[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Detonervin 10 mg/ml solution for injection for horses and cattle (AT, BE, CZ, EL, ES, HU, IE, IT, LU, NL, PL, PT, SK, UK(NI))
Detonervin vet. 10 mg/ml, solution for injection for horses and cattle (DK, FI, IS, SE)
Sedomidine 10 mg/ml, solution for injection for horses and cattle (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Detomidine	8.36 mg
(as detomidine hydrochloride	10.00 mg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Methyl parahydroxybenzoate (E218)	1.0 mg
Sodium chloride	
Hydrochloric acid (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injections	

Clear and colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Horses and cattle.

3.2 Indications for use for each target species

Sedation and analgesia in horses and cattle during various examinations and treatments, and in situations where handling of animals will be facilitated by administration of the veterinary medicinal product. For premedication before administration of injectable or inhalation anaesthetics.

3.3 Contraindications

Do not use in animals with severe cardiac insufficiency, cardiac abnormalities, pre-existing AV/SA block, severe respiratory disease or severely impaired liver or kidney function.

Do not use in combination with butorphanol in horses with colic without further monitoring of the horse for signs of clinical deterioration.

Do not use in conjunction with sympathomimetic amines or with intravenous potentiated sulfonamides. Concurrent use with intravenous potentiated sulfonamides may cause cardiac arrhythmia with a fatal outcome.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
A benefit-risk assessment should be performed by the responsible veterinarian prior to administration of the veterinary medicinal product to the following categories of animals: those approaching or in endotoxic or traumatic shock, animal with dehydration or respiratory disease, horses with pre-existing bradycardia, fever, or under extreme stress. During prolonged sedation, monitor body temperature and, if necessary, take measures to maintain normal body temperature.

When the veterinary medicinal product is administered, the animal should be allowed to rest in a maximally quiet place. Before any procedure is initiated, the sedation should be allowed to reach its peak effect (approximately 10–15 minutes following IV administration.) At the onset of the effect, it is to be noted that the animal may stagger and lower its head. Cattle, and especially young animals may become recumbent when high detomidine doses are used. In order to minimize the risk of injuries, tympany or aspiration, measures such as selecting a suitable environment for treatment, and lowering the head and neck should be taken.

For horses, fasting for 12 hours before planned anaesthesia is recommended. Food and water should be withheld until the sedative effect of the veterinary medicinal product has worn off.

For painful procedures, the veterinary medicinal product should be combined with (an) other analgesic agent(s).

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Some horses, although apparently deeply sedated, may still respond to external stimuli. Routine safety measures should be employed to protect practitioners and handlers.

Detomidine is an alpha-2 adrenoceptor agonist, which may cause sedation, somnolence, decreased blood pressure and decreased heart rate in humans.

In case of accidental ingestion or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation and changes in blood pressure may occur.

Avoid skin, eye or mucosal contact.

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 veterinary medicinal product with eyes, rinse with large amounts of fresh water. If symptoms occur, seek the advice of a doctor.

If pregnant women handle the veterinary medicinal product, special caution should be observed not to self-inject as uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure.

To the physician:
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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Horses:

Very common (>1 animal / 10 animals treated):	Arrhythmia[1], Bradycardia, Heart block[2], Hypertension (transient), Hypotension (transient) Hyperglycaemia Ataxia, Muscle tremor Urination[3] Penile prolapse (transient)[4], Uterine contraction Increased sweating (transient), Piloerection Hyperthermia, Hypothermia
Common (1 to 10 animals / 100 animals treated):	Hypersalivation (transient) Nasal discharge[5] Skin swelling[6]
Rare (1 to 10 animals / 10,000 animals treated):	Colic[7] Urticaria Hyperventilation, Respiratory depression Excitation
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction

[1,2] Causes changes in the conductivity of cardiac muscle as evidenced by partial atrioventricular and sinoatrial blocks.
[3] A diuretic effect may be observed 45 to 60 minutes after treatment.
[4] A partial penis prolapse can occur in stallions and geldings.
[5,6] Mucus discharges from the nose and oedema of the head and face may be seen because of continued lowering of the head during sedation.
[7] Substances of this class inhibit intestinal motility.

Cattle:

Very common (>1 animal / 10 animals treated):	Bradycardia, Hypertension (transient), Hypotension (transient) Hyperglycaemia Urination[1] Penile prolapse (transient)[2]
Common (1 to 10 animals / 100 animals treated):	Ruminal tympany[3], Hypersalivation (transient) Ataxia, Muscle tremor Uterine contraction Nasal discharge[4], Respiratory depression (slight)[5] Hyperthermia, Hypothermia
Rare	Arrhythmia[6] Increased sweating (transient)

(1 to 10 animals / 10,000 animals treated):	Excitation Hyperventilation (slight)[7]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Heart block[8]

[1] A diuretic effect may be observed 45 to 60 minutes after treatment.
[2] A partial, penis prolapse can occur.
[3] Substances of this class inhibit ruminal and intestinal motility. Can cause a mild bloat in cattle.
[4] Mucus discharge from the nose may be seen because of continued lowering of the head during sedation.
[5,7] Causes changes in the respiratory rate.
[6,8] Causes changes in the conductivity of cardiac muscle as evidenced by partial atrioventricular and sinoatrial blocks.

Mild adverse reactions have reportedly resolved uneventfully without treatment. Adverse reactions should be treated symptomatically.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
Do not use during the last trimester of the pregnancy as detomidine may cause uterine contractions and a decrease in foetal blood pressure.

Use only according to the benefit-risk assessment by the responsible veterinarian at other stages of gestation.

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

Lactation:
Detomidine is excreted in trace amounts into the milk. Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
The safety of the veterinary medicinal product has not been investigated in breeding horses. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Detomidine has an additive/synergistic effect with other sedatives, anaesthetics, hypnotics and analgesics and therefore an appropriate dose adjustment may be needed.

When the veterinary medicinal product is used as a premedication prior to general anaesthesia, the veterinary medicinal product may delay onset of induction.

Detomidine should not be used in conjunction with sympathomimetic amines such as adrenaline, dobutamine and ephedrine, as these agents counteract the sedative effect of detomidine, except in the case of anaesthetic incidents.

For intravenous potentiated sulfonamides, see section 3.3.'Contraindications'.

3.9 Administration routes and dosage

Intramuscular or intravenous use.

To be administered intramuscularly or by slow intravenous injection of detomidine hydrochloride at a dose of 10–80 µg/kg depending on the degree and duration of sedation and analgesia required. The effect is more rapid after intravenous administration. To ensure a correct dosage, body weight should be determined as accurately as possible.

Single use (horses and cattle)

Dose		Effect	Duration of effect (h)	Other effects
ml/100 kg	µg/kg			
0.1-0.2	10-20	Sedation	0.5-1	
0.2-0.4	20-40	Sedation and analgesia	0.5-1	Slight staggering
0.4-0.8	40-80	Deeper sedation and better analgesia	0.5-2	Staggering, sweating, piloerection, muscular tremors

The onset of action occurs 2–5 min after IV injection. The full effect is seen 10–15 min after IV injection. If necessary, detomidine hydrochloride can be administered up to a total dose of 80 µg/kg.

The following dosing instructions show different possibilities for the combination of detomidine hydrochloride. However, the simultaneous administration with other drugs should always be based on a benefit-risk assessment by the responsible veterinarian and it must be done taking into account the SPC of the relevant products.

Combinations with detomidine to increase sedation or analgesia in a standing horse

Detomidine hydrochloride 10–30 µg/kg IV in combination with either

- butorphanol 0.025–0.05 mg/kg IV or
- levomethadone 0.05–0.1 mg/kg IV or
- acepromazine 0.02–0.05 mg/kg IV

Combinations with detomidine to increase sedation or analgesia in cattle

Detomidine hydrochloride 10-30 µg/kg IV in combination with

- butorphanol 0.05 mg/kg IV

Combinations with detomidine for preanaesthetic sedation in the horse

The following anaesthetics can be used after detomidine hydrochloride premedication (10–20 µg/kg) to achieve lateral recumbency and general anaesthesia:

- ketamine 2.2 mg/kg IV or
- thiopental 3–6 mg/kg IV or
- guaifenesin IV (to effect) followed by ketamine 2.2 mg/kg IV

Administer the veterinary medicinal products prior to ketamine and allow sufficient time for sedation to develop (5 minutes). Ketamine and the veterinary medicinal product must therefore never be administered simultaneously in the same syringe.

Combinations with detomidine and inhalation anaesthetics in the horse

Detomidine hydrochloride can be used as sedative premedicant (10–30 μg/kg) before induction and maintenance of inhalation anaesthesia. Inhalation anaesthetic is given to effect. The amount of inhalation anaesthetics required is significantly reduced by premedication with detomidine.

Combination with detomidine to maintain injection anaesthesia (total intravenous anaesthesia TIVA) in the horse

Detomidine can be used in combination with ketamine and guaifenesin for maintaining total intravenous anaesthesia (TIVA).

The best-documented solution contains guaifenesin 50–100 mg/ml, detomidine hydrochloride 20 μg/ml and ketamine 2 mg/ml. 1 g ketamine and 10 mg detomidine hydrochloride are added to 500 ml of 5–10 % guaifenesin; anaesthesia is maintained by an infusion of 1 ml/kg/h.

Combinations with detomidine for induction and maintenance of general anaesthesia in cattle

Detomidine hydrochloride 20 μg/kg (0.2 ml/100 kg) with

- ketamine 0.5–1 mg/kg IV, IM or
- thiopental 6–10 mg/kg IV

The effect of detomidine-ketamine lasts for 20–30 minutes, and the effect of detomidine- thiopental for 10-20 minutes.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Over dosage is mainly manifested by delayed recovery from sedation or anaesthesia. Circulatory and respiratory depression may occur.

If recovery is delayed, it should be ensured that the animal can recover in a quiet and warm place.

Oxygen supplementation and/or symptomatic treatment may be indicated in cases of circulatory and respiratory depression.

The effects of the veterinary medicinal product can be reversed using an antidote containing the active substance atipamezole, which is an alpha-2 adrenoceptor antagonist. Atipamezole is administered at a dosage 2–10-fold that of this veterinary medicinal product, calculated in μg/kg. For example, if a horse has been given this veterinary medicinal product at a dosage of 20 μg/kg (0.2 ml/100 kg), the atipamezole dosage should be 40–200 μg/kg (0.8–4 ml/100 kg).

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

3.12 Withdrawal periods

Horses, cattle:
Meat and offal: 2 days

Milk: 12 hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN05CM90

4.2 Pharmacodynamics

The active substance of this veterinary medicinal product is detomidine. Its chemical structure is 4-(2,3-dimethylbenzyl) imidazole hydrochloride. Detomidine is an alpha-2 adrenoceptor agonist with a central effect inhibiting the transmission of noradrenalin-mediated nervous impulses. In the animal, the level of consciousness is lowered and the pain threshold is increased. The duration and level of sedation and analgesia are dose-dependent.

With detomidine administration, heart rate is decreased, blood pressure is initially elevated, and then a steady decline to normal is seen. A transient change in the conductivity of the cardiac muscle may occur, as evidenced by partial atrioventricular (AV) and sinoatrial (SA) blocks. Respiratory responses include an initial slowing of respiration within a few seconds to 1–2 minutes after administration, increasing to normal within 5 minutes. Especially at high doses, sweating, piloerection, salivation and slight muscle tremors are frequently seen. Partial, transient penis prolapse may occur in stallions and geldings. In cattle, reversible, mild tympany and increased saliva secretion have been observed. Blood sugar concentration is increased in both animal species.

4.3 Pharmacokinetics

Detomidine is rapidly absorbed after intramuscular injection, and t_{max} varies from 15 min to 30 min. Detomidine is also rapidly distributed. V_d varies between 0.75 l/kg and 1.89 l/kg. Protein binding is 75 % to 85 %. Detomidine is oxidated mainly in the liver; a small proportion is methylated in the kidneys. Most metabolites are excreted in the urine. T½ is 1–2 hours. Excretion of detomidine in milk in cattle is low. No detectable amounts are present 23 h after administration.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 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.

5.3 Special precautions for storage

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

5.4 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.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}.

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Detonervin 10 mg/ml solution for injection (AT, BE, CZ, EL, ES, HU, IE, IT, LU, NL, PL, PT, SK, UK(NI))
Detonervin vet. 10 mg/ml, solution for injection (DK, FI, IS, SE)
Sedomidine 10 mg/ml, solution for injection (FR)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Detomidine hydrochloride 10 mg

3. PACKAGE SIZE

5 ml
5 x 5 ml
20 ml
5 x 20 ml

4. TARGET SPECIES

Horses and cattle.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramuscular use or intravenous use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 2 days
Milk: 12 hours

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days.
Once broached, use by….

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

GLASS VIAL LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Detonervin (AT, BE, CZ, EL, ES, HU, IE, IT, LU, NL, PL, PT, SK, UK(NI))
Detonervin vet. (DK, FI, IS, SE)
Sedomidine (FR)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Detomidine hydrochloride 10 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached, use within 28 days.
Once broached, use by….

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Detonervin 10 mg/ml solution for injection for horses and cattle (AT, BE, CZ, EL, ES, HU, IE, IT, LU, NL, PL, PT, SK, UK(NI))
Detonervin vet. 10 mg/ml, solution for injection for horses and cattle (DK, FI, IS, SE)
Sedomidine 10 mg/ml, solution for injection for horses and cattle (FR)

2. Composition

Each ml contains:

Active substance:

Detomidine	8.36 mg
(as detomidine hydrochloride	10.00 mg)

Excipient:

Methyl parahydroxybenzoate (E218)	1.0 mg

Clear and colourless solution.

3. Target species

Horses and cattle.

4. Indications for use

Sedation and analgesia in horses and cattle during various examinations and treatments, and in situations where handling of animals will be facilitated by administration of the veterinary medicinal product. For premedication before administration of injectable or inhalation anaesthetics.

5. Contraindications

Do not use in animals with severe cardiac insufficiency, cardiac abnormalities, pre-existing AV/SA block, severe respiratory disease, or severely impaired liver or kidney function.

Do not use in combination with butorphanol in horses with colic without further monitoring of the horse for signs of clinical deterioration.

Do not use in conjunction with sympathomimetic amines or with intravenous potentiated sulfonamides. Concurrent use with intravenous potentiated sulfonamides may cause cardiac arrhythmia with a fatal outcome.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:
A benefit-risk assessment should be performed by the responsible veterinarian prior to administration of the veterinary medicinal product to the following categories of animals: those approaching or in endotoxic or traumatic shock, animal with dehydration or respiratory disease, horses with pre-existing bradycardia, fever, or under extreme stress. During prolonged sedation, monitor body temperature and, if necessary, take measures to maintain normal body temperature.

When the veterinary medicinal product is administered, the animal should be allowed to rest in a maximally quiet place. Before any procedure is initiated, the sedation should be allowed to reach its peak effect (approximately 10–15 minutes following IV administration). At the onset of the effect, it is to be noted that the animal may stagger and lower its head. Cattle, and especially young animals may become recumbent when high detomidine doses are used. In order to minimize the risk of injuries, tympany or aspiration, measures such as selecting a suitable environment for treatment, and lowering the head and neck should be taken.

For horses, fasting for 12 hours before planned anaesthesia is recommended. Food and water should be withheld until the sedative effect of the veterinary medicinal product has worn off.

For painful procedures, the veterinary medicinal product should be combined with (an)other analgesic agent(s).

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Some horses, although apparently deeply sedated, may still respond to external stimuli. Routine safety measures should be employed to protect practitioners and handlers.

Detomidine is an alpha-2 adrenoceptor agonist, which may cause sedation, somnolence, decreased blood pressure and decreased heart rate in humans.

In case of accidental ingestion or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation and changes in blood pressure may occur.

Avoid skin, eye or mucosal contact.

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 veterinary medicinal product with eyes, rinse with large amounts of fresh water. If symptoms occur, seek the advice of a doctor.

If pregnant women handle the veterinary medicinal product, special caution should be observed not to self-inject as uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure.

To the physician:
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.

Pregnancy:
Do not use during the last trimester of the pregnancy as detomidine may cause uterine contractions and a decrease in foetal blood pressure.

Use only according to the benefit-risk assessment by the responsible veterinarian at other stages of gestation.

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

Lactation:
Detomidine is excreted in trace amounts into the milk. Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
The safety of the veterinary medicinal product has not been investigated in breeding horses. Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Detomidine has an additive/synergistic effect with other sedatives, anaesthetics, hypnotics and analgesics and therefore an appropriate dose adjustment may be needed.

When the veterinary medicinal product is used as a premedication prior to general anaesthesia, the veterinary medicinal product may delay onset of induction.

Detomidine should not be used in conjunction with sympathomimetic amines such as adrenaline, dobutamine and ephedrine, as these agents counteract the sedative effect of detomidine, except in the case of anaesthetic incidents.

For intravenous potentiated sulfonamides, see section 'Contraindications'.

Overdose:
Over dosage is mainly manifested by delayed recovery from sedation or anaesthesia. Circulatory and respiratory depression may occur.

If recovery is delayed, it should be ensured that the animal can recover in a quiet and warm place.

Oxygen supplementation and/or symptomatic treatment may be indicated in cases of circulatory and respiratory depression.

The effects of the veterinary medicinal product can be reversed using an antidote, containing the active substance atipamezole, which is an alpha-2 adrenoceptor antagonist. Atipamezole is administered at a dosage 2–10-fold that of this veterinary medicinal product, calculated in µg/kg. For example, if a horse has been given this veterinary medicinal product at a dosage of 20 µg/kg (0.2 ml/100 kg), the atipamezole dosage should be 40–200 µg/kg (0.8–4 ml/100 kg).

Special restrictions for use and special conditions for use:

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products.

7. Adverse events

Horses:

Very common (>1 animal / 10 animals treated):	Arrhythmia[1], Bradycardia, Heart block[2], Hypertension (transient), Hypotension (transient) Hyperglycaemia Ataxia, Muscle tremor

	Urination[3] Penile prolapse (transient)[4], Uterine contraction Increased sweating (transient), Piloerection Hyperthermia, Hypothermia
Common (1 to 10 animals / 100 animals treated):	Hypersalivation (transient) Nasal discharge[5] Skin swelling[6]
Rare (1 to 10 animals / 10,000 animals treated):	Colic[7] Urticaria Hyperventilation, Respiratory depression Excitation
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction

[1,2] Causes changes in the conductivity of cardiac muscle as evidenced by partial atrioventricular and sinoatrial blocks.
[3] A diuretic effect may be observed 45 to 60 minutes after treatment.
[4] A partial penis prolapse can occur in stallions and geldings.
[5,6] Mucus discharges from the nose and oedema of the head and face may be seen because of continued lowering of the head during sedation.
[7] Substances of this class inhibit intestinal motility.

Cattle:

Very common (>1 animal / 10 animals treated):	Bradycardia, Hypertension (transient), Hypotension (transient) Hyperglycaemia Urination[1] Penile prolapse (transient)[2]
Common (1 to 10 animals / 100 animals treated):	Ruminal tympany[3], Hypersalivation (transient) Ataxia, Muscle tremor Uterine contraction Nasal discharge[4], Respiratory depression (slight)[5] Hyperthermia, Hypothermia
Rare (1 to 10 animals / 10,000 animals treated):	Arrhythmia[6] Increased sweating (transient) Excitation Hyperventilation (slight)[7]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Heart block[8]

[1] A diuretic effect may be observed 45 to 60 minutes after treatment.
[2] A partial, penis prolapse can occur.
[3] Substances of this class inhibit ruminal and intestinal motility. Can cause a mild bloat in cattle.
[4] Mucus discharge from the nose may be seen because of continued lowering of the head during sedation.

[5,7] Causes changes in the respiratory rate.
[6,8] Causes changes in the conductivity of cardiac muscle as evidenced by partial atrioventricular and sinoatrial blocks.

Mild adverse reactions have reportedly resolved uneventfully without treatment. Adverse reactions should be treated symptomatically.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:.

8. Dosage for each species, routes and method of administration

Intramuscular or intravenous use.

To be administered intramuscularly or by slow intravenous injection of detomidine hydrochloride at a dose of 10–80 μg/kg depending on the degree and duration of sedation and analgesia required. The effect is more rapid after intravenous administration. To ensure a correct dosage, body weight should be determined as accurately as possible.

Single use (horses and cattle)

Dose		Effect	Duration of effect (h)	Other effects
ml/100 kg	μg/kg			
0.1-0.2	10-20	Sedation	0.5-1	
0.2-0.4	20-40	Sedation and analgesia	0.5-1	Slight staggering
0.4-0.8	40-80	Deeper sedation and better analgesia	0.5-2	Staggering, sweating, piloerection, muscular tremors

The onset of action occurs 2–5 min after IV injection. The full effect is seen 10–15 min after IV injection. If necessary, detomidine hydrochloride can be administered up to a total dose of 80 μg/kg.

The following dosing instructions show different possibilities for the combination of detomidine hydrochloride. However, the simultaneous administration with other drugs should always be based on a benefit-risk assessment by the responsible veterinarian and it must be done taking into account the SPC of the relevant products.

Combinations with detomidine to increase sedation or analgesia in a standing horse

Detomidine hydrochloride 10–30 μg/kg IV in combination with either

- butorphanol 0.025–0.05 mg/kg IV or
- levomethadone 0.05–0.1 mg/kg IV or
- acepromazine 0.02–0.05 mg/kg IV

Combinations with detomidine to increase sedation or analgesia in cattle

Detomidine hydrochloride 10-30 μg/kg IV in combination with

- butorphanol 0.05 mg/kg IV

Combinations with detomidine for preanaesthetic sedation in the horse

The following anaesthetics can be used after detomidine hydrochloride premedication (10–20 μg/kg) to achieve lateral recumbency and general anaesthesia:

- ketamine 2.2 mg/kg IV or
- thiopental 3–6 mg/kg IV or
- guaifenesin IV (to effect) followed by ketamine 2.2 mg/kg IV

Administer the veterinary medicinal products prior to ketamine and allow sufficient time for sedation to develop (5 minutes). Ketamine and the veterinary medicinal product must therefore never be administered simultaneously in the same syringe.

Combinations with detomidine and inhalation anaesthetics in the horse

Detomidine hydrochloride can be used as sedative premedicant (10–30 μg/kg) before induction and maintenance of inhalation anaesthesia. Inhalation anaesthetic is given to effect. The amount of inhalation anaesthetics required is significantly reduced by premedication with detomidine.

Combination with detomidine to maintain injection anaesthesia (total intravenous anaesthesia TIVA) in the horse

Detomidine can be used in combination with ketamine and guaifenesin for maintaining total intravenous anaesthesia (TIVA).

The best-documented solution contains guaifenesin 50–100 mg/ml, detomidine hydrochloride 20 μg/ml and ketamine 2 mg/ml. 1 g ketamine and 10 mg detomidine hydrochloride are added to 500 ml of 5–10 % guaifenesin; anaesthesia is maintained by an infusion of 1 ml/kg/h.

Combinations with detomidine for induction and maintenance of general anaesthesia in cattle

Detomidine hydrochloride 20 μg/kg (0.2 ml/100 kg) with

- ketamine 0.5–1 mg/kg IV, IM or
- thiopental 6–10 mg/kg IV

The effect of detomidine-ketamine lasts for 20–30 minutes, and the effect of detomidine- thiopental for 10-20 minutes.

9. Advice on correct administration

None.

10. Withdrawal periods

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

11. Special storage precautions

Keep out of the sight and reach of children.
Keep the container in the outer carton in order to protect from light.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and the carton after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Pack sizes:
- 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.

15. Date on which the package leaflet was last revised

{DD/MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder:

Manufacturer responsible for batch release:
Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information