IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0754/005/001
Case No: 2001595

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Techno-Pharm Limited

Pharmapark, **Chapelizod**, **Dublin 20**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Propofol Technopharm 10mg/ml Emulsion for injection or infusion

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/05/2009** until **07/05/2014**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Propofol Technopharm 10mg/ml Emulsion for injection or infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of emulsion for injection or infusion contains 10mg Propofol
Each 20ml of emulsion for injection or infusion contains 200mg Propofol

Contains sodium 0.0018mmol/ml.
Contains refined Refined Soya-bean oil 100mg/ ml.

For excipients see 6.1

3 PHARMACEUTICAL FORM

Emulsion for intravenous injection or infusion.
White to off-white emulsion free from particulate matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Propofol TechnoPharm 10mg/ml is a short-acting intravenous anaesthetic agent suitable for induction and maintenance of general anaesthesia in adults and children over one month of age.
Propofol Technopharm 10mg/ml may also be used for sedation of ventilated patients receiving intensive care in adults, only for a period of 48 hours, or in rare cases up to a maximum of 7 days.
Propofol Technopharm 10mg/ml may also be used for conscious sedation for surgical and diagnostic procedures in adults only.

4.2 Posology and method of administration

Supplementary analgesic agents are generally required in addition to Propofol Technopharm 10mg/ml.

Adults:
Induction of general anaesthesia:
Propofol Technopharm 10mg/ml may be used to induce anaesthesia by slow bolus injection or infusion.

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

Maintenance of general anaesthesia:
Anaesthesia can be maintained by administering Propofol Technopharm 10mg/ml by continuous infusion or repeat bolus injection to maintain the depth of anaesthesia required.

Continuous intravenous infusion:
Propofol Technopharm 10mg/ml may be used. The required rate of administration varies considerably between patients but rates in the region of 4 to 12 mg/kg/h usually maintain satisfactory anaesthesia.

Repeat bolus intravenous injections:
If a technique involving repeat bolus injections is used, increments of 25mg to 50mg may be used according to clinical need.

Sedation of ventilated patient during intensive care
For sedation during intensive care it is advised that Propofol Technopharm 10mg/ml 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 0.3-4mg/kg/h of Propofol Technopharm 10mg/ml (see section 4.4). Propofol Technopharm 10mg/ml is not indicated for sedation in intensive care of patients of 16 years of age or younger (see section 4.3).

Conscious 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 to 1mg/kg over 1 to 5 minutes to initiate sedation.

Maintenance of sedation may be accomplished by titrating Propofol Technopharm 10mg/ml infusion to the desired level of sedation - most patients will require 1.5 to 4.5 mg/kg/h. In addition to the infusion, bolus administration of 10 to 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.

Elderly Patients:
In elderly patients the dose requirement for induction of anaesthesia with Propofol Technopharm 10mg/ml is reduced. The reduction should take account of the physical status and age of the patient. The reduced dose should be given at a slower rate and titrated against the response. Where Propofol Technopharm 10mg/ml is used for maintenance of anaesthesia or sedation the rate of infusion or “target concentration” should be 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 the elderly as this may lead to cardiorespiratory depression.

Children:
Propofol Technopharm 10mg/ml is not recommended for use in children less than one month of age.

Induction of general anaesthesia
When used to induce anaesthesia in children, it is recommended that Propofol Technopharm 10mg/ml is given slowly until the clinical signs show the onset of anaesthesia. The dose should be adjusted for age and/or weight. Most patients over 8 years of age are likely to require approximately 2.5 mg/kg of Propofol Technopharm 10mg/ml for induction of anaesthesia. Under this age the requirement may be more. Lower dosage is recommended for children of ASA grades 3 and 4.

Maintenance of general anaesthesia
Anaesthesia can be maintained by administering Propofol Technopharm 10mg/ml by intravenous infusion or repeat bolus intravenous injection to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients but rates in the region of 9 to 15 mg/kg/h usually achieve satisfactory anaesthesia. Younger children, 1 month to 3 years, may have higher dosage requirements, within the range of recommended dosages, when compared with older paediatric patients. Dosage should be adjusted individually and particular attention paid to the need for adequate analgesia.

Conscious sedation for surgical and diagnostic procedures
Propofol Technopharm 10mg/ml is not recommended for conscious sedation in children as safety and efficacy have not been demonstrated.

Sedation during intensive care
Propofol Technopharm 10mg/ml is not recommended for sedation in children as safety and efficacy have not been demonstrated. Although no causal relationship has been established, serious adverse events (including fatalities) have been observed from spontaneous reports of unlicensed use and these events were seen most often in children with respiratory tract infections given doses in excess of those recommended for adults.

Administration
When 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 Technopharm 10mg/ml may also be used diluted with 5% Dextrose Intravenous only, in PVC infusion bags or glass infusion bottles. Dilutions, which must not exceed 1 in 5, should be prepared aseptically immediately before administration. The mixture is stable for up to 6 hours.

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 Technopharm 10mg/ml. 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 dilution in the burette.

Propofol Technopharm 10mg/ml may be administered by a Y piece close to the injection site, into infusions of Dextrose 5% Intravenous Infusion, Sodium Chloride 0.9% Intravenous Infusion or Dextrose 4% with Sodium Chloride 0.18% Intravenous Infusion.

The neuromuscular blocking agents, atracurium and mivacurium should not be given through the same I.V. line as Propofol Technopharm 10mg/ml without prior flushing (see section 6.2).

Dilution and co-administration of Propofol Technopharm 10mg/ml with other drugs or infusion fluids.

Co-administration Technique	**Additive or Diluent**	**Preparation**	**Precautions**
Pre-mixing	Dextrose 5% Intravenous Infusion BP	Mix 1 part of Propofol Technopharm 10mg/ml with up to 4 parts of Dextrose 5% Intravenous Infusion BP 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 Technopharm 10mg/ml.	Prepare aseptically immediately before administration. The mixture is stable for up to 6 hours.

Co-administration via a Y-piece connector	Dextrose 5% Intravenous Infusion BP	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

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 or conscious sedation required.

In adult patients under 55 years of age, anaesthesia can usually be induced with target propofol concentrations in the region of 4 to 8 micrograms/ml.

An initial target of 4 micrograms/ml is recommended in premedicated patients and in unpremedicated patients an initial target of 6micrograms/ml is advised. Induction time with these 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 to 1.0 micrograms/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 to 6 micrograms/ml usually maintain satisfactory anaesthesia.

The predicted propofol concentration on waking is generally in the region of 1.0 to 2.0 micrograms/ml and will be influenced by the amount of analgesia given during maintenance.

Conscious Sedation for Surgical and Diagnostic Procedures
Target blood Propofol concentration settings in the range of 0.5 to 2.5 micrograms/ml will generally be required. The target concentration setting should be titrated against the response of the patient to achieve the depth of conscious sedation required.

An initial target concentration towards the upper end of this range will allow more rapid induction of conscious sedation.

An initial target concentration towards the lower end of this range should be used in elderly patients and in patients of ASA grades 3 and 4.

Routine oxygen supplementation should be provided.

4.3 Contraindications

Known hypersensitivity for any of the components of Propofol Technopharm 10mg/ml.

Propofol Technopharm 10mg/ml is contraindicated for sedation in intensive care of patients of 16 years of age or younger (see section 4.4).

Propofol Technopharm contains soya bean oil and egg lecithin and should not be used in patients who are hypersensitive to peanut, soya or egg.

4.4 Special warnings and precautions for use

Propofol Technopharm 10mg/ml is intended for hospital use only. Propofol Technopharm 10mg/ml should not be administered by the person conducting the surgical or diagnostic procedure.

Propofol Technopharm 10mg/ml 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.

When Propofol Technopharm 10mg/ml is administered for conscious sedation for surgical and diagnostic procedures, patients should be continually monitored for early signs of hypotension, airway obsturiction and oxygen desaturation.

As with other sedative agents, when Propofol Technopharm 10mg/ml 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 general anaesthesia. Very rarely the use of Propofol Technopharm 10mg/ml 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 period of wakefulness. Although recovery is spontaneous, appropriate care of an unconscious patient should be administered.

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 Technopharm 10mg/ml 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 Technopharm 10mg/ml is used in conjunction with other agents likely to cause bradycardia.

When Propofol Technopharm 10mg/ml is administered to an epileptic patient, there may be a risk of convulsion.

Propofol Technopharm 10mg/ml is not advised for general anaesthesia in children younger than 1 month of age. The safety and efficacy of Propofol Technopharm 10mg/ml for (background) sedation in children younger than 16 years of age have not been demonstrated. Although no causal relationship has been established, serious undesirable effects with (background) sedation in patients younger than 16 years of age (including cases with fatal outcome) have been reported during unlicensed use. In particular these effects concerned occurrence of metabolic acidosis, hyperlipidemia, rhabdomyolysis and/or cardiac failure. These effects were most frequently seen in children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit.

Similarly very rare reports have been received of occurrence of metabolic acidosis, rhabdomyolysis, hyperkalaemia and/or rapidly progressive cardiac failure (in some cases with fatal outcome) in adults who were treated for more than 58 hours with dosages in excess of 5 mg/kg/h. This exceeds the maximum dosage of 4mg/kg/h currently advised for sedation in the intensive care unit. The patients affected were mainly (but not only) seriously head-injured patients with raised ICP. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment. . Treating physicians are reminded if possible not to exceed the dosage of 4mg/kg/h. Prescribers should be alert to these possible undesirable effects and consider decreasing the Propofol Technopharm 10mg/ml dosage or switching to an alternative sedative at the first sign of occurrence of symptoms. Patients with raised ICP should be given appropriate treatment to support the cerebral perfusion pressure during these treatment modifications.

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 be monitored should Propofol Technopharm 10mg/ml be administered to patients thought to be at particular risk of fat overload. Administration of Propofol Technopharm 10mg/ml 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 Technopharm 10mg/ml formulation: 1.0ml of Propofol Technopharm 10mg/ml contains approximately 0.1g of fat.

Propofol Technopharm 10mg/ml is not recommended for use in neonates for induction and maintenance of anaesthesia. Data from off-label use have indicated that if the paediatric (1 month to 16 years of age) dose regimen is applied in neonates, a relative overdose could occur which may result in cardiorespiratory depression (see section 4.2 and 4.8).

Propofol Technopharm 10mg/ml contains 0.0018 mmol sodium per ml

Additional Precautions

Propofol Technopharm 10mg/ml contains no antimicrobial preservatives and supports growth of micro-organisms. When Propofol Technopharm 10mg/ml is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay.

Asepsis must be maintained for both Propofol Technopharm 10mg/ml and infusion equipment throughout the infusion period. Any infusion fluids added to the Propofol Technopharm 10mg/ml line must be administered close to the cannula site. Propofol Technopharm 10mg/ml must not be administered via a microbiological filter.

Propofol Technopharm 10mg/ml and any syringe containing Propofol Technopharm 10mg/ml are for a single use in an individual patient.

In accordance with established guidelines for other lipid emulsions a single infusion of Propofol Technopharm 10mg/ml must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner; both the reservoir of Propofol Technopharm 10mg/ml and the infusion line must be discarded and replaced as appropriate.

4.5 Interaction with other medicinal products and other forms of interaction

Propofol Technopharm 10mg/ml 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 Technopharm 10mg/ml may be required where general anaesthesia is used as an adjunct to regional anaesthetic techniques. The hypotensive effect of propofol may be potentiated by the concomitant administration of opiate analgesics. This effect may be more marked in elderly patients and when agents such as alfentanil are given by infusion.

4.6 Pregnancy and lactation

The safety of Propofol during pregnancy has not been established. Therefore, propofol should not be used in pregnant women unless clearly necessary. Propofol crosses the placenta and may be associated with neonatal depression. High doses (more than 2.5 mg/kg for induction or 6 mg/kg/h for maintenance of anaesthesia) should be avoided.

Safety to the neonate following use of Propofol Technopharm 10mg/ml in mothers who are breast feeding has not been established. Studies in breast-feeding women showed that Propofol is excreted in small amounts into the milk. Therefore, mothers should stop breast feeding and discard breast milk for 24 hours after administration of Propofol.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

General: Induction of anaesthesia is generally smooth with minimal evidence of excitation, although spontaneous movements, hiccups and coughing may be seen in some patients. The most commonly reported ADRs are pharmacologically predictable side effects of an anaesthetic agent, such as hypotension. Given the nature of anaesthesia and those patients receiving intensive care, events reported in association with anaesthesia and intensive care may also be related to the procedures being undertaken or the recipient's condition.

Very common (>1/10)	*General disorders and administration site conditions:*	Local pain on induction (1)
Common (>/100, <1/10)	*Vascular disorders:*	Hypotension (2)
	Cardiac disorders:	Bradycardia (3)
	Respiratory, thoracic and mediastinal disorders:	Transient apnoea during induction
	Gastrointestinal disorders:	Nausea and vomiting during recovery phase
	Nervous system disorders:	Headache during recovery phase
Uncommon (>1/1000, <1/100)	*Vascular disorders:*	Thrombosis and phlebitis
Rare (>1/10 000, <1/1000)	*Nervous system disorders:*	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
Very rare (<1/10 000)	*Musculoskeletal and connective tissue disorders:*	Rhabdomyolysis (4)
	Gastrointestinal disorders:	Pancreatitis
	Injury, poisoning and procedural complications:	Postoperative fever
	Renal and urinary disorders:	Discolouration of urine following prolonged administration
	Immune sytem disorders:	Anaphylaxis – may include angioedema, bronchospasm, erythema and hypotension
	Reproductive system and breast:	Sexual disinhibition
	Cardiac disorders:	Pulmonary oedema
	Nervous system disorders:	Postoperative unconsciousness

(1) May be minimised by using the larger veins of the forearm and antecubital fossa.
(2) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of Propofol Technopharm 10mg/ml.
(3) Serious bradycardias are rare. There have been isolated reports of progression to asystole.
(4) Very rare reports of rhabdomyolysis have been received where Propofol Technopharm 10mg/ml has been given at doses greater than 4 mg/kg/hr for ICU sedation. In very rare cases rhabdomyolysis, metabolic acidosis, hyperkalaemia or cardiac failure, sometimes with fatal outcome, have been observed in the intensive care unit (see section 4. 4)

Reports from off-label use of Propofol Technopharm 10mg/ml for induction of anaesthesia in neonates indicate cardiorespiratory depression may occur if the paediatric dose regimen is applied (see section 4.2 and 4.4).

The local pain which may occur during the induction phase can be minimised by the use of the larger veins in the forearm and antecubital fossa. Thrombosis and phlebitis are rare. Accidental clinical extravasation and animal studies showed minimal tissue reaction. Intra-arterial injection in animals did not induce local tissue effects.

4.9 Overdose

Accidental overdosage is likely to cause cardiorespiratory depression. Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression would require lowering of the patient's head and, if severe, use of plasma expanders and pressor agents.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

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 quantitatively similar to those of the 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 clear headed with a low incidence of headache and postoperative nausea and vomiting.
In general, there is less post-operative nausea and vomiting following anaesthesia with Propofol than following anaesthesia with inhalation agents.

Propofol, at the concentrations likely to occur clinically, does not inhibit the synthesis of adrenocortical hormones

5.2 Pharmacokinetic properties

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. The first phase is characterised by a very rapid distribution (half-life: 2-4 minutes) followed by rapid elimination (half-life: 30-60 minutes) and a slower final phase, representative of redistribution of propofol from poorly perfused tissue.

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, to form inactive conjugates of propofol and its corresponding quinol, which are excreted in urine.

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

5.3 Preclinical safety data

Propofol is a drug on which extensive clinical experience has been obtained. All relevant information is provided elsewhere in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Refined Soya-bean Oil
Egg Lecithin
Glycerol
Sodium Hydroxide
Water for Injection

6.2 Incompatibilities

Prior to administration Propofol Technopharm 10mg/ml should not be mixed with injections or infusion fluids other than 5%Dextrose, in PVC bags or glass infusion bottles. The neuromuscular blocking agents, atracurium and mivacurium should not be given through the same I.V. line as Propofol Technopharm 10mg/ml without prior flushing

6.3 Shelf Life

Unopened: 3 years.
The product should be used immediately after opening; Any portion of the contents remaining after use should be discarded.

After dilution with 5% dextrose injection in PVC bags or glass infusion bottles plastic syringes, the shelf life of the diluted product will be no greater than 6 hours when stored below 25oC. From a microbiological point of view, 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.

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.
Keep the ampoules in the outer carton in order to protect from light.
For Storage precaution for diluted product see section 6.3.

6.5 Nature and contents of container

5 x 20ml Type I (Ph. Eur. 3.2.1) glass ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For more detailed administration instructions for Propofol Technopharm and mixtures of Propofol Technopharm, please see section 4.2 Posology and Method of Administration.

In-use precautions: Containers should be shaken before use. Any portion of the contents remaining after use should be discarded.
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.

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

Asepsis for Propofol Technopharm and infusion equipment must be maintained (see Section 4.4 Special Warnings and Precautions for Use).

Propofol Technopharm 10mg/ml contains no antimicrobial preservatives and supports growth of micro-organisms. When Propofol Technopharm 10mg/ml is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the ampoule or breaking the vial seal. Administration must commence without delay. Asepsis must be maintained for both Propofol Technopharm 10mg/ml and infusion equipment throughout the infusion period. Any infusion fluids added to the Propofol Technopharm 10mg/ml line must be administered close to the cannula site. Propofol Technopharm 10mg/ml must not be administered via a microbiological filter.

In accordance with established guidelines for other liquid emulsions, a single infusion of Propofol Technopharm 10mg/ml must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner; both the reservoir of Propofol Technopharm 10mg/ml and the infusion line must be discarded and replaced as appropriate.

7 MARKETING AUTHORISATION HOLDER

Technopharm Ltd.
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Chapelizod
Dublin 20
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 754/5/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th May 2009

10 DATE OF REVISION OF THE TEXT