Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

DEXMOPET 0.5 mg/ml solution for injection for dogs and cats

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Dexmedetomidine (equivalent to 0.5 mg of dexmedetomidine hydrochloride)	0.42 mg

Excipients:

Methyl parahydroxybenzoate (E 218)	1.60 mg
Propyl parahydroxybenzoate	0.20 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

Dogs and cats.

4.2 Indications for use, specifying the target species

Non-invasive, mildly to moderately painful, procedures and examinations which require restraint, sedation and analgesia in dogs and cats.
Deep sedation and analgesia in dogs in concomitant use with butorphanol for medical and minor surgical procedures.
Premedication in dogs and cats before induction and maintenance of general anaesthesia.

4.3 Contraindications

Do not use in animals with cardiovascular disorders, severe systemic disease or impaired liver or kidney function.
Do not use in animals with mechanical disturbances or the gastrointestinal tract (torsio ventriculi, incarcerations, oesophageal obstructions).
Do not use in pregnant animals (see also section 4.7)
Do not use in animals with diabetes mellitus
Do not use in cases of state of shock, emaciation or serious debilitation.
Do not use concomitantly with sympathomimetic amines.
Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with ocular problems where an increase in intraocular pressure would be detrimental.

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals
Treated animals should be kept warm and at a constant temperature, both during the procedure and recovery.

It is recommended that animals are fasted for 12 hours prior to the product administration. Water may be given.

After treatment, the animal should not be given water or food before it is able to swallow.

The eyes should be protected by a suitable lubricant.

To be used with precaution in elderly animals.

Nervous, aggressive or excited animals should be given the possibility to calm down before initiation of treatment.

Frequent and regular monitoring of respiratory and cardiac function should be performed. Pulse oximetry may be useful but is not essential for adequate monitoring. Equipment for manual ventilation should be available in case of respiratory depression or apnoea when dexmedetomidine and ketamine are used sequentially to induce anaesthesia in cats. It is also advisable to have oxygen readily available, should hypoxaemia be detected or suspected.

Sick and debilitated dogs and cats should only be premedicated with dexmedetomidine before induction and maintenance of general anaesthesia based on a risk-benefit assessment.

Use of dexmedetomidine as a premedicant in dogs and cats significantly reduces the amount of induction drug required for induction of anaesthesia. Attention should be given during the administration of intravenous induction drugs to effect. Volatile anaesthetic requirements for maintenance anaesthesia are also reduced.

The administration of dexmedetomidine to puppies younger than 16 weeks and kittens younger than 12 weeks has not been studied.
The safety of dexmedetomidine has not been established in males intended for breeding.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
As sedation and changes in blood pressure may occur DO NOT DRIVE in case of accidental oral intake or self-injection, seek medical advice immediately and show the package insert to the physician.

In case of contact with skin, 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.
Avoid skin, eye or mucosal contact.

As uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure if pregnant women handle the product, special caution should be observed not to self-inject.

People with known hypersensitivity to dexmedetomidine or any of the excipients should administer the veterinary medicinal product with caution.

Advice to doctors:
Dexmedetomidine is an α2-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. The specific α2-adrenoceptor antagonist, atipamezole, which is approved for use in animals, has been used in humans only experimentally to antagonize dexmedetomidine-induced effects.

4.6 Adverse reactions (frequency and seriousness)

By virtue of its α2-adrenergic activity, dexmedetomidine causes a decrease in heart rate and body temperature.

In some dogs and cats, a decrease in respiratory rate may occur. Rare instances of pulmonary oedema have been reported. Blood pressure will increase initially and then return to normal or below normal. Due to peripheral vasoconstriction and venous desaturation in the presence of normal arterial oxygenation, the mucous membranes may appear pale and/or with a blue tinge.

Vomiting may occur 5-10 minutes after injection. Some dogs and cats may also vomit at the time of recovery.

Muscle tremors may occur during sedation.

In cats, corneal opacities may occur during sedation.

When dexmedetomidine and ketamine are used sequentially, with a 10 minute interval, cats may occasionally experience AV-block or extrasystole. Expected respiratory events are bradypnoea, intermittent respiratory patterns, hypoventilation, and apnoea. In clinical trials the incidence of hypoxaemia was common, especially within the 15 first minutes into dexmedetomidine-ketamine anaesthesia. Vomiting, hypothermia and nervousness have been reported after such use.

When dexmedetomidine and butorphanol are used concomitantly in dogs, bradypnoea, tachypnoea, an irregular respiratory pattern (20-30 sec apnoea followed by several rapid breaths), hypoxaemia, muscle twitch or tremor or paddling, excitation, hypersalivation, retching, vomiting, urination, skin erythema, a sudden arousal, or prolonged sedation may occur. Brady- and tachyarrhythmias have been reported. These may include profound sinus bradycardia, 1st and 2nd degree AV block, sinus arrest or pause, as well as atrial, supraventricular and ventricular premature complexes.

When dexmedetomidine is used as a premedicant in dogs bradypnoea, tachypnoea and vomiting may occur. Brady- and tachyarrhythmias have been reported and include profound sinus bradycardia, 1st and 2nd degree AV block and sinus arrest. Supraventricular and ventricular premature complexes, sinus pause and 3rd degree AV block may be observed in rare cases.

When dexmedetomidine is used as a premedicant in cats, vomiting, retching, pale mucous membranes, and low body temperature may occur. Intramuscular dosing at 40 mcg/kg (followed by ketamine or propofol) frequently resulted in sinus bradycardia and sinus arrhythmia, occasionally resulted in 1st degree atrioventricular block, and rarely resulted in supraventricular premature depolarizations, atrial bigeminy, sinus pauses, 2nd degree atrioventricular block, or escape beats/rhythms.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in the target species. Therefore, the use is not recommended during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interactions

The use of other central nervous system depressants is expected to potentiate the effects of dexmedetomidine and therefore an appropriate dose adjustment should be made. Anticholinergics should be used with caution with dexmedetomidine.

Administration of atipamezole after dexmedetomidine rapidly reverses the effects and thus shortens the recovery period. Within 15 minutes dogs and cats are normally awake and standing.

Cats: After administration of 40 micrograms dexmedetomidine/kg bw intramuscularly concurrently with 5 mg ketamine/kg bw to cats, the maximum concentration of dexmedetomidine increased twofold but there was no effect on Tmax. The mean half-life of elimination of dexmedetomidine increased to 1.6 h and the total exposure (AUC) increased by 50%.

A dose of 10 mg ketamine/kg used concurrently with 40 micrograms dexmedetomidine/kg may cause tachycardia.

4.9 Amounts to be administered and administration route

- Dogs: intravenous or intramuscular use
- Cats: intramuscular use

The product is not intended for repeat injections.

Dexmedetomidine, butorphanol and/or ketamine can be mixed in the same syringe as they have been shown to be pharmaceutically compatible.

This veterinary medicinal product is compatible with butorphanol and ketamine in the same syringe at least for two hours.

The stopper must not be punctured more than 25 times.

Dosage: the following doses are recommended:

DOGS:
Dexmedetomidine hydrochloride doses are based on body surface area:

Intravenously: up to 375 micrograms/square metre body surface area
Intramuscularly: up to 500 micrograms/square metre body surface area

When administering in conjunction with butorphanol (0.1 mg/kg bw) for deep sedation and analgesia, the intramuscular dose of dexmedetomidine hydrochloride is 300 micrograms/square metre body surface area. The premedication dose of dexmedetomidine hydrochloride is 125 – 375 micrograms/square metre body surface area, administered 20 minutes prior to induction for procedures requiring anaesthesia. The dose should be adjusted to the type of surgery, length of procedure and patient temperament.

Concomitant use of dexmedetomidine and butorphanol produces sedative and analgesic effects beginning no later than 15 minutes. The peak sedative and analgesic effects are reached within 30 minutes after administration. Sedation lasts for at least 120 minutes post administration and analgesia lasts for at least 90 minutes. Spontaneous recovery occurs within 3 hours.

Premedication with dexmedetomidine will significantly reduce the dosage of the induction agent required and will reduce volatile anaesthetic requirements for maintenance anaesthesia. In a clinical study, the requirement for propofol and thiopental was reduced by 30% and 60% respectively. All anaesthetic agents used for induction or maintenance of anaesthesia should be administered to effect. In a clinical study, dexmedetomidine contributed to postoperative analgesia for 0.5 - 4 hours. However this duration is dependent on a number of variables and further analgesia should be administered in accordance with clinical judgement.

The corresponding doses based on body weight are presented in the following tables. Use of an appropriately graduated syringe is recommended to ensure accurate dosing when administering small volumes.

Dog Weight (kg)	Dexmedetomidine hydrochloride 125 mcg/m²		Dexmedetomidine hydrochloride 375 mcg/m²		Dexmedetomidine hydrochloride 500 mcg/m²	
	Active substance (mcg/kg bw)	Product (ml)	Active substance (mcg/kg bw)	Product (ml)	Active substance (mcg/kg bw)	Product (ml)
2-3	9.4	0.04	28.1	0.12	40	0.15
3-4	8.3	0.05	25	0.17	35	0.2
4-5	7.7	0.07	23	0.2	30	0.3
5-10	6.5	0.1	19.6	0.29	25	0.4
10-13	5.6	0.13	16.8	0.38	23	0.5
13-15	5.2	0.15	15.7	0.44	21	0.6
15-20	4.9	0.17	14.6	0.51	20	0.7
20-25	4.5	0.2	13.4	0.6	18	0.8
25-30	4.2	0.23	12.6	0.69	17	0.9
30-33	4	0.25	12	0.75	16	1.0
33-37	3.9	0.27	11.6	0.81	15	1.1
37-45	3.7	0.3	11	0.9	14.5	1.2
45-50	3.5	0.33	10.5	0.99	14	1.3
50-55	3.4	0.35	10.1	1.06	13.5	1.4
55-60	3.3	0.38	9.8	1.13	13	1.5
60-65	3.2	0.4	9.5	1.19	12.8	1.6
65-70	3.1	0.42	9.3	1.26	12.5	1.7
70-80	3	0.45	9	1.35	12.3	1.8
>80	2.9	0.47	8.7	1.42	12	1.9

For deep sedation and analgesia with butorphanol		
Dog Weight (kg)	Dexmedetomidine hydrochloride 300 mcg/m² intramuscularly	
	Active substance (mcg/kg bw)	Product (ml)
2-3	24	0.12
3-4	23	0.16
4-5	22.2	0.2
5-10	16.7	0.25
10-13	13	0.3
13-15	12.5	0.35
15-20	11.4	0.4
20-25	11.1	0.5
25-30	10	0.55
30-33	9.5	0.6
33-37	9.3	0.65
37-45	8.5	0.7
45-50	8.4	0.8
50-55	8.1	0.85
55-60	7.8	0.9
60-65	7.6	0.95
65-70	7.4	1
70-80	7.3	1.1
>80	7	1.2

CATS:

The dosage for cats is 40 mcg dexmedetomidine hydrochloride/kg bw equal to a dose volume 0.08 ml of the product/kg bw when used for non-invasive, mildly to moderately painful procedures requiring restraint, sedation and analgesia.

When dexmedetomidine is used for premedication in cats, the same dose is used. Premedication with dexmedetomidine will significantly reduce the dosage of the induction agent required and will reduce volatile anaesthetic requirements for

maintenance anaesthesia. In a clinical study, the requirement for propofol was reduced by 50%. All anaesthetic agents used for induction or maintenance of anaesthesia should be administered to effect.
Anaesthesia can be induced 10 minutes after premedication by intramuscular administration of a target dose of 5 mg ketamine/ kg bw or by intravenous administration of propofol to effect. Dosing for cats is presented in the following table.

Cat Weight (kg)	Dexmedetomidine hydrochloride 40 mcg/kg intramuscularly	
	Active substance (mcg/kg bw)	Product (ml)
1-2	40	0.1
2-3	40	0.2
3-4	40	0.3
4-6	40	0.4
6-7	40	0.5
7-8	40	0.6
8-10	40	0.7

The expected sedative and analgesic effects are reached within 15 minutes after administration and are maintained up to 60 minutes after administration. Sedation may be reversed with atipamezole. Atipamezole should not be administered prior to 30 minutes following ketamine administration.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Dogs: In cases of overdosage, or if the effects of dexmedetomidine become potentially life-threatening, the appropriate dose of atipamezole is 10 times the initial dose of dexmedetomidine (micrograms/ kg bw or micrograms/ square meter body surface area). The dose volume of atipamezole at the concentration of 5 mg/ml equals the dose volume of the product that was given to the dog, regardless of route of administration of the product.

Cats: In cases of overdosage, or if the effects of dexmedetomidine become potentially life-threatening, the appropriate antagonist is atipamezole, administered by intramuscular injection, at the following dose: 5 times the initial dose dexmedetomidine in micrograms/kg bw.
After concurrent exposure to a triple (3X) overdose of dexmedetomidine and 15 mg ketamine/ kg, atipamezole can be administered at the recommended dose level for reversal of effects induced by dexmedetomidine. At high serum concentrations of dexmedetomidine sedation is not increased although the level of analgesia does increase with further dose increases. The dose volume of atipamezole at the concentration of 5 mg/ml equals one-half the volume of the product that was given to the cat.

4.11 Withdrawal period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Psycholeptics, Hypnotics and sedatives
ATCvet code: QN05CM18

5.1 Pharmacodynamic properties

This veterinary medicinal product contains dexmedetomidine as the active substance, which produces sedation and analgesia in dogs and cats. The duration and depth of the sedation and analgesia are dose-dependent. At maximal effect, the animal is relaxed, recumbent and does not respond to external stimulus.

Dexmedetomidine is a potent and selective α2-adrenoceptor agonist that inhibits the release of noradrenaline from noradrenergic neurons. Sympathetic neurotransmission is prevented and the level of consciousness decreases. Reduced heart rate and temporary AV-block can be seen after administration of dexmedetomidine. Blood pressure decreases to normal or below normal levels after an initial increase. Respiration rate can occasionally decrease. Dexmedetomidine also induces a number of other α2-adrenoceptor mediated effects, which include piloerection, depression of motor and secretory functions of the gastrointestinal tract, diuresis and hyperglycaemia.

A slight decrease in temperature may be observed.

5.2 Pharmacokinetic particulars

As a lipophilic compound, dexmedetomidine is well absorbed after intramuscular administration. Dexmedetomidine is also rapidly distributed in the body and penetrates the blood-brain barrier readily. According to studies in rats, the maximum concentration in the central nervous system is several times that of the corresponding concentration in plasma. In the circulation, dexmedetomidine is largely bound to plasma proteins (>90%).

Dogs: After an intramuscular dose of 50 micrograms/kg a maximum concentration in plasma of about 12 ng/ml is reached after 0.6 hours. The bioavailability of dexmedetomidine is 60% and the apparent volume of distribution (Vd) is 0.9 l/kg. The elimination half-life (t½) is 40-50 minutes.

Major biotransformations in the dog include hydroxylation, glucuronic acid conjugation and N-methylation in the liver. All known metabolites lack pharmacological activity. Metabolites are excreted mainly in the urine and to a lesser extent in the faeces. Dexmedetomidine has a high clearance and its elimination depends on the hepatic blood flow. A prolonged elimination half-life is therefore expected with overdoses or when dexmedetomidine is coadministered with other substances, which affect hepatic circulation.

Cats: The maximum plasma concentration is reached about 0.24 h after intramuscular administration. After a 40 micrograms/kg bw intramuscular dose the Cmax is 17 ng/ml. The apparent volume of distribution (Vd) is 2.2 l/kg and the elimination half-life (t½) is one hour.

Biotransformations in the cat occur by hydroxylation in the liver. Metabolites are excreted mainly in the urine (51% of the dose), and to a lesser extent in the faeces. As in dogs dexmedetomidine has a high clearance in cats and its elimination depends on the hepatic blood flow. A prolonged elimination half-life is therefore expected with overdoses or when dexmedetomidine is coadministered with other substances, which affect hepatic circulation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E 218)
Propyl parahydroxybenzoate
Sodium chloride
Water for injections

6.2 Major incompatibilities

None known

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Cardboard box with one colourless type I glass vial of 10 ml, closed with a bromobutyl rubber stopper and aluminium cap with a polypropylene "flip-off" seal.

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 product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health, S.L.
Les Corts, 23
08028 Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA10516/013/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 August 2016
Date of last renewal: 06 August 2021

10 DATE OF REVISION OF THE TEXT

August 2021