1. NAME OF THE VETERINARY MEDICINAL PRODUCT

MedetomidineHCl injection 10 mg/ml, vial 20 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:
Active substance: medetomidineHCl ..... 10 mg
Excipients:
Methyl parahydroxybenzoate (E218).....1.0 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection. Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Experience with large animals like elephants, rhino's, buffalo's, but also hoof stock like antelopes, giraffes and zebra's.

4.2 Indications for use, specifying the target species

Medetomidine is used for sedation and immobilisation of zoo and wild life animals, often in combination with acepromazine, ketamine and etorphine, by dart delivery systems.

4.3 Contraindications

Do not use in animals with serious cardiovascular disease, respiratory disease or hepatic or renal disorders.
Do not use in cases of obstructive disorders of the gastrointestinal tract (such as torsion of the stomach, blockage, obstruction of the oesophagus).
Do not use in animals in a state of shock, emaciation or serious debilitation.
Do not use in animals with ocular problems where an increase in intraocular pressure would be detrimental.
Do not administer concomitantly with sympathomimetics or sulphonamides and trimethoprim.

4.4 Special warning s for each target species

Medetomidine may not provide analgesia throughout the entire sedation period; therefore, the use of additional analgesics should be considered during painful surgical procedures.

4.5 Special precautions for use

Medetomidine can produce respiratory depression; in such cases, manual ventilation and administration of oxygen may be required.
Treated animals should be kept warm and at a constant temperature, both during the procedure and during recovery. Vomiting and perianesthetic reflux may occasionally lead to regurgitation of gastric contents to the mouth.
Due to decreased tear flow, the eyes should be protected by a suitable lubricant (appropriate ophthalmic ointment or artificial tear solution).
In order to reduce the recovery time after anaesthesia or sedation, the effect of the product can be reversed by the administration of an alpha-2-antagonist such as atipamezole. Atipamezole does not reverse the effect of ketamine or etorphine.

<u>Special precautions to be taken by the person administering the veterinary medicinal product to animals:</u>
In case of accidental ingestion or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. DO NOT DRIVE as sedation and changes in blood pressure may occur.

Avoid skin, eye or mucosal contact.

Wash the exposed skin immediately after exposure with large amounts of water.
Remove contaminated clothes that are in direct contact with skin.

In case of accidental contact of the product with eyes, rinse abundantly with fresh water. If symptoms occur, seek the advice of a physician.
Special precautions should be taken in pregnant women handling the product, to avoid self-injection. Uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure.

Advice to physicians:
Medetomidine is an alpha2-adrenoreceptor agonist. Symptoms after absorption may involve clinical effects including dose-dependent sedation, respiratory depression, bradycardia, hypotension, a dry mouth, and hyperglycaemia. Ventricular arrhythmias have also been reported.
Respiratory and haemodynamic symptoms should be treated symptomatically. Half life in men is approximately 3 hours.

Hazardous to the aquatic environment (H400 + H401).

4.6. Adverse reactions (frequency and seriousness)
In very rare cases the following adverse reactions may appear:
- Cardiovascular effects such as bradycardia with atrioventricular block (1st and 2nd degree) and occasionally, extrasystoles, vasoconstriction of coronary artery, decreased cardiac output and increase of blood pressure just after the administration of product (followed by a return to the normal value or slightly below).
- Felidae may vomit 5 -10 minutes after injection and may also vomit on recovery.
- Pulmonary oedema, respiratory depression and cyanosis, increase of diuresis, hypothermia, sensitivity to loud noises, reversible hyperglycaemia due to a depression of insulin secretion, pain at the injection site and muscle tremors.

In cases of cardiovascular and respiratory depression, assisted ventilation and administration of oxygen may be indicated. Atropine can increase the cardiac rate. Incidents of prolonged sedation and recurrence of sedation after initial recovery have been reported.

4.7. Use during pregnancy, lactation or lay
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Therefore, do not use the drug during pregnancy and lactation.

4.8. Interaction with other medicinal products and other forms of interaction
The concomitant administration of other central nervous system depressants should be expected to potentiate the effect of either product and appropriate dose adjustment should be made. Medetomidine has marked anaesthetic sparing effects (see section 4.5 of the SPC). The dose of compounds such as propofol and volatile anaesthetics should be reduced accordingly. The effects of medetomidine can be antagonized by the administration of atipamezole. Bradycardia may be partially prevented by prior administration (at least 5 minutes before) of an anticholinergic agent; however the administration of anticholinergic agents to treat bradycardia either simultaneously with medetomidine, or following sedation with medetomidine, could lead to adverse cardiovascular effects.

4.9 Amounts to be administered and administration route
The dose range for medetomidine in non-domestic species is wide and variable. In combination with ketamine in North American Cervidae, the dose can vary from 30mcg/kg to 80mcg/kg. Professionals are advised to refer to the Handbook of Wildlife Chemical Immobilization and the current published literature for the best information on the species, dose, and combinations that have been effective in field and clinical use.

Medetomidine may be administered intravenously and /or intramuscularly. In wildlife, dart or other

remote delivery is the method for intramuscular injection. Following injection with medetomidine or medetomidine combinations, the animal should be allowed to rest quietly for at least 15 minutes post achieving sternal recumbency, as long as the animal is in a safe position and environment.

4.10 Overdose (symptoms, emergency procedures, antidotes)

In cases of overdosage, the principal signs are prolonged anaesthesia or sedation. In some cases, cardiorespiratory effects may occur. The treatment consists of the administration of an alpha-2 antagonist, such as atipamezole, provided that reversal of sedation is not dangerous for the animal (atipamezole does not reverse the effects of ketamine). Alpha-2-antagonists should not be given less than 30-40 minutes after the administration of ketamine. Cardiovascular and/or respiratory impairment should be treated symptomatically providing the capability of assisted ventilation. Atipamezole hydrochloride is administered by the intramuscular route at dosages 2.5 - 5 times the initial dose of medetomidine hydrochloride administered.
If it is imperative to reverse bradycardia but to maintain sedation, atropine may be used.

4.11. Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Hypnotics and sedatives
ATC vet code: QN05CM91.

5.1 Pharmacodynamic properties

Medetomidine is a sedative agent which presents analgesic and myorelaxant properties. It is a selective agonist specific for, and binding with high affinity to, the alpha-2-adrenergics receptors. The activation of these receptors induces a decrease in the release and turnover of noradrenaline in the central nervous system which manifests as sedation, analgesia and bradycardia. At the peripheral level, medetomidine causes vasoconstriction by stimulation of post-synaptic alpha-2-adrenergic receptors, which produces a transitory hypertension. Blood pressure returns to normal levels, even to a moderate hypotension within 1 to 2 hours. Respiratory rate can be reduced temporarily. The time and depth of sedation and analgesia are dose dependent. When the effect is maximal, the animal is relaxed and does not respond to external stimulation. Medetomidine acts in a synergic manner with ketamine or opiates, such as fentanyl, resulting in a better anesthesia. The necessary amount of volatile anesthetics (e.g. halothane) is reduced by medetomidine. In addition to its sedative, analgesia and myorelaxant properties, medetomidine also exerts hypothermic and mydriatic effects, inhibits salivation and decreases intestinal motility.

5.2 Pharmacokinetic particulars

After intramuscular injection, medetomidine is rapidly and almost completely absorbed at the site of injection and its pharmacokinetics are very similar to that observed after intravenous injection. Maximum plasma concentrations are reached within 15 to 20 minutes. Estimated plasma half-life is 1.2 hours for dogs and 1.5 hours for cats. Medetomidine is mainly oxidised in the liver, while a small amount is methylated in the kidney. Metabolites are primarily excreted in urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate
NaOH qs
water for injections

6.2 Incompatibilities

None known. Experience with admixtures of medetomidine with ketamine, acepromazine and etorphine.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years. Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product should be stored at room temperature, with strictly controlled, limited access.

6.5 Nature and composition of immediate packaging

Polypropylene injection vial of 20ml closed with a rubber stopper and sealed with an aluminium fels and red flip-off cap.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MANUFACTURER

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10. DATE OF REVISION OF THE TEXT

October 2021