PreceDex 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**

PROPRIETARY NAME (and dosage form)

PreceDEX Concentrated solution for intravenous infusion

COMPOSITION

Each 1 ml of concentrated solution contains dexmedetomidine hydrochloride equivalent to 100 micrograms dexmedetomidine. Ampoules and vials of **PreceDEX** are intended for single patient use only.

Other ingredients include water for injections and sodium chloride.

PHARMACOLOGICAL CLASSIFICATION

A 2.9 Other Analgesics

PHARMACOLOGICAL 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.

Pharmacokinetics

Following administration, dexmedetomidine exhibits the following pharmacokinetic characteristics: rapid distribution phase with a distribution half-life ($t_{½\alpha}$) of about six minutes; terminal elimination half-life ($t_{½}$) of approximately two hours; steady-state volume of distribution (V_{ss}) of approximately 118 litres. Clearance has an estimated value of about 39 L/h. The mean body weight associated with this clearance estimate was 72 kg.

Dexmedetomidine protein binding was assessed in the plasma of normal healthy male and female human subjects: the average binding was 94 % and constant across the different concentrations tested. Protein binding was similar in males and females. The fraction of dexmedetomidine that was bound to plasma proteins was 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.

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 products of N-glucuronidation.

Hepatic Impairment

In subjects with varying degrees of hepatic impairment (Child-Pugh Class A, B, or C), clearance values were lower than in healthy subjects. The mean clearance values for subjects with mild, moderate, and severe hepatic impairment were 74 %, 64 % and 53 % respectively, of those observed in the normal healthy subjects. Mean clearances for free drug were 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 DOSAGE AND DIRECTIONS FOR USE and SPECIAL PRECAUTIONS).

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.

Gender

No difference in dexmedetomidine pharmacokinetics due to gender was observed.

Geriatrics

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

Paediatrics and Adolescents

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

INDICATIONS

PreceDEX 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 care setting for:**
    - Minor surgical procedures under local anaesthesia
    - Fibreoptic intubation

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

CONTRAINDICATIONS

PreceDEX is contraindicated in

- patients with a known hypersensitivity to dexmedetomidine
- patients with sepsis
- unstable trauma patients
- hypovolaemic patients
- heart block
- uncontrolled cardiac failure
- Imminent hepatic failure

WARNINGS

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

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

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

Elderly**:** 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 dexmedetomidine.

INTERACTIONS

Cytochrome P-450

In vitro studies indicate that clinically relevant cytochrome P450 mediated drug interactions are unlikely.

Anaesthetics/Sedatives/Hypnotics/Opioids

Co-administration of **PreceDEX** 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 dexmedetomidine and isoflurane, propofol, alfentanil, and midazolam were demonstrated. However, due to pharmacodynamic effects, when co-administered with **PreceDEX** a reduction in dosage of these agents may be required.

Neuromuscular Blockers

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

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

Pregnancy

There are no adequate and well-controlled studies in pregnant women. The use of **PreceDEX** is not recommended in pregnancy.

Labour and Delivery

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

Lactation

It is not known whether **PreceDEX** is excreted in human milk. The use of **PreceDEX** is not recommended in lactating women.

DOSAGE AND DIRECTIONS FOR USE

NOTE: PreceDEX should be administered only by health 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 **PreceDEX.**

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

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

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

PreceDEX 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 **PreceDEX**. Patients receiving **PreceDEX** 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. **PreceDEX** has been continuously infused in mechanically ventilated patients prior to extubation, during extubation, and post extubation. It is not necessary to discontinue dexmedetomidine prior to extubation.

Adults

ICU Sedation

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

Initiation:

For adult patients, it is recommended to initiate **PreceDEX** 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 microgram/kg/hr. 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/hr 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 CONTRAINDICATIONS, WARNINGS, SPECIAL PRECAUTIONS and PHARMACOKINETICS).

Conscious Sedation

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

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

Initiation

For adult patients, **PreceDEX** is generally initiated with a loading infusion of 1 (one) mcg/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 mcg/kg over 10 minutes may be suitable.

Maintenance of Conscious Sedation:

MAC - Following the load, maintenance dosing of **PreceDEX** should generally be initiated at 0,6 mcg/kg/hr and titrated to achieve desired clinical effect with doses ranging from 0,2 to 1 mcg/kg/hr 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 mcg/kg/hr should be used.

Children

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

Dosage Adjustment

Due to possible pharmacodynamic interactions a reduction in dosage of **PreceDEX** or other concomitant anesthetics, sedatives, hypnotics or opioids may be required when co-administered. (see INTERACTIONS)

Impaired Hepatic Function

Dosage reductions may need to be considered for patients with hepatic impairment, as **PreceDEX** 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.

Geriatrics

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

Directions for Use

A controlled infusion device should be used to administer **PreceDEX**.

Parenteral products should be inspected visually for particulate matter and discolouration prior to administration.

Ampoules/vials are intended for single patient use only.

Preparation of Solution

Strict aseptic technique must always be maintained during handling of **PreceDEX** 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 **PreceDEX** concentrate and add to 48 ml of 0,9 % sodium chloride solution to total 50 ml. Shake gently to mix well.

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

Administration with other fluids

PreceDEX has been shown to be compatible when administered with the following intravenous fluids and drugs:

Lactated Ringers, 5 % Dextrose in Water, 0,9 % Sodium Chloride in Water, 20 % Mannitol, thiopental sodium, etomidate, vecuronium bromide, pancuronium bromide, succinylcholine, atracurium besylate, mivacurium chloride, glycopyrrolate bromide, phenylephrine HCl, atropine sulphate, midazolam, morphine sulphate, fentanyl citrate and a plasma-substitute (i.e. Haemacel).

Compatibility studies have shown potential for adsorption of **PreceDEX** to some types of natural rubber. Although **PreceDEX** is dosed to effect, it is advisable to use components with synthetic or coated natural rubber gaskets.

Incompatibilities

PreceDEX must not be mixed with other medicinal products or diluents except those mentioned above.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side effects

ICU Sedation

Adverse event information is derived from the continuous infusion trials of **PreceDEX** when dosed at a maintenance dose range of 0,2 to 0,7 microgram/kg/hr to achieve the desired clinical effect for sedation in the ICU setting. 1007 patients received **PreceDEX**. Treatment-emergent adverse events occurring at an incidence of > 2 % are provided in Table 1. The adverse reactions are displayed by system organ class.

The most frequently observed treatment-emergent adverse events include hypotension, hypertension, bradycardia, nausea, dry mouth and hypoxia (see WARNINGS and SPECIAL PRECAUTIONS).

Table 1: Adverse Events with an Incidence > 2 % - ICU Sedation Population

	All PreceDEX N = 1007	**Randomised PreceDEX N = 798**	**Placebo N = 400**
Body System (MedDRA)/ Adverse Event	n (%)	n (%)	n (%)
Vascular disorders			
Hypotension	248 (24,6 %)	191 (23,9 %)	48 (12,0 %)
Hypertension	123 (12,2 %)	101 (12,7 %)	76 (19,0 %)
Gastrointestinal disorders			
Nausea.	90 (8,9 %)	73 (9,1 %)	36 (9,0 %)
Dry mouth	35 (3,5 %)	22 (2,8 %)	4 (1,0 %)
Vomiting	34 (3,4 %)	26 (3,3 %)	21 (5,3 %)
Cardiac disorders			
Bradycardia	52 (5,2 %)	36 (4,5 %)	10 (2,5 %)
Atrial fibrillation	44 (4,4 %)	37 (4,6 %)	13 (3,3 %)
Tachycardia	20 (2,0 %)	15 (1,9 %)	17 (4,3 %)
Sinus tachycardia	6 (0,6 %)	6 (0,8 %)	2 (0,5 %)
Ventricular tachycardia	4 (0.4 %)	4 (0,5 %)	3 (0,8 %)
General disorders and administration site conditions			
Pyrexia	35 (3,5 %)	31 (3,9 %)	15 (3,8 %)
Hyperthermia	19 (1,9 %)	16 (2,0 %)	12 (3,0 %)
Chills	17 (1,7 %)	14 (1,8 %)	13 (3,3 %)
Oedema peripheral	4 (0,4 %)	2 (0,3 %)	2 (0,5 %)
Metabolism and nutrition disorders			

Body System (MedDRA)/ Adverse Event	All PreceDEX N = 1007	Randomised PreceDEX N = 798	Placebo N = 400
Hypovolaemia	31 (3,1 %)	22 (2,8 %)	9 (2,3 %)
Hyperglycaemia	17 (1,7 %)	15 (1,9 %)	7 (1,8 %)
Hypocalcaemia	7 (0,7 %)	7 (0,9 %)	0
Acidosis	6 (0,6 %)	5 (0,6 %)	4 (1,0 %)
Respiratory, thoracic and mediastinal disorders			
Atelectasis	29 (2,9 %)	23 (2,9 %)	13 (3,3 %)
Pleural effusion	23 (2,3 %)	16 (2,0 %)	4 (1,0 %)
Hypoxia	16 (1,6 %)	13 (1,6 %)	8 (2,0 %)
Pulmonary oedema	9 (0,9 %)	9 (1,1 %)	3 (0,8 %)
Wheezing	4 (0,4 %)	4 (0,5 %)	1 (0,3 %)
Psychiatric disorders			
Agitation	20 (2,0 %)	16 (2,0 %)	11 (2,8 %)
Blood and lymphatic system disorders			
Anaemia	19 (1,9 %)	18 (2,3 %)	7 (1,8 %)
Injury, poisoning and procedural complications			
Post-procedural haemorrhage	15 (1,5 %)	13 (1,6 %)	10 (2,5 %)
Investigations			
Urine output decreased	6 (0,6 %)	6 (0,8 %)	0

Conscious Sedation

Adverse event information is derived from the two primary Phase III trials for conscious sedation in which 318 patients received **PreceDEX**.

Treatment-emergent adverse events occurring at an incidence of > 2 % are provided in Table 2. The adverse reactions are displayed by system organ class. The majority of the adverse events were

assessed as mild in severity. The most frequent adverse events were hypotension, bradycardia, and dry mouth. (See WARNINGS and SPECIAL PRECAUTIONS)

Table 2 : Adverse Events with an Incidence > 2 % - Conscious Sedation Population

Body System (MedDRA) / Adverse Event	**PreceDEX** **N = 318** n (%)
Vascular disorders	
Hypotension[1]	173 (54,4 %)
Hypertension[2]	41 (12,9 %)
Respiratory, thoracic and mediastinal disorders	
Respiratory depression[5]	117 (36,8 %)
Hypoxia[6]	7 (2,2 %)
Bradypnoea	5 (1,6 %)
Cardiac disorders	
Bradycardia[3]	45 (14,2 %)
Tachycardia[4]	17 (5,3 %)
Gastrointestinal disorders	
Nausea	10 (3,1 %)
Dry mouth	8 (2,5 %)

1. Hypotension was defined in absolute and relative terms as Systolic blood pressure of < 80 mmHg or < 30 % lower than pre-study drug infusion value, or Diastolic blood pressure of < 50 mmHg.
2. Hypertension was defined in absolute and relative terms as Systolic blood pressure > 180 mmHg or > 30 % higher than pre-study drug infusion value or Diastolic blood pressure of > 100 mmHg.
3. Bradycardia was defined in absolute and relative terms as < 40 bpm or < 30 % lower than pre-study drug infusion value.
4. Tachycardia was defined in absolute and relative terms as > 120 bpm or > 30 % greater than pre-study drug infusion value.

5. Respiratory Depression was defined in absolute and relative terms as RR < 8 bpm or > 25 % decrease from baseline.

6. Hypoxia was defined in absolute and relative terms as SpO2 < 90 % or 10 % decrease from baseline.

Post-marketing Experience

Table 3 : Adverse Events Experienced During Post-approval Use of PreceDEX

Body System (WHOART)	**Preferred Term**
Body as a Whole – general disorders	Allergic reaction, ascites, fever, hyperpyrexia, hypovolaemia, light anaesthesia, oedema, peripheral oedema, pain, syncope, withdrawal syndrome, rigors
Cardiovascular Disorders, General	Blood pressure fluctuation, circulatory failure, cyanosis, abnormal ECG, heart disorder, hypertension, aggravated hypertension, pulmonary hypertension, hypotension, postural hypotension, pulmonary hypertension, myocardial infarction
Central and Peripheral Nervous System Disorders	Convulsion, dizziness, headache, neuralgia, neuritis, neuropathy, paraesthesia, paralysis, paresis, speech disorder
Gastrointestinal System Disorders	Abdominal pain, diarrhoea, eructation, mucosal ulceration, nausea, vomiting
Heart Rate and Rhythm Disorders	Dysrhythmia, atrial dysrhythmia, atrial fibrillation, AV block, bradycardia, bundle branch block, cardiac arrest, extrasystoles, heart block, hypoxia, supraventricular tachycardia,T wave inversion, tachycardia, ventricular dysrhythmia, ventricular tachycardia
Liver and Biliary System Disorders	Increased AG ratio, increased GGT, abnormal hepatic function, hyperbilirubinaemia, alanine transaminase, aspartate aminotransferase, increased aspartate transaminase (AST), increased alanine transaminase (ALT), jaundice
Metabolic and Nutritional Disorders	Acidosis, lactic acidosis, respiratory acidosis, diabetes

	mellitus, hyperglycaemia, hypoglycaemia, hypokalaemia, hyperkalaemia, hypoproteinaemia, increased alkaline phosphatase, increased Non-protein nitrogen (NPN), thirst
Musculoskeletal System Disorders	Muscle weakness
Myo-,Endo-, Pericardial & Valve Disorders	Angina pectoris, myocardial infarction, myocardial ischaemia
Platelet, Bleeding & Clotting Disorders	Coagulation disorders, disseminated intravascular coagulation, haematoma, abnormal platelets, decreased prothrombin, thrombocytopenia
Psychiatric Disorders	Agitation, anxiety, confusion, delirium, depression, hallucination, illusion, nervousness
Red Blood Cell Disorders	Anaemia
Renal disorders	Increased blood urea, oliguria
Resistance Mechanism Disorders	Infection, fungal infection, sepsis
Respiratory System Disorders	Adult respiratory distress syndrome, apnoea, bronchial obstruction, bronchospasm, coughing, dyspnoea, emphysema, haemoptysis, hypercapnia, hypoventilation, hypoxia, pharyngitis, pleurisy, pneumonia, pneumothorax, pulmonary congestion, pulmonary oedema, respiratory depression, respiratory disorder, respiratory insufficiency, increased sputum, stridor
Skin and Appendages Disorders	Rash erythematous, increased sweating
Urinary System Disorders	Haematuria, acute renal failure, abnormal renal function, urinary retention
Vascular (extracardiac) Disorders	Haemorrhage, cerebral haemorrhage, peripheral ischaemia, vascular disorder, vasodilation
Vision Disorders	Diplopia, photopsia, abnormal vision
White Cell & RES Disorders	Leukocytosis

Withdrawal

ICU Sedation

Although not specifically studied, withdrawal symptoms similar to those reported for another alpha$_2$ adrenergic agent (clonidine) may result when **PreceDEX** 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 **PreceDEX** (< 6 hours).

SPECIAL PRECAUTIONS

NOTE: PreceDEX should be administered only by health professionals 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 **PreceDEX**.

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 CONTRA-INDICATIONS).

Hypotension, Bradycardia and Sinus arrest

Clinical events of bradycardia and sinus arrest have been associated with **PreceDEX** administration in young, healthy volunteers with high vagal tone, or with different routes of administration including rapid intravenous or bolus administration of **PreceDEX** (see WARNINGS).

Decreased blood pressure and/or heart rate may occur with the administration of **PreceDEX**. Based on clinical experience with **PreceDEX**, if medical intervention is required, treatment may include decreasing or stopping the infusion of **PreceDEX**, increasing the rate of intravenous fluid administration, elevation of the lower extremities and use of pressor agents. Because PreceDEX has the potential to augment bradycardia

induced by vagal stimuli, clinicians should be prepared to intervene. The intravenous administration of anticholinergic agents should be considered to modify vagal tone. In clinical trials, atropine and glycopyrrolate were effective in the treatment of most episodes of PreceDex-induced bradycardia. However, in some patients with significant cardiovascular dysfunction, more advanced resuscitative measures were required.

PreceDEX 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 **PreceDEX**. Patients who are hypovolaemic may become hypotensive under **PreceDEX** therapy. Therefore, fluid supplementation should be administered prior to and during the administration of **PreceDEX**.

Additionally, in situations where other vasodilators or negative chronotropic agents are administered, co-administration of **PreceDEX** could have an additive pharmacodynamic effect and should be administered with caution and careful titration (see INTERACTIONS).

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

Transient Hypertension

Transient hypertension has been observed primarily during the loading infusion, associated with initial peripheral vasoconstrictive effects of **PreceDEX** 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 **PreceDEX** dominate and the blood pressure usually decreases.

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

Driving and operating machinery

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

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

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

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

IDENTIFICATION

A clear, colourless concentrated solution for intravenous infusion.

PRESENTATION

Available in colourless 2 ml glass ampoules and vials in packs of 5 and 25.

STORAGE INSTRUCTIONS

PreceDEX should be stored in the original container at room temperature (at or below 25 °C). Do not refrigerate. Once diluted, the diluted solution should be used immediately. If not used immediately, the diluted solution may be stored at 2 – 8 °C during the 24 hour "in use" period. Discard any unused diluted solution after 24 hours.

Keep out of reach of children.

REGISTRATION NUMBER

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