1.3 Product Information

1.3.1 Summary Of product characteristics (SmPC)

1.3.1.1 Name of the medicinal product

Propofol Injection BP 10 mg/ ml

1.3.1.2 Qualitative and Quantitative composition:

Each ml contains:
Propofol BP.....10 mg
Excipients…. q.s.

Qualitative and Quantitative formula:

Batch size: 50 Liters/2475 Vials						
Sr. No.	**Ingredient**	**Reference**	**Quantity/ml**	**Overages %**	**Quantity/ Batch**	**Function**
1.	Propofol	BP	10 mg/ml	3%	515.00* gm	Active Ingredient
2.	Refined Soya Oil	BP	100 mg/ml	--	5000.0 gm	Vehicle
3.	Egg Lecithin 80% (Lipoid E 80)	USP	12 mg/ml	--	600 gm	Emulsifying Agent
4.	Glycerol	BP	22.5 mg/ml	--	1125.00	Tonicity Agent
5.	Disodium Hydroxide	BP	0.05 mg/ml	--	2.5	Antimicrobial Agent
6.	Sodium Hydroxide	BP	Q.s. to adjust pH	--	12.00	pH Adjusting
7.	Water for Injection	BP	q.s. to make volume	--	50.00	Vehicle

1.3.1.3 Pharmaceutical form

Liquid Injection

1.3.1.4 Clinical particulars

1.3.1.4.1 Therapeutic indication

Suppression of ventricular extra systoles and ventricular tachycardia, especially after an acute myocardial infarction.

Local anaesthesia by surface infiltration, regional, epidural and caudal routes, dental anaesthesia, either alone or in combination with adrenaline.

Lidocaine may also be administered by subcutaneous, intramuscular or intravenous injection.

Not intended for use in the eye.

1.3.1.4.2 Posology and method of administration

Propofol 10 mg / ml may only be administered by doctors that have been trained in anaesthesiology intensive care . Sedation or anaesthesia with Propofol 10 mg / ml and the surgical or diagnostic procedure may not be performed by the same person.

The cardiac , circulatory and respiratory functions should be continuously monitored (e.g.ECG,pulseoxymetry) . The customary equipment for possible accidents during anaesthesia or sedation must be ready for use at all times.

The dosage should be adjusted individually while taking the premedication and the patient's reaction into consideration . Normally , the additional administration of analgesics is necessary .

Anaesthesia for adults :

Induction of anaesthesia :

For the induction of anaesthesia , Propofol 10 mg / ml is administered , titrate data speed of 20 – 40 mg propofol every 10 seconds , until unconsciousness occurs .

Most adults less than 55 years of age would normally require a total dose of 1.5 to 2.5 mg propofol / kg of body weight.

For patients in risk groups ASA III and IV , especially in the case of prior cardiac damage and elderly patients , it may be necessary to reduce the total dosage of Propofol 10mg/ml down to 1mg propofol / kg body of mass ,Where by Propofol 10 mg/ml is administered at slower infusion speed(approximately 20 mg propofol every 10 seconds).

Maintenance of anaesthesia:

The anaesthesia can be maintained with a long-term infusion or repeated bolus injections of Propofol 10 mg/ml.

Continuous infusion

For maintenance of anaesthesia by means of continuous infusion, the dosage and infusion speed must be adjusted for each individual. Normally, the dosage is 4-12 mg propofol/kg of body mass per hour in order to maintain a satisfactory level of anaesthesia.

In the case of elderly patients in a poor general state of health or with hypovolemia and patients in the risk groups ASA III and IV, the dosage of Propofol 10 mg/ml may be reduced down to 4 mg Propofol/kg of body mass per hour.

Repeated bolus injection

For maintenance of anaesthesia by means of repeated bolus injection, generally 25 - 50 mg propofol (2.5 - 5 ml Propofol 10 mg/ml) are subsequently injected.

Anaesthesia in children from 1 month of age

Induction of anaesthesia

For the induction of anaesthesia, Propofol 10 mg/ml is titrated slowly until clinical signs can be seen that indicate the start of anaesthesia. The dose should be adjusted based on the age and/or body weight. Most children over 8 years of age require approximately 2.5 mg Propofol/kg of body mass for induction of anaesthesia. In the case of younger children, especially those in the age range of 1 month to 3 years, the required dose may be higher (2.5 - 4 mg Propofol/kg of body mass). Lower doses are recommended for patients in the risk groups ASA III and IV .

Maintenance of anaesthesia

Maintenance of the required depth of anaesthesia can be achieved with the administration of Propofol 10 mg/ml by means of an infusion or repeated bolus administration. The required dosage rates vary considerably among patients, however a satisfactory state of anaesthesia is normally achieved at doses in the range of 9 - 15 mg/kg of body mass per hour. In the case of younger children, especially those in the age range of 1 month to 3 years, the required dose may be higher. Lower doses are recommended for patients in the risk groups ASA III and IV (see section 4.4).

Sedation of patients over 16 years of age during intensive care:

For the sedation of ventilated patients during intensive care, Propofol 10 mg/ml should be administered as a continuous infusion. The dosage is based on the required depth of sedation. Normally, the desired depths of sedation can be achieved with doses in the range of 0.3 to 4.0 mg propofol/kg of body mass per hour. (see section 4.4).

Propofol 10 mg/ml may not be used for the sedation of children aged 16 years or younger as part of intensive care.

The administration of Propofol 10 mg/ml by means of a TCI system is not recommended for sedation as part of intensive care.

Sedation of adults for surgical and diagnostic procedures:

During the administration of Propofol 10 mg/ml, the patient must be continually monitored for signs of a decrease in blood pressure, respiratory tract obstruction and oxygen deficiency and the customary emergency equipment for accidents must be

kept ready.
For induction of anaesthesia, generally 0.5 – 1.0 mg propofol/kg of body mass are administered for 1 -5 minutes. . For the maintenance of anaesthesia, the dosage is determined based on the desired depth of sedation and is generally in the range between 1.5 - 4.5 mg propofol/kg of body mass per hour.
In addition to the infusion, 10 – 20 mg may be injected as a bolus if a quick increase in the depth of sedation is necessary.
A lower dosage and slower administration may be necessary for patients in risk groups ASA III and IV. A lower dosage may also be necessary in patients over 55 years of age.

Note
In the case of elderly patients, smaller doses are required for the induction of anaesthesia with Propofol 10 mg/ml. The patient's general state of health and age should be taken into account. The lowered dose should be administered more slowly and
titrated according to the reaction.
Even when using Propofol 10 mg/ml for maintenance of anaesthesia and for sedation, the infusion rate and the selected Propofol concentration in the blood should be decreased.
An additional lowering of the dosage and the infusion rate is necessary for patients in risk groups ASA III and IV. Elderly patients should not be given any bolus injections (individual or multiple), since circulatory and respiratory depression may result.

Sedation of children from 1 month of age for surgical and diagnostic procedures
The dosage and the periods between doses are selected based on the desired depth of sedation and the clinical response. For the induction of sedation, a dose of 1 - 2 mg Propofol/kg of body weight is necessary for most paediatric patients. Maintenance of the sedation is achieved with the titration of Propofol 10 mg/ml via an infusion until the desired depth of sedation is reached.
For most patients, 1.5 - 9 mg Propofol /kg of body mass per hour is required. The infusion can be supplemented with bolus administration of up to 1 mg Propofol/kg of body mass, if a rapid increase in the depth of sedation is required.
Lower doses may be necessary for patients in the risk groups ASA III and IV.
Propofol 10 mg/ml may not be used for the sedation of children aged 16 years or younger as part of intensive care.

1.3.1.4.3 Contraindication
•Do not use Propofol 10 mg/ml
• In the case of hypersensitivity to active substance, soybeans, peanuts, or to any of the other ingredients of the emulsion listed.
• For the sedation of patients aged 16 years or younger as part of intensive care

1.3.1.4.4 Special warning and precautions for use

During the use of Propofol 10 mg/ml for sedation for surgical and diagnostic procedures, the patient must be continually monitored for the first signs of a decrease in blood pressure, respiratory tract obstruction and oxygen deficiency.

As is also the case with other sedatives, spontaneous movements of the patient during surgical procedures may occur with the use of Propofol 10 mg/ml for sedation. For procedures that require an immobile patient, these movements may jeopardise the success of the operation.

Misuse and dependency on Propofol has been reported, primarily among healthcare personnel. As with all medications for general anaesthesia, it may not be used without securing an airway; otherwise, there is the risk of deadly respiratory complications.

After the use of Propofol 10 mg/ml, it should be ensured that the patient has fully recovered from the anaesthesia prior to discharge.

In individual cases, a postoperative unconsciousness phase can occur with the use of Propofol 10 mg/ml, which may be accompanied by increased muscle tone. The occurrence of this is dependent on whether or not the patient was previously awake. Even though the patient will spontaneously regain consciousness, an unconscious patient should be kept under intensive observation.

The impairments caused by Propofol 10 mg/ml are usually not observed for longer than 12 hours. When explaining the effect of Propofol 10 mg/ml to the patient, and when making the following recommendations, the doctor should take into consideration the type of procedure, the concomitant medication, the age and the condition of the patient.

The patient should only return home when accompanied by another person.

The patient should be made aware of when manual activities or activities requiring dexterity / risky activities (e.g. operating a motor vehicle) can be carried out again.

The patient should be made aware that taking other sedatives (e.g. benzodiazepine, opiates, alcohol) may prolong and increase the impairments. As with other intravenous anaesthetics, Propofol 10 mg/ml should be administered in a slower manner than usual and used with particular caution in patients with cardiac, respiratory, renal and hepatic disorders, hypovolemia or who are in a reduced general state of health .

Heart, circulatory and respiratory insufficiency as well as hypovolaemia should be compensated prior to administration of the drug, if possible.

In the case of patients with severe cardiac damage, Propofol 10 mg/ml must be administered with corresponding caution and in combination with intensive monitoring.

A pronounced drop in blood pressure may necessitate the administration of plasma substitutes, possibly of vasoconstrictors, and slower administration of Propofol 10 mg/ml. The possibility of a massive drop in blood pressure should be taken into consideration for patients with reduced coronary or cerebral perfusion or with hypovolemia. The Propofol clearance is dependent on the blood flow. Therefore, if drugs are used at the same time that reduce the cardiac output, the Propofol clearance will also be reduced.

1.3.1.4.5 Interaction with other medicinal products and other forms of interaction

Propofol 10 mg/ml is compatible with other agents for anaesthesia (premedication, muscle relaxants, inhaled anaesthesia, analgesics, local anaesthetics). In the case of regional anaesthesia procedures, smaller doses of Propofol 10mg/ml may be necessary. No indications of severe interactions have been observed. Some of the agents mentioned may decrease the blood pressure or impair respiration , so that there can be cumulative effects with the use of Propofol 10 mg/ml. A pronounced decrease in blood pressure when inducing anaesthesia with Propofol has been reported in patients that were treated with rifampicin.

If opiates are additionally administered prior to the anaesthesia, apnoea can occur more frequently and for a longer period of time.

In patients that take valproate, the necessity of lower doses of Propofol has been observed. In the case of simultaneous use, a reduction of in the propofol dose may be considered.

1.3.1.4.6 Fertility, pregnancy and lactation

There is no epidemiological evidence for the safety of pentazocine in human pregnancy The safety of propofol during pregnancy has not been proven. Therefore, Propofol 10 mg/ml should only be used during pregnancy if absolutely necessary. Propofol 10 mg/ml crosses the placenta and may be associated with the depression of vital functions in newborns (see also section 5.3). Propofol can be employed as anaesthesia in the case of termination of pregnancy.

High dosages (more than 2.5 mg Propofol/kg body mass for induction or 6 mg Propofol/kg of body mass per hour for maintenance of anaesthesia) should be avoided.

Studies in animals have shown reproductive toxicity.

Breast-feeding Studies with breast-feeding women have shown that propofol passes into breast milk in small quantities . Therefore, mothers should suspend breast-feeding for up to 24 hours after administration of propofol and discard the corresponding breast milk.

1.3.1.4.7 Effect on ability to drive and use medicines

After the administration of Propofol 10 mg/ml, the patient should be observed for an appropriate period of time. Patients should be made aware of fact that the ability to participate in traffic and use machinery may be impaired for some time after the administration of Propofol 10 mg/ml. The impairments caused by Propofol 10 mg/ml are usually not observed for longer than 12 hours The patient may only return home when accompanied by another person and may not drink any alcohol.

1.3.1.4.8 Undesirable effects

The induction and maintenance of anaesthesia and sedation with Propofol is normally gentle with only a few signs of excitation.The most frequently reported undesirable effects are pharmacologically foreseeable effects of anaesthetics / sedatives, such as, for example, hypotension and respiratory depression. The type, severity and frequency of these effects, which were observed in patients during the use of Propofol, are dependent on the patient's state of health, type of procedure and the therapeutic measures taken. The frequency of the occurrence of undesirable effects is based on the following categories:

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).
The following undesirable effects were particularly observed:

System Organ Classes	Indications of Frequency	Undesirable effects
Immune system disorders	Very rare	severe allergic reactions (anaphylaxis), which can include angiooedema, bronchospasm, erythemas and hypotension
Metabolism and nutrition disorders	Not known	Metabolic acidosis5, hyperkalaemia5, hyperlipidaemia5
Psychiatric disorders	Not known	euphoric mood during the waking phase, abuse of the drug and dependency on the drug8
Nervous system disorders	Common	Spontaneous movements and muscle spasms during induction of anaesthesia,

		headache during the waking phase
	Rare	Feeling of dizziness, chills and perception of cold during the waking phase, episodes similar to epilepsy with seizures and opisthotonus during induction, maintenance and the waking phase (very rarely delayed by hours to a few days)
	Very rare	postoperative unconsciousness (also see section 4.4)
	Not known	Involuntary movements
Cardiac disorders	Common	Bradycardia1
	Very rare	Pulmonary oedema
	Not known	Arrhythmia5, heart failure 5,7
Vascular disorders	Common	Hypotension2
	Uncommon	Thrombosis and phlebitis
Respiratory, thoracic and mediastinal disorders	Common	Hyperventilation and coughing during induction of anaesthesia, temporary apnoea during induction of anaesthesia
	Uncommon	Coughing during maintenance therapy
	Rare	Coughing during the waking phase
	Not known	Respiratory depression (depending on the dosage)
Gastrointestinal tract disorders	Common	Singultation during the induction, nausea and vomiting during the waking phase
	Very rare	Pancreatitis
Hepatobiliary disorders	Not known	Hepatomegaly5
Musculoskeletal and connective tissue disorders	Not known	Rhabdomyolysis 3,5

Renal and urinary disorders	Very rare	Discolouration of urine after longer periods of administration of Propofol 10 mg/ml
	Not known	Renal failure5
Reproductive tract and breast disorders	Very rare	Sexual disinhibition
	Not known	Priapism
General disorders and administration site conditions	Very common	Local pain during the first injection4
	Common	Hot flushes during the induction of anaesthesia
	Very rare	Severe tissue reactions and tissue necrosis9 after erroneous extravascular application
	Not known	Local pain, swelling after erroneous extravascular application
Investigations	Not known	Brugada-type ECG5,6
Injury, poisoning and complications as a result of a procedure	Very rare	Postoperative fever

After simultaneous administration of, the following side effects can occur: dizziness, vomiting, drowsiness, convulsions, bradycardia, arrhythmia and shock.

Soybean oil may trigger allergic reactions very rarely.

1. Severe bradycardia is rare; in some individual cases, progression up to and including asystole has been reported.

2.Occasionally, a decrease in blood pressure can make volume replacement therapy and a decrease in the speed of administering Propofol 10 mg/ml necessary.

3.Rhabdomyolysis was reported very rarely if Propofol 10 mg/ml was administered in high doses as 4 mg Propofol/kg of body mass per hour for sedation as part of intensive care.

4.This can be avoided for the most part by administering imultaneously and by administering the drug in larger veins in the forearm or the cubital fossa.

5.A combination of these events, which is also called "Propofol infusion syndrome", occurs in severely ill patients who often have multiple risk factors for the development of these events.

6.Brugada syndrome - elevated ST segment and concave T waves in the ECG.

7.Quickly progressing heart failure (in some cases with a deadly outcome) in adults, which was usually not able to be treated with supportive inotropic therapeutic measures.

8.Misuse and dependency on Propofol, primarily by healthcare personnel.

9.In cases where viability of the tissue was impaired, necrosis has been reported.

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

1.3.1.4.9 Overdose

An overdose can lead to circulatory and respiratory depression. Apnoea requires artificial ventilation. In the case of circulatory depression, the usual measures should be taken of lowering the head position or/and plasma substitution and vasoconstrictors.

1.3.1.5 Pharmacological properties

1.3.1.5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Other general anaesthetics,

ATC-code N0lAXl0.

After intravenous injection of Propofol 10 mg/ml, a hypnotic effect occurs quickly. The induction time is dependent on the injection speed and is normally 30 - 40 seconds. The duration of effect is short as a result of rapid metabolisation and excretion (4-6 minutes). The mechanism of action is not completely known, as with all general anaesthetics. However, it is believed that Propofol produces its sedative or anaesthetic effect by means of positive modulation of the inhibitory effect of the neurotransmitter GABA through the ligand-gated GABA receptors.

When the dosing guidelines are followed, a clinically relevant accumulation of propofol after multiple repeated injections or infusion can be ruled out.

Limited studies on the duration of action of anaesthesia with propofol in children indicate that the safety and efficacy remain unchanged up to duration of 4 hours.
References in literature regarding the use of Propofol in children also indicate that there are no changes with respect to the safety and efficacy when Propofol is used with longer treatments.
Most patients awake quickly in a clearly conscious state.
The occasionally observed bradycardia and drop in blood pressure when inducing anaesthesia are most likely attributed to a central vagotonic effect or to an inhibition of the activity of the sympathetic nervous system. The circulatory situation generally normalises when continuing the anaesthesia.

1.3.1.5.2 Pharmacokinetic properties

Propofol is up to 98 % bound to plasma protein.
After intravenous administration, the initial progression of the blood concentration (alpha phase) is characterised by a large decrease due to the rapid distribution in the organism. The half-life of the alpha phase is 1.8 - 4.1 minutes.
The decrease in the blood concentration is slower during the elimination or beta phase. The half-life for this phase was calculated at 34 to 64 minutes.
A so-called deep compartment can be identified over a longer period of observation. The half-life for this phase (gamma phase) of the blood concentration is 184 - 382 minutes.
The initial distribution volume V amounts to 22 - 76 l, and the total distribution volume Vd is 387 - 1,587l. Propofol has a large distribution volume and is quickly eliminated from the body (total clearance: 1.5 - 2 l/min). The elimination occurs through metabolisation, primarily in the liver, where inactive conjugates of Propofol and the corresponding hydroquinone
are formed depending on the blood flow, which undergo renal excretion.
After a single intravenous dose of 3 mg Propofol/kg, the Propofol clearance per kg of body weight increased depending on the patient's age in the following manner: the mean clearance in newborns < 1 month of age (n=25), at 20 ml/kg/min was considerably lower in comparison to older children (n=36, aged 4 months to 7 years). In the case of newborns, the data additionally exhibit considerable variability (3.7 - 78 ml/kg/min). Due to these limited study results, which indicate a large degree of variability, no dosage recommendation can be provided for this age class.
In the case of older children, the mean clearance of Propofol after a single bolus administration of 3 mg Propofol/kg was 37.5 ml/kg/min in children in the age of 4 - 24 months (n=8), 38.7 ml/kg/min in children in the age of 11 - 43 months (n=6), 48 ml/kg/min in children in the age of 1 - 3 years (n=12) and 28.2 ml/kg/min in children in the age of 4 - 7 years (n=10). In
comparison, the mean clearance in adults was 23.6 ml/kg/min (n=6)

1.3.1.5.3 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.

Published studies in animals (including primates) at doses resulting in light to moderate anaesthesia demonstrate that the use of anaesthetic agents during the period of rapid brain growth or synaptogenesis results in cell loss in the developing brain that can be associated with prolonged cognitive deficiencies. The clinical significance of these nonclinical findings is not known.

1.3.1.6 Pharmaceutical particulars

1.3.1.6.1 List of excipients

Refined Soya Oil BP
Egg Lecithin 80% (Lipoid E 80) USP
Glycerol BP
Disodium Hydroxide BP
Sodium Hydroxide BP
Water for Injection BP

1.3.1.6.2 Incompatibilities

Not Available

1.3.1.6.3 Shelf life

24 months.

1.3.1.6.4 Special precautions for storage

Store at a temperature not exceeding 25°C. Protect from light.

1.3.1.6.5 Nature and contents of container

A milky white emulsion is filled in 20 ml flint Tubular vial with 20 mm grey bromo butyl rubber plugs with 20 mm flip off aluminium seals.

6.6 Special precautions for disposal and other handling

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

1.3.1.7 Marketing authorization holder

M/s. T.P DRUGS LIMITED,
Shop No. A1 & A2 13, Murtala Mohammed Way, Kano, Nigeria.

Manufacturer:

M/s. Kamla Lifesciences Ltd.

Plot no.G-84/1, Tarapur M.I.D.C, Boisar,

Tal. & Dist. Palghar, Maharashtra, India -401 506.