Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Domitor 1 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Medetomidine hydrochloride (equivalent to 0.85 mg/ml medetomidine)	1 mg/ml

Excipients:

Methyl parahydroxybenzoate (E218)	1 mg/ml
Propyl parahydroxybenzoate	0.2 mg/ml

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

Dogs:

- For restraint, sedation and analgesia associated with clinical examinations and procedures, minor surgery and as premedication before general anaesthesia
- In combination with butorphanol for sedation and analgesia

Cats:

- For restraint and sedation
- In combination with ketamine for the induction of general anaesthesia prior to surgical procedures
- In combination with butorphanol for sedation and analgesia, and combined with both butorphanol and ketamine for general anaesthesia
- As a premedication before alfaxalone or alfadolone for general anaesthesia

4.3 Contraindications

Do not use in animals with cardiovascular disease, respiratory disease or impaired liver or kidney function, animals in shock, seriously debilitated animals, or animals that are stressed due to extreme heat, cold or fatigue.

Do not use in conjunction with sympathomimetic amines.

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

Before using any combinations consult the contraindications and warnings that appear on the other product's data sheet.

4.4 Special warnings 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.

When the veterinary medicinal product is administered, the animal should be allowed to rest in a maximally quiet place. Before any procedure is started or other drugs are administered, sedation should be allowed to reach its peak effect, which occurs at about 10 to 30 minutes, depending on the route of administration.

In extremely nervous, excited or agitated animals, the levels of endogenous catecholamines may be high. The pharmacological response elicited by alpha-2 agonists (e.g. medetomidine) in such animals is often reduced, with depth and duration of sedative and analgesic effects ranging from slightly diminished to non-existent. Highly agitated animals should therefore be put at ease and allowed to rest quietly prior to receiving the veterinary medicinal product. Allowing animals to rest quietly for 10 to 15 minutes after injection may improve the response to the veterinary medicinal product.

4.5 Special precautions for use

Special precautions for use in animals

A clinical examination should be carried out in all animals before the use of drugs for sedation and/or general anaesthesia.

Care should be taken when using medetomidine with other anaesthetics or sedatives. Medetomidine has marked anaesthetic sparing effects. The dose of the anaesthetic should be reduced accordingly.

Special care is recommended when treating very young animals and older animals. The veterinary medicinal product should not be used in dogs under 12 weeks of age.

Fasting is recommended before administration of the veterinary medicinal product. After treatment, the animal should not be given water or food before it is able to swallow properly.

Treated animals should be kept in a warm and even temperature during the procedure and for 12 hours after sedation.

During prolonged procedures an ophthalmic preparation should be administered at regular intervals to lubricate the cornea especially in cats and sometimes also in dogs if their eyes remain open.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

In the case of accidental oral intake or self-injection, seek medical advice immediately and show the package leaflet to the doctor but 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 the case of accidental contact of the product with eyes, rinse abundantly with fresh water. If symptoms occur, seek the advice of a physician.

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

Advice to doctors:

Medetomidine hydrochloride is an alpha-2 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.

4.6 Adverse reactions (frequency and seriousness)

Blood pressure will increase initially and then return to normal or slightly below.

Bradycardia with occasional atrioventricular block may occur. Cyanosis has been reported.

Some dogs and most cats vomit 5 to 15 minutes after injection. Some cats may also vomit upon recovery.

Body temperature is slightly or moderately decreased and prolonged recovery may lead to hypothermia.

An increase in blood glucose concentration is seen due to alpha-2-adrenoreceptor mediated inhibition of insulin secretion.

Urination typically occurs during recovery at about 90 to 120 minutes post-treatment.

Some animals experience muscle tremors and may be sensitive to loud sounds.

Incidents of prolonged sedation and recurrence of sedation after initial recovery have been reported.

Isolated cases of hypersensitivity, paradoxical response (excitation) and lack of efficacy have been reported.

Death from circulatory failure with severe congestion of the lungs, liver, or kidney has been reported. Decreased respiratory rates with or without transient apnoea periods may occur. If the animal has a pre-existing subclinical respiratory disease, administration of the veterinary medicinal product can cause some significant respiratory depression which could predispose the animal to adverse effects such as cardiac arrest. Pulmonary oedema has been reported.

In cats, when the veterinary medicinal product is used in combination with ketamine, laryngeal and pharyngeal reflexes are retained during anaesthesia. The combination is reported to elicit a pain response in some cats when administered intramuscularly. Heart rates will generally decrease to approximately 50% of pre-anaesthetic levels and in some cats very slow respiratory rates are observed (4-6 breaths per minute).

In dogs, when the veterinary medicinal product is used in combination with propofol, movement of the forelegs may occur during induction of anaesthesia. In some cases at higher dosages, a decline in arterial oxygen tension may occur.

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

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy or lactation. The use is not recommended during pregnancy or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Domitor should not be used in conjunction with sympathomimetic amines. The concomitant use of other central nervous system depressants should be expected to potentiate the effect of either product and appropriate dose adjustment should be made.

The veterinary medicinal product has marked anaesthetic sparing effects. The dose of compounds such as propofol and volatile anaesthetics should be reduced accordingly.

Although bradycardia may be partially prevented by prior administration (at least 5 minutes before the veterinary medicinal product) of an anticholinergic agent, 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

Domitor is intended for injection by intramuscular, intravenous and subcutaneous routes in the dog, and by the intramuscular and subcutaneous route in the cat.

Dosage: the following dose ranges are recommended for Domitor

When used alone for sedation and analgesia

Animal	**Dose µg/kg**	**Effect**	**Quantity**
Dog	10-30	Slight sedation	0.1 - 0.3 ml/10 kg
	30-80	Moderate to deep sedation and analgesia	0.3 - 0.8 ml/10 kg
	10-20	Pre-anaesthesia	0.1 - 0.2 ml/10 kg
Cat	50-100	Moderate sedation	0.25 - 0.5 ml/5 kg
	100-150	Deep sedation	0.50 – 0.75 ml/5kg

Maximal effect is obtained within 10 - 15 minutes. The clinically useful effect is dose-related, lasting 30 - 180 minutes, but injection may be repeated if necessary. Animals should be fasted for 12 hours prior to anaesthesia.

Premedication dosing guide: Domitor has marked anaesthetic-sparing effects. It is essential to reduce appropriately the dose of anaesthetic induction and maintenance agents in animals that have been given Domitor.

Dosing guide:

DOMITOR AS PREMEDICANT BEFORE PROPOFOL IN DOGS
Domitor is administered either intravenously at least 10 minutes before propofol (induction agent) or intramuscularly at least 20 minutes before propofol to allow sedation to develop. Domitor may be administered at a dose rate of 10, 20 or 40 micrograms/kg. The following table is a guideline for doses of Domitor and Propofol:

Domitor		Propofol (Induction) Dose in mg/kg
Dose µg/kg	Quantity ml/10 kg	
10	0.1	1.5
20	0.2	1.1
40	0.4	1.0

Following premedication with Domitor, doses of propofol of up to 4 mg/kg have been safely used when a greater depth of anaesthesia is required.

NB: The induction time is increased following Domitor premedication, propofol should be administered slowly and up to 2.5 minutes should be allowed before a further dose is given.

Once jaw relaxation is adequate, tracheal intubation can be undertaken. It is advisable to administer oxygen during anaesthesia.
For maintenance of anaesthesia the dose of propofol is markedly reduced by medetomidine premedication. Infusion doses of 0.06 to 0.35 mg/kg/minute will provide stable anaesthesia for dogs sedated with between 40 and 10 µg/kg Domitor, respectively. For intermittent bolus administration, a dose of 1 mg/kg at intervals of between 4 and 12 minutes will provide stable anaesthesia.
Recovery from anaesthesia may take from 20 to > 60 minutes.
Food should be withheld for 12 hours prior to anaesthesia.
Antisedan administered intramuscularly at 50 – 200 µg/kg (0.1 - 0.4 ml per 10 kg) in the post-operative phase will hasten the recovery from anaesthesia.

DOMITOR WITH BUTORPHANOL FOR CANINE SEDATION
Dose rate: by intramuscular or intravenous injection, Domitor 10 - 25 µg/kg bodyweight, depending on the degree of sedation required, plus 0.1 mg/kg butorphanol. Allow 20 minutes for sedation to develop before commencing the procedure.
Reversal with an equal volume of Antisedan to that of Domitor used results in sternal recumbency approximately 5 minutes later and standing approximately a further 2 minutes later.

DOMITOR WITH KETAMINE IN CATS:
Domitor and Vetalar (ketamine) are administered concomitantly, in the same syringe, by the intramuscular route. To minimise the possibility of cross contamination, the vials of each product should have separate needles inserted for withdrawal. Domitor should be administered at a rate of 80 µg/kg with a concomitant dose of 5 - 7.5 mg/kg of Vetalar.

Using this regime the average onset of anaesthesia is 3 - 4 minutes and surgical anaesthesia can be expected to last between 30 and 50 minutes. If required, anaesthesia may be prolonged with inhalational anaesthetics.

Food should be withheld for 12 hours prior to anaesthesia

DOMITOR WITH BUTORPHANOL FOR FELINE SEDATION
Dose rate: by intramuscular or subcutaneous injection: Domitor 50 µg/kg, depending on the degree of sedation required, plus 0.4 mg/kg butorphanol. Allow 20 minutes for sedation to develop before commencing the procedure.
Local anaesthetic infiltration should be used for wound suturing.
Reversal with half volume of Antisedan to that of Domitor used, results in sternal recumbency approximately 4 minutes later and standing approximately a further 2 minutes later.

Feline doses (ml) for sedation:

Weight (kg)		**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**
Domitor 1 mg/ml	50µg/kg	0.05	0.08	0.10	0.13	0.15	0.18	0.20	0.23	0.25
butorphanol 10 mg/ml	0.4 mg/kg	0.04	0.06	0.08	0.10	0.12	0.14	0.16	0.18	0.20

DOMITOR, BUTORPHANOL AND KETAMINE FOR FELINE ANAESTHESIA
a) *Intramuscular*
Dosage: Domitor 80 µg/kg, and ketamine 5 mg/kg should be given in a single syringe, and butorphanol 0.4 mg/kg in a separate one.
Cats become recumbent in 2 - 3 minutes following injection. Loss of pedal reflex occurs 3 minutes post injection.

Reversal by 200 µg/kg Antisedan (0.04 ml/kg i/m) results in return of pedal reflex 2 minutes later, sternal recumbency 6 minutes later and standing 31 minutes later.

Feline doses (ml) for I/M ketamine anaesthesia:

Weight (kg)		**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**
Domitor 1 mg/ml	80 µg/kg	0.08	0.12	0.16	0.2	0.24	0.28	0.32	0.36	0.40
butorphanol 10mg/ml	0.4 mg/kg	0.04	0.06	0.08	0.1	0.12	0.14	0.16	0.18	0.20
ketamine 100 mg/ml	5 mg/kg	0.05	0.075	0.1	0.125	0.15	0.175	0.2	0.225	0.25

b) *Intravenous*
Dosage: Domitor 40 µg/kg, butorphanol 0.1 mg/kg and ketamine (depending on depth of anaesthesia required) from 1.25 to 2.5 mg/kg.

Reversal by 100 µg/kg of Antisedan results in return of pedal reflex 4 minutes later, sternal recumbency 7 minutes later and standing 18 minutes later.

Feline doses (ml) for I/V ketamine anaesthesia:

Weight (kg)		**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**
Domitor 1 mg/ml	40 µg/kg	0.04	0.06	0.08	0.10	0.12	0.14	0.16	0.18	0.20
butorphanol 10 mg/ml	0.1 mg/kg	0.01	0.02	0.02	0.03	0.03	0.04	0.04	0.05	0.05
EITHER ketamine 100 mg/ml	1.25 mg/kg	0.01	0.02	0.03	0.03	0.04	0.04	0.05	0.06	0.06
OR ketamine 100 mg/ml	2.5 mg/kg	0.03	0.04	0.05	0.06	0.08	0.09	0.10	0.11	0.13

Approximate time scales in intravenous Domitor/butorphanol/ketamine anaesthesia:

ketamine dose	time to recumbency	time to loss of pedal reflex	time to return of pedal reflex	time to sternal recumbency	time to standing
1.2 mg/kg	32 secs	62 secs	26 mins	54 mins	74 mins
2.5 mg/kg	22 secs	39 secs	28 mins	62 mins	83 mins

DOMITOR FOLLOWED BY ALFAXALONE/ALFADOLONE FOR GENERAL ANAESTHESIA
Dosage: Administer Domitor 80 µg/kg by intramuscular or subcutaneous injection. 15 - 60 minutes later administer 2.5 – 5.0 mg/kg alfaxalone/alfadolone intravenously. Anaesthesia may be maintained by further intravenous injections of alfaxalone/alfadolone, or by administration of halothane in oxygen.

Feline doses (ml) for alfaxalone/alfadolone anaesthesia:

Weight (kg)		**1**	**1.5**	**2**	**2.5**	**3**	**3.5**	**4**	**4.5**	**5**
Domitor 1 mg/ml	80 µg/kg	0.08	0.12	0.16	0.2	0.24	0.28	0.32	0.36	0.40
alfaxalone 9 mg/ml /alfadolone 3 mg/ml	minimum dose = 2.5 mg/kg	0.21	0.31	0.42	0.52	0.63	0.73	0.83	0.94	1.04
alfaxalone 9 mg/ml /alfadolone 3 mg/ml	maximum dose = 5 mg/kg	0.42	0.63	0.83	1.04	1.25	1.46	1.67	1.88	2.08

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

Overdose is mainly manifested by delayed recovery after sedation or anaesthesia. In a few individuals, circulatory and respiratory depression may occur.

In cases of overdosage, or if the effects of medetomidine become life-threatening, the appropriate dose of atipamezole is recommended provided that reversal of sedation and analgesia is not dangerous to the patient. For example, atipamezole does not reverse the effects of ketamine. In the dog, the atipamezole dosage calculated in ml is the same as that of medetomidine (expressed in mcg the dosage of atipamezole is 5 times that of medetomidine). In the cat, the atipamezole dosage in ml is half that of medetomidine (expressed in mcg the dosage of atipamezole is 2.5 times that of medetomidine).

If it is imperative to reverse bradycardia but maintain sedation, atropine may be used (see section 4.8).

Considering the seriousness of the situation, the animal can be ventilated with oxygen and given intravenous fluids. Maintaining the normal body temperature both in sedation and recovery is important. If the animal is hypothermic, elevation of the body temperature will speed up the recovery.

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other hypnotics and sedatives
ATC vet code: QN05CM91

5.1 Pharmacodynamic properties

The active ingredient of Domitor is medetomidine. Medetomidine is an alpha-2 adrenergic agonist with central and peripheral effects inhibiting the transmission of noradrenaline-mediated nerve impulses by activating pre-and post-synaptic alpha-2 adrenoceptors. In the animal, the level of consciousness is lowered and the pain threshold is raised. The action of medetomidine is dose−dependent: small doses cause mild sedation and analgesia, while larger doses produce high levels of sedation and analgesia.

Medetomidine lowers the heart rate and initially elevates the blood pressure; blood pressure returns to baseline or slightly below baseline over fifteen minutes. The cardiovascular changes observed are either centrally mediated (bradycardia, hypotension) or due to direct effects on alpha-2 receptors (vasoconstriction, increased systemic vascular resistance).

The vasoconstriction may turn the mucous membranes pale or slightly bluish. Dogs may develop benign conductivity disturbances (first or second degree AV block). The respiratory rate is lowered. Local muscular twitching may occur in a few individuals. Blood glucose levels are elevated in both animal species. Body temperature is decreased in a dose dependent manner and intestinal motility is also reduced.

5.2 Pharmacokinetic properties

Medetomidine is rapidly absorbed after intramuscular injection; the t_{max} varies from 15 to 30 min. Medetomidine is also rapidly distributed. The V_d varies between 2.8 and 3.6 L/kg. Protein binding is 85 to 90%. Medetomidine is oxidised in the liver and a small proportion is methylated in the kidneys. Most metabolites are excreted in the urine. The $T_{½}$ is 1-2 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Sodium chloride
Water for injection

6.2 Incompatibilities

The product must not be mixed with other drugs with the exception of Vetalar (ketamine) injection and butorphanol.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packed for sale: 3 years.
Shelf life after opening the immediate packing: 3 months.

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and composition of immediate packaging

The product is presented in Type I (Ph. Eur.) clear glass vials of 10 ml capacity. Vials are fitted with a fluoropolymer coated bromobutyl rubber stopper and sealed with an aluminium seal.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

Orion Corporation
Orionintie 1
FI-02200 Espoo
Finland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10664/005/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22nd October 2010

10 DATE OF REVISION OF THE TEXT

April 2017