Baxter **Baxter Pharmaceuticals India Private Limited**

Artwork Code : 140000XXXX	
Quality of Paper/Board : Super Sun Shine	**Size of Artwork (In mm) : 400x175**
Quality of Gum :	**GSM of Paper/Board : 60 GSM**

Colour Code : BLACK ■ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐ | Pantone ☐

Barcode Information:

Barcode Scan Report:

Packing: 20 ml Glass Vial	**Plant Location : BA 1**
Country: Malaysia	**Language : English**

Date: 28/11/24

Baxter

For the use of an Anaesthesiologist attached to Hospitals, Institutions and Nursing homes only.

Propofol Emulsion for Injection or Infusion (1% w/v) with MCT-LCT (1% w/v)

Spiva™

Description

SPIVA™, is a white milky emulsion, practically free from extraneous particulate contamination and large oil droplets.

Composition:

Each ml (of emulsion) contains:

Propofol BP 10 mg

Excipients

Soybean Oil USP, Medium chain triglycerides BP, Glycerol USP, Egg Lecithin, Sodium Oleate, Sodium Hydroxide BP, Water for Injections BP q.s.

Pharmacodynamics

Pharmacotherapeutic group: Anaesthetics, general

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 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.

Pharmacokinetics

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 to 4 minutes), rapid elimination (half-life 30 to 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.

Preclinical Safety Data

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 non-clinical findings is not known.

Indication

SPIVA™ is a short-acting intravenous anaesthetic agent suitable for induction and maintenance of general anaesthesia.

SPIVA™ may also be used for sedation of ventilated adult patients receiving intensive care.

SPIVA™ may also be used for conscious sedation for surgical and diagnostic procedures.

Recommended Dose

Supplementary analgesic agents are generally required in addition to SPIVA™.

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

A. Adults

INDUCTION OF GENERAL ANAESTHESIA

SPIVA™ may be used to induce anaesthesia by slow bolus injection or infusion. In unpremedicated and premedicated patients, it is recommended that SPIVA™ should be titrated (approximately 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 SPIVA™. 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 SPIVA™ either by continuous infusion or by repeat bolus injections to maintain the depth of anaesthesia required.

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 anaesthesia.

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

SEDATION DURING INTENSIVE CARE

When used to provide sedation for ventilated adult patients undergoing intensive care, it is recommended that SPIVA™ be given by continuous infusion. The infusion rate should be adjusted according to the depth of sedation required but rates in the region of 0.3 to 4.0 mg/kg/h should achieve satisfactory sedation in most adult patients.

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

Maintenance of sedation may be accomplished by titrating SPIVA™ 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 in ASA grades 3 and 4 the rate of administration and dosage may need to be reduced

B. Elderly Patients

In elderly patients the dose requirement for induction of anaesthesia with SPIVA™ 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 SPIVA™ is used for maintenance of anaesthesia or sedation the rate of infusion or 'target concentration' should also be reduced. Patients of ASA grades 3 and 4 will require further reductions in dose and dose rate. Rapid bolus administration (single or repeated) should not be used in the elderly as this may lead to cardiorespiratory depression.

C. Children

INDUCTION OF GENERAL ANAESTHESIA

SPIVA™ is not recommended for use in children less than 3 years of age (see 'Side Effects').

When used to induce anaesthesia in children, it is recommended that SPIVA™ 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 SPIVA™ 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

SPIVA™ is not recommended for use in children less than 3 years of age. Anaesthesia can be maintained by administering SPIVA™ by infusion or repeat 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 to 15 mg/kg/h usually achieve satisfactory anaesthesia.

CONSCIOUS SEDATION FOR SURGICAL & DIAGNOSTIC PROCEDURES.

SPIVA™ is not recommended for conscious sedation in children as safety and efficacy have not been demonstrated.

SEDATION DURING INTENSIVE CARE

SPIVA™ 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.

D. Administration

SPIVA™ can be used for infusion undiluted from plastic syringes or glass infusion bottles.

When SPIVA™ 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.

SPIVA™ may also be used 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/ml) 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 SPIVA™. 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.

SPIVA™ may be administered via 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.

SPIVA™ 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.

To reduce pain on initial injection, SPIVA™ used for induction may be mixed with Lidocaine Injection in a plastic syringe in the ratio of 20 parts SPIVA™ with up to one part of either 0.5% or 1% Lidocaine Injection immediately prior to administration.

DILUTION AND CO-ADMINISTRATION OF SPIVA™ WITH OTHER DRUGS OR INFUSION FLUIDS (See also 'Additional Precautions' Section)

Co-administration Technique	Additive or Diluent	Preparation	Precautions
Pre-mixing.	Dextrose 5% Intravenous Infusion	Mix 1 part of SPIVA™ with up to 4 parts of Dextrose 5% Intravenous Infusion in either PVC infusion bags or glass infusion bottles. When diluted in PVC bags it is recommended that the bag should be full and that the dilution be prepared by withdrawing a volume of infusion fluid and replacing it with an equal volume of SPIVA™	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 SPIVA™ 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 SPIVA™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

Route of Administration

Intravenous (IV)

Contraindications

SPIVA™ is contraindicated in patients with a known hypersensitivity to propofol or any of the excipients.

SPIVA™ is contraindicated for sedation in intensive care of patients of 16 years of age or younger (see 'Warnings & Precautions').

SPIVA™ contains soya oil and should not be used in patients who are hypersensitive to peanut or soya.

Warnings & Precautions

SPIVA™ 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. SPIVA™ should not be administered by the person conducting the diagnostic or surgical procedure.

When SPIVA™ 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 SPIVA™ 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 SPIVA™.

SPIVA™ 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 SPIVA™ 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 SPIVA™ is combined with centrally depressant drugs administered parenterally, severe respiratory and cardiovascular depression may occur. It is recommended that SPIVA™ is administered following the analgesic and the dose should be carefully titrated to the patient's response (see 'Interactions with other Medicaments').

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 SPIVA™ 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 SPIVA™ 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 SPIVA™ 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 SPIVA™ 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 SPIVA™ is used in conjunction with other agents likely to cause a bradycardia.

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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.
SPIVA™ is not advised for general anaesthesia in children younger than 1 month of age.
The safety and efficacy of SPIVA™ 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.
SPIVA™ 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.
There are no clinical trials data to support the use of SPIVA™ for the sedation of children with croup or epiglottitis receiving intensive care.

Advisory statement concerning Intensive Care Unit management:

Very rare reports of metabolic acidosis, rhabdomyolysis, hyperkalaemia, ECG changes*,and/or cardiac failure, in some cases with a fatal outcome, have been received concerning seriously ill patients receiving SPIVA™ for ICU sedation. The following appear to be the major risk factors for the development of these events: decreased oxygen delivery to tissues; serious neurological injury and/or sepsis; high dosages of one or more of the following pharmacological agents - vasoconstrictors, steroids, inotropes and/or propofol. All sedative and therapeutic agents used in the ICU (including SPIVA™) should be titrated to maintain optimal oxygen delivery and haemodynamic parameters
*Coved ST segment elevation (similar to ECG changes of the Brugada syndrome)

ADDITIONAL PRECAUTIONS

SPIVA™ contains no antimicrobial preservatives and supports growth of microorganisms.
When SPIVA™ 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 SPIVA™ and infusion equipment throughout the infusion period. Any infusion fluids added to the SPIVA™ line must be administered close to the cannula site. SPIVA™ must not be administered via a microbiological filter.
SPIVA™ and any syringe containing SPIVA™ 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 SPIVA™ be discarded and replaced at regular intervals.
There have been very rare reports of epileptiform movement in epileptics and epileptics occurring during induction orbemergence from anaesthesia induced by Propofol.

Interactions with Other Medicaments

SPIVA™ 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 SPIVA™ 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 (see 'Warnings & Precautions').
A need for lower propofol doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of propofol may be considered.

Pregnancy and Lactation

Pregnancy

The safety of SPIVA™ during pregnancy has not been established. Studies in animals have shown reproductive toxicity (see *Section Preclinical Safety Data*). Therefore SPIVA™ should not be used in pregnancy unless clearly necessary. SPIVA™ has been used, however, during termination of pregnancy in the first trimester.

Obstetrics

SPIVA™ 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 SPIVA™ in mothers who are breast feeding.

Side Effects

General

Induction of anaesthesia with SPIVA™ 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.

Frequency	System Organ Class	Event
Very common (≥1/10)	*General disorders and administration site conditions:*	Local pain on induction (a)
Common (≥1/100, <1/10)	*Vascular disorders:*	Hypotension (b)
	Cardiac disorders:	Bradycardia (c)
	Respiratory, thoracic and Mediastinal	Transient apnoea during induction
	Gastrointestinal disorders:	Nausea and vomiting during recovery phase
	Nervous system disorders:	Headache during recovery phase
	General disorders and administration site conditions:	Withdrawal symptoms in children(d)
	Vascular disorders:	Flushing in children (d)
Uncommon (≥1/1000, <1/100)	*Vascular disorders:*	Thrombosis and phlebitis
Rare (≥1/10000, <1/1000)	*Nervous system disorders:*	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	Psychiatric disorders:	Euphoric mood
Very rare (<1/10 000)	*Musculoskeletal and connective tissue disorders:*	Rhabdomyolysis (e)
	Gastrointestinal disorders:	Pancreatitis
	Injury, poisoning and procedural complications:	Post-operative fever
	Renal and urinary disorders:	Discolouration of urine following prolonged administration
	Immune system disorders:	Anaphylaxis - may include angioedema, bronchospasm, erythema and hypotension
	Reproductive system and breast disorders:	Sexual disinhibition
	Cardiac disorders:	Pulmonary oedema
	Nervous system disorders:	Postoperative unconsciousness
Not known (cannot be estimated from the available data)	*Reproductive system and breast disorders:*	Priapism
	Hepatobiliary disorders	Hepatomegaly
		Hepatitis, acute hepatic failure (f)

(a) May be minimised by using the larger veins of the forearm and antecubital fossa. With SPIVA™ local pain can also be minimised by the co-administration of Lidocaine (see 'Recommended Dose' part D).
(b) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of SPIVA™.
(c) Serious bradycardias are rare. There have been isolated reports of progression to asystole.
(d) Following abrupt discontinuation of SPIVA™ during intensive care.
(e) Very rare reports of rhabdomyolysis have been received where SPIVA™ has been given at doses greater than 4 mg/kg/hr for ICU sedation.
(f) After both long- and short-term treatment and in patients without underlying risk factors.

Reports from off-label use of SPIVA™ for induction of anaesthesia in neonates indicates that cardio-respiratory depression may occur if the paediatric dose regimen is applied. (See 'Recommended Dose' and 'Warnings & Precautions').

Symptoms and Treatment of 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.

Effects on Ability to Drive and Use Machine

Patients should be advised that performance at skilled tasks, such as driving and operating machinery, may be impaired for some time after use of SPIVA™.

Incompatibilities

The neuromuscular blocking agents, atracurium and mivacurium should not be given through the same intravenous line as SPIVA™ without prior flushing.

Instructions for Use

In-use precautions
Containers should be shaken before use.
Any portion of the contents remaining after use should be discarded.
Asepsis for SPIVA™ and infusion equipment must be maintained (see 'Additional Precautions').

Storage Condition

Store below 30°C. Do not freeze.

Presentation

It is available in 20ml Glass Vial. (20ml in a vial x 5 vial)

Shelf Life

24 Months.

Date of Revision:

11/2024

140000XXXX

Manufactured by:
Baxter Pharmaceuticals India Private Limited
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Ahmedabad-382213, India.

Product Registration Holder:
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