ICU care. Maintenance of normothermia, provision of carbohydrates and good hydration are recommended for such patients. The early presentations of mitochondrial disease exacerbation and of the 'propofol infusion syndrome' may be similar.

Propofol contains no antimicrobial preservatives and permits the growth of micro-organisms.

When propofol must be aspirated, it must be drawn up aseptically in a sterile syringe, or an infusion set immediately after breach of the seal of the vial. Administration must be started without delay. Asepsis must be maintained for both propofol and the infusion set throughout the infusion period. Infusion fluid that is added to the propofol line must be administered close to the cannula site. Propofol must not be administered via a microbiological filter. Propofol and every syringe that contains propofol is for single use in a single patient. In accordance with the current guidelines for the use of lipid emulsions, infusion via the same infusion system must not exceed 12 hours. After one infusion (max. 12 hours) every residue of propofol and the infusion equipment must be discarded. The infusion may be resumed if necessary.

Propofol Hospira 1% w/v contains approximately 0.016 mmol (0.4 mg) per ml of sodium.

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 pre-medication, neuromuscular blockers, inhalational anaesthetics and analgesics; no pharmacological incompatibilities have been seen. Lower doses of propofol may be required where general anaesthesia or sedation is used as supplement to regional anaesthesia techniques. Profound hypotension has been reported following anesthetic induction with propofol in patients treated with rifampicin.

A need for lower propofol doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of propofol may be considered.

4.6 Fertility, 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 may, however be used in an induced abortion.

Breastfeeding

Studies of breastfeeding 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 ability to drive and use machines

Patients must be told to avoid driving, using machines or potentially hazardous situations. Impaired functions due to propofol cannot normally be detected after 12 hours (see section 4.4).

4.8 Undesirable effects

Induction and maintenance of anaesthesia or sedation with propofol generally proceeds smoothly with minimal signs of excitation. The most commonly reported undesirable effects are pharmacologically predictable undesirable effects of an anaesthetic or sedative, such as hypotension. The nature, severity and incidence of the undesirable effects that are observed in patients receiving propofol may be related to the patient's condition and the surgical or therapeutic procedure.
Adverse reactions are ranked under headings of frequency, the most frequent first, using the following convention: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Table of Adverse Drug Reactions

System Organ Class	Frequency	Undesirable Effects
Immune system disorders:	Very rare	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
Endocrine disorders:	Frequency not known (9)	Diabetes insipidus
Metabolism and nutritional disorders:	Frequency not known (9)	Metabolic acidosis (5), hyperkalaemia (5), hyperlipidaemia (5)
Psychiatric disorders:	Frequency not known (9)	Euphoria Drug abuse and drug dependence (8)
Nervous system disorders:	Common	Headache during recovery phase
	Rare	Epileptiform movement, including convulsions, opisthotonus during induction, maintenance and recovery
	Very rare	Post-operative unconsciousness
	Frequency not known (9)	Involuntary movements
Cardiac disorders:	Common	Bradycardia (1)
	Very rare	Pulmonary oedema
	Frequency not known (9)	Cardiac arrhythmia (5), cardiac failure (5), (7)
Vascular disorders:	Common	Hypotension (2)
	Uncommon	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders:	Common	Transient apnoea during induction
	Frequency not known (9)	Respiratory depression (dose dependant)
Gastrointestinal disorders:	Common	Nausea and vomiting during recovery phase
	Very rare	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	Discolouration of urine after long-term administration
	Frequency not known (9)	Renal failure (5)
Reproductive system and breast disorders	Very rare	Sexual disinhibition
General disorders and	Very common	

administration site conditions:		Local pain during induction[4]
	Very rare	Tissue necrosis[10] following accidental extravascular administration
	Frequency not known [9]	Local pain, swelling, following accidental extravascular administration
Investigations	Frequency not known [9]	Brugada type ECG [5], [6]
Injury, poisoning and procedural complications:	Very rare	Post-operative fever

[1] Severe bradycardia is 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 local pain can also be minimised by the co-administration of lidocaine.
[5] The combination of these undesirable effects has been reported as “propofol infusion syndrome” and can occur in severely ill patients, who often have several risk factors for developing these undesirable effects, see section 4.4.
[6] Brugada-type ECG - elevated ST-segment and T-wave inversion in the 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] Abuse of and drug dependence on propofol, especially by healthcare professionals.
[9] Not known as it cannot be estimated from the available clinical research data.
[10] Tissue necrosis has been reported where tissue viability has been impaired.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: http://www.hpra.ie/, e-mail: medsafety@hpra.ie.

4.9 Overdose

Unintended overdose is likely to cause circulatory and respiratory depression.

Respiratory depression must be treated with controlled ventilation with oxygen. Circulatory depression is treated by lowering the patient’s head and in serious cases using plasma substitutes and vasopressors.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other general anesthetics, ATC code: N01AX10

Propofol (2, 6-diisopropylphenol) is a short-acting general anaesthetic agent with a rapid onset of action of approximately 30 seconds. Recovery from anaesthesia is usually rapid. The mechanism of action, like all general anaesthetics, is poorly understood. However, propofol is thought to produce its sedative/anaesthetic effects by the positive modulation of the inhibitory function of the neurotransmitter GABA through the ligand-gated $GABA_A$ receptors.

In general, falls in mean arterial blood pressure and slight changes in heart rate are observed when propofol is

administered for induction and maintenance of anaesthesia. However, the haemodynamic parameters normally remain relatively stable during maintenance and the incidence of untoward haemodynamic changes is low.

Although ventilatory depression can occur following administration of propofol, any effects are qualitatively similar to those of other intravenous anaesthetic agents and are readily manageable in clinical practice.

Propofol reduces cerebral blood flow, intracranial pressure and cerebral metabolism. The reduction in intracranial pressure is greater in patients with an elevated baseline intracranial pressure.

Recovery from anaesthesia is usually rapid and the patient rapidly regains consciousness with a low occurrence of postoperative nausea and vomiting.

In general, there is less post-operative nausea and vomiting following anaesthesia with propofol than following anaesthesia with inhalational agents. There is evidence that this may be related to a reduced emetic potential of propofol.
Propofol, at the concentrations likely to occur clinically, does not inhibit the synthesis of adrenocortical hormones.

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

Propofol is extensively distributed and rapidly cleared from the body (total body clearance 1.5 – 2 litres/minute). Clearance occurs by metabolic processes, mainly in the liver where it is blood flow dependent to form inactive conjugates of propofol and its corresponding quinol, which are excreted in urine.

The decline in propofol concentrations following a bolus dose or following the termination of an infusion can be described by a three compartment open model with very rapid distribution (half-life 2 – 4 minutes), rapid elimination (half-life 30 – 60 minutes), and a slower final phase, representative of redistribution of propofol from poorly perfused tissue.

When propofol is used to maintain anaesthesia, blood concentrations asymptotically approach the steady-state value for the given administration rate. The pharmacokinetics are linear over the recommended range of infusion rates of propofol.

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 under 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

Non-clinical data reveal no special hazard for humans based on conventional studies on repeated dose toxicity or genotoxicity.

Carcinogenicity studies have not been conducted.

Reproductive toxicity studies have shown effects related to pharmacodynamic properties of propofol only at high doses.
Teratogenic effects have not been observed.

In local tolerance studies, intramuscular injection resulted in tissue damage around the injection site.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Soya-bean Oil, Refined
Egg Phospholipids
Glycerol
Sodium Hydroxide
Water for Injections

6.2 Incompatibilities

The neuromuscular blocking agents, atracurium and mivacurium should not be given through the same intravenous line as Propofol Hospira 1% w/v without prior flushing.

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

6.3 Shelf life

Unopened:
2 years

After first opening:
The product should be used immediately after first opening.

After dilution:
Chemical and physical in-use stability has been demonstrated for not more than 6 hours at 25°C.

From a microbiological point of view, unless the method of opening/ dilution preludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user.

Unused solution should be discarded.

6.4 Special precautions for storage

Do not freeze.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

20 ml, 50 ml or 100 ml Type I clear glass vials with bromobutyl rubber stoppers and aluminium seals.

Pack Sizes: 1, 5, 10 or 20 vials per carton or tray

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Containers should be shaken before use.

Parenteral products should be inspected visually for particulate matter prior to administration. If particulate matter is evident emulsion should not be used.

If two layers can be seen after shaking, the emulsion should not be used.

Propofol Hospira 1% w/v is for single use in an individual patient. All contents that may be left over after a single use must be destroyed.

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

Prior to use, the rubber stopper should be disinfected using a medicinal alcohol (spray or dipped swab).

Dilution and Co-Administration of Propofol Hospira 1% w/v with Other Drugs or Infusion Fluids (see also 'Further Precautions' section under 4.4 Special warnings and precautions for use)

Co-administration Technique	**Additive or Diluent**	**Preparation**	**Precautions**
Pre-mixing.	Dextrose 5% Intravenous Infusion	Mix 1 part of Propofol Hospira 1% w/v with up to 4 parts of Dextrose 5% Intravenous Infusion B.P in glass infusion bottles.	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 Hospira 1% w/v 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.
	Alfentanil injection (500 microgram/ml).	Mix Propofol Hospira 1% w/v 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

7 MARKETING AUTHORISATION HOLDER

HOSPIRA UK Ltd
Queensway
Royal Leamington Spa
Warwickshire CV31 3RW
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0437/073/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th December 2014

10 DATE OF REVISION OF THE TEXT

June 2017