SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Rominervin 10 mg/ml solution for injection for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Romifidine hydrochloride 10 mg
equivalent to 8.76 mg romifidine

Excipient(s):
Chlorocresol 2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear colourless to slight yellow solution

4. CLINICAL PARTICULARS

4.1 Target species

Horses

4.2 Indications for use, specifying the target species

Sedative to facilitate handling, examination, minor surgical interventions and minor procedures.
For premedication prior to administration of injectable or inhalation anaesthetics.
Romifidine can also be used with synthetic opiates (e.g. butorphanol) to provide deeper sedation/analgesia.

4.3 Contraindications

Do not use in horses in the last month of pregnancy.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Do not use TMP/S-containing products intravenously when horses have been sedated with romifidine.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Sedation with α2 agonist drugs, such as romifidine may increase the sensitivity of the hind legs to tactile stimuli. Occasionally, defensive reactions, i.e. kicking, may occur even in apparently well sedated animals.
The veterinary medicinal product should be used with caution in animals suffering from cardiovascular or respiratory diseases, hepatic or renal insufficiency and in animals in shock.
When used as a pre-anaesthetic agent, sedation should be apparent before the induction of anaesthesia.
When the veterinary medicinal product is used as part of the anaesthetic procedure, care should be taken during the recovery phase to ensure that the horse is kept in a warm and quiet environment.

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 insert to the physician 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 thoroughly 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 the physician:
Romifidine is an alpha2-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)

As with other veterinary medicinal products of this class, the following adverse events may occur:

- Bradycardia, which may be profound
- Benign, reversible cardiac arrhythmias (second degree AV block and to a lesser extent sino-atrial block)
- Hypotension, following a short period of hypertension

- Incoördination of the limbs/ataxia
- Sweating and increased salivation
- Hyperglycemia and diuresis
- In male horses, a reversible, partial penile prolapse can occur.
- Increased sensitivity of the hind legs (defensive movements)
- In very rare cases mild symptoms of colic, as the intestinal motility is temporarily inhibited.

Hypersensitivity may occur in very rare cases.

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

Do not use during the last month of pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

The sedative effect of the veterinary medicinal product may be potentiated by other psychoactive compounds, such as tranquillisers, other sedatives or morphine-like analgesics, therefore reducing the required dose of subsequent anaesthetic agents.

The concurrent intravenous use of potentiated sulphonamides with alpha2-agonists has been reported to cause cardiac arrhythmias which may be fatal. Intravenous administration of TMP/S containing products is therefore contra-indicated when horses have been sedated with romifidine.

The concomitant use of romifidine and phenothiazines (e.g. acepromazine) can result in severe hypotension.
The product should not be used in association with other substances belonging to the same pharmacological class (sympathicomimetic amines, including alpha-2-agonist, such as xylazine, detomidine..).

4.9 Amounts to be administered and administration route

For intravenous use.
A dose range of 0.04 – 0.12 mg romifidine HCl/kg bodyweight (0.4 – 1.2 ml product/100 kg bodyweight) gives a dose-related response.
Onset of action, which is independent of dose, is 1 – 2 minutes. Maximum sedation is achieved after 5 - 10 minutes. Please see the Table below.

Recommended dose

Sedation

Dose	Depth of Sedation	Duration of Sedation
0.04 mg romifidine HCl/kg bw (i.e. **0.4 ml product/100 kg** bw)	Light	0.5 - 1 hour
0.08 mg romifidine HCl/kg bw (i.e. **0.8 ml product/100 kg** bw)	Deep	0.5 – 1.5 hours
0.12 mg romifidine HCl/kg bw (i.e. **1.2 ml product/100 kg** bw)	Deep sedation of prolonged duration	At this dose residual sedation may persist for up to 3 hours

When romifidine is used in combination with butorphanol for deeper sedation and analgesia, a dose of 0.04 mg – 0.12 mg romifidine HCl/kg bw (0.4 – 1.2 ml product per 100 kg bw) should be used followed by butorphanol.

Premedication

Premedication with ketamine for induction
When romifidine is used as premedication prior to ketamine induced anaesthesia, a dose of 0.1 mg romifidine HCl/ kg bw (1 ml product/100 kg bw) should be used followed by ketamine after 5-10 minutes.

Premedication with other agents for induction
When romifidine is used as premedication in combination with other agents such as injectable or inhalation anaesthetics, a dose of 0.04 mg – 0.08 mg romifidine HCl/kg bw (0.4 – 0.8 ml product per 100 kg bw) should be used followed by induction of anaesthesia after 5-10 minutes.

Maintenance of anaesthesia

To maintain or deepen surgical anaesthesia with romifidine/ketamine, when facilities for gaseous anaesthesia are not available, romifidine can be administered at a dose of 0.025 mg/kg romifidine HCl (0.25 ml product/100 kg bodyweight) followed immediately by ketamine intravenously (50% of the initial ketamine premedication dose). Administer the romifidine/ketamine top-up dose immediately prior to commencement of surgical incision or when signs of returning consciousness appear.

The stopper should not be punctured more than 40 times

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

Dosages up to 5 times the highest recommended dose caused transient adverse reactions, such as sweating, bradycardia, second degree atrio-ventricular heart blocks, hypotension, ataxia, hyperglycaemia and diuresis.
In case of overdose, adverse reactions, as listed in section 4.6, are expected to be more severe and more frequent.

In such cases, symptomatic treatment should be initiated; an alpha-2 adrenergic antagonist may be useful in reducing such effects.

4.11 Withdrawal period(s)

Meat and offal: 6 days.

Not authorised for use in animals producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Hypnotics and sedatives
ATC vet code: QN05CM93

5.1 Pharmacodynamic properties

Romifidine is an alpha-2-agonist of the imino-imidazolidine class. It exerts sedative and analgesic effects. Its sedative effect is induced by stimulation of alpha-2-adrenoreceptors in the central nervous system. The substance possesses a strong specific affinity for these receptors.
After administration of romifidine, blood pressure increases initially due to its effect on peripheral postsynaptic α1-receptors in combination with activation of extrajunctional α2b-adrenoceptors located on smooth muscle cells in the arteriolar resistance vessels. Subsequently, blood pressure decreases due to the effect on peripheral presynaptic receptors (inhibition of noradrenaline release from sympatic nerve endings) and decrease of sympathetic tone resulting in vasodilatation.

5.2 Pharmacokinetic particulars

Approximately 20% of romifidine is bound to plasma proteins. Romifidine is found predominantly in the kidney and muscle, whereas the liver contains only traces of the parent compound. The main hepatic metabolites, SHT 2130, STH 2337 and ESR 1235, have been shown to be pharmacologically inactive.
Following intravenous injection, romifidine is rapidly eliminated: approximately 80% of the administered dose is eliminated via urine and the remainder via the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Sodium chloride
Hydrochloric acid, diluted (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injection

6.2 Major Incompatibilities

Do not mix with any other veterinary medicinal product.

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: 56 days

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Colourless type I glass vials closed with a coated bromobutyl rubber stopper and aluminium cap. One glass vial in a cardboard box.
Pack size
Box with 1 vial 10 ml
Box with 1 vial of 20 ml
Box with 1 vial of 50 ml

Multi-pack with 6 boxes each containing 1 vial of 10 mL
Multi-pack with 6 boxes each containing 1 vial of 20 mL
Multi-pack with 6 boxes each containing 1 vial of 50 mL

Multi-pack with 10 boxes each containing 1 vial of 10 mL
Multi-pack with 10 boxes each containing 1 vial of 20 mL
Multi-pack with 10 boxes each containing 1 vial of 50 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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 41821/4062

9. DATE OF FIRST AUTHORISATION

24 October 2018

10. DATE OF REVISION OF THE TEXT

October 2018

Approved: 24 October 2018