1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

Diprivan 2 % 50 ml infusion parenteral

Diprivan 2 % PFS 10 ml intravenous infusion

Diprivan 2 % PFS 50 ml intravenous infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of DIPRIVAN 2 % 50 ml contains 20 mg/ml of propofol.

Each pre-filled syringe of DIPRIVAN 2 % PFS 10 ml-contains 20 mg/ml of propofol.

Each pre-filled syringe of DIPRIVAN 2 % PFS 50 ml-contains 20 mg/ml of propofol.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection or infusion

DIPRIVAN 2 % is a white or almost white, homogenous emulsion, practically free from extraneous particulate contamination and large oil droplets. Slight creaming may be visible on prolonged standing.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

DIPRIVAN 2 % is indicated for:

a) Induction and maintenance of general anaesthesia as part of a balanced anaesthetic technique.

b) Sedation of ventilated adult patients receiving intensive care, for a period of up to 72 hours.

4.2. Posology and method of administration

Posology

Supplementary analgesic medicines are required in addition to DIPRIVAN 2 %, where analgesia is required (see section 4.5).

Adults

Induction of general anaesthesia:

DIPRIVAN 2 % should be used to induce anaesthesia by infusion and only in those patients who will receive DIPRIVAN 2 % for maintenance of anaesthesia.

In unpremedicated and premedicated patients:

Most adult patients aged less than 55 years are likely to require 1,5 to 2,5 mg/kg (0,075 to 0,125 ml/kg) of DIPRIVAN 2 %, (approximately 40 mg every 10 seconds in an average healthy adult) by infusion titrated against the response of the patient until clinical signs show onset of anaesthesia. The total dose required can be reduced by lower rates of administration (20 to 50 mg/min (1 to 2,5 mL/min). Over the age of 55 years the requirement will generally be less. In patients of ASA Grades 3 and 4, lower rates of administration should be used (approximately 20 mg (1 ml) every 10 seconds).

Maintenance of general anaesthesia:

Anaesthesia can be maintained by administering DIPRIVAN 2 % by continuous infusion to prevent the clinical signs of light anaesthesia.

Slightly higher rates of administration may be required for 10 to 20 minutes after induction of anaesthesia.

Continuous infusion:

The average rate of administration varies between patients, but rates in the region of 4 to 12 mg/kg/hr (0,2 to 0,6 ml/kg/hr) usually maintain satisfactory anaesthesia.

Slightly higher rates of administration may be required for 10 to 20 minutes after induction of anaesthesia.

Sedation during intensive care:

To provide sedation for ventilated adult patients undergoing intensive care, it is recommended that DIPRIVAN 2 % be given by continuous infusion, for up to 72 hours. Adjust infusion rate according to the depth of sedation required. Rates of 0,3 to 4,0 mg/kg/hr should achieve satisfactory sedation. Rates above 4,0 mg/kg/hr are not recommended (see section 4.4).

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 2 % infusion to the desired level of sedation - most patients will require 1,5 to 4,5 mg/kg/hr. 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.

Special populations

Elderly population

In elderly patients the dose requirement for induction of anaesthesia with DIPRIVAN 2 % 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 2 % 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.

Paediatric population

Induction of general anaesthesia

DIPRIVAN 2% is not recommended for use in children less than 3 years of age (see section 4.3 and 4.4).

It is recommended that DIPRIVAN 2 % be given slowly until the clinical signs show the onset of anaesthesia. Adjust dose for age and/or weight. Most patients over 8 years of age are likely to require approximately 2,5 mg/kg (0,125 ml/kg) of DIPRIVAN 2 % for induction. Between the ages of 3 and 8 years the requirement may be more. Lower dosage is recommended for children of ASA Grades 3 and 4.

Maintenance of general anaesthesia:

DIPRIVAN 2% is not recommended for use in children less than 3 years of age.

Administer DIPRIVAN 2 % by infusion to maintain the depth of anaesthesia required. The required rate of administration varies considerably between patients. Rates in the region of 9 to 15 mg/kg/hr (0,45 to 0,75 mL/kg/hr) usually achieves satisfactory anaesthesia.

Sedation during intensive care:

DIPRIVAN 2 % 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.

Associated findings include metabolic acidosis, lipaemia, rhabdomyolysis, cardiac irregularities and renal failure.

Method of administration

Administration of DIPRIVAN 2 % by bolus injection is not recommended. DIPRIVAN 2 % must be used undiluted. It is recommended that equipment such as drop counters, syringe pumps or volumetric infusion pumps should always be used to control infusion rates. DIPRIVAN 2 % can be used for infusion undiluted from glass infusion bottles, plastic syringes, or DIPRIVAN 2 % pre-filled syringes.

DIPRIVAN 2 % may be administered via a Y-piece close to the injection site, into intravenous infusions of dextrose 5 %, sodium chloride 0,9 % intravenous infusion or dextrose 4 % with sodium chloride 0,18 % (see DOSING TABLE BELOW).

Co-administration of DIPRIVAN with other infusion fluids:

Co-administration technique	**Additive or diluent**	**Preparation**	**Precautions**
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		
	Dextrose 4 % with sodium chloride 0,18% intravenous infusion		

The glass pre-filled syringe (PFS) has a lower frictional resistance than plastic disposable syringes and operates more easily. Therefore, if DIPRIVAN 2 % is administered using a hand held pre-filled syringe, the line between the syringe and the patient must not be left open if unattended.

Patients with hypovolaemia should have fluid-volume deficits corrected prior to administration of DIPRIVAN 2 %.

In use precautions

General

Containers should be gently shaken before use. DIPRIVAN 2 % should be inspected for particulate matter and discolouration before administration. Do not use if there is evidence of separation of the phases of the emulsion.

General anaesthesia

In accordance with established guidelines for other lipid emulsions, a single infusion of DIPRIVAN 2 % must not exceed 12 hours. At the end of the surgical procedure or at 12 hours, whichever is the sooner, both the reservoir of DIPRIVAN 2 % and the infusion line must be discarded and replaced as appropriate.

Intensive care sedation

Administration should commence promptly and must be completed within 12 hours after the vial has been spiked. The tubing and any unused portions of DIPRIVAN 2 % must be discarded after 12 hours.
If DIPRIVAN 2 % is transferred to a syringe or other container prior to administration, the handling procedures for *"General anaesthesia"* (above) should be followed and the product should be discarded, and administration lines changed after 6 hours.

4.3. Contraindications

DIPRIVAN 2 % is contraindicated in:

- Patients with hypersensitivity to propofol or to any of the excipients in DIPRIVAN 2 % (see section 6.1).
- Patients who are hypersensitive to peanut or soya as DIPRIVAN 2 % contains soya oil (see section 6.1).
- DIPRIVAN 2 % is not recommended in children under the age of 3 years.
- Patients of 16 years of age or younger for sedation in intensive care (see section 4.4).
- For the sedation of children of all ages with croup or epiglottitis receiving intensive care (see section 4.4).
- Pregnant women (see section 4.6).

4.4. Special warnings and precautions for use

DIPRIVAN 2 % should be given by those trained in anaesthesia (or, where appropriate, doctors trained in the care of patients in intensive care).

Patients should be constantly monitored and facilities for maintenance of a patent airway, artificial ventilation and oxygen enrichment and other resuscitative facilities should be readily available at all times. DIPRIVAN 2 % should not be administered by the person conducting the diagnostic or surgical procedure.

Abuse of, and dependence on DIPRIVAN 2 %, predominantly by healthcare professionals, have been reported. As with other general anaesthetics, the administration of DIPRIVAN 2 % without airway care may result in fatal respiratory complications.

When DIPRIVAN 2 % 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.

An adequate period is needed prior to discharge of the patient to ensure full recovery after general anaesthesia. Very rarely the use of DIPRIVAN 2 % 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.

DIPRIVAN 2 % induced impairment is not generally detectable beyond 12 hours. The effects of DIPRIVAN 2 %, the procedure, concomitant medications, the age and the condition of the patient should be considered when advising patients on:

- The advisability of being accompanied on leaving the place of administration.
- The timing of recommencement of skilled or hazardous tasks such as driving (see section 4.7).
- The use of other medicine that may sedate (E.g., benzodiazepines, opiates, alcohol.)

Caution should be applied in patients with cardiac, respiratory, renal or hepatic impairment or in hypovolaemic or debilitated patients. The pharmacokinetics of propofol, as in DIPRIVAN 2 %, may be prolonged in people with chronic hepatic cirrhosis or chronic renal impairment. Recovery times may double as a result. The effects of acute hepatic or renal failure on the pharmacokinetics of propofol, as in DIPRIVAN 2 %, have not been studied.

DIPRIVAN 2 % lacks vagolytic activity and has been associated with reports of bradycardia, occasionally profound and also asystole. The intravenous administration of an anticholinergic medicine before induction, or during maintenance of anaesthesia should be considered, especially in situations where vagal tone is likely to predominate or when DIPRIVAN 2 % is used in conjunction with other medicines likely to cause bradycardia.

Respiration will be depressed and must be monitored to ensure adequate gas exchange. Special care should be exercised when used with other respiratory depressants.

A generalised systemic reaction which may be anaphylactic in nature (including angio-oedema, bronchospasm, erythema and hypotension) may occur following DIPRIVAN 2 % administration - estimated as 1 in 15 000 (see section 4.8).

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

Occasionally, hypotension may require use of intravenous fluids and reduction of the rate of administration of DIPRIVAN 2 % during the period of anaesthetic maintenance.

When DIPRIVAN 2 % is administered to an epileptic patient, there may be a risk of convulsion.

In the elderly, debilitated or ASA Grades 3 or 4 patients, rapid single or repeated bolus administration should not be used in order to minimise undesirable cardio-respiratory side effects.

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

Fat metabolism may be disturbed in conditions such as renal insufficiency, uncompensated diabetes mellitus, certain forms of liver insufficiency, metabolic disorders, severe trauma including long-bone and multiple fractures, and sepsis.

It is recommended that blood lipid levels be monitored routinely should DIPRIVAN 2 % be administered to patients thought to be at particular risk of fat overload. Administration of DIPRIVAN 2 % 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 2 % formulation; 1,0 ml of DIPRIVAN 2 % contains 0,1 g of fat.

Use is not recommended with electroconvulsive treatment.

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

Advisory statement concerning Intensive Care Unit management:
Use of propofol emulsion infusions, as in DIPRIVAN 2 %, for ICU sedation has been associated with a constellation off metabolic derangements and organ system failures that may result in death. Reports have been received of combinations of the following: metabolic acidosis, rhabdomyolysis, hyperkalaemia, hepatomegaly, renal failure, hyperlipidaemia, cardiac arrhythmia, brugada-type ECG (elevated ST-segment and coved T-wave) and rapidly progressive cardiac failure usually unresponsive to inotropic supportive treatment.

Combinations of these events have been referred to as the Propofol Infusion Syndrome. These events were mostly seen in patients with serious head injuries and children with respiratory tract infections who received dosages in excess of those advised in adults for sedation in the intensive care unit.

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 medicines - vasoconstrictors, steroids, inotropes and/or DIPRIVAN 2 % (usually at dose rates greater than 4mg/kg/h for more than 48 hours).

The healthcare provider should be alert to these events in patients with the above risk factors and promptly consider decreasing or stopping the DIPRIVAN 2 % dosage when the above signs develop.

Treating healthcare professionals are reminded, if possible, not to exceed the dosage of 4 mg/kg/h.

Caution should be taken when treating patients with mitochondrial disease. These patients may be susceptible to exacerbations of their disorder when undergoing anaesthesia, surgery and ICU care. Maintenance of normothermia, provision of carbohydrates and good hydration are recommended for such patients. The early presentations of mitochondrial disease exacerbation and of the 'Propofol Infusion Syndrome' may be similar.

DIPRIVAN 2 % contains no antimicrobial preservatives and supports growth of microorganisms.

EDTA is a chelator of metal ions, including zinc. The need for supplemental zinc should be considered during prolonged administration of DIPRIVAN 2 %, particularly in patients who are predisposed to zinc deficiency, such as those with burns, diarrhoea and/or major sepsis

When DIPRIVAN 2 % is to be aspirated, it must be drawn aseptically into a sterile syringe or giving set immediately after opening the vial seal. Administration must commence without delay.

Asepsis must be maintained for both DIPRIVAN 2 % and infusion equipment throughout the infusion period. Any infusion fluids added to the DIPRIVAN 2 % line must be administered close to the cannula site. DIPRIVAN 2 % must not be administered via a microbiological filter.

Any container or syringe containing DIPRIVAN 2 % is for single use in a single patient only.

Paediatric population

DIPRIVAN 2 % is not recommended for use in neonates or children under 3 years of age for induction and maintenance of anaesthesia.

DIPRIVAN 2 % must not be used in patients of 16 years of age or younger for sedation for intensive care as the safety and efficacy of propofol, as in DIPRIVAN 2 %, for sedation in this age group have not been demonstrated.

4.5. Interaction with other medicines and other forms of interaction

Profound hypertension has been reported following anaesthetic with propofol, as in DIPRIVAN 2 %, in patients treated with rifampicin.

A need for lower propofol, as in DIPRIVAN 2 %, doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of DIPRIVAN 2 % may be considered.

Where general anaesthesia with DIPRIVAN 2 % is used simultaneously with a regional anaesthetic technique, lower doses of DIPRIVAN 2 % may be required.

DIPRIVAN 2 % has been used in association with spinal and epidural anaesthesia and with commonly used premedication, neuromuscular blocking medicines, inhalation, and analgesic medicines; no pharmacological incompatibility has been encountered. Dosage adjustment may be necessary when used together particularly with the narcotics (e.g. morphine, meperidine and fentanyl), combinations of opioids and sedatives (e.g. benzodiazepines, barbiturates, droperidol etc.), supplementary analgesic medicines

(e.g. nitrous oxide or opioids) and the potent inhalation medicines (e.g. isoflurane, enflurane and halothane).

4.6. Fertility, pregnancy, and lactation

Pregnancy

DIPRIVAN 2 % should not be used in pregnancy (see section 4.3). DIPRIVAN 2 % has been used, however, during termination of pregnancy in the first trimester.

Obstetrics

DIPRIVAN 2 % crosses the placenta and may be associated with neonatal depression. DIPRIVAN 2 % should not be used for obstetric anaesthesia.

Breastfeeding

Safety to the neonate following the use of DIPRIVAN 2 % in mothers who are breastfeeding has not been established. It has been reported that small quantities of DIPRIVAN 2 % are excreted in human milk. Women should therefore not breastfeed for 24 hours after administration of DIPRIVAN 2 %. Milk produced during this period should be discarded.

Fertility

No data are available.

4.7. Effects on ability to drive and use machines

DIPRIVAN 2% has high influence on the ability to drive and use machines

Since adverse reactions such as postoperative unconsciousness have been reported in patients receiving DIPRIVAN 2 %, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that DIPRIVAN 2 %, does not adversely affect their ability to do so

(see section 4.8).

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown [9]
Immune system disorders		Anaphylaxis - may include angioedema, bronchospasm, erythema, hypotension	
Metabolism and nutrition disorders			Metabolic acidosis[5], hyperkalaemia[5], hyperlipidaemia[5]
Psychiatric disorders			Euphoric moods, drug abuse and drug dependence[8]
Nervous system disorders	Headache during recovery phase,	Epileptiform movements, including convulsions and opisthotonus during induction, maintenance and recovery postoperative unconsciousness	Involuntary movement
Cardiac disorders	Bradycardia [1]		Cardiac arrhythmia [5], cardiac failure [5][7]
Vascular disorders	Flushing in children[11], hypotension [2]	Phlebitis, thrombosis	
Respiratory, thoracic and mediastinal disorders	Transient apnoea during induction	Pulmonary oedema	Respiratory depression (dose dependent)
Gastrointestinal disorders	Nausea and vomiting during recovery phase	Pancreatitis	
Hepatobiliary disorders			Hepatomegaly [5]
Musculoskeletal, connective tissue and bone disorder			Dystonia/dyskinesia Rhabdomyolysis [3][5]
Renal and urinary disorders		Urine discolouration following prolonged administration	Renal failure [5]
Reproductive system and breast disorders		Sexual disinhibition	Priapism

General disorders and administration site conditions	Local pain on induction [4] Withdrawal symptoms in children[11]	Tissue necrosis [10] following accidental extravascular administration	Local pain, swelling following accidental extravascular administration
Investigations			Brugada type ECG [5], [6]
Injury and poisoning		Postoperative fever	

1) *Serious bradycardias are rare. There have been isolated reports of progression to asystole.*

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

3) *Very rare reports of rhabdomyolysis have been received where DIPRIVAN has been given at doses greater than 4 mg/kg/hr for ICU sedation.*

4) *May be minimised by using the larger veins of the forearm and antecubital fossa.*

5) *Combinations of these events, reported as "Propofol Infusion Syndrome", may be seen in seriously ill patients who often have multiple risk factors for the development of the events.*

6) *Brugada-type ECG - elevated ST-segment and coved T-wave in ECG.*

7) *Rapidly progressive cardiac failure (in some cases with fatal outcome) in adults. The cardiac failure in such cases was usually unresponsive to inotropic supportive treatment.*

8) *Abuse of and drug dependence on propofol, predominantly by healthcare professionals.*

9) *Not known as it cannot be estimated from the available clinical trial data.*

10) *Necrosis has been reported where tissue viability has been impaired.*

11) *Following abrupt discontinuation of DIPRIVAN during intensive care.*

b) Description of selected adverse reactions

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.

Reports from off-label use of DIPRIVAN 2 % for induction of anaesthesia in neonates indicates that cardiorespiratory depression may occur if the dose regimen recommended for children 3 years and over is applied (see section 4.2)

General side effects may also include excitation and hypertension.

Less frequently, tachycardia, premature ventricular contractions, premature atrial contractions, syncope, abnormal ECG, and ST segment depression may occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to **SAHPRA** via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org. za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

Accidental overdosage is likely to cause cardiorespiratory depression.

Treatment

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 medicines.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 2.1 Anaesthetics

Pharmacotherapeutic group: Central nervous system depressants

ATC code: N01AX10

Mechanism of action

Propofol 2,6-diisopropylphenol) is a short-acting sedative and general anaesthetic medicine with a rapid onset of action of approximately 30 seconds. The mechanism of action is poorly understood.

Falls in mean arterial blood pressure and changes in heart rate are observed when propofol is administered.

Ventilatory depression can occur following administration of propofol.

Propofol, reduces cerebral blood flow, intracranial pressure and cerebral metabolism. The reduction in intracranial pressure is greater in patients with an elevated baseline intracranial pressure.

Recovery from anaesthesia is usually rapid and clear-headed.

Propofol , has an anti-emetic effect.

Studies have shown that propofol at the concentrations likely to occur clinically, does not inhibit the synthesis of adrenocortical hormones.

5.2. Pharmacokinetic properties

Absorption

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. The first phase is characterised by a rapid distribution (half-life: 2 to 4 minutes) followed by rapid elimination (half-life: 30 to 60 minutes) and a slower final phase, representative of redistribution of propofol from poorly perfused tissue.

Distribution

Propofol is extensively distributed and rapidly cleared from the body (total body clearance: 1,5 to 2 litres/minute).

The pharmacokinetics are linear over the recommended range of infusion rates of propofol.

Under the usual maintenance regimens, significant accumulation of propofol does not occur.

Elimination

Clearance occurs by metabolic processes, mainly in the liver, to form inactive conjugates of propofol and its corresponding quinol, which are excreted in the urine.

Summary of pre-clinical studies

Published studies in animals demonstrate that the use of anaesthetic medicine 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 neonatal primates, exposure to 3 hours of an anaesthetic regimen that produced a light surgical plane of anaesthesia did not increase neuronal cell loss, however, treatment regimens of 5 hours or longer increased neuronal cell loss. Data in foetal and neonatal rodents and primates suggest that the neuronal and oligodendrocyte cell losses are associated with subtle but prolonged cognitive deficits in learning and memory.

The clinical significance of these preclinical findings is not known.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium edetate (anhydrous) 0,005 % *m/v*, glycerol, purified egg phosphatide, sodium hydroxide (for

pH adjustment), soya-bean oil, water for injection

6.2. Incompatibilities

DIPRIVAN 2 % should not be mixed prior to administration with injections or infusion fluids.

The neuromuscular blocking medicines, atracurium and mivacurium should not be given through the same intravenous line as DIPRIVAN 2 % without prior flushing.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 ºC. Do not freeze.

Keep in original packaging until required for use.

6.5. Nature and contents of container

DIPRIVAN 2 % 50 ml: 1 x 50 ml colourless, clear Type 1 glass vial with an aluminium seal, grey bromobutyl rubber stopper and a polypropylene snap off cap. 1 vial is packed in an outer cardboard carton.

DIPRIVAN 2 % PFS 10 ml: 1 x 10 ml pre-filled glass syringe, plunger rod and luer connector pack. 1 pre-filled syringe is packed in an outer cardboard carton.

DIPRIVAN 2 % PFS 50 ml: 1 x 50 ml pre-filled glass syringe, plunger rod and luer connector pack. 1 pre-filled syringe is packed in an outer cardboard carton.

Not all strengths, packs and pack sizes are necessarily marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBERS

DIPRIVAN 2 % 50 ml: 36/2.1/0084

DIPRIVAN 2 % PFS 10 ml: 36/2.1/0085

DIPRIVAN 2 % PFS 50 ml: 36/2.1/0086

9. DATE OF FIRST AUTHORISATION

Date of registration: 20 September 2002

10. DATE OF REVISION OF TEXT

12 April 2023

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