[Version 9,03/2022]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dexdormostart 0.5 mg/ml solution for injection for dogs and cats (AT, BE, BG, CY, CZ, DE, EL, ES, HU, HR, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI))
Dexdormostart Vet 0,5 mg/ml solution for injection for dogs and cats (DK, FI, IS, NO, SE)
Dexdormostart solution for injection for dogs and cats (FR)
Dexdormostart, 0.5 mg/ml solution for injection for dogs and cats (EE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Dexmedetomidine hydrochloride 0.5 mg
(equivalent to 0.42 mg dexmedetomidine)

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Methyl parahydroxybenzoate (E218)	1.6 mg
Propyl parahydroxybenzoate	0.2 mg
Sodium chloride	
Hydrochloric acid, diluted (for pH-adjustment)	
Sodium hydroxide (for pH-adjustment)	
Water for injections	

Clear, colourless and practically free from particles solution for injection.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats

3.2 Indications for use for each 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.

3.3 Contraindications

Do not use in animals with cardiovascular disorders.
Do not use in animals with severe systemic disease or in animals that are moribund.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

The administration of dexmedetomidine to puppies younger than 16 weeks and kittens younger than 12 weeks has not been studied.

3.5 Special precautions for use

Special precautions for safe use in the target species
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 administration of the veterinary medicinal product. Water may be given.

After treatment, the animal should not be given water or food before it is able to swallow.
Corneal opacity may occur during sedation. 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 pre-medicant 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This veterinary medicinal product is a sedative and can cause skin and/or eye irritation. Care should be taken to avoid skin, eye, mucosal contact and self-injection. The use of impermeable gloves is advisable.
In case of accidental contact of the veterinary medicinal product with the skin or eyes, rinse with large amounts of fresh water. Remove contaminated clothes that are in direct contact with skin. If symptoms occur, seek medical advice. In case of accidental oral exposure or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation and changes in blood pressure may occur.

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

People with known hypersensitivity to the active substance and/or parabens should administer the veterinary medicinal product with caution.

Advice to physicians: The veterinary medicinal product is an a2-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 a2- adrenoceptor antagonist, atipamezole, which is approved for use in animals, has been used in humans only experimentally to antagonize dexmedetomidine-induced effects.

Special precautions for the protection of the environment:
Not applicable

3.6 Adverse events

Dogs:

Very common (> 1 animal / 10 animals treated):	Bradycardia[1] Pale or cyanotic mucous membranes[2]
Rare (1 to 10 animals / 10,000 animals treated):	Pulmonary oedema.
Undetermined frequency (cannot be estimated from the available data)	Change in blood pressure[3]. Bradypnoea. Hypothermia[1]. Vomiting[4]. Muscle tremor[5]. Corneal opacity[6].
When dexmedetomidine and butorphanol are used concomitantly:	
Common (1 to 10 animals / 100 animals treated):	Arrhythmias[7]
Undetermined frequency (cannot be estimated from the available data)	Bradypnoea, tachypnoea, irregular breathing[8], hypoxia. Muscle twitching or tremor or paddling. Excitation, sudden arousal, prolonged sedation. Hypersalivation. Retching, vomiting. Urination. Erythema.
When dexmedetomidine is used as a pre-medicant:	
Rare (1 to 10 animals / 10,000 animals treated):	Arrhythmia[9].
Undetermined frequency (cannot be estimated from the available data)	Arrhythmia[10]. Bradypnoea, tachypnoea. Vomiting.

[1] By virtue of the α2-adrenergic activity of dexmedetomidine.
[2] Due to peripheral vasoconstriction and venous desaturation in the presence of normal arterial oxygenation.
[3] Blood pressure will increase initially and then return to normal or below normal.
[4] May occur 5–10 minutes after injection. Some dogs and cats may also vomit at the time of recovery.
[5] May occur during sedation.
[6] May occur if the eyes stay open during sedation. The eyes should be protected by a suitable eye lubricant (see also section 3.5).
[7] Brady- and tachyarrhythmias. 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.
[8] 20-30 sec apnoea followed by several rapid breaths.
[9] Supraventricular and ventricular premature complexes, sinus pause and 3rd degree AV block.
[10] Brady- and tachyarrhythmias have been reported and include profound sinus bradycardia, 1st and 2nd degree AV block and sinus arrest.

Cats:

Very common (> 1 animal / 10 animals treated):	Bradycardia[1]. Vomiting[2]. Pale or cyanotic mucous membranes[3].
Rare (1 to 10 animals / 10,000 animals treated):	Pulmonary oedema.
Undetermined frequency (cannot be estimated from the available data)	Change in blood pressure[4]. Bradypnoea. Hypothermia[1]. Muscle tremor[5]. Corneal opacity[6].
When dexmedetomidine and ketamine are used sequentially (with a 10 min interval):	
Very common (> 1 animal / 10 animals treated):	AV-block.
Common (1 to 10 animals / 100 animals treated):	Hypoxia/Decreased pulse oxygenation[7]. Hypothermia.
Uncommon (1 to 10 animals / 1,000 animals treated)	Apnoea.
Undetermined frequency (cannot be estimated from the available data)	Bradypnoea, irregular breathing, hypoventilation. Vomiting. Extrasystole. Nervousness.
When dexmedetomidine is used as a pre-medicant:	
Very common (> 1 animal / 10 animals treated):	Arrhythmia[8, 9].
Common (1 to 10 animals / 100 animals treated)	Sinus bradycardia[8], sinus arrhythmia[8], supraventricular and nodal arrhythmia. Retching.
Uncommon (1 to 10 animals / 1,000 animals treated)	1st degree AV block[8].
Undetermined frequency (cannot be estimated from the available data)	Vomiting. Pale mucous membranes. Hypothermia.

[1] By virtue of the α2-adrenergic activity of dexmedetomidine.
[2] May occur 5–10 minutes after injection. Some dogs and cats may also vomit at the time of recovery.
[3] Due to peripheral vasoconstriction and venous desaturation in the presence of normal arterial oxygenation.
[4] Blood pressure will increase initially and then return to normal or below normal.
[5] May occur during sedation.
[6] May occur if the eyes stay open during sedation. The eyes should be protected by a suitable eye lubricant (see also section 3.5).
[7] Especially within the 15 first minutes of anaesthesia.
[8] After intramuscular dosing at 40 micrograms/kg (followed by ketamine or propofol).

[9] Supraventricular premature complexes, atrial bigeminy, sinus pauses, 2nd degree AV block, escape beats/rhythms.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy or lactation

The safety of dexmedetomidine has not been established during pregnancy and lactation in the target species.

Pregnancy and lactation:
The use is not recommended during pregnancy and lactation.

Fertility:
The safety of dexmedetomidine has not been established in males intended for breeding.

3.8 Interaction with other medicinal products and other forms of interaction

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 T_{max}. 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.

3.9 Administration routes and dosage

Dogs: intravenous or intramuscular use
Cats: intramuscular use

The product is not intended for repeat injections.
To ensure a correct dosage, body weight should be determined as accurately as possible.

Dosage: the following doses are recommended:

Dogs:
Dexmedetomidine 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) for deep sedation and analgesia, the intramuscular dose of dexmedetomidine is 300 micrograms/square metre body surface area. The premedication dose of dexmedetomidine 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 after administration. 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 125 mcg/m²**		**Dexmedetomidine 375 mcg/m²**		**Dexmedetomidine 500 mcg/m²**	
	(mcg/kg)	**(ml)**	**(mcg/kg)**	**(ml)**	**(mcg/kg)**	**(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 300 mcg/m² intramuscularly**	
	(mcg/kg)	**(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 micrograms dexmedetomidine hydrochloride/kg bw equal to a dose volume 0.08 ml 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 40 mcg/kg intramuscularly (mcg/kg)**	**(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.
The stoppers should not broached more than 30 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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 this veterinary medicinal product that was given to the dog, regardless of route of administration of dexmedetomidine.

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 this veterinary medicinal product that was given to the cat.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN05CM18

4.2 Pharmacodynamics

The 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 a2-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 a2-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.

4.3 Pharmacokinetics

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 nanograms/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 co-administered 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 C_{max} is 17 nanograms/ml. The apparent volume of distribution (Vd) is 2.2 l/kg and the elimination half-life (t½) is one hour.

Biotransformation in the cat occurs 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 co-administered with other substances, which affect hepatic circulation.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Cardboard box with one clear Type I glass vial of 10 ml or 20 ml with grey fluorinated coated bromobutyl rubber stopper and aluminium cap.

Pack sizes:
5 ml (in a 10 ml sized vial)
10 ml
20 ml

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).