SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Equimidine 10 mg/ml Solution for Injection for Horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance
Detomidine hydrochloride 10.0 mg

Excipient
Methyl parahydroxybenzoate 1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear, almost colourless, sterile, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Target species

Horse,

4.2 Indications for use, specifying the target species

Sedation and slight analgesia of horses with or without butorphanol to facilitate the handling of horses for examination, minor surgical interventions and other manipulations.

Equimidine is also indicated for use with ketamine for short duration anaesthesia to carry out surgical procedures such as castration.

4.3 Contraindications

Do not use with sympathomimetic amines.
Do not use with potentiated sulphonamides.
Do not mix with other products.
Do not use in animals with cardiac abnormalities (including pre-existing atrio-ventricular blocks and coronary insufficiency) or respiratory disease.
Do not use in animals with liver insufficiency or renal failure.
Do not use in animals with general health problems (e.g. dehydration).
Do not use in the last 3 months of pregnancy.
Do not use in combination with butorphanol in horses suffering from colic.
Do not offer food or water until drug effect has passed.

See also sections 4.7 and 4.8.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals

As sedation begins, horses may start to sway and lower the head rapidly while remaining standing. In order to prevent self injury the location where the procedure is to be performed should be chosen carefully.
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 animal from heat or cold.

ii) 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. The use of impermeable gloves is advisable especially in the case of damaged skin.
Immediately after exposure wash the exposed skin with large amounts of fresh water.
Remove contaminated clothes that are in direct contact with skin.
In the case of accidental contact of the product with eyes, rinse with large amounts of fresh water. If symptoms occur, seek the advice of a doctor.
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 hydrochloride is an alpha-2-adrenoreceptor agonist. Symptoms after absorption may involve clinical effects including dose-dependent sedation, respiratory depression, bradycardia and 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,
- Cardiac arrhythmia, atrioventricular and sino-atrial block.
- Transient hypo- and/or hypertension,
- Respiratory depression, rarely hyperventilation especially in febrile horses,
- Increase in blood glucose,
- Sweating,
- Ataxia,
- Uterine contractions,

As with other sedatives, in rare cases paradoxical reactions (excitations) can develop.

At doses above 40 μg/kg bodyweight, the following symptoms can also be observed: sweating, pilo-erection and tremor of muscles. Transient penis prolapse in stallions and geldings.
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 pregnancy. Use only according to a benefit/risk assessment by the responsible veterinary surgeon during the other months of pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

The concurrent use of certain potentiated sulphonamides may cause potentially fatal dysrhythmias. Do not use in combination with sulphonamides.
The product should be used with care with other sedatives and anaesthetics because of an additive/synergistic effect.
Concurrent use of other sedatives should proceed only after consultation of the warnings and precautions of the product concerned and according to the benefit/risk assessment of the veterinary surgeon.
Detomidine should not be used in combination with sympathomimetic amines such as adrenaline, dobutamine and ephedrine.
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

Give by slow intravenous injection. As this is a multi dose bottle the surface of the bung should be cleaned and disinfected prior to penetration of the bung with a sterile needle. The needle should be passed carefully into the bottle prior to withdrawal of the dose and then withdrawn carefully to avoid damage. (See also 4.5, above). Return bottle to cardboard carton after use.

The following procedure is recommended. Use two sterile needles, one to fill the syringe from the bottle and one to inject the patient. Once the required dose has been withdrawn from the vial, the syringe should be removed from the needle. A separate sterile needle should be inserted into the injection site and the syringe connected to it. The needles should be discarded.

Use alone for sedation

Dosage table

Anticipated Level of Sedation	Light	Moderate	Profound
Dosage (IV) mcg/kg	10 – 20	20 – 40	40 – 80
Dose (IV) ml/100kg	0.1 – 0.2	0.2 – 0.4	0.4 – 0.8
Commencement of effect (mins)	3	2	1
Duration of action (hrs)	0.5 – 1	0.5 - 1	0.5 – 2

Use with butorphanol for sedation

Use only after reading all the information provided in section 4, Clinical Particulars.

Dosage 0.12 ml /100kg (12 mcg/kg detomidine hydrochloride) intravenously followed within 5 minutes by 25 mcg/kg butorphanol (e.g. 0.25 ml/100kg of a 10mg/ml solution) intravenously. Clinical experience has shown that 5 mg detomidine HCl (0.5 ml of the product) and 10 mg (e.g. 1 ml of a 10 mg/ml solution) of butorphanol affords effective and very safe sedation in horses above 200 kg bodyweight.

Warnings

Do not use combination in horses with a history of liver disease. The combination should not be used in pregnant mares or in animals suffering from colic.
Routine cardiac auscultation should be performed prior to use of this combination. Do not use in horses with a pre-existing cardiac dysrhythmia or bradycardia.
Mild to severe ataxia may be encountered but clinical studies have shown that horses are unlikely to collapse. Normal precautions should be observed to prevent patient self-injury.

Use with ketamine (short duration anaesthesia)

Use only after reading all the information provided in section 4, Clinical Particulars.
Ketamine should not be used as the sole anaesthetic agent in horses. It is important to adhere to the following procedures to obtain satisfactory surgical anaesthesia.
Administer the product at a dose rate of 20 mcg/kg by slow intravenous injection.
Allow 5 minutes for the horse to become deeply sedated then administer ketamine at a dose rate of 2.2 mg/kg as an intravenous bolus. Onset of anaesthesia is gradual

with the horse taking approximately 1 minute to become recumbent. (In large fit horses recumbency may take up to 3 minutes).
Anaesthesia will deepen for a further 1-2 minutes and during this time the horse should be left quietly.
Horses regain sternal recumbency approximately 20 minutes after ketamine injection.
The period of surgical anaesthesia is about 10-15 minutes and if it is necessary to prolong anaesthesia, thiopentone sodium can be given as IV boluses of 1 mg/kg as required. Total doses of 5 mg/kg (5 x 1 mg/kg injections) have been given. Doses greater than this may reduce the quality of recovery. Thiopentone can also be given (as above) to deepen anaesthesia if needed.

The horse should be allowed to stand in its own time. Ataxia may be a problem if it stands prematurely and it should be encouraged to remain recumbent.
To facilitate handling and administration some horses have received acepromazine by intramuscular injection at a dose rate of 0.03 mg/kg at least 45 minutes prior to induction of anaesthesia.

Warnings

Allow sedation to develop. The two agents should never be co-administered in the same syringe.
It is recommended that feed is withdrawn for at least 12 hours prior to anaesthesia.
Excitable horses can be poor subjects for anaesthesia. Considerate, quiet and careful handling during the administration of the agents is necessary so as to cause the minimum upset possible. If sedation with the product fails to occur then the procedure should be abandoned. In these circumstances ketamine must not be injected into the horse

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

In cases of suspected overdose, cardiac arrhythmias, hypotension, delayed recovery and profound CNS and respiratory depression may occur. Should the effects of detomidine become life-threatening, an alpha-2-antagonist (atipamizole) is recommended at 5 -10 times the dose of detomidine in mcg/kg.
Atrio-ventricular blocks may be prevented by IV administration of atropine at 0.02 mg/kg.

4.11 Withdrawal periods

Meat and offal: 2 days
Milk: 12 hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: {group}. Hypnotics and sedatives
ATCvet code: QN05CM90

5.1 Pharmacodynamic properties

Detomidine hydrochloride is an alpha 2 adrenergic agonist drug. Its chemical structure is 4-(2,3-dimethylbenzyl)-1*H*-imidazole hydrochloride. Detomidine affects the central nervous system by inhibiting noradrenaline mediated neurotransmission. This leads to a decrease in the level of consciousness and an increase in pain threshold.

Reduced heart rate and temporary AV-blocks can be seen after administration of detomidine. The result of the fall in the pulse rate is an increase of blood pressure. This is a temporary phenomenon, which returns back to initial level or little lower after 15 minutes. The respiratory rate decreases. Horses can sweat and pilo-erection can be observed particularly following high dosages. Prolapse of the penis can occur in stallions and geldings. The level of blood sugar can be elevated.

5.2 Pharmacokinetic particulars

In the horse kinetics were studied following intramuscular and intravenous injection of 80µg/kg and measuring levels with a sensitive radio-immunoassay. Following I/M injection the absorption half-life was 0.15 hours. Distribution was rapid with half-life of 0.15 hrs post IV injection. The elimination half-life in the horse was 1.19 hours with less than 1% parent compound in urine. Detomidine is metabolised nearly completely in the liver and the metabolites mainly excreted via the urine and faeces. All tissue concentrations measured 48 hours post treatment were less than 3% of original dose/unit volume. The magnitude of and duration of effects mirrored serum pharmacokinetics. (Salonen J. S. et al J Vet Pharmacol Therap 12, 65-72, 1989)

The volume of distribution (Vd) ranges from 0.75 – 1.89 l/kg and protein binding is 75-85%. Metabolism takes place mainly in the liver and excretion via the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate
Sodium hydroxide (for pH adjustment)
Sodium chloride
Water for Injections

6.2 Incompatibilities

This veterinary medicinal product must 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

6.4. Special precautions for storage

Store the product in the carton in order to protect from light.
Protect from light.
Store in a dry place.
Following withdrawal of the first dose, use the product within 28 days. Discard unused material.

6.5 Nature and composition of immediate packaging

Multidose vials, either,

i) Clear, Type I glass injection vial containing 10 ml solution
or
ii) Clear, cyclic olefin copolymer injection vial containing 15 ml solution.

The vials are closed with red bromobutyl rubber or grey chlorobutyl rubber stoppers secured with aluminium crimps.

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

Provivo Oy
Liedontie 45
04600 Mäntsälä
Finland

8. MARKETING AUTHORISATION NUMBER

Vm 25929/4000

9. DATE OF RENEWAL OF THE AUTHORISATION

Date: 09 December 2010

10. DATE OF REVISION OF THE TEXT

Date: December 2014

APPROVED T. NASH **2/12/2014**