Treated animals should be kept in a warm and even temperature during the procedure.

Special care is recommended when treating very young animals and older animals. Medetomidine has marked anaesthetic-sparing effects. The dose of the anaesthetic should be reduced accordingly, by up to 50-90%, depending on the individual animal.

Care should be taken when combining medetomidine with other anaesthetics or sedatives. Avoid skin, eye or mucosal contact. 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 normal. 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 may occur.
If the animal has a pre-existing subclinical respiratory disease, administration of Domitor can cause some significant respiratory depression which could predispose the animal to cardiac arrest. Pulmonary oedema has been reported.

The combination of Domitor and ketamine 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 Domitor 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.

Reporting suspected adverse reactions after autorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://forms.gov.il/qlglobadata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il.

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

4.8 Interaction with other medicinal products and other forms of interaction
Medetomidine 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. Medetomidine must not be mixed with other products, with the exception of Ketaset Injection and Torbugesic injection.

Medetomidine has marked anaesthetic-sparing effects. The dose of compounds such as propofol and volatile anaesthetics should be reduced accordingly, up to 50-90%, depending on the individual animal.
Although bradycardia may be partially prevented by prior administration (at least 5 minutes before Domitor) 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
An appropriately graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting small volumes. Administration by intramuscular (IM), intravenous (IV) and subcutaneous (SC) routes are possible. The effect is most rapid after IV administration and slowest after SC administration. The dosage is dependent on the degree of sedation and analgesia required.

<table>
<thead>
<tr>
<th>Domitor</th>
<th>Dose mcg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs</td>
<td>10-80</td>
</tr>
<tr>
<td>Cats</td>
<td>50-150</td>
</tr>
</tbody>
</table>

For sedation, small dogs require more Domitor per kg of body weight than large dogs, thus the dosage per square meter of body surface could be more accurate. If this approach is used, the dosage is 750 to 1000 mcg/square meter.

The following table gives the dosage for dogs on the basis of body weight.

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Injection volume (ml)</th>
<th>Body weight (kg)</th>
<th>Injection volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV administration</td>
<td>IM/SC administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5-2.2</td>
<td>0.1</td>
<td>1.5-2.2</td>
<td>0.1</td>
</tr>
<tr>
<td>2.3-3.5</td>
<td>0.15</td>
<td>2.3-3.5</td>
<td>0.15</td>
</tr>
<tr>
<td>3.6-5.1</td>
<td>0.2</td>
<td>3.6-5.1</td>
<td>0.2</td>
</tr>
<tr>
<td>5.2-6.9</td>
<td>0.25</td>
<td>5.2-6.9</td>
<td>0.25</td>
</tr>
<tr>
<td>7.0-9.9</td>
<td>0.3</td>
<td>7.0-9.9</td>
<td>0.3</td>
</tr>
<tr>
<td>10.0-14.4</td>
<td>0.4</td>
<td>10.0-14.4</td>
<td>0.4</td>
</tr>
<tr>
<td>14.5-19.5</td>
<td>0.5</td>
<td>14.5-19.5</td>
<td>0.5</td>
</tr>
<tr>
<td>19.6-25.1</td>
<td>0.6</td>
<td>19.6-25.1</td>
<td>0.6</td>
</tr>
<tr>
<td>25.2-31.1</td>
<td>0.7</td>
<td>25.2-31.1</td>
<td>0.7</td>
</tr>
<tr>
<td>31.2-37.6</td>
<td>0.8</td>
<td>31.2-37.6</td>
<td>0.8</td>
</tr>
<tr>
<td>37.7-44.4</td>
<td>0.9</td>
<td>37.7-44.4</td>
<td>0.9</td>
</tr>
<tr>
<td>44.5-55.3</td>
<td>1.0</td>
<td>44.5-55.3</td>
<td>1.0</td>
</tr>
<tr>
<td>55.4-71.1</td>
<td>1.2</td>
<td>55.4-71.1</td>
<td>1.2</td>
</tr>
<tr>
<td>71.2-88.2</td>
<td>1.4</td>
<td>71.2-88.2</td>
<td>1.4</td>
</tr>
<tr>
<td>88.3 +</td>
<td>1.6</td>
<td>88.3 +</td>
<td>1.6</td>
</tr>
<tr>
<td>2.0</td>
<td>75.9 +</td>
<td>2.0</td>
<td>75.9 +</td>
</tr>
</tbody>
</table>

Anaesthesia:
Domitor is suitable for use as an anaesthetic premedication prior to general anaesthesia.

Premedication dosing guide: Medetomidine 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 the product.

<table>
<thead>
<tr>
<th>Combinant</th>
<th>Dosage (Dogs) (mcg/kg)</th>
<th>Dosage (Cats) (mcg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Propofol</td>
<td>10-40</td>
<td>1-4</td>
</tr>
</tbody>
</table>

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.

The effects of Domitor can be eliminated using the specific alpha-2 adrenergic antagonist atipamezole (Antisedan). In the dog, the Antisedan dosage expressed in mcg is 5 times that of Domitor. In the cat, the Antisedan dosage expressed in mcg is 2.5 times that of Domitor.

4.11 Withdrawal period
Not applicable.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: sedative and analgesic.
ATC vet Code: QN05CM91.

5.1 Pharmacodynamic properties
The active ingredient of Domitor is medetomidine. Its chemical structure is 4-[1(2,3-dimethylphenyl)ethyl]H imidazole hydrochloride. 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 decreases.

5.2 Pharmacokinetic particulars
Medetomidine is rapidly absorbed after intramuscular injection; the t1/2 varies from 15 to 30 min. Medetomidine is also rapidly distributed in the organism. The Vd 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 t1/2 is 1-2 hours.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Methyl parahydroxybenzoate
Propyl parahydroxybenzoate
Sodium chloride
Water for injections

6.2 Incompatibilities
Medetomidine must not be mixed with other products with the exception of Ketaset injection.

6.3 Shelf-life
Do not use the veterinary medicinal product after the expiry date (exp. Date) mentioned on the package. The expiry date refers to the last day of that month.
Shelf-life after first opening the immediate packaging: 28 days. Discard unused material.

6.4 Special precautions for storage
Do not store above 25°C. Protect from freezing.
This medicine and any other medicine must be kept in a safe place out of the reach of children and/or infants to avoid poisoning.

6.5 Nature and composition of immediate packaging
Sterile aqueous solution and presented in clear, Type I glass vials of 10 ml capacity. Vials are fitted with a chlorobutyl rubber bung and sealed with an aluminium seal.

7. MARKETING AUTHORISATION HOLDER
Zoetis Israel Holding B.V.
5 Atir Yeda Street, Kfar Saba, Israel

8. MARKETING AUTHORISATION NUMBER
082 58 92306 00

9. MANUFACTURER
Orion Corporation Orion Pharma, Finland
Orionintie 1, 02200 Espoo, Finland

10. VETERINARY USE
The veterinary medicine is dispensed with a veterinarian’s prescription only