Product Monograph

Including Patient Medication Information

[Pr]PROPOFOL INJECTION

Propofol injectable emulsion

For intravenous use, 10 mg / mL

Mfr. Std.

General Anesthetic

Fresenius Kabi Canada Ltd.

165 Galaxy Blvd, Suite 100

Toronto, ON M9W 0C8

Date of Authorization:

Dec. 19, 2025

Submission Control Number: 301681

Recent Major Label Changes

7 Warnings and Precautions, General	2024-07

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Recent Major Label Changes 2

Table of Contents 2

Part 1: Healthcare Professional Information 4

1. Indications 4

1.1 Pediatrics 4

1.2 Geriatrics 4

2. Contraindications 5

4. Dosage and Administration 5

4.1 Dosing Considerations 5

4.2 Recommended Dose and Dosage Adjustment 6

4.3 Reconstitution 11

4.4 Administration 11

5. Overdose 12

6. Dosage forms, Strengths, Composition, and Packaging 13

7. Warnings and Precautions 13

7.1 Special Populations 16

7.1.1 Pregnancy 16

7.1.2 Breastfeeding 16

7.1.3 Pediatrics 16

7.1.4 Geriatrics 17

8. Adverse Reactions 17

8.1 Adverse Reaction Overview 17

8.2 Clinical Trial Adverse Reactions 18
8.2.1 Clinical Trial Adverse Reactions – Pediatrics 20
8.3 Less Common Clinical Trial Adverse Reactions 20
8.5 Post-Market Adverse Reactions 22

9. Drug Interactions 22
9.2 Drug Interactions Overview 22
9.3 Drug-Behaviour Interactions 22
9.4 Drug-Drug Interactions 22
9.5 Drug-Food Interactions 23
9.6 Drug-Herb Interactions 23
9.7 Drug-Laboratory Test Interactions 23

10. Clinical Pharmacology 24
10.1 Mechanism of Action 24
10.2 Pharmacodynamics 24
10.3 Pharmacokinetics 25

11. Storage, Stability, and Disposal 26

12. Special Handling Instructions 26

Part 2: Scientific Information 27

13. Pharmaceutical Information 27

14. Clinical Trials 27

16. Non-Clinical Toxicology 27

17. Supporting Product Monographs 30

Patient Medication Information 31

Part 1: Healthcare Professional Information

1. Indications

Propofol Injection (propofol injectable emulsion) is indicated for:

- Induction and maintenance of general anesthesia
- Conscious sedation for surgical and diagnostic procedures
- Sedation during intensive care

Propofol Injection is a short-acting intravenous general anesthetic agent, that can be used for both induction and maintenance of anesthesia as part of a balanced anesthesia technique, including total intravenous anesthesia (TIVA), for inpatient and outpatient surgery.

Propofol Injection, when administered intravenously as directed, can be used to initiate and maintain sedation in conjunction with local/regional anesthesia in adult patients undergoing surgical procedures. Propofol Injection may also be used for sedation during diagnostic procedures in adults (see 7 WARNINGS AND PRECAUTIONS, General).

Propofol Injection should only be administered to intubated, mechanically ventilated, adult patients in the Intensive Care Unit (ICU) to provide continuous sedation and control of stress responses. In this setting, Propofol Injection should be administered only by or under the supervision of persons trained in general anesthesia or critical care medicine.

1.1 Pediatrics

Pediatrics (3 to ≤ 18 years of age):

Propofol Injection is only indicated for anesthesia in children 3 years of age and older.

Propofol Injection is not indicated for sedation or during surgical/diagnostic procedures in children under the age of 18, as safety and efficacy have not been established in this patient population. (See 7.1.3 Pediatrics and 4 Dosage and Administration.)

(See 2 Contraindications).

1.2 Geriatrics

Geriatrics (> 55 years of age): Elderly patients should be given reduced doses of propofol, commensurate with their age and physical condition (see 7.1.4 Geriatrics and 4 Dosage and Administration).

2. Contraindications

Propofol Injection is contraindicated:

- In patients who are hypersensitive or allergic to this drug, lipid emulsions or to any other ingredient in the formulation, including any non-medicinal ingredient (including eggs or egg products, and soybeans or soy products), or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition and Packaging.
- For the sedation of children 18 years or younger receiving intensive care (see 4 Dosage and Administration).
- When sedation or general anesthesia are contraindicated.

4. Dosage and Administration

4.1 Dosing Considerations

For general anesthesia or sedation for surgical/diagnostic procedures, Propofol Injection should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of surgical/diagnostic procedures. Patients should be continuously monitored and facilities for maintenance of a patent airway, artificial ventilation, and oxygen enrichment and circulatory resuscitation must be immediately available.

For sedation of intubated, mechanically ventilated, adult patients in the ICU, Propofol Injection should be administered only by persons trained in general anesthesia or critical care medicine.

As with other general anesthetics, the administration of Propofol Injection without airway care may result in fatal respiratory complications.

Strict aseptic techniques must always be maintained during handling as Propofol Injection is a single-use parenteral product, for use in an individual patient, and contains no antimicrobial preservatives. The vehicle is capable of supporting rapid growth of microorganisms. Failure to follow aseptic handling procedures may result in microbial contamination causing fever/infection/sepsis which could lead to life-threatening illness.

Propofol Injection should be visually inspected for particulate matter, emulsion separation and/or discolouration prior to use. Do not use if any of these things are seen. If no signs of particulate matter, emulsion separation and/or discolouration are seen, shake gently before use.

Dosage and rate of administration should be individualized and titrated to the desired effect according to clinically relevant factors including preinduction and concomitant medications, age, ASA status and level of debilitation of the patient. In heavily premedicated patients, both the induction and maintenance doses should be reduced.

Propofol Injection should not be co-administered through the same intravenous catheter with blood or plasma because compatibility has not been established. *In vitro* tests have shown that aggregates of the globular component of the emulsion vehicle have occurred with blood/plasma/serum from humans and animals. The clinical significance is not known.

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

The administration of Propofol Injection should be initiated as a continuous infusion and changes in the rate of administration made slowly (>5 min) in order to minimize hypotension and avoid acute overdosage.

Since Propofol Injection is formulated in an oil-water emulsion, patients should be monitored for lipemia. Administration of Propofol Injection should be adjusted if fat is being inadequately cleared from the body. A reduction in the quantity of concurrently administered lipids is indicated to compensate for the amount of lipid infused as part of the Propofol Injection formulation; 1 mL of Propofol Injection contains approximately 0.1 g of fat (1.1 kcal).

In adults and children, attention should be paid to minimize pain on administration of propofol. Transient local pain during intravenous injection may be reduced by prior injection of intravenous lidocaine (1 mL of a 1% solution).

Concomitant use of midazolam, has been reported to prolong the anesthesia and to reduce the respiratory rate. (see 9.4 Drug-Drug Interactions).

4.2 Recommended Dose and Dosage Adjustment

Induction of general anethesia

As with most anesthetic agents, the effects of Propofol Injection may be potentiated in patients who have received intravenous sedative or narcotic premedications shortly prior to induction.

Adults (< 55 years of age):

Most adult patients under 55 years of age and classified ASA I and II are likely to require 2 to 2.5 mg/kg of Propofol Injection for induction when unpremedicated or when premedicated with oral benzodiazepines or intramuscular narcotics. For induction, Propofol Injection should be titrated (approximately 40 mg every 10 seconds by bolus injection or infusion) against the response of the patient until the clinical signs show the onset of general anesthesia.

Geriatric, Debilitated, and ASA Classes III and IV Adults

It is important to be familiar and experienced with the appropriate intravenous use of Propofol Injection before treating elderly, debilitated and/or adult patients in ASA Physical Status Classes III and IV. These patients may be more sensitive to the effects of Propofol Injection; therefore, the dosage of Propofol Injection should be reduced in these patients by approximately 50% (20 mg every 10 seconds) according to their condition and clinical response. A rapid bolus should not be used as this will increase the likelihood of undesirable cardiorespiratory depression including hypotension, apnea, airway obstruction and/or oxygen desaturation (see 7 Warnings and Precautions and Table 1: Dosage Guide for Induction of General Anesthesia).

Cardiac anesthesia

During cardiac anesthesia, a rapid bolus induction should be avoided. A slow rate of approximately 20 mg every 10 seconds until induction onset (0.5 to 1.5 mg/kg) should be used.

Pediatrics (3-18 years of age):

Most children over 8 years of age require approximately 2.5 mg/kg of Propofol Injection for induction of anesthesia. Children 3 to 8 years of age may require somewhat higher doses; however, the dose should be titrated by administering Propofol Injection slowly until the clinical signs show the onset of anesthesia. Reduced dosage is recommended for children of ASA Classes III and IV.

Pediatrics (< 3 years of age):

Propofol Injection is not indicated for induction of anesthesia in children less than 3 years of age.

Table 1: Dosage Guide for Induction of General Anesthesia

Dosage should be individualized:	
Adult Patients < 55 Years of Age	Are likely to require 2 to 2.5 mg/kg (approximately 40 mg every 10 seconds until induction onset).
Elderly, Debilitated and/or Adult ASA III or IV Patients	Are likely to require 1 to 1.5 mg/kg (approximately 20 mg every 10 seconds until induction onset) but dose should be carefully titrated to effect.
Cardiac Anesthesia	Patients are likely to require 0.5 to 1.5 mg/kg (approximately 20 mg every 10 seconds until induction onset).
Neurosurgical Patients	Are likely to require 1 to 2 mg/kg (approximately 20 mg every 10 seconds until induction onset).
Pediatric Patients 3-8 and 8-18 Years of Age	Children over 8 years of age require approximately 2.5 mg/kg. Children 3 to 8 years of age may require somewhat higher doses but doses should be titrated slowly to the desired effect. Reduced dosage is recommended for children of ASA Classes III and IV.
Pediatric Patients < 3 Years of Age	Propofol Injection is not indicated for induction of anesthesia in children less than 3 years of age (see 1.1 Pediatrics and 7 Warnings and Precautions).

MAINTENANCE OF GENERAL ANESTHESIA

Anesthesia can be maintained by administering Propofol Injection by infusion or intermittent intravenous bolus injection. The patient's clinical response will determine the infusion rate or the amount and frequency of incremental injections.

When administering Propofol Injection by infusion, drop counters, syringe pumps or volumetric pumps must be used to provide controlled infusion rates.

Continuous Infusion

Propofol Injection 0.1 to 0.2 mg/kg/min (6 - 12 mg/kg/h) administered in a variable rate infusion with 60% - 70% nitrous oxide and oxygen provides anesthesia for patients undergoing general surgery. Maintenance by infusion of Propofol Injection should immediately follow the induction dose in order to provide satisfactory or continuous anesthesia during the induction phase. During this initial period following the induction injection, higher rates of infusion are generally required (0.15 - 0.2 mg/kg/min; 9 - 12 mg/kg/h) for the first 10 to 15 minutes. Infusion rates should subsequently be decreased by 30% - 50% during the first half-hour of maintenance. Changes in vital signs (increases in pulse rate, blood pressure, sweating and/or tearing) that indicate a response to surgical stimulation or lightening of anesthesia may be controlled by the administration of Propofol Injection 25 mg (2.5 mL) to 50 mg (5 mL) incremental boluses and/or by increasing the infusion rate. If vital sign changes are not controlled after a five-minute period, other means such as a narcotic, barbiturate, vasodilator or inhalation agent therapy should be initiated to control these responses.

For minor surgical procedures (i.e., body surface) 60% to 70% nitrous oxide can be combined with a variable rate Propofol Injection infusion to provide satisfactory anesthesia. With more stimulating surgical procedures (i.e., intra-abdominal) supplementation with intravenous analgesic agents should be considered to provide a satisfactory anesthetic and recovery profile. When supplementation with nitrous oxide is not provided,

administration rate(s) of Propofol Injection and/or opioids should be increased in order to provide adequate anesthesia.

Infusion rates should always be titrated downward in the absence of clinical signs of light anesthesia until a mild response to surgical stimulation is obtained in order to avoid administration of Propofol Injection at rates higher than are clinically necessary. Generally, rates of 0.05 to 0.1 mg/kg/min should be achieved during maintenance in order to optimize recovery times.

During *cardiac anesthesia*, when Propofol Injection is used as the primary agent, maintenance infusion rates should not be less than 0.1 mg/kg/min and should be supplemented with analgesic levels of continuous opioid administration. When an opioid is used as the primary agent, Propofol Injection maintenance rates should not be less than 0.05 mg/kg/min. Higher doses of Propofol Injection will reduce the opioid requirements.

For *children (>3 years of age)*, the average rate of administration varies considerably but rates between 0.1 to 0.25 mg/kg/min (6 - 15 mg/kg/h) should achieve satisfactory anesthesia. These infusion rates may be subsequently reduced depending on patient response and concurrent medication.

Intermittent Bolus

Increments of Propofol Injection 25 mg (2.5 mL) to 50 mg (5 mL) may be administered with nitrous oxide in patients undergoing general surgery. The incremental boluses should be administered when changes in vital signs indicate a response to surgical stimulation or light anesthesia.

Propofol Injection has been used in conjunction with a wide variety of agents commonly used in anesthesia such as atropine, scopolamine, glycopyrrolate, diazepam, depolarizing and nondepolarizing muscle relaxants, and narcotic analgesics, as well as with inhalational and regional anesthetic agents. No pharmacological incompatibilities have been encountered.

Lower doses of Propofol Injection may be required when used as an adjunct to regional anesthesia.

Table 2: Dosage Guide for Maintenance of General Anesthesia

Infusion: Variable rate infusion titrated to the desired clinical effect	
Adult Patients < 55 Years of Age	Generally, 0.1 to 0.2 mg/kg/min (6 to 12 mg/kg/h)
Elderly, Debilitated and/or Adult ASA III or IV Patients	Generally, 0.05 to 0.1 mg/kg/min (3 to 6 mg/kg/h)
Cardiac Anesthesia	Most patients require: • Primary Propofol Injection with Secondary Opioid – 0.1 to 0.15 mg/kg/min (6 to 9 mg/kg/h) • Low Dose Propofol Injection with Primary Opioid – 0.05 to 0.1 mg/kg/min (3 to 6 mg/kg/h)
Neurosurgical Patients	Generally, 0.1 to 0.2 mg/kg/min (6 to 12 mg/kg/h)
Pediatric Patients 3-18 Years of Age	Generally, 0.1 to 0.25 mg/kg/min (6 to 15 mg/kg/h)

Intermittent Bolus: Increments of 25 mg to 50 mg, as needed.

Surgical/Diagnostic Sedation

During sedation, attention must be given to the cardiorespiratory effects of Propofol Injection. Hypotension, apnea, airway obstruction, and/or oxygen desaturation can occur, especially with a rapid bolus injection. During initiation of sedation, slow infusion or slow injection techniques are preferable over rapid bolus administration, and during maintenance of sedation, a variable rate infusion is preferable over intermittent bolus administration in order to minimize undesirable cardiorespiratory effects. In the elderly, debilitated and ASA III or IV patients, rapid (single or repeated) bolus dose administration should not be used for sedation (see 7 Warnings and Precautions, General).

Adults

When Propofol Injection is administered for sedation, rates of administration should be individualized and titrated to clinical response. In most patients, the rates of Propofol Injection administration will be approximately 25 to 30% of those used for maintenance of general anesthesia.

During initiation of sedation, slow injection or slow infusion techniques are preferable over rapid bolus administration. During maintenance of sedation, a variable rate infusion is preferable over intermittent bolus dose administration.

Initiation of Sedation

Slow injection: most adult patients will generally require 0.5 to 1 mg/kg administered over 3 to 5 minutes and titrated to clinical response.

In the elderly, debilitated, hypovolemic and ASA III or IV patients, the dosage of Propofol Injection should be reduced to approximately 70% to 80% of the adult dosage and administered over 3 to 5 minutes.

Infusion: sedation may be initiated by infusing Propofol Injection at 0.066 to 0.1 mg/kg/min (4 - 6 mg/kg/h) and titrating to the desired level of sedation while closely monitoring respiratory function.

Maintenance of Sedation

Patients will generally require maintenance rates of 0.025 to 0.075 mg/kg/min (1.5 - 4.5 mg/kg/h) during the first 10 to 15 minutes of sedation maintenance.

Infusion rates should always be titrated downward in the absence of clinical signs of light sedation until mild responses to stimulation are obtained in order to avoid sedative administration of Propofol Injection at rates higher than are clinically necessary.

In addition to the infusion, bolus administration of 10 to 15 mg may be necessary if a rapid increase in sedation depth is required.

In the elderly, debilitated, hypovolemic and ASA III or IV patients, the rate of administration and the dosage of Propofol Injection should be reduced to approximately 70% to 80% of the adult dosage according to their condition, responses, and changes in vital signs. Rapid (single or repeated) bolus dose administration should not be used for sedation in these patients (see 7 Warnings and Precautions).

Table 3: Dosage Guide for Surgical/Diagnostic Sedation

Dosage and rate should be individualized and titrated to the desired clinical effect:	
Adult Patients < 55 Years of Age	Are likely to require 0.5 to 1 mg/kg over 3 to 5 min to initiate sedation, followed by 0.025 to 0.075 mg/kg/min (1.5 - 4.5 mg/kg/h) for continued sedation.
Elderly, Debilitated, Hypovolemic and/or ASA III or IV patients	The dosage and rate of administration may need to be reduced in these patients by approximately 20 to 30% (see previous section for details).
Pediatric Patients < 18 Years of Age	Propofol Injection is not indicated for sedation during surgical/diagnostic procedures in children under the age of 18, as safety and efficacy have not been established (see 1.1 Pediatrics and 2 Contraindications).

Initiation and maintenance of ICU sedation in intubated, mechanically ventilated adult patients Propofol Injection should be individualized according to the patient's condition and response, blood lipid profile, and vital signs.

Adults

For intubated, mechanically ventilated, adult patients, Intensive Care Unit (ICU) sedation should be initiated slowly with a continuous infusion in order to titrate to desired clinical effect and minimize hypotension. When indicated, initiation of sedation should begin at 0.005 mg/kg/min (0.3 mg/kg/h). The infusion rate should be increased by increments of 0.005 to 0.01 mg/kg/min (0.3 - 0.6 mg/kg/h) until the desired level of sedation is achieved. A minimum period of 5 minutes between adjustments should be allowed for onset of peak drug effect.

Most adult patients require maintenance rates of 0.005 to 0.05 mg/kg/min (0.3 - 3 mg/kg/h). Administration of Propofol Injection for ICU sedation in adult patients should not exceed 4 mg/kg/hour. Dosages of Propofol Injection should be reduced in patients who have received large dosages of narcotics. As with other sedative medications, there is interpatient variability in dosage requirements and these requirements may change with time. (See Table 4: Dosage Guide for Initiation and Maintenance of ICU Sedation in Intubated, Mechanically Ventilated Adult Patients).

Bolus administration of 10 to 20 mg should only be used to rapidly increase sedation depth in patients where hypotension is not likely to occur. A rapid bolus should not be used, as this will increase the likelihood of hypotension. Patients with compromised myocardial function, intravascular volume depletion or abnormally low vascular tone (e.g., sepsis) may be more susceptible to hypotension.

Children Under 18 Years of Age

Propofol is contraindicated for the sedation of children 18 years or younger receiving intensive care.

Table 4: Dosage Guide for Initiation and Maintenance of ICU Sedation in Intubated, Mechanically Ventilated Adult Patients

Dosage and rate of infusion should be individualized:	
Adult Patients	• For initiation, most patients require an infusion of 0.005 mg/kg/min (0.3 mg/kg/h) for at least 5 minutes. Subsequent increments of 0.005 to 0.01 mg/kg/min (0.3 - 0.6 mg/kg/h) over 5 to 10 minutes may be used until desired level of sedation is achieved. Administration of Propofol Injection for ICU sedation in adult patients should not exceed 4 mg/kg/hour. • For maintenance, most patients require 0.005 to 0.05 mg/kg/min (0.3 - 3 mg/kg/h). • The long-term administration of Propofol Injection to patients with renal failure and/or hepatic insufficiency has not been evaluated.

4.3 Reconstitution

Dilution Prior to Administration

When Propofol Injection is diluted prior to administration, it should only be diluted with 5% Dextrose Injection, USP, and it should not be diluted to a concentration less than 2 mg/mL because it is an emulsion. Dilutions should be prepared aseptically immediately before administration and should not be used beyond 6 hours of preparation. In diluted form, it has been shown to be more stable when in contact with glass than with plastic (95% potency after 2 hours of running infusion in plastic).

Pre-mixing with Alfentanil

Propofol Injection may be pre-mixed with alfentanil injection containing 500 mcg/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.

Propofol Injection can be pre-mixed with alfentanil. Propofol Injection should not be mixed with other therapeutic agents prior to administration.

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

4.4 Administration

Handling Procedures

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. Do not freeze.

Propofol Injection should be visually inspected for particulate matter, emulsion separation and/or discolouration prior to use. Do not use if any of these changes are seen. If no signs of particulate matter, emulsion separation and/or discolouration are seen, shake gently before use.

Aseptic techniques must be applied to the handling of the drug. Propofol Injection contains no antimicrobial preservatives and the vehicle supports growth of microorganisms. When Propofol Injection is to be aspirated, it

should be drawn aseptically into a sterile syringe or intravenous administration set immediately after breaking the vial seal. Administration should commence without delay. Asepsis must be maintained for both Propofol Injection and the infusion equipment throughout the infusion period. Any drugs or fluids added to the infusion line must be administered close to the cannula site. Propofol Injection must not be administered via a microbiological filter.

Propofol Injection is for single use in an individual patient only. If a vial is utilized for infusion, both the reservoir of Propofol Injection and the infusion line must be discarded and replaced as appropriate at the end of the procedure or at 12 hours, whichever is sooner. (When using **diluted** Propofol Injection, see 4.3 Reconstitution).

Administration into a Running Intravenous Catheter

Compatibility of Propofol Injection with the co-administration of blood/serum/plasma has not been established (see 7 Warnings and Precautions, General). Propofol Injection has been shown to be compatible with the following intravenous fluids when administered into a running intravenous catheter:

- 5% Dextrose Injection, USP
- Lactated Ringer's Injection, USP
- Lactated Ringer's and 5% Dextrose Injection
- 5% Dextrose and 0.45% Sodium Chloride Injection, USP
- 5% Dextrose and 0.2% Sodium Chloride Injection, USP

Since Propofol Injection contains no preservative or bacteriostatic agents, any unused portions of Propofol Injection or solutions containing Propofol Injection should be discarded at the end of the surgical procedure.

5. Overdose

To date, no specific information on emergency treatment of overdosage is available. If accidental overdosage occurs, Propofol Injection administration should be discontinued immediately. Overdosage is likely to cause cardiorespiratory depression. Respiratory depression should be treated by artificial ventilation with oxygen. Cardiovascular depression may require repositioning of the patient by raising the patient's legs, increasing the flow rate of intravenous fluids and, if severe, may require the administration of plasma volume expanders and/or pressor agents.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage forms, Strengths, Composition, and Packaging

Table 5: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Intravenous	Emulsion 10 mg / mL (1% w / v)	Glycerol, medium-chain triglycerides, oleic acid, purified egg phospholipids, sodium hydroxide, soybean oil, and water for injection.

Composition

Propofol Injection is a white, oil in water emulsion. Each mL contains 10 mg of propofol for intravenous administration. In addition to the active component, propofol, the formulation also contains soybean oil (50 mg/mL), medium-chain triglycerides (50 mg/mL), glycerol (22.5 mg/mL), purified egg phospholipids (12 mg/mL), oleic acid (0.4 mg/mL for pH adjustment and as co-emulsion), and water for injection with sodium hydroxide to adjust pH. It is isotonic with a pH of 6 - 8.5.

Dosage Forms and Packaging

Propofol Injection is available as propofol 1% w/v in 20 mL glass vial, 50 mL and 100 mL glass bottles for single use infusion only. Each vial and bottle contains 10 mg/mL of propofol.

The stopper is not made with natural rubber latex.

7. Warnings and Precautions

General

Very rarely, reports of metabolic acidosis, rhabdomyolysis, hyperkalemia, Brugada-type ECG changes (coved ST segment elevation, similar to the Brugada syndrome) and cardiac failure, in some cases with a fatal outcome, have been received concerning seriously ill patients receiving propofol for ICU sedation (see 8.5 Post-Market Adverse Reactions). The combinations of these events have been referred to as Propofol Infusion Syndrome (PIS). 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 doses of one or more of the following pharmacological agents – vasoconstrictors, steroids, inotropes and/or propofol.

All sedatives and therapeutic agents used in the ICU (including propofol) should be titrated to maintain optimal oxygen delivery and hemodynamic parameters.

Patients should be followed up post-operatively after exposure to Propofol Injection as appropriate to identify potential adverse effects.

Cardiovascular

Extreme care should be used in administering Propofol Injection in patients with impaired left ventricular function because Propofol Injection may produce a negative inotropic effect.

Extreme care should be used in administering Propofol Injection in patients who are hypotensive, hypovolemic or in shock because Propofol Injection may cause excessive arterial hypotension.

Propofol injectable emulsion 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 anesthesia should be considered, especially in situations where vagal tone is likely to predominate or when Propofol Injection is used in conjunction with other agents likely to cause bradycardia.

Patients should be monitored for early signs of significant hypotension and/or cardiovascular depression, which may be profound. These effects are responsive to discontinuation of Propofol Injection, intravenous fluid administration, and/or vasopressor therapy.

Cardiac Anesthesia

Propofol injectable emulsion was evaluated in 328 patients undergoing coronary artery bypass graft (CABG). Of these patients 85% were males (mean age 61, range 32-83) and 15% were females (mean age 65, range 42-86). The majority of patients undergoing CABG had good left ventricular function. Experience in patients with poor left ventricular function, as well as in patients with hemodynamically significant valvular or congenital heart disease, is limited.

Slower rates of administration should be utilized in premedicated patients, geriatric patients, patients with recent fluid shift, or patients who are hemodynamically unstable. Any fluid deficits should be corrected prior to the administration of Propofol Injection. In those patients where additional fluid therapy may be contraindicated, other measures, e.g., elevation of lower extremities or use of pressor agents, may be useful to offset the hypotension which is associated with the induction of anesthesia with Propofol Injection.

Dependence, Tolerance and/or Abuse Liability

There are reports of the abuse of propofol for recreational and other improper purposes, which have resulted in fatalities and other injuries. Instances of self -administration of propofol injectable emulsion by health care professionals have also been reported, which have resulted in fatalities and other injuries.

Driving and Operating Machinery

Patients receiving Propofol Injection on an outpatient basis should not engage in hazardous activities requiring complete mental alertness such as driving a motor vehicle or operating machinery until the effects of Propofol Injection have completely subsided.

Endocrine and Metabolism

Propofol Injection should not be used for Intensive Care Unit (ICU) sedation in patients who have severe lipidemia or severely disordered fat metabolism because the vehicle of Propofol Injection is a lipid emulsion. Therefore, the restrictions that apply to lipid emulsions should also be considered when using Propofol Injection in the ICU. Propofol Injection should be given with caution in conditions of impaired lipid metabolism as in renal insufficiency, uncompensated diabetes mellitus, pancreatitis, impaired liver function, hypothyroidism (if hypertri-glyceridemic) and sepsis. If given to patients with these conditions, close monitoring of the serum triglyceride concentration is obligatory: fat elimination should be checked daily and the dosage adjusted to the patient's capacity for fat elimination. In cases of verified or suspected liver insufficiency, liver function must be closely followed.

Hepatic/Biliary/Pancreatic

The long-term administration of propofol injectable emulsion to patients with hepatic insufficiency has not been evaluated.

Immune

Use of propofol injectable emulsion has been associated with both fatal and life-threatening anaphylactic and anaphylactoid reactions.

Neurologic

Neurosurgical Anesthesia

When using Propofol Injection in patients with increased intracranial pressure (ICP) or impaired cerebral circulation, significant decreases in mean arterial pressure should be avoided because of the resultant decreases in cerebral perfusion pressure. When increased ICP is suspected, hyperventilation and hypocarbia should accompany the administration of Propofol Injection (see 4 Dosage and Administration).

Epilepsy

Since various manifestations of seizures have been reported during propofol injectable emulsion anesthesia, special care should be taken when giving the drug to epileptic patients.

Ophthalmologic

Preliminary findings in patients with normal intraocular pressure indicate that propofol anesthesia produces a decrease in intraocular pressure which may be associated with a concomitant decrease in systemic vascular resistance.

Peri-Operative Considerations

As with other sedative medications, there is wide interpatient variability in Propofol Injection dosage requirements, and these requirements may change with time.

Patients who receive large doses of narcotics during surgery may require very small doses of Propofol Injection for appropriate sedation.

When Propofol Injection is administered as a sedative for surgical or diagnostic procedures, patients should be continuously monitored by persons not involved in the conduct of the surgical/diagnostic procedure. Oxygen supplementation should be immediately available and provided where clinically indicated; and oxygen saturation should be monitored in all patients. Patients should be continuously monitored for early signs of hypotension, apnea, airway obstruction and/or oxygen desaturation. These cardiorespiratory effects are more likely to occur following rapid initiation (loading) boluses or during supplemental maintenance boluses, especially in the elderly, debilitated and ASA III or IV patients.

Patients should be continuously monitored for early signs of significant hypotension and/or bradycardia. Treatment may include increasing the rate of intravenous fluid, elevation of lower extremities, use of pressor agents or administration of anticholinergic agents (e.g., atropine) or use of plasma volume expanders. Apnea often occurs during induction and may persist for more than 60 seconds. Ventilatory support may be required. Because Propofol Injection is a lipid emulsion, caution should be exercised in patients with disorders of lipid metabolism such as primary hyperlipoproteinemia, diabetic hyperlipemia and pancreatitis.

As with other sedative agents, when Propofol Injection 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.

Abrupt discontinuation of Propofol Injection infusion prior to weaning should be avoided since, due to the rapid clearance of Propofol Injection, it may result in rapid awakening with associated anxiety, agitation and resistance to mechanical ventilation. Infusions of Propofol Injection should be adjusted to maintain a light level of sedation throughout the weaning process.

Since Propofol Injection is rarely used alone, an adequate period of evaluation of the awakened patient is indicated to ensure satisfactory recovery from general anesthesia or sedation prior to discharge of the patient from the recovery room or to home. Very rarely, the use of Propofol Injection 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.

Propofol Infusion Syndrome (PIS)

Use of propofol injectable emulsion infusions for both adult and pediatric ICU sedation has been associated with a constellation of metabolic derangements and organ system failures, referred to as Propofol Infusion Syndrome, that have resulted in death.

The syndrome is characterized by severe metabolic acidosis, hyperkalemia, lipemia, rhabdomyolysis, hepatomegaly, cardiac and renal failure. The syndrome is most often associated with prolonged, high-dose infusions (> 5 mg/kg/h for > 48 h) but has also been reported following large-dose, short-term infusions during surgical anesthesia. 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.

Renal

The long-term administration of propofol injectable emulsion to patients with renal failure has not been evaluated.

7.1 Special Populations

7.1.1 Pregnancy

Propofol Injection should not be used during pregnancy unless absolutely necessary. Propofol injectable emulsion has been used during termination of pregnancy in the first trimester.

Propofol Injection should not be used in obstetrics including Caesarean section deliveries, because Propofol Injection crosses the placenta and may be associated with neonatal depression. Studies in animals have shown reproductive toxicity. See 16 Non-Clinical Toxicology, Reproductive and Developmental Toxicology.

7.1.2 Breastfeeding

Propofol Injection is not recommended for use in breast-feeding women because preliminary findings indicate that it is excreted in human milk and the effects of oral absorption of small amounts of propofol injectable emulsion are not known.

7.1.3 Pediatrics

Pediatrics (≤ 18 years of age): In the absence of sufficient clinical experience, Propofol Injection is not indicated for anesthesia in children less than 3 years of age (see 1.1 Pediatrics and 4 Dosage and Administration).

Propofol Injection is not indicated for sedation or during surgical/diagnostic procedures in children under the age of 18, as safety and efficacy have not been established in this patient population. (see 1.1 Pediatrics).

7.1.4 Geriatrics

Geriatrics (> 55 years of age): Elderly patients may be more sensitive to the effects of Propofol Injection; therefore, the dosage of Propofol Injection should be reduced in these patients according to their condition and clinical response (see 10.3 Pharmacokinetics and 4 Dosage and Administration).

Elderly, Debilitated, or Other ASA III or IV Patients

Extreme care should be used in administering Propofol Injection in elderly, debilitated or other ASA III or IV patients. In the elderly, debilitated and ASA III or IV patients, rapid (single or repeated) bolus administration should not be used during general anesthesia or sedation in order to minimize undesirable cardiorespiratory depression including hypotension, apnea, airway obstruction and/or oxygen desaturation.

Age is highly correlated with the fall in blood pressure. In elderly subjects, both the incidence and degree of hypotension are greater than in younger subjects. Thus, a lower induction dose and a slower maintenance rate of administration should be used in the elderly (see 4 Dosage and Administration). Particular caution should be exercised in elderly patients with severe coronary and/or cerebral arteriosclerosis; reduction in perfusion pressure may impair adequate blood supply to these organs.

Insufficient data are available regarding the cardiovascular effects of propofol when used for induction and/or maintenance of anesthesia or sedation in elderly, hypotensive, debilitated or other ASA III and IV patients. However, limited information suggests that these patients may have more profound cardiovascular responses. It is recommended that, if propofol is used in these patients, a lower induction dose and a slower maintenance rate of administration of the drug be used.

8. Adverse Reactions

8.1 Adverse Reaction Overview

Anesthesia and Sedation for Surgical/Diagnostic Procedures

During induction of anesthesia in clinical trials, hypotension and apnea occurred in the majority of patients. The incidence of apnea varied considerably, occurring in between 30 and 100% of patients depending upon premedication, speed of administration and dose (see 10 Clinical Pharmacology). Decreases in systolic and diastolic pressures ranged between 10 and 28%, but were more profound in the elderly and in ASA III and IV patients.

Excitatory phenomena occurred in up to 14% of adult patients and in 33 to 90% of pediatric patients; they consisted most frequently of spontaneous musculoskeletal movements and twitching and jerking of the hands, arms, feet or legs. Epileptiform movements including convulsions and opisthotonus have occurred rarely, but a causal relationship with propofol injectable emulsion has not been established. A feeling of euphoria occurred rarely in patients.

Flushing and rash have occurred in 10 to 25% of pediatric patients. Local pain occurred during intravenous injection of propofol injectable emulsion at an incidence of 28% when veins of the dorsum of the hand were used and 5% when the larger veins of the forearm and the antecubital fossa were used. Propofol injectable emulsion increased plasma glucose concentrations significantly, but no other significant changes in hematological or biochemical values were observed.

In the sedation clinical trials, the adverse reaction profile of propofol injectable emulsion was similar to that seen during anesthesia. The most common adverse reactions included hypotension, nausea, pain and/or

hotness at injection site and headache. Respiratory events included upper airway obstruction, apnea, hypoventilation, dyspnea and cough.

Rarely, clinical features of anaphylaxis, which may include angioedema, bronchospasm, erythema and hypotension, occur following propofol injectable emulsion administration. In addition, a feeling of euphoria occurred rarely in patients.

Very rarely, the use of propofol injectable emulsion 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.

There have been reports of post-operative fever.

Pulmonary edema may be a potential side effect associated with the use of propofol injectable emulsion.

As with other anesthetics, sexual disinhibition may occur during recovery.

Intensive Care Unit (ICU) Sedation-Adults

The most frequent adverse reactions during Intensive Care Unit (ICU) sedation were hypotension (31.5%), hypoxia (6.3%), and hyperlipemia (5.5%). In some patients, hypotension was severe. Other reactions considered severe were observed in single patients and included ventricular tachycardia, decreased cardiac output, decrease in vital capacity and negative inspiratory force, increase in triglycerides, and agitation. Two patients with head injury suffered renal failure with severe increases in BUN accompanied in one patient by an increase in creatinine.

There have been very rare reports of rhabdomyolysis when propofol injectable emulsion has been administered at doses greater than 4 mg/kg/hr for ICU sedation.

Very rarely, pancreatitis has been observed following the use of propofol injectable emulsion for induction and maintenance of anesthesia, and for intensive care sedation. A causal relationship has not been clearly established.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

The following table compares the overall occurrence rates of adverse reactions in propofol injectable emulsion patients from non-ICU and ICU clinical trials where the rate of occurrence was greater than 1%. Major differences include lack of metabolic/nutritional (hyperlipemia) and respiratory events in the non-ICU group and lack of nausea, vomiting, headache, movement and injection site events in the ICU group.

Table 6: Non-ICU vs. ICU Adverse Events Occurring in Greater than 1% of Propofol Injectable Emulsion Patients

Body System	Event	Non-ICU	ICU
Number of patients		2588	127
Cardiovascular	Hypotension	7.38%	31.5%
	Bradycardia	2.82%	3.94%
	Hypertension	2.82%	1.57%

Body System	Event	Non-ICU	ICU
	Arrhythmia	1.24%	0.79%
	Tachycardia	0.81%	3.15%
	Cardiovascular Disorder	0.23%	2.36%
	Hemorrhage	0.23%	1.57%
	Atrial Fibrillation	0.15%	1.57%
	Cardiac Arrest	0.12%	3.15%
	Ventricular Tachycardia	0.08%	1.57%
Digestive	Nausea	14.57%	0%
	Vomiting	8.31%	0%
	Abdominal Cramping	1.24%	0%
Nervous	Movement	4.44%	0%
	Headache	1.78%	0%
	Dizziness	1.7%	0%
	Twitching	1.47%	0%
	Agitation	0.19%	2.36%
	Intracranial Hypertension	0%	3.94%
Metabolic/Nutritional	Hyperlipemia	0.08%	5.51%
	Acidosis	0.04%	1.57%
	Creatinine Increased	0%	2.36%
	BUN Increased	0%	1.57%
	Hyperglycemia	0%	1.57%
	Hypernatremia	0%	1.57%
	Hypokalemia	0%	1.57%
Respiratory	Dyspnea	0.43%	1.57%
	Hypoxia	0.08%	6.3%
	Acidosis	0%	1.57%
	Pneumothorax	0%	1.57%
Other	Injection Site:		
	Pain	8.11%	0%
	Burning/stinging	7.77%	0%
	Fever	1.89%	2.36%

Body System	Event	Non-ICU	ICU
	Hiccough	1.78%	0%
	Cough	1.55%	0%
	Rash	1.2%	1.57%
	Anemia	0.35%	1.57%
	Kidney Failure	0%	1.57%

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Propofol Injection is only indicated for anesthesia in children 3 years of age and older.

Generally the adverse experience profile from reports of 506 propofol injectable emulsion pediatric patients from 6 days through 16 years of age in the US/Canadian anesthesia clinical trials is similar to the profile established with propofol injectable emulsion during anesthesia in adults.

Although not reported as an adverse event in clinical trials, apnea is frequently observed in pediatric patients.

Although propofol injectable emulsion is not indicated for sedation or during surgical/diagnostic procedures in children under the age of 18, a randomised, controlled, clinical trial that evaluated the safety and effectiveness of propofol injectable emulsion versus standard sedative agents (SSA) in pediatric ICU patients has been conducted. In that study, a total of 327 pediatric patients were randomised to receive either propofol injectable emulsion 2% (113 patients), propofol injectable emulsion 1% (109 patients), or an SSA (e.g., lorazepam, chloral hydrate, fentanyl, ketamine, morphine, or phenobarbital). Propofol injectable emulsion therapy was initiated at an infusion rate of 5.5 mg/kg/hr and titrated as needed to maintain sedation at a standardized level. The results of the study showed an increase in the number of deaths in patients treated with propofol injectable emulsion as compared to SSAs. A total of 25 patients died during the trial or within the 28-day follow-up period: 12 (11%) in the propofol injectable emulsion 2% treatment group, 9 (8%) in the propofol injectable emulsion 1% treatment group, and 4 (4%) in the SSA treatment group.

8.3 Less Common Clinical Trial Adverse Reactions

Less Common Clinical Trial Adverse Drug Reactions (≤ 1 %) reported during anesthesia and sedation for surgical/diagnostic procedures:

Cardiovascular System

Significant hypotension, premature atrial contractions, premature ventricular contractions, tachycardia, syncope, abnormal ECG, bigeminy, edema.

Central Nervous System

Confusion, dizziness, paresthesia, somnolence, shivering, abnormal dreams, agitation, delirium, euphoria, fatigue.

Digestive System

Hypersalivation, dry mouth.

Excitatory

Hypertonia, dystonia, rigidity, tremor.

Injection Site

Phlebitis, thrombosis, hives/itching, redness/discolouration.

Musculoskeletal

Myalgia.

Respiratory System

Burning in throat, tachypnea, dyspnea, upper airway obstruction, wheezing, bronchospasm, laryngospasm, hypoventilation, hyperventilation, sneezing.

Senses (Ear and Eye)

Diplopia, amblyopia, tinnitus

Skin and Subcutaneous Tissue

Flushing/rash (for incidence in children, see above), urticaria, pruritus.

Special Senses

Diplopia, amblyopia, tinnitus.

Urogenital

Urine retention, discolouration of urine.

Less Common Adverse Drug Reactions (≤ 1%) reported during ICU sedation.

Body as a Whole

Sepsis, trunk pain, whole body weakness.

Cardiovascular

Arrhythmia, extrasystole, heart block, right heart failure, bigeminy, ventricular fibrillation, heart failure, myocardial infarction.

Central Nervous System

Seizure, thinking abnormal, akathisia, chills, anxiety, confusion, hallucinations.

Digestive

Ileus, hepatomegaly.

Metabolic/Nutritional

Osmolality increased.

Respiratory

Lung function decreased, respiratory arrest.

Urogenital

Green urine, urination disorder, oliguria.

8.5 Post-Market Adverse Reactions

Propofol Infusion Syndrome (PIS)

There are several publications identifying an association in adults between high infusion rates (greater than 5 mg/kg/h) of propofol for more than 48 hours in ICUs and a potentially fatal constellation of adverse events characterized by metabolic acidosis, rhabdomyolysis, hyperkalemia, and cardiovascular collapse (see 7 Warnings and Precautions).

The majority of the above-reported cases occurred in adults with head injury. These patients were treated with propofol at infusion rates greater than 5 mg/kg/h in an attempt to control intracranial hypertension. It is unclear at this time whether propofol at these high infusion rates can provide enhanced intracranial pressure reduction. A causal relationship between these adverse events and propofol and/or the lipid carrier cannot yet be established.

Similar findings were first reported in the literature in 1992 in children who received high doses of propofol in the ICU. Since the 1992 publication, several similar reports have been published, including an article that summarized 18 cases of children who received propofol infusions and suffered serious adverse events, including death.

Drug Abuse and Dependence

Rare cases of self-administration of propofol injectable emulsion by health care professionals have been reported, including some fatalities.

Priapism

Cases of priapism have been observed.

Hepatic/Biliary/Pancreatic

Hepatitis and acute hepatic failure

9. Drug Interactions

9.2 Drug Interactions Overview

Propofol may increase the CNS depressant, respiratory depressant, or hypotensive effects of other medications.

9.3 Drug-Behaviour Interactions

Concomitant use of central nervous depressants such as alcohol will result in intensification of their sedative effects.

9.4 Drug-Drug Interactions

Propofol injectable emulsion has been used in association with spinal and epidural anesthesia and with a range of premedicants, muscle relaxants, inhalational agents, analgesic agents and with local anesthetic agents.

The concurrent administration of Propofol Injection with these and other central nervous system depressants such as alcohol and anesthetic agents may add to the sedative, anesthetic and cardiorespiratory depressant effects of Propofol Injection. During induction of anesthesia, hypotension and transient apnea may occur depending on the dose and use of premedicants and other agents.

The combination of propofol and alfentanil is likely to produce greater sedation and anesthetic effects. In addition, alfentanil enhances the depressant effects of propofol on systolic blood pressure and heart rate. When used concomitantly, a dose adjustment of propofol or alfentanil should be considered. Furthermore, in the presence of propofol injectable emulsion, alfentanil concentrations were higher than expected based upon the rate of infusion. However, alfentanil did not affect the pharmacokinetics of propofol injectable emulsion (see 4.4 Dosage and Administration, Administration).

Propofol dose required for sedation and induction of anesthesia may need to be reduced in the presence of dexmedetomidine. In addition, based on literature reports and case analyses, co-administration of dexmedetomidine with propofol is linked with pyrexia and hyperpyrexia.

Propofol and sevoflurane causes additive effects on anesthesia when used in combination. Hence, when used concomitantly, a dose adjustment of propofol or sevoflurane should be considered.

A need for lower propofol doses has been observed in patients taking midazolam. The co-administration of propofol with midazolam is likely to result in enhanced sedation and respiratory depression. When used concomitantly, a dose reduction of propofol should be considered. Concomitant use also decreases the clearance of midazolam.

In the presence of a potent opioid (e.g. fentanyl), the blood pressure lowering effect of propofol is substantially increased. Fentanyl also decreases heart rate and this might lead to a significant decrease in cardiac output.

In pediatric patients, administration of fentanyl concomitantly with Propofol Injection may result in serious bradycardia.

Opioid premedication - in the presence of hyoscine - affected respiratory function (rate of respiration and minute volume) substantially more than atropine premedication. Respiratory function was more depressed when these premedicants were combined with propofol than when they were combined with thiopental. Enhanced respiratory depression with propofol and an opioid have been observed in the post-operative period.

9.5 Drug-Food Interactions

Interactions of propofol with food have not been established.

9.6 Drug-Herb Interactions

Interactions of propofol with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions of propofol with laboratory tests have not been established.

10. Clinical Pharmacology

10.1 Mechanism of Action

Propofol is an intravenous hypnotic agent for use in the induction and maintenance of general anesthesia or sedation.

The mechanism of action, like all general anesthetics, is poorly understood. However, propofol is thought to produce its sedative/anesthetic effects by the positive modulation of the inhibitory function of the neurotransmitter GABA through the ligand-gated $GABA_A$ receptors.

Intravenous injection of a therapeutic dose of propofol produces hypnosis rapidly and smoothly, usually within 40 seconds from the start of an injection (one arm-brain circulation time), although induction times > 60 seconds have been observed.

10.2 Pharmacodynamics

Propofol induces anesthesia in a dose-dependent manner. In unpremedicated, ASA I or II patients, propofol induced anesthesia in 87% and 95% of patients at doses of 2 and 2.5 mg/kg, respectively. Elderly patients require lower doses; for unpremedicated patients older than 55 years of age, the mean dose requirement was 1.66 mg/kg. Premedication profoundly alters dose requirements; at 1.75 mg/kg, propofol induced anesthesia in 65% of patients who had no premedication and in 85% and 100% of patients who received diazepam or papaveretum-hyoscine premedication, respectively.

During induction of anesthesia, the hemodynamic effects of propofol vary. If spontaneous ventilation is maintained, the major cardiovascular effects are arterial hypotension (sometimes greater than a 30% decrease) with little or no change in heart rate and no appreciable decrease in cardiac output. If ventilation is assisted or controlled (positive pressure ventilation), the degree and incidence of decrease in cardiac output are accentuated. Maximal fall in blood pressure occurs within the first few minutes of the administration of a bolus dose. The fall in arterial pressure is greater under propofol anesthesia than under anesthesia induced by thiopental or methohexital. Increases in heart rate with propofol are generally less pronounced or absent after an induction dose, than after equivalent doses of these other two agents.

During maintenance of anesthesia with propofol, systolic and diastolic blood pressures generally remain below pre-anesthetic levels, although the depth of anesthesia, the rate of maintenance infusion as well as stimulation from tracheal intubation and/or surgery may increase or decrease blood pressure. Heart rate may also vary as a function of these factors but will generally remain below pre-anesthetic levels (see 7 Warnings and Precautions and 4 Dosage and Administration).

The first respiratory disturbance after a bolus dose of propofol is a profound fall in tidal volume leading to apnea in many patients. There has been no accompanying cough or hiccough and otherwise anesthesia is smooth. However, there might be some difficulty in uptake of volatile agents if respiration is not assisted.

In unpremedicated healthy patients, there is a steep dose-response relationship regarding apnea; 0% and 44% of patients had apnea after receiving 2 and 2.5 mg/kg of propofol, respectively. Fentanyl enhanced both the incidence and the onset of apnea and the episode lasted for > 60 seconds in the majority of patients.

During maintenance, propofol (0.1 to 0.2 mg/kg/min; 6 - 12 mg/kg/h) caused a decrease in ventilation usually associated with an increase in carbon dioxide tension which may be marked depending upon the rate of

administration and other concurrent medication (e.g., narcotics, sedatives, etc.). Propofol was not evaluated in patients with any respiratory dysfunction.

Clinical and preclinical studies suggest that propofol is rarely associated with elevation of plasma histamine levels and does not cause signs of histamine release.

Clinical and preclinical studies show that propofol does not suppress the adrenal response to ACTH.

Propofol is devoid of analgesic or antanalgesic activity.

10.3 Pharmacokinetics

The pharmacokinetic profile of propofol can be described by a 3-compartment open model. After a single-bolus dose, there is fast distribution from blood into tissues ($t_{½}$ α: 1.8 to 8.3 min), high metabolic clearance ($t_{½}$ β: 34 to 66 min) and a terminal slow elimination from poorly perfused tissues ($t_{½}$ γ: 184 to 480 min). With 12- and 24-hour samplings, $t_{½}γ$ values of 502 and 674 min, respectively, were observed.

When given by an infusion for up to two hours, the pharmacokinetics of propofol appear to be independent of dose (0.05 - 0.15 mg/kg/min; 3 - 9 mg/kg/h) and similar to intravenous bolus pharmacokinetics. Pharmacokinetics are linear over recommended infusion rates.

Propofol is highly protein-bound (97 - 99%); the degree of binding seems to be unrelated to either sex or age.

Pharmacokinetics in Adult Patients in Intensive Care Unit (ICU)

Regarding most parameters, the pharmacokinetics of propofol in these patients are similar to those of patients undergoing anesthesia/sedation for short surgical procedures. However, the terminal half-life ($t_{½}γ$) is substantially prolonged after long-term infusion, reflecting extensive tissue distribution.

Distribution:

Propofol has large volumes of distribution as would be expected with a highly lipophilic anesthetic agent. The volume of central compartment (V_c) is between 21 and 56 L (0.35 - 0.93 L/kg based on a 60 kg patient), and the volume of distribution at steady state (V_{ss}) is between 171 and 364 L (2.85 - 6.07 L/kg). Values for volume of distribution during the terminal phase (V_d) are two to three times the corresponding V_{ss} values.

Metabolism:

The termination of the anesthetic or sedative effects of propofol after a single intravenous bolus or a maintenance infusion is due to extensive redistribution from the CNS to other tissues and high metabolic clearance, both of which will decrease blood concentrations. The mean propofol concentration at time of awakening is 1 mcg/mL (range: 0.74 to 2.2 mcg/mL). Recovery from anesthesia or sedation is rapid. When propofol is used for both induction (2 to 2.5 mg/kg) and maintenance (0.1 to 0.2 mg/kg/min) of anesthesia, the majority of patients are generally awake, responsive to verbal command and oriented in approximately 7 to 8 minutes. Recovery from the effects of propofol occurs due to rapid metabolism and is not dependent on the terminal elimination half-life since the blood levels achieved in this phase are not clinically significant.

Elimination:

A study in six subjects showed that 72% and 88% of the administered radio-labelled dose was recovered in the urine within 24 hours and 5 days, respectively. Less than 2% was excreted in the feces. Unchanged drug was less than 0.3%. Propofol is chiefly metabolized by conjugation in the liver to inactive metabolites which are excreted by the kidney. Propofol glucuronide accounts for about 50% of the administered dose. The remainder consists of the 1- and 4-glucuronide and 4-sulphate conjugates of 2,6-diisopropyl-1,4-quinol.

The total body clearance (Cl) of propofol ranges from 1.6 L/min to 2.3 L/min (0.026 - 0.038 L/min/kg based on a 60 kg patient). This clearance exceeds estimates of hepatic blood flow, suggesting possible extrahepatic metabolism.

Special Populations and Conditions

- **Pediatrics** The results were obtained in ASA I children, ranging in age from 3 to 10 years, who received a single-bolus dose of propofol, 2.5 mg/kg. Propofol was rapidly distributed from blood into tissue ($t_{½}\alpha$: 1.5 - 4.1 min), metabolic clearance was high ($t_{½}\beta$: 9.3 - 56.1 min) and terminal elimination slow ($t_{½}\gamma$: 209 - 735 min). The volume of central compartment (V_c) ranged between 0.53 - 0.72 L/kg, the volume of distribution at steady state (V_{ss}) was between 2.1 - 10.9 L/kg and clearance (Cl) ranged between 0.032 - 0.04 L/min/kg. The mean plasma concentration of propofol at awakening was 2.3 mcg/mL.
- **Geriatrics** With increasing age, the dose of propofol injectable emulsion needed to achieve a defined anesthetic endpoint (dose-requirement) decreases. Elderly patients had higher propofol blood concentrations at 2 minutes than young ones (6.07 versus 4.15 mcg/mL), probably due to a significantly lower initial distribution volume (20 L versus 26 L). The relatively high blood concentrations during the first few minutes can predispose elderly patients to cardiorespiratory effects including hypotension, apnea, airway obstruction and/or oxygen desaturation. The clearance of propofol injectable emulsion also decreased from a mean ± S.D. of 1.8 ± 0.4 L/min in young patients (18 - 35 years) to 1.4 ± 0.4 L/min in elderly patients (65 - 80 years). The reduced clearance could decrease maintenance propofol requirements and prolong recovery if inappropriate infusions are used. Obesity is associated with significantly larger volumes of distribution (399 L versus 153 L) and clearance rates (2.8 L/min versus 1.8 L/min) but there is no change in the elimination half-life.
- **Sex** The pharmacokinetics of propofol injectable emulsion do not appear to be altered by sex.
- **Hepatic Insufficiency** The pharmacokinetics of propofol injectable emulsion do not appear to be altered by chronic hepatic cirrhosis. The effects of acute hepatic failure on the pharmacokinetics of propofol injectable emulsion have not been studied.
- **Renal Insufficiency** In renal failure, the data is based on very limited findings. There was a trend towards longer half-lives, although the differences versus control patients did not reach statistical significance.

11. Storage, Stability, and Disposal

Store at 2 °C to 25 °C; do not freeze. The emulsion should be visually inspected for particulate matter, emulsion separation and/or discolouration prior to use. Do not use if any of these things are seen. If no signs of particulate matter, emulsion separation and/or discolouration are seen, shake gently before use. Any unused portions of Propofol Injection or solutions containing Propofol Injection should be discarded at the end of the surgical procedure.

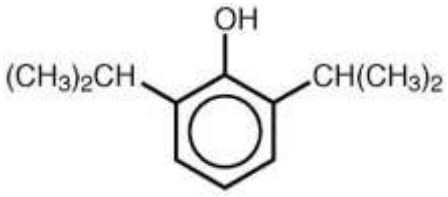
12. Special Handling Instructions

There are no special handling instructions for Propofol Injection.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Proper name:	Propofol
Chemical name:	2,6-diisopropylphenol or 2,6-bis(1-methylethyl)phenol
Molecular formula and molecular mass:	$C_{12}H_{18}O$, 178.27 g/mol
Structural formula:	
Physicochemical properties:	Colourless or very lightly yellow clear liquid. Very soluble in methanol and in ethanol, slightly soluble in cyclohexane and in isopropyl alcohol, very slightly soluble in water, miscible with hexane. pK_a of 11.1 in water and a Melting Point of 18 °C.
Pharmaceutical standard:	Mfr. Std.

14. Clinical Trials

Information on clinical trials is unavailable.

16. Non-Clinical Toxicology

General Toxicology:

Studies in Rats and Mice

Rats and mice of the Alderley Park Albino strain received graded intravenous or oral doses of propofol. At each dose level, six male and six female animals were used. The drug was available as an emulsion for the intravenous studies and as a solution in soya bean oil for the oral studies. At the doses used, all animals became anaesthetized. Several rats and mice, both in the intravenous and oral studies, regained consciousness and then became re-anaesthetized before fully recovering. The LD_{50} values and observations are summarized in Table 7 below.

Table 7: LD_{50} Values and Observations in Rats and Mice

Species	Route of administration	LD_{50} mg/kg (95% Confidence Limits)	Observations
Rats	Intravenous	42 (38-46)	Death occurred within 5 minutes of dosing.
	Oral	600 (540-660)	The majority of rats died 1 to 3 days after propofol administration. Following recovery from anesthesia, several rats exhibited decreased activity, piloerection, hunched posture and tremors.
Mice	Intravenous	53 (46-60)	Death occurred within 2 minutes of dosing and was due to respiratory depression.
	Oral	1230 (1010-1500)	The majority of mice died 1 to 2 days after propofol administration. During anesthesia, both the rate and depth of respiration was decreased. Following recovery from anesthesia, several mice exhibited locomotor incoordination and tremors.

Single-Dose Tolerance Study in Rabbits

Three male and three female Dutch rabbits received propofol, 15 mg/kg, by the intravenous route. The drug was given at a rate of 0.5 mg/kg/second. All rabbits became lightly anaesthetized, with 6/6 rabbits retaining their pedal reflex and 2/6 rabbits retaining their palpebral reflex. Ten to 15 minutes after dosing, all rabbits recovered completely without any untoward effect.

Long-Term Toxicology

One-Month Toxicity Study in Rats

Five groups of albino rats were dosed daily for 28 days. Injections were given intravenously into the tail vein. Group I received saline, Group II the emulsion vehicle, Groups III, IV and V propofol at doses of 5, 10 and 15 mg/kg/day, respectively.

Propofol induced anesthesia in a dose-dependent manner; at 5 mg/kg rats were not anaesthetized while the duration of anesthesia was significantly longer at the 15 mg/kg than at the 10 mg/kg dose. With repeated administration, the duration of anesthesia became prolonged and on Day 26, anesthesia lasted significantly longer than on Day 1.

High dose male rats gained slightly but significantly less weight than control rats (131 versus 150 g). In female rats, weight gain was slightly less in all treated animals, however, the effect was not dose-related. Urine volume was significantly but not dose-dependently elevated on Day 26 in all propofol-treated rats. In female rats, relative kidney weights were significantly and dose-dependently elevated in all propofol-treated groups.

One-Month Toxicity Study in Dogs

Five groups of Beagle dogs were dosed intravenously over a 30-day period. Group I received saline, Group II the emulsion vehicle, and Groups III and IV propofol at doses of 5 and 10 mg/kg/day, respectively. Group V received propofol, 30 mg/kg 3 times weekly for a total of 13 doses.

Each dose consisted of a 7.5 mg/kg bolus dose and an infusion of 0.5 mg/kg/min for a total of 22.5 mg/kg.

Each group was comprised of 5 male and 5 female dogs. In addition, 3 dogs/sex were used to evaluate recovery in the control and high dose groups.

Propofol induced anesthesia in a dose-dependent manner. With repeated administration, the duration of anesthesia became prolonged and on Day 28, anesthesia lasted significantly longer than on Day 1.

During the 30-day treatment period, Hb, RBC and PCV values declined below the normal range in a few animals. On Day 30, abnormally low values were recorded in 3/10 dogs in both Groups III and IV. (In both groups, the same three dogs were affected.) In Groups II and V, 1/16 dogs each showed similar changes.

Reproductive and Developmental Toxicology:

Fertility and Reproductive Performance in Rats

Three groups of 50 rats each were dosed intravenously with the vehicle or propofol at doses of 10 or 15 mg/kg/day for two weeks prior to mating, during the mating period to untreated males and up to Day 7 of gestation. Generally, reproductive studies require that treatment be continued during both gestation and lactation, thus, this study provides information about propofol's effect upon fertility but not necessarily upon reproduction.

Approximately half of the females of the F_0 generation were sacrificed on Day 21 of pregnancy. The remainder were allowed to litter and rear their offspring to weaning at Day 22 of lactation. At weaning, two females and one male were selected from each litter to form the F_1 generation. These animals were kept until sexually mature and then mated. As with the F_0 generation, approximately half the females were sacrificed on Day 21 of pregnancy and the remainder were allowed to litter and rear their young to weaning, when the F_1 dams and their pups (the F_2 generation) were sacrificed.

The administration of propofol was associated with the following changes:

In the F_0 generation, treated rats gained significantly less weight than controls prior to mating (9.7, -0.8 and 1.7 g in the control, low and high dose groups, respectively). However, weight gains between Days 7 and 16, or 1 to 21 of pregnancy, were similar in all three groups.

Gestation period was dose-dependently decreased. In the control, low and high dose groups 9.5, 16 and 33% of the rats, respectively delivered on Day 21, rather than Day 22.

Survival of the F_1 generation pups was lower in the treated groups. On Day 1, the number of alive pups was similar in all three groups. From Day 5 on, survival in treated groups was lower. Numerical values on Day 22 were as follows: 73, 49 and 52% of pups were alive in the control, low and high dose groups, respectively.

Pups which died, were subjected to necropsy. None showed soft tissue abnormalities, however, reduced vertebral ossification was present in 13, 38 and 40% of pups in the control, low and high dose groups, respectively.

Post-implantation loss (as a % of implants) in the F_1 generation was higher in rats born to high dose animals (2.3, 1.2 and 15.6% in control, low and high dose rats, respectively).

Teratology Study in Rats

Four groups of 40 mated female rats each were dosed intravenously with the vehicle or propofol at doses of 5, 10 or 15 mg/kg/day from Day 6 to Day 15 of pregnancy. The rats were sacrificed on Day 20 of pregnancy and the pups checked for internal and skeletal anomalies.

Maternal weight gain during Days 6 to 15 was significantly less in propofol-treated rats than in controls. The incidence of abnormal cranial ossification was higher in fetuses born to high dose dams than in control fetuses (19.9% versus 11%).

In rats, sacrificed on Day 15 of pregnancy, 10 minutes after the last dose, propofol was detected in maternal blood, amniotic fluid and the developing embryo. Drug concentrations increased linearly with increasing doses.

The study indicated that propofol is not teratogenic in rats at the doses studied.

Teratology Study in Rabbits

Four groups of 22 mated female rabbits each were dosed intravenously with the vehicle or propofol at doses of 5, 10 or 15 mg/kg/day from Day 6 to Day 18 of pregnancy. The rabbits were sacrificed on Day 28 of pregnancy.

Maternal weight gain during Days 6 to 18 was less in propofol-treated rabbits than in controls. Incomplete sternebral ossification increased dose-dependently in fetuses born to propofol-treated dams as compared to control fetuses.

Propofol was detected in maternal blood, amniotic fluid and embryonic tissue. Drug concentrations increased in a dose-dependent manner.

The study indicated that propofol is not teratogenic in rabbits at the doses studied.

Perinatal and Post-natal Study in Rats

Three groups of 22 rats each were dosed intravenously with the vehicle or propofol at doses of 10 to 15 mg/kg/day from Day 16 of gestation through Day 22 of lactation. The number of rats in whom treatment was completed was 18, 16 and 12, in the control, low and high dose groups, respectively. In the high dose group, four dams died during dosing, the cause of death might have been due to respiratory depression. In addition, mothers were sacrificed if the litters died. Maternal weight gain, during the last week of pregnancy, was significantly less in high dose rats than in control animals (47.1 versus 60.3 g). Litter survival on Day 22 was slightly but dose-dependently decreased; the percent of litters which survived was 65, 61 and 53% in the control, low and high dose groups, respectively.

Propofol did not affect the gestation period, maternal weight gain during lactation or the weight gain and developmental landmarks of the litter.

Studies in rodents demonstrate that the use of anesthetic agents during the period of rapid brain growth or synaptogenesis results in widespread neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis. Based on comparisons across species, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester through the first several months of life, but may extend out to approximately 3 years of age in humans.

In primates, three hours exposure to an anesthetic regimen that produced a light surgical plane of anesthesia did not increase neuronal cell loss; however, treatment regimens of five hours or longer increased neuronal cell loss. Data in rodents and in primates suggest that the neuronal and oligodendrocyte cell losses are associated with subtle but prolonged cognitive deficits in learning and memory. See 7.1 Special Populations.

17. Supporting Product Monographs

[Pr]DIPRIVAN® 1% (propofol), Emulsion, 10 mg/mL, submission control 295642, Product Monograph, Aspen Pharmacare Canada Inc., (July 28, 2025).

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrPROPOFOL INJECTION

Propofol injectable emulsion

This Patient Medication Information is written for the person who will be taking **Propofol Injection**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **Propofol Injection**, talk to a healthcare professional.

What Propofol Injection is used for:

Propofol Injection is used:

- in adults and children 3 years of age and older during surgery and other medical procedures to make the patient become unconscious (asleep).
- in adults in the Intensive Care Unit (ICU) and in other medical settings to keep patients sedated (a very relaxed state of calm, drowsiness or sleep).

How Propofol Injection works:

Propofol Injection belongs to a group of medicines called general anesthetics. These types of medicines work by causing a loss of feeling and awareness that feels like being in a deep sleep.

The ingredients in Propofol Injection are:

Medicinal ingredient (s): Propofol

Non-medicinal ingredients: glycerol, medium-chain triglycerides, oleic acid, purified egg phospholipids, sodium hydroxide, soybean oil, and water for injection.

Propofol Injection comes in the following dosage form(s):

Emulsion; 10 mg/mL

Do not use Propofol Injection:

- In children under the age of 18 years for sedation during surgical/diagnostic procedures or in the intensive care unit (ICU).
- If you have ever received Propofol Injection before and have experienced an allergic reaction to its use or if you know that you are allergic to propofol or any of the nonmedicinal ingredients (including eggs or egg products and soybeans or soy products) in Propofol Injection (see **The ingredients in Propofol Injection are**).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Propofol Injection. Talk about any health conditions or problems you may have, including:

- All health problems you have now or have had in the past.
- Other medicines you take, including ones you can buy without a prescription.
- If you have any other health problems such as problems with your:

- heart,
- pancreas,
- thyroid,
- breathing,
- kidneys or liver

or if you have been generally unwell for some time.

- If you have ever had an epileptic fit or seizures.
- If you have ever been told that either you have very high fat levels in your blood or your body has problems in breaking down fat adequately.
- If you have diabetes.
- If you are pregnant, plan to become pregnant or are breastfeeding.

Other warnings you should know about:

Driving and using machines: Propofol Injection may temporarily interfere with your ability to drive or operate tools or machinery. You should not drive or operate machinery until all the effects of Propofol Injection have worn off.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Propofol Injection:

- Alfentanil (used as painkillers for initiating and/or maintaining general anesthesia).
- Dexmedetomidine (used to induce sedation (a very relaxed state of calm, drowsiness or sleep))
- Sevoflurane (used to induce and maintain general anesthesia)
- Midazolam (used to induce sedation (a very relaxed state of calm, drowsiness or sleep) and relieves anxiety and muscle tension).
- Opioid medicines, such as fentanyl (used to treat severe pain).
- Other medicines that have an effect on the nervous system, breathing and blood pressure.
- Avoid alcohol before and for at least 8 hours after receiving Propofol Injection.

How to take Propofol Injection:

Propofol Injection will be given to you by your anesthesiologist or intensive care doctor.

Usual dose:

The dose given is decided by the healthcare professional based on the medical procedure it is being used for and your physical condition.

<u>When Receiving Propofol Injection</u>

Propofol Injection will be given to you as an injection into a vein, usually in the back of the hand or in the forearm. Your anesthesiologist may use a needle. For long operations and for use in intensive care situations, an electric pump may be used to control the rate at which the injection is given.

Your anesthesiologist or intensive care doctor will closely control the amount of Propofol Injection that is given to you. The amount will be adjusted according to how deeply your anesthesiologist or intensive care doctor wishes you to sleep or be sedated. He/she will also take account of your age and physical fitness and adjust the amount accordingly.

Several different medicines may be needed in order to keep you asleep or sedated, free from pain, breathing in a healthy way and to keep your blood pressure steady. Your anesthesiologist or intensive care doctor will decide which medicines to use as the need arises.

If Propofol Injection is used for a long time in intensive care situations, certain patients may need to be given zinc (a mineral) supplements.

After Receiving Propofol Injection

You may feel some pain in the arm into which Propofol Injection is given; this is normal.

Overdose:

If you think you, or a person you are caring for, have taken too much Propofol Injection, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

What are possible side effects from using Propofol Injection?

These are not all the possible side effects you may have when taking Propofol Injection. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Frequency/Side Effect/Symptom	**Talk to your healthcare professional**		**Stop taking this drug (if applicable) and get immediate medical help**
	Only if severe	**In all cases**	
During Use of PROPOFOL INJECTION			
Very common			
A feeling of pain near the injection site	✓		
Common			
A fall in blood pressure		✓	
A slower heart beat		✓	
Changes in your breathing pattern		✓	
Rare			
Some twitching and shaking		✓	
Feeling of euphoria (sense of happiness)		✓	
Very rare			

Serious side effects and what to do about them			
Frequency/Side Effect/Symptom	**Talk to your healthcare professional**		**Stop taking this drug (if applicable) and get immediate medical help**
	Only if severe	**In all cases**	
Allergic reactions: swelling of face, hives, rash and itchiness, including anaphylactic shock and anaphylactoid reaction			✓
Fluid in the lungs: severe shortness of breath, difficulty breathing and wheezing, especially when lying down			✓
Unknown			
Discolouration of the urine		✓	
Breakdown of muscle cells (rhabdomyolysis): muscle pain, muscle weakness and dark urine			✓
After use of PROPOFOL INJECTION			
Common			
Nausea and vomiting	✓		
Headache	✓		
Uncommon			
Redness or soreness where Propofol Injection was given	✓		
Rare			
Some twitching and shaking		✓	
Feeling of euphoria (sense of happiness)		✓	
Very rare			
Inflammation of the pancreas (pancreatitis): long periods of pain in the stomach and/or intestine area may go around to your back. You may also vomit.		✓	
Fluid in the lungs: severe shortness of breath, difficulty breathing and wheezing, especially when lying down		✓	
Feeling hot, have increased body temperature or fever, or flushed skin		✓	
A feeling of sexual arousal or long-lasting penile erection		✓	

Serious side effects and what to do about them			
Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug (if applicable) and get immediate medical help
	Only if severe	In all cases	
Fainting or loss of consciousness		✓	
Unknown			
Hepatitis (inflammation of the liver), acute liver failure (symptoms can include yellowing skin and eyes, itching, dark coloured urine, stomach pain and liver tenderness (indicated by pain under the front of the rib cage on your right-hand side), sometimes with loss of appetite)		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store Propofol Injection at 2 °C to 25 °C; do not freeze.

Keep out of reach and sight of children.

If you want more information about Propofol Injection:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html), the manufacturer's website https://www.fresenius-kabi.com/en-ca, or by calling 1-877-821-7724.

This leaflet was prepared by:

Fresenius Kabi Canada Ltd.
165 Galaxy Blvd, Suite 100
Toronto, ON M9W 0C8

Date of Authorization: Dec. 19, 2025