SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Detonervin 10 mg/ml, solution for injection for Horses and Cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:
Active substance:
Detomidine hydrochloride: 10.0 mg
(equivalent to 8.36 mg detomidine)

Excipients:
Methyl parahydroxybenzoate (E218): 1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Horse, cattle.

4.2 Indications for use, specifying the target species

For the sedation and slight analgesia of horses and cattle, to facilitate physical examinations and treatments, such as minor surgical interventions.
Detomidine can be used for:
- Examinations (e.g. endoscopy, rectal and gynaecological examinations, X-rays).
- Minor surgical procedures (e.g. treatment of wounds, dental treatment, tendon treatment, excision of skin tumours, teat treatment).
- Before treatment and medication (e.g. stomach tube, horse shoeing).

For premedication prior to administration of injection- or inhalation anaesthetics.

See section 4.5 before use.

4.3 Contraindications

- Do not use in animals with cardiac abnormalities or respiratory diseases.
- Do not use in animals with liver insufficiency or renal failure.
- Do not use in animals with general health problems (e.g. dehydrated animals).
- Do not use in combination with butorphanol in horses suffering from colic.

- Do not use in the last trimester of pregnancy.

See also section 4.7. and 4.8.

4.4 Special warnings

None.

4.5 Special precautions for use

Special precautions for use in animals

- As sedation begins, especially horses may start to sway and lower the head rapidly while they remain standing. Cattle and especially young cattle will try to lie down. To prevent injuries the location should therefore be chosen carefully. Especially for horses usual precautionary measures should be taken to prevent human or animal injury. To avoid ruminal bloat and aspiration of feed or saliva, cattle should be maintained in sternal recumbency during and following treatment and head and neck of recumbent cattle should be lowered.
- Animals suffering from shock or liver or kidney disease should only be treated according to the benefit risk assessment by the responsible veterinarian.
- The product should not be used in animals suffering from cardiac diseases (with pre-existing bradycardia and risk of atrioventricular block), respiratory-, liver- or renal insufficiencies, shock or any other extraordinary stress conditions.
- Detomidine/butorphanol combination should not be used in horses with a history of liver disease or cardiac irregularities.
- It is recommended that feed should be withheld for at least 12 hours prior to anaesthesia. Water or food should not be offered to treated animals until the drug effect has passed.
- In painful procedures detomidine should be used only in combination with an analgesic or a local anaesthetic.
- While waiting for sedation animals should remain in calm surroundings.
- In case of sustained effect it is necessary to protect the animals from heat or cold.

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 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.
- 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:
Detomidine is an alpha2-adrenoreceptor agonist, which 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)

Injection of detomidine may cause the following side effects:
- Bradycardia
- Transient hypo- and/or hypertension
- Respiratory depression, rarely hyperventilation
- Increase in blood glucose
- As with other sedatives, in rare cases paradoxical reactions (excitations) can develop
- Ataxia
- Uterine contractions
- In horses: Cardiac arrhythmia, atrioventricular and sino-atrial block
- In cattle: Inhibition of rumen motility, tympany, paralysis of the tongue.

At doses above 40 µg/kg bodyweight, the following symptoms can also be observed: sweating, pilo-erection and tremor of muscles, transient penis prolaps in stallions and geldings and mild, transient tympany of rumen and increased salivation in cattle.
In very rare cases horses may show mild symptoms of colic following administration of alpha-2 sympathomimetics because substances of this class transiently inhibit the motility of the intestines. Detomidine should be prescribed with caution in horses which present with signs of colic or impaction.
A diuretic effect is usually observed within 45 to 60 minutes after treatment.

4.7 Use during pregnancy, lactation or lay

Do not use during the last trimester of pregnancy. Use only according to the benefit/risk assessment by the responsible veterinarian during the other months of pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of other sedatives only after consultation of the warnings and precautions of the product concerned.
Detomidine should not be used in combination with sympathomimetic amines such as adrenaline, dobutamine and ephedrine.
The concurrent use of certain potentiated sulphonamides may cause cardiac arrhythmia with fatal outcome. Do not use in combination with sulphonamides.
Detomidine in combination with other sedatives and anaesthetics should be used carefully because additive/synergistic effects may be possible. Where anaesthesia is induced with a combination of detomidine and ketamine, prior to maintenance with halothane, the effects of halothane may be delayed and care must be taken to avoid overdosage. When detomidine is used as a premedicant prior to general anaesthesia, the product may delay the onset of induction.

4.9 Amounts to be administered and administration route

For intravenous (IV) or intramuscular (IM) use. The product should be injected slowly. Onset of effect is more rapid following intravenous use.

Dosage in µg detomidine hydrochloride/kg	Dosage in ml/100 kg	Level of sedation	Commencement of effect (min)	Duration of effect(hrs)

			horse	cattle	
10-20	0.1-0.2	Light	3-5	5-8	0.5-1
20-40	0.2-0.4	Moderate	3-5	5-8	0.5-1

When prolonged sedation and analgesia is required, doses of 40 to 80 µg detomidine hydrochloride /kg can be used. The duration of effect is up to 3 hours.
For combination with other product to intensify the sedation or for premedication prior to general anaesthesia, doses of 10 to 30 µg detomidine hydrochloride /kg can be used.
It is recommended to wait 15 minutes after the detomidine administration before starting the planned procedure.

The bodyweight of the animal to be treated should be determined as accurately as possible to avoid overdosing.

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

In the event of an accidental overdose, cardiac arrhythmias, hypotension, delayed recovery and profound CNS and respiratory depression may occur. Should the effects of detomidine become life-threatening, general measures for circulatory and respiratory stabilization and administration of an alpha2-adrenergic antagonist is recommended.

4.11 Withdrawal period(s)

Horse, cattle:
Meat and offal: 2 days
Milk: 12 hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: sedative and analgesic
ATCvet code: QN05CM90

5.1 Pharmacodynamic properties

The active ingredient of the product is 4-(2,3-dimethylbenzyl)-imidazole-hydrochloride (INN: Detomidine). Detomidine leads to sedation of the treated animals and relieves pain. Duration and intensity of the effects are dose related. Mode of action of Detomidine is a pronounced stimulation of alpha-2 adrenoceptors. Its analgesic effects are due to an inhibition of transmission of the pain impulse within the CNS.

Detomidine also reveals its effects on peripheral alpha-receptors, therefore increase in blood glucose levels and at higher dosages piloerection, sweating and diuresis may occur. Following an initial increase in mean blood pressure, it will return to normal or slightly below normal, and heart frequency will decrease. The ECG shows an enlarged PR-interval, and in the horse mild atrio-ventricular blocks may be seen. The above mentioned changes are transient. A respiratory response includes an initial decrease of respiration rate and is increasing to normal or slightly increased values within a few minutes.

5.2 Pharmacokinetic particulars

Detomidine is absorbed rapidly after intramuscular injection. Tmax is 15 - 30 min. Bioavailability after intramuscular administration is 66-85%. After rapid distribution of detomidine into the tissues, it is metabolised nearly completely mainly in the liver, t½ is 1 to 2 hours. Metabolites are mainly excreted via urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E 218)
Sodium chloride
Hydrochloric acid (for pH-adjustment)
Sodium hydroxide (for pH-adjustment)
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products in the same syringe.

6.3 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
Discharge any product remaining in the container at this time.

6.4. Special precautions for storage

Keep the container in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Clear colourless glass (type I) vials closed with a coated bromobutyl rubber stopper (type I) and an aluminium cap with a polypropylene lid.

1 x 1 glass vial with 5 ml.
5 x 1 glass vials with 5 ml.
1 x 1 glass vial with 20 ml.
5 x 1 glass vials with 20 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product 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. MARKETING AUTHORISATION HOLDER

Le Vet B.V.
Wilgenweg 7

3421 TV Oudewater
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 19994/4015

9. DATE OF FIRST AUTHORISATION

19 January 2011

10. DATE OF REVISION OF THE TEXT

June 2016

Approved: 09 June 2016