BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

Summary of the product characteristics

1. Name of Medicinal Product

TROYPOFOL 20 ml [Propofol Injection BP I.V. (1% w/v)]

2. Qualitative and quantitative composition

1 ml (of emulsion) contains 10mg of propofol

For the full list of excipients, see section 6.1

3. Pharmaceutical Form:

Emulsion for injection or infusion.

A milky white emulsion.

4. Clinical Particulars:

4.1 Therapeutic indications

Propofol is a short-acting intravenous anaesthetic agent suitable suitable for induction and maintenance of general anaesthesia. Propofol may also be used for sedation of ventilated patients receiving intensive care. Propofol may also be used for sedation for surgical and diagnostic procedures.

4.2 Posology and method of administration

Induction of General Anaesthesia

Adults

In unpremedicated 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 to 2.5 mg/kg of propofol. The total dose required can be reduced by lower rates of administration (2 to 5 ml/min [20 to 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).

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

Elderly Patients

In elderly patients the dose requirement for induction of anaesthesia with propofol is reduced. The reduction should take into 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.

Children

Propofol is not recommended for induction of anaesthesia in children aged less than 1 month. When used to induce anaesthesia in children, it is recommended that propofol be 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 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

Adults

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 to 12 mg/kg/h usually maintain satisfactory anesthesia.

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.

Elderly Patients

When propofol is used for maintenance of anaesthesia 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 the elderly as this may lead to cardiorespiratory depression.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

Children

Propofol is not recommended for maintenance of anaesthesia in children less than 1 month old.

Anaesthesia can be maintained in children over 1 month of age by administering propofol by infusion or repeat bolus injection to prevent the clinical signs of light anaesthesia. 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, less than 3 years, may have higher dosage requirements within the range of recommended dosages, as compared with older paediatric patients. Dosage should be adjusted individually and particular attention paid to the need for adequate analgesia. A maximum duration of use of approximately 60 minutes should not be exceeded except where there is a specific indication for longer use e.g. malignant hyperthermia where volatile agents must be avoided.

For ASA 3 and 4 patients lower doses are recommended

Sedation during Intensive Care

Adults

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. Propofol is not indicated for sedation in intensive care of patients of 16 years of age or younger.

Propofol may be diluted with 5% Dextrose.

It is recommended that blood lipid levels be monitored should propofol be administered to patients thought to be at particular risk of fat overload. Administration of propofol should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation. If the duration of sedation is in excess of 3 days, lipids should be monitored in all patients.

Elderly Patients

When propofol 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 the elderly as this may lead to cardiorespiratory depression.

Children

Propofol 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 individualized and titrated to clinical response.

Most patients will require 0.5 to 1 mg/kg over 1 to 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 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

When propofol 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 the elderly as this may lead to cardio respiratory depression.

Children

Propofol is not recommended for sedation in children as safety and efficacy have not been demonstrated.

Administration

Propofol has no analgesic properties and therefore supplementary analgesic agents are generally required in addition to propofol.

Propofol can be used for infusion undiluted or diluted with 5% Dextrose (Intravenous Infusion) 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.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

It is recommended that, when using diluted propofol, the volume of 5% Dextrose removed from the infusion bag during the dilution process is totally replaced in volume by propofol emulsion.

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

- Dextrose 5% Intravenous Infusion
- Sodium Chloride 0.9% Intravenous Infusion
- Dextrose 4% with Sodium Chloride 0.18% Intravenous Infusion BP

Propofol may be premixed with alfentanil injection containing 500 micrograms/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 may be mixed with preservative-free Lidocaine Injection 0.5% or 1%.

Dilution and Co-administration of propofol with Other Drugs or Infusion Fluids

Co-administration Technique	**Additive or Diluent**	**Preparation**	**Precautions**
Pre-mixing.	Dextrose 5% Intravenous	Mix 1 part of propofol with up to 4 parts of Dextrose 5% Intravenous infusion in either PVC infusion	Prepare aseptically immediately before administration. The mixture is stable for upto 6 hours.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

		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.	
	Lidocaine hydrochloride injection (0.5% or 1% without preservatives).	Mix 20 parts of propofol 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 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.
	Sodium chloride 0.9% intravenous infusion	As above	As above
	Dextrose 4% with sodium chloride 0.18% intravenous infusion.	As above	As above

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

4.3 Contraindications:

- Propofol is contraindicated in patients with a known hypersensitivity to propofol or any of the excipients.
- Propofol is contraindicated for sedation in intensive care of patients of 16 years of age or younger.
- Propofol contains soya oil and should not be used in patients who are hypersensitive to peanut or soya.

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 patient 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.

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

As with other sedative agents, when propofol is used for sedation during operative procedures, involuntary patient movements may occur. During procedures requiring immobility these movements may be hazardous to the operative site.

As with other intravenous anaesthetic and sedative agents, patients should be instructed to avoid alcohol before and for at least 8 hours after administration of propofol.

Propofol should be used with caution when used to sedate patients undergoing some procedures where spontaneous movements are particularly undesirable, such as ophthalmic surgery.

As with other intravenous sedative agents, when propofol is given along with central nervous system depressants, such as potent analgesics, the sedative effect may be intensified and the possibility of severe respiratory or cardiovascular depression should be considered.

During bolus administration for operative procedures, extreme caution should be exercised in patients with acute pulmonary insufficiency or respiratory depression.

Concomitant use of central nervous system depressants e.g., alcohol, general anaesthetics, narcotic analgesics will result in accentuation of their sedative effects. When propofol is combined with centrally depressant drugs administered parenterally, severe respiratory and cardiovascular depression may occur. It is recommended that propofol is administered

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

following the analgesic and the dose should be carefully titrated to the patient's response.

During induction of anaesthesia, hypotension and transient apnoea may occur depending on the dose and use of premedicants and other agents.

Occasionally, hypotension may require use of intravenous fluids and reduction of the rate of administration of propofol during the period of anaesthetic maintenance. An adequate period is needed prior to discharge of the patient to ensure full recovery after general anaesthesia. Very rarely the use of propofol may be associated with the development of a period of post-operative unconsciousness, which may be accompanied by an increase in muscle tone. This may or may not be preceded by a period of wakefulness. Although recovery is spontaneous, appropriate care of an unconscious patient should be administered.

When propofol is administered to an epileptic patient, there may be a risk of convulsion. As with other intravenous anaesthetic agents, caution should be applied in patients with cardiac, respiratory, renal or hepatic impairment or in hypovolaemic, elderly or debilitated patients.

The risk of relative vagal overactivity may be increased because propofol lacks vagolytic activity; it has been associated with reports of bradycardia (occasionally profound) and also asystole. The intravenous administration of an anticholinergic agent before induction, or during maintenance of anaesthesia should be considered, especially in situations where vagal tone is likely to predominate, or when propofol is used in conjunction with other agents likely to cause a bradycardia.

Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. Use is not recommended with electroconvulsive treatment. As with other anaesthetics, sexual disinhibition may occur during recovery. 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 4 mg/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. If possible, the dosage should not exceed 4 mg/kg/h. Alertness is advised to these possible Propofol is not advised for general anaesthesia in children younger than 1 month of age. The safety and efficacy of propofol for (background) sedation in children younger than 16 years of age have not been demonstrated. Although no causal relationship has been established, serious undesirable effects with (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. Propofol 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 cardio-respiratory depression.

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 4 mg/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. If possible, the dosage should not exceed 4 mg/kg/h. Alertness is advised to these possible undesirable effects and consider decreasing the propofol 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.

Additional Precautions

Troypofol contains no antimicrobial preservatives and supports growth of micro-organisms. When propofol is to be aspirated, it must be drawn aseptically into a sterile syringe. Administration must commence without delay. Asepsis must be maintained for both propofol and infusion equipment throughout the infusion period. Any drugs or fluids added to the propofol line must be administered close to the cannula site. Propofol must not be administered via a microbiological filter. Propofol and any syringe containing propofol are for single use in an individual patient. For use in long term maintenance of anaesthesia or sedation in intensive care it is recommended that the infusion line and reservoir of propofol be discarded and replaced at regular intervals.

4.5 Interaction with other medicinal products and other forms of interaction

Propofol has been used in association with spinal and epidural anaesthesia and with commonly used premedicants, neuromuscular blocking drugs, inhalational agents and analgesic agents; no pharmacological incompatibility has been encountered. Lower doses of propofol may be required where general anaesthesia is used as an adjunct to regional anaesthetic techniques.

The concurrent administration of other CNS depressants such as pre-medication drugs,

inhalation agents, analgesic agents may add to the sedative, anaesthetic and cardiorespiratory depressant effects of propofol.

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The concurrent administration of other CNS depressants such as pre-medication drugs, inhalation agents, analgesic agents may add to the sedative, anaesthetic and cardiorespiratory depressant effects of propofol.

4.6 Pregnancy and Lactation

Pregnancy

The safety of propofol during pregnancy has not been established. Therefore propofol should not be used in pregnancy unless clearly necessary. Propofol has been used, however, during termination of pregnancy in the first trimester.

Obstetrics

Propofol crosses the placenta and may be associated with neonatal depression. It should not be used for obstetric anaesthesia unless clearly necessary.

Lactation

Safety to the neonate has not been established following the use of propofol in mothers who are breast feeding

4.7 Effects on ability to drive and use machines

Propofol has moderate influence on the ability to drive and use machines. Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after general anaesthesia.

4.8 Undesirable effects

General

Induction of anaesthesia is generally smooth with minimal evidence of excitation. 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.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

Very common(>1/10)	General disordersand administrationsite conditions:	Local pain oninduction (1)
Common(>1/100, <1/10)	Vascular disorder:	Hypotension (2)
	Cardiac disorders:	Bradycardia (3)
	Respiratory, thoracicand mediastinaldisorders:	Transientapnoea duringinduction
	Gastrointestinaldisorders:	Nausea and vomitingduring recovery phase
	Nervous systemdisorders:	Headache duringrecovery phase
	General disordersand administrationsite conditions:	Withdrawalsymptoms inchildren (4)
	Vascular disorders:	Flushing in children (4)
Uncommon(>1/1000, <1/100)	Vascular disorders:	Thrombosis andphlebitis
Rare (>1/10 000,<1/1000)	Nervous systemdisorders:	Epileptiformmovements, includingconvulsions andopisthotonus duringinduction,maintenance andrecovery
Very rare(<1/10 000)	Musculoskeletal and connective tissuedisorders:	Rhabdomyolysis(5)
	Gastrointestinaldisorders:	Pancreatitis
	Injury, poisoning and proceduralcomplications:	Post-operative fever
	Renal and urinarydisorders:	Discolouration of urinefollowing prolongedadministration
	Immune systemdisorders:	Anaphylaxis - mayinclude angioedema,bronchospasm,erythema andhypotension
	Reproductive system and breast disorders:	Sexual disinhibition
	Cardiac disorders:	Pulmonary oedema
	Nervous systemdisorders:	Postoperative Unconsciousness

(1) May be minimised by using the larger veins of the forearm and antecubital fossa. With propofol, local pain can also be minimized by the co-administration of lidocaine.

(2) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of propofol.

(3) Serious bradycardias are rare. There have been isolated reports of progression to asystole.

(4) Following abrupt discontinuation of propofol during intensive care.

(5) Very rare reports of rhadbomyolysis have been received where propofol has been given at doses greater than 4 mg/kg/hr for ICU sedation.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

Local

The local pain which may occur during the induction phase of propofol anaesthesia can be minimised by the coadministration of lidocaine and by the use of the larger veins of the forearm and antecubital fossa. Thrombosis and phlebitis are rare. Accidental clinical extravasation showed minimal tissue reaction.

4.9 Overdose

Accidental overdosage is likely to cause cardio respiratory 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.

5.0 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other general anaesthetics

ATC code: N01AX10

Mechanism of action

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.

Pharmacodynamic properties

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.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

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 clear headed with a low incidence of headache and post-operative 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.

5.2 Pharmacokinetic properties

Absorption

When propofol is used to maintain anaesthesia, blood concentrations asymptotically approach the steady-state value for the given administration rate.

Distribution

Propofol is extensively distributed and rapidly cleared from the body (total body clearance 1.5–2 litres/minute).

Elimination

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.

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.

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

5.3 Preclinical safety data

No data available

6. Pharmaceutical particulars

6.1 List of excipients

1.Lipoid E 80 (Egg lecithin)
2.Lipoid Sodium Oleate B
3.Glycerol
4.Disodium Edetate
5.Lipoid Purified Soyabean Oil 700
6.Sodium Hydroxide (pellets)
7.Water for Injection

6.2 Incompatibilities:

No data available

6.3 Shelf-life:

36 Months

6.4 Special precautions for storage

Store below 30°C. Do not freeze.

6.5 Nature and contents of container:

BRAND NAME	TROYPOFOL 20ML
GENERIC NAME	Propofol Injection BP I.V. (1% w/v)

20 ml flint vial USP Type I with 20 mm Bromo butyl rubber closure and 20 mm blue flip off aluminium seal with Troikaa logo.

6.6 Special precautions for disposal and other handling

No special requirements

7. Applicant

Artemis Laboratories Limited, formerly known as Sewell Pharmaceuticals Ltd Plot 4, Block 4, Ogun State Housing Corporation & Industrial Estate, Ota, Ogun State, Nigeria.

8. Manufacturer

Troikaa Pharmaceuticals Limited C-1, Sara Industrial Estate, Selaqui, Dehradun-248 197, Uttarakhand, India.

9. Date of first authorization: 26-Feb-2015
Date of renewal of the authorization: 28-Oct-2021

10. Date of revision of text: ---