1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS: S5

1. NAME OF THE MEDICINE

ADCOPRES 200 mcg (Solution for intravenous infusion)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2 ml vial of ADCOPRES contains 236 mcg of dexmedetomidine hydrochloride, equivalent to 200 mcg of dexmedetomidine.

The concentration of the final solution after dilution should be either 4 micrograms/ml or 8 micrograms/ml.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

ADCOPRES 200 mcg (Solution for intravenous infusion)

Clear, sterile, colourless solution for injection, free from visible extraneous matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ADCOPRES 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.

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- **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 of ADCOPRES has not been studied in children under 18 years of age.

4.2 Posology and method of administration

Posology

ADCOPRES 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 ADCOPRES. Patients in receipt of ADCOPRES have been observed to be arousable and alert when stimulated. This is a predictable component of dexmedetomidine sedation and should not be considered as evidence of lack of efficacy in the absence of other clinical signs and symptoms. ADCOPRES has been continuously infused in mechanically ventilated patients before extubation, during extubation, and after extubation. It is not deemed necessary to cease dexmedetomidine prior to extubation. In order to minimise undesirable pharmacologic side effects, bolus injections of ADCOPRES should not be used.

The administration of ADCOPRES may be associated with clinical signs of bradycardia and sinus arrest in young, healthy volunteers with high vagal tone, or by administration through different routes, including rapid intravenous or bolus administration of ADCOPRES.

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

To ensure normovolaemia, the supplementation of fluid should be administered prior to and during administration of ADCOPRES.

Adults

ICU Sedation

Dosage of ADCOPRES should be individualised and titrated to the desired clinical effect.

Initiation:

For initiation in adult patients, a loading dose of 1,0 mcg/kg over a period of 10 minutes is recommended.

Maintenance of ICU sedation:

A maintenance infusion, ranging of 0,2 to 0,7 microgram/kg/hr will generally be required in adults. The infusion maintenance rate can be adjusted in order to achieve the desired clinical effect. Dosages as low as 0,05 micrograms/kg/hr may be used. A reduction in dose for both the loading and maintenance infusions should be considered in patients with impaired hepatic or renal function and in elderly patients (over 65 years of age) (see section 4.3, 4.4 and 5.2).

Conscious Sedation

Monitored anaesthesia care (MAC) with an adequate nerve block and awake fibreoptic intubation (AFI). Dosage of ADCOPRES should be individualised and titrated to the preferred clinical effect.

Initiation

For initiation in adult patients, a loading dose of 1,0 mcg/kg over a period of 10 minutes is recommended. For elderly 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 suitable.

Maintenance of Conscious Sedation

For MAC, following the load, a maintenance dose of ADCOPRES 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 every procedure. The infusion rate for maintenance should be adjusted to achieve the targeted level of

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sedation. For AFI, following the load in awake fibreoptic intubation, a fixed maintenance dose of 0,7 mcg/kg/hr should be used.

Special Populations

Paediatrics

Safety and efficacy of ADCOPRES has not been established. ADCOPRES is not suitable for administration to individuals below 18 years of age.

Elderly

Elderly patients (over 65 years) often require lower doses of dexmedetomidine as in ADCOPRES.

Impaired Hepatic Function

The dose may have to be reduced when considering patients with hepatic impairment, ADCOPRES is primarily metabolised in the liver.

Impaired Renal Function

Considering that the majority of metabolites are eliminated in the urine, dose reductions may be needed for patients with renal impairment.

Dosage Adjustment

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

Method of Administration

For intravenous infusion

Only a controlled infusion device is to be used when ADCOPRES is administered. A visual inspection should be performed on parenteral products, prior to administration for any particulate matter and

discolouration. Glass vials are intended for single patient use ONLY. For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

ADCOPRES is contraindicated in

- patients known to be hypersensitive to dexmedetomidine or to any of the excipients listed in section 6.1
- patients with sepsis
- patients with unstable trauma
- hypovolaemic patients
- heart block
- uncontrolled cardiac failure
- imminent hepatic failure
- pregnancy and lactation

4.4 Special warnings and precautions for use

ADCOPRES shouldn't be used outside an Intensive Care Unit setting or surgical operating theatres. The vital parameters of the patient must be monitored constantly. Administration of ADCOPRES should only be performed by health professionals experienced in the management of patients in the intensive care setting. Continuous cardiac monitoring is vital during infusion of ADCOPRES. In order to minimise undesirable pharmacological side effects, bolus injections of ADCOPRES should not be used. ADCOPRES glass vials are intended for single patient use only.

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

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Respiration should be monitored in non-intubated patients due to the risk of respiratory depression and in some case apnoea.

Special Precautions

Elderly

Elderly patients are more susceptible to cardiovascular adverse events e.g., hypotension and bradycardia and the dosage must be carefully titrated to ensure the desired effect is obtained. Continuous monitoring of the cardiovascular system is required.

Cardio-vascular effects

Dexmedetomidine as in ADCOPRES reduces heart rate and blood pressure through central sympatholysis but at higher concentrations causes peripheral vasoconstriction leading to hypertension (see section 5.1). Dexmedetomidine as in ADCOPRES is therefore not suitable in patients with severe cardiovascular instability.

Caution should be exercised when administering dexmedetomidine to patients with pre-existing bradycardia disorders (i.e., advanced heart block). The hypotensive effects of dexmedetomidine may be of greater significance in those patients with pre-existing hypotension (especially if not responsive to vasopressors), hypovolaemia, chronic hypotension or reduced functional reserve such as patients with pre-existing severe ventricular dysfunction including congestive heart failure and cardiac failure in whom sympathetic tone is critical for maintaining haemodynamic balance. Patients with high physical fitness and slow resting heart rate may be particularly sensitive to bradycardic effects of alpha-2 receptor agonists.

Dose reduction or discontinuation should be considered in a patient developing signs of myocardial or cerebral ischaemia.

Patients with impaired peripheral autonomic activity (e.g., due to spinal cord injury) should be monitored closely, as they may have more pronounced haemodynamic changes after starting dexmedetomidine as in ADCOPRES.

Local vasoconstriction, at higher concentration, may be of greater significance in patients with ischaemic heart disease or severe cerebrovascular disease. Care should be taken.

Hypotension, Bradycardia and Sinus arrest

Decreased blood pressure and/or heart rate may occur with the administration of ADCOPRES. Based on clinical experience with ADCOPRES, if medical intervention is required, treatment may include decreasing or stopping the infusion of ADCOPRES, increasing the rate of intravenous fluid administration, elevation of the lower extremities and use of pressor agents. Because ADCOPRES has the potential to augment bradycardia induced by vagal stimuli, medical practitioner 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 dexmedetomidine-induced bradycardia. However, in some patients with significant cardiovascular dysfunction, more advanced resuscitative measures were required.

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

Additionally, in situations where other vasodilators or negative chronotropic agents are administered, coadministration of ADCOPRES could have an additive pharmacodynamic effect and should be administered with caution and careful titration (see section 4.5).

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

Transient Hypertension

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

Hyperthermia or pyrexia

ADCOPRES may induce hyperthermia or pyrexia, which may be resistant to traditional cooling methods, such as administration of cooled intravenous fluids and antipyretic medicines. Discontinue ADCOPRES if medicine-related hyperthermia or pyrexia is suspected and monitor patients until body temperature normalises. ADCOPRES may cause reduced lacrimation. Lubrication of the patient's eyes may be considered when administering dexmedetomidine to avoid corneal dryness.

Hepatic impairment

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

Patients with neurological disorders

Dexmedetomidine as in ADCOPRES may reduce cerebral blood flow and intracranial pressure and this should be considered when selecting therapy. Caution should be exercised when administering ADCOPRES to patients with severe neurological disorders such as head injury and after neurosurgery, especially if deep sedation is required.

ADCOPRES should not be used as a general anaesthetic induction agent for intubation or to provide sedation during muscle relaxant use. Dexmedetomidine lacks the anticonvulsant action of some other sedatives and so will not suppress underlying seizure activity.

ADCOPRES contains less than 1 mmol sodium (23 mg) per dose.

4.5 Interactions with other medicines and other forms of interaction

Anaesthetics/Sedatives/Hypnotics/Opioids

Co-administration of ADCOPRES with anaesthetics, sedatives, hypnotics and opioids is likely to lead to an enhancement of effects. 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 possible pharmacodynamic interaction, when co-administered with ADCOPRES a reduction in dosage of ADCOPRES or these medicines may be required.

Neuromuscular Blockers

No clinically significant increase in the magnitude of neuromuscular blockade and no pharmacokinetic interactions with ADCOPRES and rocuronium administration were observed.

Cardiovascular medicines

The possibility of enhanced hypotensive and bradycardic effects should be considered in patients receiving other medicines causing these effects, for example beta blockers.

Cytochrome P-450

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

Inhibition of CYP 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety of ADCOPRES in pregnancy and lactation has not been established. 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 ADCOPRES in labour and delivery has not been studied and it is therefore not recommended for obstetrics, including caesarean section deliveries.

Breastfeeding

Dexmedetomidine as in ADCOPRES is excreted in human milk, however levels will be below the limit of detection by 24 hours following treatment discontinuation. There is no information regarding the effects of ADCOPRES on the breastfed infant or the effects on milk production. The risk to infants cannot be excluded and therefore healthcare professionals must advise women to monitor the breastfed infant for irritability. A decision must be made whether to discontinue breastfeeding or to discontinue ADCOPRES therapy.

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Fertility

In the rat fertility study, dexmedetomidine had no effect on male or female fertility. No human data on fertility are available.

4.7 Effects on ability to drive and use machines

Patients should be advised to refrain from driving or other hazardous tasks for a suitable period of time after receiving ADCOPRES for procedural sedation.

4.8 Undesirable effects

a. Summary of the safety profile

ICU Sedation

The most frequently observed treatment-emergent adverse events include hypotension, hypertension, bradycardia, nausea, dry mouth and hypoxia (see section 4.4).

Procedural/awake sedation

The most frequently reported adverse reactions with ADCOPRES in procedural sedation are hypotension, respiratory depression, bradycardia.

b. Tabulated list of adverse reactions

The adverse reactions below are classified where appropriate by system organ class and frequency according to the following convention.

System Organ Class	Frequency	Adverse Event
Blood and lymphatic system disorders	Frequent	Anaemia
Metabolism and nutrition disorders	Frequent	Hyperglycaemia, hypercalcaemia, acidosis, hypovolaemia
	Less frequent	Hypoalbuminaemia
Psychiatric disorders	Frequent	Agitation

	Less frequent	Hallucination
Cardiac disorders	Frequent	Bradycardia, atrial fibrillation, sinus tachycardia, ventricular tachycardia, myocardial ischaemia or infarction, tachycardia
	Less frequent	Atrioventricular block, cardiac output decreased, cardiac arrest
Vascular disorders	Frequent	Hypotension, hypertension
Respiratory, thoracic and mediastinal disorders	Frequent	Respiratory depression, atelectasis, pleural effusion, wheezing, pulmonary oedema, hypoxia
	Less frequent	Dyspnoea, apnoea
Gastrointestinal disorders	Frequent	Nausea, vomiting, dry mouth
	Less frequent	Abdominal distension
Renal and urinary disorders	Less frequency	Polyuria
General disorders and administration site conditions	Frequent	Withdrawal syndrome, hyperthermia, pyrexia, chills, oedema peripheral
	Less frequent	Drug ineffective, thirst
Investigations	Frequent	Urine output decreased
Injury, poisoning and procedural complications	Frequent	Post-procedural haemorrhage

Post-marketing experience

System Organ Class	**Preferred term**

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Infections and infestations	Infection, fungal infection, sepsis
Blood and the lymphatic system disorders	Anaemia, leukocytosis, coagulation, disorders, disseminated intravascular coagulation, haematoma, abnormal platelets, decreased prothrombin, thrombocytopenia
Immune system disorders	Allergic reactions
Metabolism and nutrition disorders	Hyperglycaemia, hypoglycaemia, acidosis, lactic acidosis, respiratory acidosis, diabetes mellitus, hypokalaemia, hyperkalaemia, hypoproteinaemia, increased alkaline phosphate, increased Non-protein nitrogen (NPN), thirst
Psychiatric disorders	Agitation, anxiety, confusion, delirium, depression, hallucination, illusion, nervousness
Nervous system disorders	Convulsion, dizziness, headache, neuralgia, neuritis, neuropathy, paraesthesia, paralysis, paresis, speech disorder, syncope
Eye disorders	Diplopia, photopsia, abnormal vision
Cardiac disorders	Bradycardia, myocardial ischaemia, myocardial infarction, tachycardia, angina pectoris, dysrhythmia, atrial dysrhythmia, atrial fibrillation, AV block, bundle branch block, cardiac arrest, extrasystoles, heart block, hypoxia, supraventricular tachycardia, T-wave inversion, ventricular dysrhythmia, ventricular tachycardia

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Vascular disorders	Hypotension, hypertension, haemorrhage, cerebral haemorrhage, peripheral ischaemia, vascular disorder, vasodilation, circulatory failure, cyanosis, abnormal ECG, heart disorder, aggravated hypertension, pulmonary hypertension, postural hypotension, pulmonary hypertension
Respiratory, thoracic and mediastinal disorders	Adult respiratory distress syndrome, apnoea, bronchial obstruction, bronchospasm, coughing, dyspnoea, emphysema, haemoptysis, hypercapnia, pharyngitis, pleurisy, pneumonia, pneumothorax, pulmonary congestion, pulmonary oedema, respiratory depression, respiratory disorder, respiratory insufficiency, increased sputum, stridor
Gastrointestinal disorders	Abdominal pain, diarrhoea, eructation, mucosal ulceration, nausea, vomiting
Hepato-biliary disorders	Increased albumin to globulin (AG) ratio, increased gamma-glutamyl transpepsidase (GGT), abnormal hepatic function, hyperbilirubinaemia, increased aspartate transaminase (AST), increased alanine transaminase (ALT), jaundice.
Skin and subcutaneous tissue disorders	Rash erythematous, increased sweating
Musculoskeletal, connective tissue and disorders	Muscle weakness

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Renal and urinary disorders	Increased blood urea, oliguria, haematuria, acute renal failure, abnormal renal function, urinary retention
General disorders and administration site conditions	Ascites, fever, hyperpyrexia, hypovolaemia, light anaesthesia, oedema, peripheral oedema, pain, withdrawal syndrome, rigors.

c. Description of selected adverse reactions

Bradycardia and hypotension

Clinically significant hypotension or bradycardia should be treated as described in section 4.4. In relatively healthy non-ICU subjects treated with ADCOPRES, bradycardia has occasionally led to sinus arrest or pause. The symptoms responded to leg raising and anticholinergics such as atropine or glycopyrrolate. In isolated cases bradycardia has progressed to periods of asystole in patients with pre-existing bradycardia. Also, cases of cardiac arrest, often preceded by bradycardia or atrioventricular block, have been reported. Hypertension has been associated with the use of a loading dose and this reaction can be reduced by avoiding such a loading dose or reducing the infusion rate or size of the loading dose.

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 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
For reporting of side effects directly to the HCR, contact +27 11 635 0134 or email Adcock.aereports@adcock.com

4.9 Overdose

Symptoms

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First-degree AV block and second-degree heart block may occur. Bradycardia, with or without hypotension, and cardiac arrest may occur. ADCOPRES has the potential to augment bradycardia induced by vagal stimuli, therefore medical practitioner should be prepared to intervene. In clinical trials, atropine and glycopyrrolate were effective in the treatment of ADCOPRES induced bradycardia.

5. Pharmacological properties

5.1 Pharmacodynamic properties

A 2.9 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. It has a sympatholytic effect through decrease of the release of noradrenaline in sympathetic nerve endings The sedative effects of dexmedetomidine are attributed to the decreased firing of locus coeruleus, the predominant noradrenergic nucleus, situated in the brainstem.

Dexmedetomidine as in ADCOPRES has analgesic and anaesthetic/ analgesic-sparing effects. 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. The cardiovascular effects depend on the dose; with lower infusion rates, the central effects dominate leading to decrease in heart rate and blood pressure. With higher doses, peripheral vasoconstricting effects prevail leading to an increase in systemic vascular resistance and blood pressure, while the bradycardic effect is further emphasised. Dexmedetomidine has no affinity for beta adrenergic, muscarinic, dopaminergic, or serotonin receptors.

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5.2 Pharmacokinetic properties

Distribution

Following administration, dexmedetomidine exhibits the following pharmacokinetic characteristics: rapid distribution phase with a distribution half-life (t ½ α) of about six minutes; terminal elimination half-life (t ½) of approximately two hours; steady-state volume of distribution (Vss) 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 binds to both human serum albumin and Alpha-1-acid glycoprotein with serum albumin as the major binding protein of dexmedetomidine in plasma. Protein binding was similar in males and females.

Biotransformation and Elimination

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 products of N-glucuronidation.

Special Populations

Hepatic Impairment

Dexmedetomidine plasma protein binding is decreased in subjects with hepatic impairment compared with healthy subjects. The mean percentage of unbound dexmedetomidine in plasma ranged from 8.5 % in healthy subjects to 17.9 % in subjects with severe hepatic impairment. Subjects with varying degrees of hepatic impairment (Child-Pugh Class A, B, or C) had decreased hepatic clearance and prolonged plasma elimination $t_{1/2}$. The mean plasma clearance values of unbound dexmedetomidine for subjects with mild, moderate, and severe hepatic impairment were 59 %, 51 % and 32 % of those observed in the normal healthy subjects, respectively. The mean $t_{1/2}$ for the subjects with mild, moderate or severe hepatic impairment was prolonged to 3.9, 5.4, and 7.4 hours, respectively. Although ADCOPRES is

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dosed to effect, it may be necessary to consider initial/maintenance dose reduction in patients with hepatic impairment depending on the degree of impairment and the response.

Renal Impairment

Dexmedetomidine pharmacokinetics (C_{max}, T_{max}, AUC, t½, CL and Vss) 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.

5.3 Preclinical safety data

Not applicable.

Environmental Risk Assessment

Not Applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium chloride

Water for injections

6.2 Incompatibilities

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

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

6.3 Shelf life

24 months

After dilution

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C. From a microbiological point of view, the product 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° to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store 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

1 Vial

2 mL tubular, USP type I flint glass vial with13 mm Teflon coated rubber stopper (ready to sterilize) and 13 mm Aluminium flip-off seals.

Pack size

25 labelled vials

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6.6 Special precautions for disposal <and other handling>

Preparation of Solution

Strict aseptic technique must always be maintained during handling of ADCOPRES 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 ADCOPRES concentrate and add to 48 ml of 0,9 % sodium chloride solution to total 50 ml to achieve the required concentration of 4 micrograms/ml. Shake gently to mix well. ADCOPRES is intended for immediate use after dilution, and should be discarded after 24 hours.

Administration with other fluids

ADCOPRES 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, 100mg/ml magnesium sulphate solution and 0.3% potassium chloride solution.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Critical Care (Pty) Ltd

1 Sabax Road,

Aeroton, Johannesburg,

2013

Tel: 011 494 8000

8. REGISTRATION NUMBER(S)

53/2.9/0717

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 September 2024

10. DATE OF REVISION OF THE TEXT

Dharmisha Bhaga