ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Equimidine 10 mg/ml Solution for Injection for Horses

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Detomidine hydrochloride 10 mg/ml.
Methyl parahydroxybenzoate 1 mg/ml.

3. PHARMACEUTICAL FORM

Solution for injection.

4. PACKAGE SIZE

10 ml
15 ml

5. TARGET SPECIES

Horses.

6. INDICATION(S)

A sedative with analgesic properties for I/V use in horses.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

-

8. WITHDRAWAL PERIOD

Meat and offal: 2 days
Milk 12 hours

9. SPECIAL WARNING(S), IF NECESSARY

READ PACKAGE LEAFLET BEFORE USE.

User warnings
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 contact with the skin. In case of accidental contact with the eyes, rinse with large amounts of fresh

water. If symptoms occur seek the advice of a doctor. See package leaflet for full user warnings.

10. EXPIRY DATE

EXP: End {month/year}

11. SPECIAL STORAGE CONDITIONS

Store in a dry place in the original carton to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

FOR ANIMAL TREATMENT ONLY.
To be supplied only on veterinary prescription.

POM-V

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Provivo Oy
Liedontie 45
04600 Mäntsälä
Finland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 25929/4000

17. MANUFACTURER'S BATCH NUMBER

BN:

Distributed in the UK by:
Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Equimidine 10 mg/ml Solution for Injection for Horses

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Detomidine hydrochloride 10 mg/ml
Methyl parahydroxybenzoate 1 mg/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml
15 ml

4. ROUTE(S) OF ADMINISTRATION

For IV injection.

5. WITHDRAWAL PERIOD

Withdrawal periods: Meat & offal - 2 days; Milk – 12 hours

6. BATCH NUMBER

BN:

7. EXPIRY DATE

EXP: End
Following withdrawal of the first dose, use the product within 28 days. Discard unused material.
Once opened, use by….

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.
To be supplied only on veterinary prescription POM-V
Vm 25929/4000

Store in a dry place in the original carton to protect from light.
Read the package leaflet before use.
Keep out of the sight and reach of children.

Zoetis UK Limited
1st Floor, Birchwood Building
Springfield Drive
Leatherhead
Surrey
KT22 7LP

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Equimidine 10 mg/ml Solution for Injection for Horses

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Provivo Oy, Liedontie 45, 04600 Mäntsälä, Finland

Manufacturer responsible for batch release:
Ballinskelligs Veterinary Products, Co Kerry, Ireland

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Equimidine 10 mg/ml Solution for Injection for Horses

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

A clear, colourless solution for intravenous injection containing detomidine hydrochloride 10 mg/ml and methyl parahydroxybenzoate 1 mg/ml as preservative.

4. INDICATION(S)

Equimidine has sedative and mild analgesic properties and is indicated for use either alone or in combination with butorphanol to facilitate the handling of horses for clinical examinations, minor surgical procedures and other manipulations. It can also be used with ketamine for short duration general anaesthesia appropriate for short surgical procedures such as castration.

5. 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.

6. ADVERSE REACTIONS

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.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Horses

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Equimidine 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

Equimidine with butorphanol for sedation
Dosage 0.12 ml Equimidine/100 kg (12 mcg/kg detomidine hydrochloride) intravenously followed within 5 minutes by 25 mcg/kg butorphanol (e.g. 0.25 ml/100 kg of a 10 mg/ml solution) intravenously. Clinical experience has shown that 5 mg detomidine HCl (0.5 ml Equimidine) 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.

Equimidine with ketamine (short duration anaesthesia)
Ketamine should not be used as the sole anaesthetic agent in horses. It is important to follow the following procedures to obtain satisfactory surgical anaesthesia. Administer Equimidine at a dose rate of 20 mcg/kg by slow intravenous injection. Allow 5 minutes for the hose 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 intra-venous 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 be given (as above) to deepen the 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.

9. ADVICE ON CORRECT ADMINISTRATION

For 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 operator warnings below). 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. Return bottle to cardboard carton after use.

Equimidine with butorphanol for sedation
Do not use this combination in horses intended for human consumption or in horses with a history of liver disease.
This combination should not be used in pregnant mares or in animals suffering from colic.
Routine cardiac auscultation should be used prior to use of this combination. Do not use in horses with 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 taken to prevent patient self-injury. Refer to (i) **Special warnings for us in animals** for additional advice on the use of detomidine in combination with butorphanol.

Equimidine with ketamine
Allow sedation to develop for at least 5 minutes before giving ketamine. 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 are poor subjects for anaesthesia. Considerate, quiet and careful handling during the administration of agents is necessary to cause the minimum upset possible. If sedation with Equimidine fails to occur, then the procedure should be abandoned. In these circumstances ketamine must not be injected into the horse.
Refer to (i) **Special warnings for us in animals** for additional advice on the use of detomidine in combination with ketamine.

10. WITHDRAWAL PERIOD

Meat and offal: 2 days
Milk: 12 hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

When the container is broached (opened) for the first time, using the in-use shelf life which is specified on this package leaflet, the date on which any product remaining in the carton should be worked out. This discard date should be written in the space provided.

12. SPECIAL WARNING(S)

Special precautions for use in animals:
Before using any combination, read the contraindications and warnings appearing on the other product's information sheets (Summary of Product Characteristics (SPC) or package leaflet)
For animal treatment only. Give by slow intravenous injection.
The concurrent use of certain potentiated sulphonamides may cause potentially fatal dysthythmias.
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.
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.
Where anaesthesia is induced with a combination of detomidine and ketamine, prior to maintenance with halothane, the effect 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.
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.
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.
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.
In painful procedures detomidine should be used only in combination with an analgesic or a local anaesthetic.
Do not use during the last trimester of pregnancy. Use only according to a benefit/risk assessment by the responsible veterinary surgeon during the other months of pregnancy.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
1. 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.
2. Avoid skin, eye or mucosal contact. The use of impermeable gloves is advisable especially in case of damaged skin.
3. Immediately after exposure wash the exposed skin with large amounts of fresh water.
4. Remove contaminated clothes that are in direct contact with skin.
5. 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.
6. 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.
7. 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, hypotension, a dry mouth and hyperglycaemia. Ventricular arrhythmias have also been reported. Respiratory and haemodynamic symptoms should be treated symptomatically.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Dispose of any unused product and empty containers in accordance with guidance from your local waste regulation authority.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

December 2020

15. OTHER INFORMATION

Where appropriate, Equimidine may be used with local anaesthetics.
In cases of suspected overdose or if 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/ml.

Package quantities

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.

To be supplied only on veterinary prescription. POM-V
Vm 25929/4000

Marketing authorisation holder:
Provivo Oy
Liedontie 45
04600 Mäntsälä
Finland.

Distributed by:
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Approved 23 December 2020