PROFESSIONAL INFORMATION

DEXSEDATE 100 µg/ml should not be used outside an Intensive Care Unit setting or surgical operating theatres. There should be continuous monitoring of vital parameters.

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

DEXSEDATE 100 µg/ml concentrate for solution for infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of concentrate for solution for infusion contains dexmedetomidine hydrochloride equivalent to 100 µg dexmedetomidine.

Each 2 ml ampoule contains 200 µg of dexmedetomidine.

Each 5 ml vial contains 500 µg of dexmedetomidine.

Each 10 ml vial contains 1 000 µg of dexmedetomidine.

The ampoules and vials are intended for single patient use only.

Sugar free.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.

A clear, colourless solution, free from visible particles and fibers.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

DEXSEDATE is an alpha$_2$ adrenoreceptor agonist sedative with analgesic properties

indicated for:

Intensive care unit sedation

- Sedation of intubated and mechanically ventilated adult post-surgical patients during treatment in an intensive care setting.

Monitored anaesthesia care (MAC)/Conscious sedation in a theatre or intensive case setting for:

- Minor surgical procedures under local anaesthesia
- Fibreoptic intubation

Efficacy and safety have not been studied in children under 18 years of age.

4.2 Posology and method of administration

Posology

NOTE: DEXSEDATE should be administered only by health care professionals skilled in the management of patients in the intensive care setting. Continuous monitoring of vital signs, in particular blood pressure, heart rate and oxygen saturation is mandatory during infusion of DEXSEDATE.

In order to minimise undesirable pharmacologic side effects, bolus injection of DEXSEDATE should not be used. Clinically significant events of bradycardia and sinus arrest have been associated with DEXSEDATE administration in young healthy volunteers with high vagal tone, or with different routes of administration including rapid intravenous or bolus administration of DEXSEDATE.

DEXSEDATE should be administered by continuous intravenous infusion not to exceed 24 hours.

Fluid supplementation should be administered prior to and during administration of DEXSEDATE to ensure normovolaemia.

DEXSEDATE has been administered to patients requiring mechanical ventilation as well as to patients breathing spontaneously after extubation. There is no respiratory depression associated with the administration of DEXSEDATE. Patients receiving DEXSEDATE have been observed to be arousable and alert when stimulated. This is an expected component of dexmedetomidine sedation and should not be considered as evidence of lack of efficacy in the absence of other clinical signs and symptoms. DEXSEDATE has been continuously infused in mechanically ventilated patients prior to extubation, during extubation, and post extubation. It is not necessary to discontinue DEXSEDATE prior to extubation.

Posology

Adults

ICU sedation

DEXSEDATE dosage should be individualised and titrated to the desired clinical effect.

Initiation

For adult patients, it is recommended to initiate DEXSEDATE with a loading dose of 1,0 microgram/kg over ten minutes.

Maintenance of ICU sedation

Adult patients will generally require a maintenance infusion in the range of 0,2 to 0,7 micrograms/kg/h. The rate of the maintenance infusion can be adjusted in order to achieve the desired clinical effect. Dosages as low as 0,05 micrograms/kg/h have been used in clinical studies.

A dose reduction for both the loading and maintenance infusions should be considered in patients with impaired hepatic or renal function and in patients over 65 years of age (see sections 4.3, 4.4 and 5.2).

Conscious sedation

Monitored anaesthesia care (MAC) with an adequate nerve block and awake fibreoptic intubation (AFI).

DEXSEDATE dosing should be individualised and titrated to the desired clinical effect.

Initiation

For adult patients, DEXSEDATE is generally initiated with a loading infusion of 1 (one) microgram/kg over 10 minutes.

For patients over 65 years of age or those undergoing less invasive procedures such as ophthalmic surgery, a loading infusion of 0,5 micrograms/kg over 10 minutes may be suitable.

Maintenance of conscious sedation

MAC

Following the load, maintenance dosing of DEXSEDATE should generally be initiated at 0,6 micrograms/kg/h and titrated to achieve desired clinical effect with doses ranging from 0,2 to 1 micrograms/kg/h for all procedures. The rate of the maintenance infusion should be adjusted to achieve the targeted level of sedation.

AFI

Following the load in awake fibreoptic intubation, a fixed maintenance dose of 0,7 micrograms/kg/h should be used.

Dosage adjustment

Due to possible pharmacodynamics interactions a reduction in dosage of DEXSEDATE or other concomitant anaesthetics, sedatives, hypnotics or opioids may be required when co-administered (see section 4.5).

Special populations

Impaired hepatic function

Dosage reductions may need to be considered for patients with hepatic impairment, as DEXSEDATE is metabolised primarily in the liver.

Impaired renal function

Since the majority of metabolites are excreted in the urine, dosage reductions may need to be considered for patients with renal impairment.

Elderly population

Since the elderly are more sensitive to the effects of DEXSEDATE dosage reductions may need to be considered.

Paediatric population

Safety and efficacy of DEXSEDATE has not been studied in children and adolescents and is therefore not recommended for patients under 18 years of age.

Method of administration

For intravenous infusion.

For instructions on preparation and dilution of the product before administration, see section 6.6.

4.3 Contraindications

DEXSEDATE is contraindicated in:

- Patients with a known hypersensitivity to dexmedetomidine or to any of the excipients (see section 6.1)
- Patients with sepsis
- Unstable trauma patients

- Hypovolaemic patients
- Heart block
- Uncontrolled cardiac failure
- Imminent hepatic failure
- Uncontrolled hypotension
- Acute cerebrovascular conditions

4.4 Special warnings and precautions for use

DEXSEDATE should be administered only by healthcare professionals skilled in the management of patients in the intensive care setting and who have received complete training in the use of DEXSEDATE in the ICU setting.

Safety and efficacy of DEXSEDATE in non-surgical intensive care patients have not been established.

Clinical events of bradycardia and sinus arrest have been associated with DEXSEDATE administration in some young, healthy volunteers with high vagal tone, or with different routes of administration including rapid intravenous or bolus administration of DEXSEDATE. Bolus injections of DEXSEDATE should not be used, in order to minimise undesirable pharmacological side effects.

Elderly population

The elderly are more prone to cardiovascular adverse events e.g. hypotension and bradycardia and the dose must be carefully titrated to obtain the desired effect. Close CVS monitoring is required. Elderly patients (over 65 years) often require lower doses of DEXSEDATE.

Special precautions

NOTE: DEXSEDATE should be administered only by health care providers skilled in the management of patients in the intensive care setting. Continuous electrocardiogram (ECG), blood pressure and oxygen saturation monitoring are mandatory during infusion of DEXSEDATE.

Caution should be exercised in patients with pre-existing severe bradycardia disorders (i.e. advanced heart block), or patients with pre-existing severe ventricular dysfunction (e.g. ejection fraction < 30 %) including congestive heart failure and cardiac failure in whom sympathetic tone is critical for maintaining haemodynamic balance (see section 4.3).

Hypotension, bradycardia and sinus arrest

Clinical events of bradycardia and sinus arrest have been associated with DEXSEDATE administration in some young, healthy volunteers with high vagal tone, or with different routes of administration including rapid intravenous or bolus administration of DEXSEDATE. Bolus injections of DEXSEDATE should not be used, in order to minimise undesirable pharmacological side effects.

Decreased blood pressure and/or heart rate may occur with the administration of DEXSEDATE. If medical intervention is required, treatment may include decreasing or stopping the infusion of DEXSEDATE, increasing the rate of intravenous fluid administration, elevation of the lower extremities and use pressor medicines. Because DEXSEDATE has the potential to augment bradycardia induced by vagal stimuli, medical practitioners should be prepared to intervene. The intravenous administration of anticholinergic medicines should be considered to modify vagal tone. In clinical trials, atropine and glycopyrrolate were effective in the treatment of most episodes of dexmedetomidine-induced bradycardia. However, in some patients with significant

cardiovascular dysfunction, more advanced resuscitative measures were required.

DEXSEDATE decreases sympathetic nervous activity and therefore, these effects may be expected to be most pronounced in patients with desensitised autonomic nervous system control (i.e. elderly, diabetes, chronic hypertension, severe cardiac disease).

Prevention of hypotension and bradycardia should take into consideration the haemodynamic stability of the patient and normovolaemia must be ensured prior to the administration of DEXSEDATE. Patients who are hypovolaemic may become hypotensive under DEXSEDATE therapy. Therefore, fluid supplementation should be administered prior to and during the administration of DEXSEDATE.

Additionally, in situations where other vasodilators or negative chronotropic medicines are administered, co-administration of DEXSEDATE could have an additive pharmacodynamics effect and should be administered with caution and careful titration (see section 4.5).

Clinical events of bradycardia or hypotension may be potentiated when DEXSEDATE is used concurrently with propofol or midazolam. Therefore, consider a dose reduction of propofol or midazolam (see section 4.5).

Patients with impaired peripheral autonomic activity (e.g. due to spinal cord injury) may have more pronounced haemodynamic changes after starting DEXSEDATE and so should be treated with care.

Transient hypertension

Transient hypertension has been observed primarily during the loading infusion, associated with initial peripheral vasoconstrictive effects of DEXSEDATE and relatively

higher plasma concentrations achieved during the loading infusion. If intervention is necessary, reduction of the loading infusion rate may be considered. Following the loading infusion, the central effects of DEXSEDATE dominate and the blood pressure usually decreases.

Local vasoconstriction at higher concentration may be of greater significance in patients with ischaemic heart disease or severe cerebrovascular disease who should be monitored closely. Dose reduction or discontinuation should be considered in a patient developing signs of myocardial or cerebral ischaemia.

Caution is advised when administering DEXSEDATE together with spinal or epidural anaesthesia due to possible increased risk of hypotension or bradycardia.

DEXSEDATE may cause reduced lacrimation. Lubrication of the patient's eyes may be considered when administering DEXSEDATE to avoid corneal dryness.

Patients with hepatic impairment

Care should be taken in severe hepatic impairment as excessive dosing may increase the risk of adverse reactions, over-sedation, or prolonged effect as a result of reduced DEXSEDATE clearance.

Patients with neurological disorders

Experience of DEXSEDATE in severe neurological disorders such as head injury and after neurosurgery is limited and it should be used with caution here, especially if deep sedation is required. DEXSEDATE may reduce cerebral blood flow and intracranial pressure, and this should be considered when selecting therapy.

Other

Alpha-2 agonists have less frequently been associated with withdrawal reactions when stopped abruptly after prolonged use. This possibility should be considered if the patient develops agitation and hypertension shortly after stopping DEXSEDATE.

DEXSEDATE may induce hyperthermia that may be resistant to traditional cooling methods. DEXSEDATE treatment should be discontinued in the event of a sustained unexplained fever and is not recommended for use in malignant hyperthermia-sensitive patients.

Diabetes insipidus has been reported in association with DEXSEDATE treatment. If polyuria occurs, it is recommended to stop DEXSEDATE and check serum sodium level and urine osmolality.

DEXSEDATE contains less than 1 mmol sodium (23 mg) per ml, essentially “sodium free”.

4.5 Interaction with other medicines and other forms of interaction

Cytochrome P-450

Inhibition of GYP enzymes including CYP2B6 by dexmedetomidine has been studied in human liver microsome incubations. *In vitro* study suggests that interaction potential *in vivo* exists between dexmedetomidine and substrates with dominant CYP2B6 metabolism.

Induction of dexmedetomidine *in vitro* was observed on CYP1A2, CYP2B6, CYP2C8, CYP2C9 and CYP3A4, and induction *in vivo* cannot be excluded. The clinical significance is unknown.

The possibility of enhanced hypotensive and bradycardic effects should be considered in patients receiving other medicines causing these effects, for example beta blockers, although additional effects in an interaction study with esmolol were modest.

Anaesthetics/sedatives/hypnotics/opioids

Co-administration of DEXSEDATE is likely to lead to an enhancement of effects with anaesthetics, sedatives, hypnotics and opioids. Specific studies have confirmed these effects with sevoflurane, isoflurane, propofol, alfentanil, and midazolam. No pharmacokinetic interactions between DEXSEDATE and isoflurane, propofol, alfentanil, and midazolam were demonstrated. However, due
to pharmacodynamic effects, when co-administered with DEXSEDATE a reduction in dosage of these medicines may be required.

Neuromuscular blockers

No clinically meaningful increases in the magnitude of neuromuscular blockade and no pharmacokinetic interactions were observed with DEXSEDATE and rocuronium administration.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Pregnancy

Available data from published randomized controlled trials and case reports over several decades of use with intravenously administered dexmedetomidine during pregnancy have not identified a drug-associated risk of major birth defects and miscarriage; however, the reported exposures occurred after the first trimester. Most of the available data are based on studies with exposures that occurred at the time of caesarean section delivery, and these studies have not identified an adverse effect on maternal outcomes or infant Apgar

scores. Available data indicate that dexmedetomidine crosses the placenta.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

Labour and delivery

The safety of DEXSEDATE in labour and delivery has not been studied and it is therefore not recommended for obstetrics, including caesarean section deliveries.

Breastfeeding

Available published literature reports the presence of DEXSEDATE in human milk following intravenous administration. There is no information regarding the effects of DEXSEDATE on the breastfed infant or the effects on milk production. Advise women to monitor the breastfed infant for irritability. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DEXSEDATE and any potential adverse effects on the breastfed infant from DEXSEDATE or from the underlying condition.

In two published clinical studies, a total of 14 women were given intravenous dexmedetomidine 6 micrograms/kg/hour for 10 minutes after delivery followed by continuous infusion of 0,2 – 0,7 microgram/kg/hour. Breast milk and maternal blood samples were collected at 0, 6, 12, and 24 hours after discontinuation of dexmedetomidine. Plasma and milk dexmedetomidine concentrations were detectable up to 6 hours in most subjects, up to 12 hours in one subject and undetectable in all at 24 hours. The milk-to-plasma ratio from single paired maternal milk and plasma concentrations at each time point ranged from 0,53 to 0,95. The relative infant dose was estimated to range from 0,02 to 0,098 %.

Fertility

In a rat fertility study, there was no effect on male or female fertility. No human data on

fertility are available.

4.7 Effects on ability to drive and use machines

The patient should not drive or operate machinery or make legal decisions until 24 hours after recovery from a surgical procedure in which DEXSEDATE was used.

4.8 Undesirable effects

a. Summary of the safety profile

ICU sedation

The most frequently reported adverse reactions with dexmedetomidine in ICU setting are hypotension, hypertension, bradycardia, nausea, dry mouth and hypoxia (see section 4.4).

Conscious sedation

The majority of the adverse events were assessed as mild in severity. The most frequent adverse events were hypotension, bradycardia, and dry mouth (see section 4.4)

b. Tabulated summary of adverse reactions

The frequency of adverse reactions listed below is defined using the following convention: frequent; less frequent or frequency unknown (cannot be estimated from the available data).

MedDRA system organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Frequency unknown	Infection, fungal infection, sepsis

MedDRA system organ class	**Frequency**	**Adverse reactions**
Blood and lymphatic system disorders	Frequent	Anaemia
	Frequency unknown	Coagulation disorders, disseminated intravascular coagulation, haematoma, abnormal platelets, decreased prothrombin, thrombocytopenia, leukocytosis
Endocrine disorders	Frequency unknown	Diabetes mellitus, diabetes insipidus
Metabolism and nutrition disorders	Frequent	Hypoglycaemia, hyperglycaemia
	Less frequent	Hypocalcaemia, hypoalbuminaemia, metabolic acidosis
	Frequency unknown	Lactic acidosis, respiratory acidosis, hypokalaemia, hyperkalaemia, hypoproteinaemia, increased alkaline phosphatase, increased nonprotein nitrogen (NPN)
Psychiatric disorders	Frequent	Agitation
	Frequency unknown	Anxiety, confusion, delirium, depression, illusion, nervousness, hallucination
Nervous system disorders	Frequency unknown	Convulsion, dizziness, headache, neuralgia, neuritis, neuropathy, paraesthesia, paralysis, paresis, speech disorder
Eye disorders	Frequency unknown	Diplopia, photopsia, abnormal vision

MedDRA system organ class	**Frequency**	**Adverse reactions**
Cardiac disorders	Frequent	Atrial fibrillation, bradycardia, tachycardia
	Less frequent	Sinus tachycardia, ventricular tachycardia, decreased cardiac output
	Frequency unknown	Dysrhythmia, atrial dysrhythmia, AV block, bundle branch block, extrasystoles, heart block, supraventricular tachycardia, T-wave inversion, ventricular dysrhythmia, angina pectoris, abnormal ECG, heart disorder, myocardial ischaemia or infarction, atrioventricular block, cardiac arrest
Vascular disorders	Frequent	Hypovolaemia, hypotension, hypertension
	Frequency unknown	Blood pressure fluctuation, circulatory failure, cyanosis, aggravated hypertension, pulmonary hypertension, postural hypotension, pulmonary hypertension, haemorrhage, cerebral haemorrhage, peripheral ischaemia, vascular disorder, vasodilation
Respiratory, thoracic and mediastinal disorders	Frequent	Atelectasis, pleural effusion, hypoxia, bradypnoea, respiratory depression
	Less frequent	Pulmonary oedema, wheezing,

MedDRA system organ class	**Frequency**	**Adverse reactions**
		dyspnoea, apnoea
	Frequency unknown	Syncope, adult respiratory distress syndrome, bronchial obstruction, bronchospasm, coughing, emphysema, haemoptysis, hypercapnia, hypoventilation, pharyngitis, pleurisy, pneumonia, pneumothorax, pulmonary congestion, respiratory disorder, respiratory insufficiency, increased sputum, stridor
Gastrointestinal disorders	Frequent	Nausea, vomiting, dry mouth
	Less frequent	Abdominal distension
	Frequency unknown	Abdominal pain, diarrhoea, eructation, mucosal ulceration
Hepato-biliary disorders	Frequency unknown	Increased AG ratio, increased GGT, abnormal hepatic function, hyperbilirubinaemia, increased aspartate transaminase (AST), increased alanine transaminase (ALT), jaundice
Skin and subcutaneous tissue disorders	Frequency unknown	Rash erythematous, increased sweating
Musculoskeletal and connective tissue disorders	Frequency unknown	Muscle weakness

MedDRA system organ class	**Frequency**	**Adverse reactions**
Renal and urinary disorders	Frequency unknown	Increased blood urea, oliguria, haematuria, acute renal failure, abnormal renal function, urinary retention
General disorders and administration site conditions	Frequent	Pyrexia, chills, hyperthermia
	Less frequent	Peripheral oedema, medicine ineffective
	Frequency unknown	Allergic reaction, ascites, hyperpyrexia, light anaesthesia, oedema, pain, rigors, thirst, withdrawal syndrome
Investigations	Less frequent	Decreased urine output
Injury, poisoning and procedural complications	Frequent	Post-procedural haemorrhage

Withdrawal

ICU sedation

Although not specifically studied, withdrawal symptoms similar to those reported for another alpha$_2$ adrenergic medicine (clonidine) may result when DEXSEDATE is administered in excess of 24 hours and stopped abruptly. These symptoms include nervousness, agitation and headache accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma.

Conscious sedation

Withdrawal symptoms were not seen after discontinuation of short-term infusions of DEXSEDATE (< 6 hours).

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

First-degree AV block and second-degree heart block may occur.

Bradycardia, with or without hypotension, and cardiac arrest may occur.

Because DEXSEDATE has the potential to augment bradycardia induced by vagal stimuli, medical practitioners should be prepared to intervene. In clinical trials, atropine and glycopyrrolate were effective in the treatment of DEXSEDATE-induced bradycardia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A2.9 Other Analgesics.

Pharmacotherapeutic group: Psycholeptics, other hypnotics and sedatives, ATC code: N05CM18.

Mechanism of action

Dexmedetomidine is an alpha$_2$-adrenoreceptor agonist.

The sedative actions of dexmedetomidine are believed to be mediated primarily by post-synaptic alpha$_2$-adrenoreceptors, which in turn act on inhibitory pertussis-toxin-sensitive G protein, thereby increasing conductance through potassium channels. The site of the sedative effects of dexmedetomidine has been attributed to the locus ceruleus. The analgesic actions are believed to be mediated by a similar mechanism of action at the brain and spinal cord level.

Alpha$_2$ selectivity is demonstrated following low and medium doses given slowly. Alpha$_2$

and alpha$_1$ activity is seen following rapid administration. Dexmedetomidine has no affinity for beta adrenergic, muscarinic, dopaminergic, or serotonin receptors.

5.2 Pharmacokinetic properties

Distribution

Following administration, dexmedetomidine exhibits the following pharmacokinetic characteristics: rapid distribution phase with a distribution half-life ($t_{1/2\alpha}$) of about 6 minutes; terminal elimination half-life ($t_{1/2}$) of approximately two hours; steady state volume of distribution (V_{ss}) of approximately 118 L. Clearance has an estimated value of about 39 L/h. The mean body weight associated with this clearance estimate is 72 kg.

Dexmedetomidine protein binding is on average 94 %. Protein binding is similar in males and females. The fraction of dexmedetomidine that is bound to plasma proteins is statistically significantly decreased in subjects with hepatic impairment compared with healthy subjects.

Dexmedetomidine is unlikely to cause clinically significant changes in the plasma protein binding of fentanyl, ketorolac, theophylline, digoxin, lidocaine, phenytoin, warfarin, ibuprofen and propranolol.

Elimination

Dexmedetomidine is eliminated almost exclusively by metabolism with 95 % of a radio-labelled dose being excreted in the urine and 4 % in the faeces. Approximately 34 % of the excreted metabolites are medicines of N-glucuronidation.

Special populations

Gender

No major pharmacokinetic differences have been observed based on gender.

Hepatic impairment

In subjects with varying degrees of hepatic impairment (Child-Pugh Class A, B, or C), clearance values are lower than in healthy subjects. The mean clearance values for subjects with mild, moderate, and severe hepatic impairment are 74 %, 64 % and 53 % respectively, of those observed in the normal healthy subjects. Mean clearances for free medicine are 59 %, 51 %, and 32 % respectively, of those observed in the normal healthy subjects. Although dexmedetomidine is dosed to effect, it may be necessary to consider dose reduction depending on the degree of hepatic impairment (see section 4.2 and section 4.4).

Renal impairment

Dexmedetomidine pharmacokinetics (C_{max}, T_{max}, AUC, $t_{½}$, CL and V_{ss}) were not different in subjects with severe renal impairment (Cr Cl: < 30 mL/min) compared with healthy subjects.

Elderly population

The pharmacokinetic profile of dexmedetomidine was not altered by age. The elderly are more sensitive to the effects of dexmedetomidine. There was a higher incidence of bradycardia and hypotension in elderly patients (> 65 years of age).

Paediatric population

The pharmacokinetic profile of dexmedetomidine has not been studied in subjects less than 18 years.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (pH adjustment)

Sodium chloride

Sodium hydroxide (pH adjustment)

Water for injection

6.2 Incompatibilities

DEXSEDATE must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life

24 months

After dilution

Chemical and physical in-use stability has been demonstrated for 24 hours at or below 25 °C. From a microbiological point of view, the medicine should be used immediately. If not used immediately, in-use storage times and conditions prior to the use are the responsibility of the user and would not normally be longer than 24 hours at 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the vials in the outer carton in order to protect from light.

For storage conditions after dilution of the medicine, see section 6.3.

6.5 Nature and contents of container

DEXSEDATE is packed in 2 ml type I clear glass ampoules with a white colour dot, 5 ml or 10 ml type I clear vials with grey colour rubber stoppers and aluminium flip-off white seals.

Pack size: 5 x 2 ml ampoules, 5 x 5 ml vials or 5 x 10 ml vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The ampoules and vials are intended for single patient use only.

Preparation of solution

Strict aseptic technique must always be maintained during handling of DEXSEDATE infusion.

Preparation of infusion solutions is the same, whether for the loading dose or for the maintenance dose.

To prepare the infusion, withdraw 2 ml of DEXSEDATE concentrate and add to 48 ml of 0,9 % sodium chloride solution to total 50 ml. Shake gently to mix well.

After dilution, DEXSEDATE is intended for immediate use and should be discarded after 24 hours.

Administration with other fluids

DEXSEDATE has been shown to be compatible when administered with the following intravenous fluids:

0,9 % Sodium chloride injection, Lactated Ringers, 5 % Dextrose in water and 20 % mannitol.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Pharma-Q (Pty) Ltd

50 Commando Road

Industria West 2093

Johannesburg

South Africa

info@pharmaq.co.za

Tel: 011 247 1600

8 REGISTRATION NUMBER

57/2.9/0783

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 September 2025

10 DATE OF REVISION OF THE TEXT

To follow