

DIPRIVAN 10mg/ml (1%) emulsion for injection or infusion

QUALITATIVE AND QUANTITATIVE COMPOSITION

Propofol 10mg / mL

PHARMACEUTICAL FORM

Emulsion for injection or infusion.

White aqueous isotonic oil-in-water emulsion containing Propofol 10mg/mL.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS

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

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

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

POSODOLOGY AND METHOD OF ADMINISTRATION

Supplementary analgesic agents are generally required in addition to DIPRIVAN.

DIPRIVAN 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 DIPRIVAN may be required where general anaesthesia is used as an adjunct to regional anaesthetic techniques.

A. Adults

INDUCTION OF GENERAL ANAESTHESIA

DIPRIVAN may be used to induce anaesthesia by slow bolus injection or infusion.

In unpremedicated and premedicated patients, it is recommended that DIPRIVAN 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 DIPRIVAN. 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 DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN 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

DIPRIVAN is not recommended for use in children less than 3 years of age (see 'Undesirable Effects').

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

DIPRIVAN is not recommended for use in children less than 3 years of age. Anaesthesia can be maintained by administering DIPRIVAN 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

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

SEDATION DURING INTENSIVE CARE

DIPRIVAN 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

DIPRIVAN can be used for infusion undiluted from plastic syringes or glass infusion bottles. When DIPRIVAN 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.

DIPRIVAN 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 DIPRIVAN. 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.

DIPRIVAN 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.

DIPRIVAN may be premixed with alfentanil injection containing 500 micrograms/ml alfentanil ('Rapifen'; Janssen Pharmaceuticals Ltd.) 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, DIPRIVAN used for induction may be mixed with Lidocaine Injection in a plastic syringe in the ratio of 20 parts DIPRIVAN with up to one part of either 0.5% or 1% Lidocaine Injection immediately prior to administration.

DILUTION AND CO-ADMINISTRATION OF DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN.	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 DIPRIVAN 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 DIPRIVAN 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

CONTRAINDICATIONS

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

DIPRIVAN is contraindicated for sedation in intensive care of patients of 16 years of age or younger (see 'Special Warnings and Precautions for Use').

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

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

DIPRIVAN should be given by those trained in anaesthesia or, where appropriate, doctors trained in the care of patients in Intensive Care. Patients should be constantly monitored and facilities for maintenance of a patient airway, artificial ventilation, oxygen enrichment and other resuscitative facilities should be readily available at all times. DIPRIVAN should not be administered by the person conducting the diagnostic or surgical procedure.

When DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN.

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

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 DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN 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 over activity may be increased because DIPRIVAN 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 DIPRIVAN is used in conjunction with other agents likely to cause a bradycardia.

Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously.

It is recommended that blood lipid levels should be monitored if DIPRIVAN is administered to patients thought to be at particular risk of fat overload. Administration of DIPRIVAN should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from

the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the DIPRIVAN formulation; 1.0 ml of DIPRIVAN contains approximately 0.1 g of fat.

Use is not recommended with electroconvulsive treatment.

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

DIPRIVAN is not advised for general anaesthesia in children younger than 1 month of age. The safety and efficacy of DIPRIVAN 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.

DIPRIVAN 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 DIPRIVAN 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 DIPRIVAN for ICU sedation. The combination 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 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 DIPRIVAN) 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

DIPRIVAN contains no antimicrobial preservatives and supports growth of micro-organisms. DIPRIVAN contains disodium edetate 0.005% w/v (EDTA) as a microbial inhibitor. EDTA is a chelator of metal ions, including zinc; during prolonged administration of DIPRIVAN the need for supplemental zinc should be considered in patients predisposed to zinc deficiency, such as those with burns, diarrhoea and /or sepsis.

When DIPRIVAN 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 DIPRIVAN and infusion equipment throughout the infusion period. Any infusion fluids added to the DIPRIVAN line must be administered close to the cannula site. DIPRIVAN must not be administered via a microbiological filter.

DIPRIVAN and any syringe containing DIPRIVAN 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 DIPRIVAN be discarded and replaced at regular intervals.

There have been very rare reports of epileptiform movement in epileptics and non-epileptics occurring during induction or emergence from anaesthesia induced by propofol.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

DIPRIVAN 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 DIPRIVAN 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 'Special Warnings and Precautions for Use').

A need for lower Propofol doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of Propofol may 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. Co-administration with dexmedetomidine is likely to lead to an enhancement of effects. Propofol dose required for sedation may have to be reduced in the presence of dexmedetomidine.

PREGNANCY AND LACTATION

Pregnancy

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

Obstetrics

DIPRIVAN 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 DIPRIVAN in mothers who are breast feeding.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

UNDESIRABLE EFFECTS

Summary of the safety profile

Induction of anaesthesia with DIPRIVAN 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.

Tabulated summary of adverse reactions

The following convention has been utilized for the classification of frequency: Very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ and $< 1/1000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

Frequency	System Organ Class	Event
Very common ($\geq 1/10$)	<i>General disorders and administration site conditions:</i>	Local pain on induction (a)
Common ($\geq 1/100$, $< 1/10$)	<i>Vascular disorders:</i>	Hypotension (b)
	<i>Cardiac disorders:</i>	Bradycardia (c)
	<i>Respiratory, thoracic and mediastinal disorders:</i>	Transient apnoea during induction
	<i>Gastrointestinal disorders:</i>	Nausea and vomiting during recovery phase
	<i>Nervous system disorders:</i>	Headache during recovery phase
	<i>General disorders and administration site conditions:</i>	Withdrawal symptoms in children ^(d)
	<i>Vascular disorders:</i>	Flushing in children (d)
Uncommon ($\geq 1/1000$, $< 1/100$)	<i>Vascular disorders:</i>	Thrombosis and phlebitis
Rare ($\geq 1/10000$, $< 1/1000$)	<i>Nervous system disorders:</i>	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery
	<i>Psychiatric disorders:</i>	Euphoric mood
Very rare ($< 1/10\ 000$)	<i>Musculoskeletal and connective tissue disorders:</i>	Rhabdomyolysis (e)
	<i>Gastrointestinal disorders:</i>	Pancreatitis
	<i>Injury, poisoning and procedural complications:</i>	Post-operative fever
	<i>Renal and urinary disorders:</i>	Discolouration of urine following prolonged administration
	<i>Immune system disorders:</i>	Anaphylaxis - may include angioedema, bronchospasm, erythema and hypotension
	<i>Reproductive system and breast</i>	Sexual disinhibition

Not known (cannot be estimated from the available data)	<i>disorders:</i>	
	<i>Cardiac disorders:</i>	Pulmonary oedema
	<i>Nervous system disorders:</i>	Postoperative unconsciousness
	<i>Reproductive system and breast disorders:</i>	Priapism
	<i>Immune system disorders:</i>	Anaphylactic shock
	<i>Hepatobiliary disorders:</i>	Hepatitis, acute hepatic failure ^(f)

- (a) May be minimised by using the larger veins of the forearm and antecubital fossa. With DIPRIVAN local pain can also be minimised by the co-administration of Lidocaine (see 'Posology and Method of Administration' part D).
- (b) Occasionally, hypotension may require use of intravenous fluids and reduction of the administration rate of DIPRIVAN.
- (c) Serious bradycardias are rare. There have been isolated reports of progression to asystole.
- (d) Following abrupt discontinuation of DIPRIVAN during intensive care.
- (e) Very rare reports of rhabdomyolysis have been received where DIPRIVAN 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 DIPRIVAN for induction of anaesthesia in neonates indicates that cardio-respiratory depression may occur if the paediatric dose regimen is applied. (See 'Posology and Method of Administration' and 'Special Warnings and Precautions for Use').

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.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Anaesthetics, general
ATC Code: N01A X10

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 DIPRIVAN 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 DIPRIVAN, any effects are qualitatively similar to those of other intravenous anaesthetic agents and are readily manageable in clinical practice.

DIPRIVAN 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 DIPRIVAN than following anaesthesia with inhalational agents. There is evidence that this may be related to a reduced emetic potential of propofol.

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

PHARMACOKINETIC PROPERTIES

The decline in propofol concentrations following a bolus dose or following the termination of an infusion can be described by a three compartment open model 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 DIPRIVAN 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 DIPRIVAN.

PRE-CLINICAL 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.

PHARMACEUTICAL PARTICULARS

LIST OF EXCIPIENTS

Glycerol
Purified Egg Phosphatide
Sodium Hydroxide
Soya-bean Oil, Refined
Water for Injections
Disodium Edetate

INCOMPATIBILITIES

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

SHELF-LIFE

The expiry date is indicated on the packaging.

STORAGE CONDITIONS

Store below 25°C. Do not freeze.

NATURE AND CONTENTS OF CONTAINER

Glass ampoules (20 mL) (boxes of 5)

INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

Containers should be shaken before use.

Any portion of the contents remaining after use should be discarded.

Asepsis for DIPRIVAN and infusion equipment must be maintained (see 'Additional Precautions').

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MANUFACTURER

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