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

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet. 10 mg/ml, Solution for injection for Horses, Dogs and Cats
Alvegesic 10 mg/ml, Solution for injection for Horses, Dogs and Cats (ES, PT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Butorphanol 10 mg
(equivalent to butorphanol tartrate 14.58 mg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzethonium chloride	0.10 mg
Citric acid monohydrate	
Sodium citrate	
Sodium chloride	
Water for injections	

Clear, colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Horses, Dogs, Cats.

3.2 Indications for use for each target species

HORSE
As an analgesic: For relief of moderate to severe abdominal pain (alleviates abdominal pain associated with colic of gastrointestinal origin).
As a sedative: For sedation after the administration of certain alpha2-adrenoceptor agonists (detomidine, romifidine).
DOG
As an analgesic: For relief of moderate visceral pain.
As a sedative: For sedation in combination with certain alpha2-adrenoceptor agonists (medetomidine).
As a pre-anaesthetic: For pre-anaesthesia as sole agent and in combination with acepromazine.
As an anaesthetic: For anaesthesia in combination with medetomidine and ketamine.
CAT
As an analgesic for the relief of moderate pain: For pre-operative analgesia in combination with acepromazine/ketamine or xylazine/ketamine.
For post- operative analgesia after small surgical procedures.
As a sedative: For sedation in combination with certain alpha2-adrenoceptor agonists (medetomidine).
As an anaesthetic: For anaesthesia in combination with medetomidine and ketamine.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients. Do not use in animals with severe dysfunction of the liver or kidneys.

Use of butorphanol is contraindicated in case of cerebral injury or organic brain lesions and in animals with obstructive respiratory disease, heart dysfunction or spastic conditions.
Horse:
Butorphanol/Detomidine hydrochloride combination: Do not use in pregnant animals.
Do not use in horses with pre-existing cardiac dysrhythmia or bradycardia.

The combination will cause a reduction in gastrointestinal motility and consequently should not be used in cases of colic associated with impaction.
Due to a possible depressive effect on the respiratory system, the veterinary medicinal product is contraindicated for use in horses with emphysema.
Butorphanol/Romifidine combination:
The combination should not be used during the last month of pregnancy.

3.4 Special warnings

Butorphanol is intended for use where short duration analgesia (horse, dog) or short to medium duration analgesia (cat) is required.
Marked sedation does not occur in cats when butorphanol is used as a sole agent.
In cats, individual response to butorphanol may be variable. In the absence of an adequate analgesic response, an alternative analgesic agent should be used.

In cats increasing of the dose will not increase intensity or duration of desired effects.

3.5 Special precautions for use

Special precautions for safe use in the target species :
Before using any combinations consult the contraindications and warnings that appear on the other product's Summary of Product Characteristics or data sheets.

Due to its antitussive properties, butorphanol may lead to an accumulation of mucous in the respiratory tract. Therefore, in animals with respiratory diseases associated with increased mucous production or in animals that are being treated with expectorants, butorphanol should only be used on the basis of a risk- benefit analysis by the responsible veterinarian.

For the concomitant use of other central nervous depressants refer to section 3.8.
For the combination of butorphanol and α2-adrenoceptor agonists refer to section 3.8. Special care should be taken when administering the veterinary medicinal product to animals with impaired liver or kidney function.
FOR ALL TARGET SPECIES
The safety of the veterinary medicinal product in puppies, kitten and foals has not been established. Use of the product in these groups should be on the basis of a benefit/risk analysis by the responsible veterinarian.

Horse:
- The use of the veterinary medicinal product at the recommended dose may lead to transient ataxia and/or excitement.
- Therefore, to prevent injuries in patient and people when treating horses, the location for the treatment should be chosen carefully.

Dog:
- When administered as an intravenous injection, the veterinary medicinal product must be injected slowly. Do not inject as a bolus.
- The dose must be reduced by 25-50% for dogs with MDR1 mutation.

Cat:

- When administered as an intravenous injection, the veterinary medicinal product must be injected slowly. Use of either insulin syringes or 1 ml graduated syringes is recommended.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Butorphanol has opioid activity. Precautions should be taken to avoid accidental injection / self-injection with this potent drug. The most frequent adverse effects of butorphanol in humans are drowsiness, sweating, nausea, dizziness and vertigo and may occur following unintended self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

DO NOT DRIVE. Effects can be reversed with an opioid (e.g. naloxone). antagonist. Wash splashes from skin and eyes immediately.

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

3.6 Adverse events

Horses:

Very common (>1 animal / 10 animals treated):	Ataxia[1,2], Sedation[3]
Undetermined frequency (cannot be estimated from available data) :	Pacing[4], Restlessness Cardiac depression Digestive tract disorder[5] Shivering Respiratory depression

[1] Mild, may persist for 3 -10 minutes, may last 1-2 hours in some cases.
[2] Mild to severe, may be encountered in combination with detomidine, but clinical studies have shown that horses are unlikely to collapse. Normal precautions should be observed to prevent self-injury.
[3] may occur in about 15% of horses.
[4]Excitatory locomotor effects after IV bolus injection at the maximum recommended dose (0.1 mg/kg body weight).
[5] No reduction in gastrointestinal transit time is seen. These effects are dose dependent and are generally minor and transient.

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Diarrhoea Ataxia[1] Anorexia
Undetermined frequency (cannot be estimated from available data) :	Injection site pain[2] Cardiac depression[3,4] Digestive tract disorder[5] Sedation[6] Respiratory depression[3,4]

[1] Transient clinical sign.
[2] Localised pain following intramuscular injection.

[3]As evidenced by a decrease in respiratory rate, development of bradycardia (slow heart rate) and a decrease in diastolic pressure may occur. The degree of depression is dose dependent. The extent of depression is dose dependent. Naloxone may be used as an antidote.
[4] Moderate to severe cardiopulmonary depression may occur during rapid intravenous injection.
[5] Reduction in gastrointestinal motility.
[6] Mild intensity.

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Diarrhoea Ataxia Anorexia
Undetermined frequency (cannot be estimated from available data) :	Injection site pain[1] Agitation[2] Mydriasis, Sedation[2] Respiratory depression[3] Dysphoria

[1] Localised pain following intramuscular injection.
[2] Mild intensity
[3] Naloxone may be used as an antidote

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 and lactation:

The safety of the veterinary medicinal product has not been established in the target species during pregnancy and lactation. The use is not recommended during pregnancy and lactation.For use of the veterinary medicinal product in combination with alpha2-adrenoceptor agonists, see section 3.3 .

3.8 Interaction with other medicinal products and other forms of interaction

Butorphanol must be used with caution when used in combination with other sedatives or analgesics (see section 3.5) . Reduce appropriately dosages of both butorphanol and alpha-agonists to avoid any adverse synergistic effect.
Use of butorphanol may influence subsequent administration of other analgesics e.g. higher doses of pure agonist opioid analgesics such as morphine or oxymorphone may be necessary.
Because of its antagonist properties at the opiate μ-opioid receptor, butorphanol may remove the analgesic effect in animals which have already received pure μ-opioid agonists.

The concomitant use of other central nervous depressants would be expected to potentiate the effects of butorphanol and such drugs should be used with caution. A reduced dose should be used when administering these agents concurrently.
The combination of butorphanol and α2-adrenoceptor agonists should be used with caution in animals with cardiovascular disease. The concurrent use of anticholinergic drugs, e.g atropine should be considered.

3.9 Administration routes and dosage

Horse: Intravenous use (IV)
Dog and cat: Intravenous (IV), intramuscular (IM) and subcutaneous use (SC).
To ensure a correct dosage, body weight should be determined as accurately as possible.

HORSE
For analgesia
Analgesic effects are seen within 15 minutes of injection and last approximately 2 hours.

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment
IV	0.10	**0.01 ml**	Dose may be repeated after 3-4 hours. Treatment should not exceed 48 hours.

For sedation (intravenous use) when used in combination with other drugs

Combination sedation agent (given 5 minutes before Alvegesic vet. 10mg/ml Solution for Injection)	IV Dose of Combination Agent mg/kg body weight	IV Dose Butorphanol mg/kg body weight	**IV Dose Alvegesic vet. 10mg/ml** **ml/100 kg body weight**
Detomidine hydrochloride*	0.012	0.025	**0.25 ml / 100 kg bw**
Romfidine	0.04-0.12	0.02	**0.20 ml / 100 kg bw**

* Clinical experience has shown that a total dose rate of 5 mg detomidine hydrochloride and 10 mg butorphanol affords effective, safe sedation in horses above 200 kg body weight.

DOG
For analgesia
Analgesic effects are seen within 15 minutes post injection.

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml** **ml/kg body weight**	Comment
IV, IM or SC	0.20-0.30	**0.02-0.03 ml**	Avoid rapid IV injection.(see section 3.6) Administer 15 minutes before terminating anaesthesia to provide analgesia in the recovery phase. Repeat dose as required.

For sedation when used in combination with other drugs

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine hydrochloride mg/kg body weight	Comment
IM or IV	0.1	**0.01 ml**	0.01-0.025 (depends on degree of sedation required)	Allow 20 minutes for profound sedation to develop before commencing the procedure

For use as a premedicant/pre-anaesthetic

1. when Alvegesic vet 10mg/ml Solution for Injection is used as the sole agent:

Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Route	Time of administration
0.1-0.20	**0.01-0.02 ml**	IV, IM or SC	15 minutes prior to induction

2. when Alvegesic vet 10mg/ml Solution for Injection is used together with 0.02 mg/kg acepromazine:

Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Route	Time of administration
0.10*	**0.01 ml***	IV or IM	Allow at least 20 minutes before the onset of action but the time between pre- medication and induction is flexible from 20-120 minutes

* The dose may be increased to 0.2 mg/kg (equivalent to 0.02 ml/kg) if the animal is already experiencing pain before the procedure commences or if a higher plane of analgesia is required during surgery.

For anaesthesia in combination with medetomidine & ketamine

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine mg/kg body weight	Dose Ketamine mg/kg body weight	Comments
IM	0.10	**0.01 ml**	0.025	5.0*	**Reversal with atipamezole is not recommended**

* Ketamine should be administered 15 minutes after IM administration of the butorphanol/medetomidine combination.

Post IM administration of the combination of the veterinary medicinal product with edetomidine, recumbency and loss of pedal reflex occurs in approximately 6 minutes and 14 minutes, respectively. Post administration of ketamine, the pedal reflex returns in approximately 53 minutes, followed by sternal recumbency a further 35 minutes later and standing a further 36 minutes later.

CAT

For analgesia

Pre-operative:

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment

IM or SC	0.4	**0.04 ml**	Administer 15-30 minutes prior to the administration of IV induction anaesthetic agents Administer 5 minutes before induction with IM induction anaesthetic agents such as combinations of IM acepromazine/ ketamine or xylazine/ketamine

Preclinical model studies and clinical field trials in cats demonstrated that the analgesic effect of butorphanol tartrate is seen within 20 minutes.

Post-operative

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment
SC or IM	0.4	**0 04 ml**	Administer 15 minutes before recovery
IV	0.1	**0.01 ml**	Administer 15 minutes before recovery

For sedation when used in combination with other drugs

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine hydrochloride mg/kg body weight	Comment
IM or SC	0.4	**0.04 ml**	0.05	Local anaesthetic infiltration should be used for wound suturing

For anaesthesia in combination with medetomidine & ketamine

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine mg/kg body weight	Dose Ketamine mg/kg body weight	Comments
IM	0.40	**0.04 ml**	0.08	5.0*	Recumbency and loss of pedal reflex occurs within 2-3 minutes and 3 minutes, respectively, post injection. Reversal with atipamezole results in return of the pedal reflex 2 minutes later, sternal recumbency 6 minutes later and standing 31 minutes later.
IV	0.10	**0.01 ml**	0.04	1.25-2.50 (depending on depth of anaesthesia required)	Reversal with atipamezole results in return of the pedal reflex 4 minutes later, sternal recumbency 7 minutes later and standing 18 minutes later.

* Ketamine should be administered 15 minutes after IM administration of the butorphanol/medetomidine combination.

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

The most important result of overdosage is respiratory depression. This can be reversed with naloxone. To reverse the effect of combinations with detomidine/medetomide atipamezole may be used, except when a combination of butorphanol, medetomidine, and ketamine has been used intramuscularly to produce anaesthesia in the dog. In this case, atipamezole should not be used(see section 3.9).

Other possible signs of overdose in the horse include restlessness/excitability, muscle tremor, ataxia, hypersalivation, decrease of gastrointestinal motility and seizures.

In the cat, the main signs of overdose are incoordination, salivation, and mild convulsions.

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

Not applicable.

3.12 Withdrawal periods

Horse: Meat and offal: Zero days
Milk: Zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN02AF01

4.2 Pharmacodynamics

Butorphanol is an opioid agonist- antagonist drug with intrinsic agonist activity at the κ opioid receptor and antagonist activity at the μ opioid receptor. The activity of endogenous and exogenous opioids is mediated by binding at opioid receptors in the brain, the spinal cord and in the periphery. The activation of opioid receptors is coupled to changes in ion conductance and G-protein interactions, leading to inhibition of pain transmission.

4.3 Pharmacokinetics

Post parenteral administration, absorption of the veterinary medicinal product is rapid and almost complete with serum peak levels occurring after 0.5-1.5 hours. It has a large apparent volume of distribution (V_d > 1l/kg) and is widely distributed in the animal. Butorphanol undergoes extensive hepatic metabolism. The metabolites (hydroxybutorphanol and norbutorphanol) presumably have no pharmacological activity. Thus, in cases where there is clinically significant hepatic impairment, the dose of butorphanol should be reduced and/or the dose interval should be increased.

Elimination of intact drug from the plasma is rapid in animals. The veterinary medicinal product is primarily excreted via the kidneys. Only 10-14 % of parenterally administered butorphanol is excreted by biliary excretion.

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: 4 years
Shelf-life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

Keep the vial in the outer carton in order to protect from light. Do not refrigerate or freeze.

5.4 Nature and composition of immediate packaging

Cardboard box with 1 glass (Type II) vial of 10 ml with a bromobutyl rubber stopper and aluminium cap.

Package size:

Cardboard box containing 1 vial of 10 mL.

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

V.M.D. n.v.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

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 OF 10 ML

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet. 10 mg/ml; solution for injection.

2. STATEMENT OF ACTIVE SUBSTANCES

Butorphanol 10 mg/ml
(as butorphanol tartrate 14.58 mg/ml)

3. PACKAGE SIZE

10 ml

4. TARGET SPECIES

Horses, dogs, cats.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Horse: intravenous use
Dog and cat: intravenous, intramuscular and subcutaneous use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Horse: Meat and offal: Zero days
Milk: Zero hours

8. EXPIRY DATE

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

9. SPECIAL STORAGE PRECAUTIONS

Keep vial in the outer carton in order to protect from light.
Do not refrigerate or freeze.

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

V.M.D. n.v.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

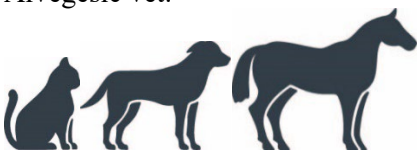
Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Type II colourless glass vials (10ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet.



2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Butorphanol (as tartrate) 10 mg/ml

3. BATCH NUMBER

Lot

4. EXPIRY DATE

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

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Alvegesic vet. 10 mg/ml, Solution for injection for Horses, Dogs and Cats
Alvegesic 10 mg/ml, Solution for injection for Horses, Dogs and Cats (ES, PT)

2. Composition

Each ml contains :
Active substance:
Butorphanol 10 mg
(equivalent to butorphanol tartrate 14.58 mg)

Excipient:
Benzethonium chloride 0.10 mg

Clear colourless solution.

3. Target species

Horses, dogs, cats.

4. Indications for use

HORSE
As an analgesic: For relief of moderate to severe abdominal pain (alleviates abdominal pain associated with colic of gastrointestinal origin).
As a sedative: For sedation after the administration of certain alpha2-adrenoceptor agonists (detomidine, romifidine).
DOG
As an analgesic: For relief of moderate visceral pain.
As a sedative: For sedation in combination with certain alpha2-adrenoceptor agonists (medetomidine).
As a pre-anaesthetic: For pre-anaesthesia as sole agent and in combination with acepromazine.
As an anaesthetic: For anaesthesia in combination with medetomidine and ketamine.
CAT
As an analgesic for the relief moderate pain: For pre-operative analgesia in combination with acepromazine/ketamine or xylazine/ketamine. For post- operative analgesia after small surgical procedures.
As a sedative: For sedation in combination with certain alpha2-adrenoceptor agonists (medetomidine). As an anaesthetic: For anaesthesia in combination with medetomidine and ketamine.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with severe dysfunction of the liver or kidneys.
Use of butorphanol is contraindicated in case of cerebral injury or organic brain lesions and in animals with obstructive respiratory disease, heart dysfunction or spastic conditions.

HORSE
Butorphanol/Detomidine hydrochloride combination:Do not use in pregnant animals.
Do not use with pre-existing cardiac dysrhythmia or bradycardia (slow heart rate).
The combination will cause a reduction in gastrointestinal motility and consequently should not be used in cases of colic associated with impaction.
Due to a possible depressive effect on the respiratory system, the veterinary medicinal product is

contraindicated for use in horses with emphysema.

Butorphanol/Romifidine combination:
The combination should not be used during the last month of pregnancy.

6. Special warnings

Special warnings:

Butorphanol is intended for use where short duration analgesia (horse, dog) or short to medium duration analgesia (cat) is required.
Marked sedation does not occur in cats when Butorphanol is used as a sole agent.

In cats, individual response to butorphanol may be variable. In the absence of an adequate analgesic response, an alternative analgesic agent should be used.

In cats increasing of the dose will not increase intensity or duration of desired effects.

Before using any combinations consult the contraindications and warnings that appear on the other veterinary medicinal product's Summary of Product Characteristics or data sheets.
Due to its antitussive properties, butorphanol may lead to an accumulation of mucous in the respiratory tract. Therefore, in animals with respiratory diseases associated with increased mucous production or in animals that are being treated with expectorants, butorphanol should only be used on the basis of a risk- benefit analysis by the responsible veterinarian.
For the concomitant use of other central nervous depressants refer to section *Interaction with other medicinal products and other forms of interaction.*
For the combination of butorphanol and α2-adrenoceptor agonists refer to section *Interaction with other medicinal products and other forms of interaction.*
Special care should be taken when administering the veterinary medicinal product to animals with impaired liver or kidney function.

Special precautions for safe use in the target species:

FOR ALL TARGET SPECIES
The safety of the veterinary medicinal product in puppies, kitten and foals has not been established. Use of the product in these groups should be on the basis of a benefit/risk analysis by the responsible veterinarian.

Horse:
- The use of the veterinary medicinal product at the recommended dose may lead to transient ataxia and/or excitement. Therefore, to prevent injuries in patient and people when treating horses, the location for the treatment should be chosen carefully.

Dog:
- When administered as an intravenous injection, the veterinary medicinal product must be injected slowly. The dose must be reduced by 25-50% for dogs with MDR1 mutation.

Cat:
- When administered as an intravenous injection, the veterinary medicinal product must be injected slowly. Use of either insulin syringes or 1 ml graduated syringes is recommended.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Butorphanol has opioid activity. Precautions should be taken to avoid accidental injection / self-injection with this potent drug. The most frequent adverse effects of butorphanol in humans are

drowsiness, sweating, nausea, dizziness and vertigo and may occur following unintended self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
DO NOT DRIVE. Effects can be reversed with an opioid antagonist Wash splashes from skin and eyes immediately.
An opioid antagonist (e.g. naloxone) may be used as an antidote.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in the target species during pregnancy and lactation. The use is not recommended during pregnancy and lactation.
For use of the veterinary medicinal product in combination with alpha2-adrenoceptor agonists, (see section *Contraindication).*

Interaction with other medicinal products and other forms of interaction:
Butorphanol must be used with caution when used in combination with other sedatives or analgesics. Reduce appropriately dosages of both butorphanol and alpha-agonists to avoid any adverse synergistic effect.

Use of Butorphanol may influence subsequent administration of other analgesics e.g. higher doses of pure agonist opioid analgesics such as morphine or oxymorphine may be necessary.
Because of its antagonist properties at the opiate μ-opioid receptor, butorphanol may remove the analgesic effect in animals which have already received pure μ-opioid agonists.
The concomitant use of other central nervous depressants would be expected to potentiate the effects of butorphanol and such drugs should be used with caution. A reduced dose should be used when administering these agents concurrently.
The combination of butorphanol and alpha 2-adrenoceptor agonists should be used with caution in animals with cardiovascular disease. The concurrent use of anticholinergic drugs, e.g atropine should be considered.

Overdose:
The most important result of overdosage is respiratory depression. This can be reversed with an opioid antagonist (e.g.naloxone). To reverse the effect of combinations with detomidine/medetomide, atipamezole may be used, except when a combination of butorphanol, medetomidine, and ketamine has been used intramuscularly to produce anaesthesia in the dog. In this case, atipamezole should not be used. (see section 8 *Dosage for each species, routes and method of administration*). Other possible signs of overdose in the horse include restlessness/excitability, muscle tremor, ataxia, hypersalivation, decrease of gastrointestinal motility and seizures.

In the cat, the main signs of overdose are incoordination, salivation, and mild convulsions.

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

7. Adverse events

Horses:

Very common (>1 animal / 10 animals treated):	Ataxia[1,2], Sedation[3]
Undetermined frequency (cannot be estimated from available data) :	Pacing[4], Restlessness Cardiac depression Digestive tract disorder[5] Shivering Respiratory depression

[1] Mild, may persist for 3 -10 minutes, may last 1-2 hours in some cases.

[2] Mild to severe, may be encountered in combination with detomidine, but clinical studies have shown that horses are unlikely to collapse. Normal precautions should be observed to prevent self-injury.
[3] may occur in about 15% of horses.
[4] Excitatory locomotor effects after IV bolus injection at the maximum recommended dose (0.1 mg/kg body weight).
[56] No reduction in gastrointestinal transit time is seen. These effects are dose dependent and are generally minor and transient.

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Diarrhoea Ataxia (incoordination)[1] Anorexia (losss of appetite)
Undetermined frequency (cannot be estimated from available data) :	Injection site pain[2] Cardiac depression[3,4] Digestive tract disorder[5] Sedation[6] Respiratory depression[3,4]

[1] Transient clinical sign.
[2] Localised pain following intramuscular injection.
[3]As evidenced by a decrease in respiratory rate, development of bradycardia (slow heart rate) and a decrease in diastolic pressure may occur. The degree of depression is dose dependent. The extent of depression is dose dependent. Naloxone may be used as an antidote.
[4] Moderate to severe cardiopulmonary depression may occur during rapid intravenous injection.
[5] Reduction in gastrointestinal motility.
[6] Mild intensity.

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Diarrhoea Ataxia (incoordination) Anorexia (loss of appetite)
Undetermined frequency (cannot be estimated from available data) :	Injection site pain[1] Agitation[2] Mydriasis, Sedation[2] Respiratory depression[3] Dysphoria (uneasiness)

[1] Localised pain following intramuscular injection.
[2] Mild intensity
[3] Naloxone may be used as an antidote

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal 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: *[listed in Appendix I*]*>.

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

Horse: Intravenous use(IV)
Dog and cat: Intravenous(IV), intramuscular (IM)and subcutaneous use. (SC).
To ensure a correct dosage, body weight should be determined as accurately as possible.

HORSE

For analgesia

Analgesic effects are seen within 15 minutes of injection and last approximately 2 hours.

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment
IV	0.10	**0.01 ml**	Dose may be repeated after 3-4 hours. Treatment should not exceed 48 hours.

For sedation (intravenous use) when used in combination with other drugs

Combination sedation agent (given 5 minutes before Alvegesic vet. 10mg/ml Solution for Injection)	IV Dose of Combination Agent mg/kg body weight	IV Dose Butorphanol mg/kg body weight	**IV Dose Alvegesic vet. 10mg/ml** **ml/100 kg body weight**
Detomidine hydrochloride*	0.012	0.025	**0.25 ml / 100 kg bw**
Romfidine	0.04-0.12	0.02	**0.20 ml / 100 kg bw**

* Clinical experience has shown that a total dose rate of 5 mg detomidine hydrochloride and 10 mg butorphanol affords effective, safe sedation in horses above 200 kg body weight.

DOG

For analgesia

Analgesic effects are seen within 15 minutes post injection.

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml** **ml/kg body weight**	Comment
IV, IM or SC	0.20-0.30	**0.02-0.03 ml**	Avoid rapid IV injection. (see section “Special Warnings”). Administer 15 minutes before terminating anaesthesia to provide analgesia in the recovery phase. Repeat dose as required.

For sedation when used in combination with other drugs

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine hydrochloride mg/kg body weight	Comment
IM or IV	0.1	**0.01 ml**	0.01-0.025	Allow 20 minutes for profound sedation to

			(depends on degree of sedation required)	develop before commencing the procedure

For use as a premedicant/pre-anaesthetic

1. when Alvegesic vet 10mg/ml Solution for Injection is used as the sole agent:

Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Route	Time of administration
0.1-0.20	**0.01-0.02 ml**	IV, IM or SC	15 minutes prior to induction

2. when Alvegesic vet 10mg/ml Solution for Injection is used together with 0.02 mg/kg acepromazine:

Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Route	Time of administration
0.10*	**0.01 ml***	IV or IM	Allow at least 20 minutes before the onset of action but the time between pre-medication and induction is flexible from 20-120 minutes

* The dose may be increased to 0.2 mg/kg (equivalent to 0.02 ml/kg) if the animal is already experiencing pain before the procedure commences or if a higher plane of analgesia is required during surgery.

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine mg/kg body weight	Dose Ketamine mg/kg body weight	Comments
IM	0.10	**0.01 ml**	0.025	5.0*	**Reversal with atipamezole is not recommended**

***** Ketamine should be administered 15 minutes after IM administration of the butorphanol/medetomidine combination.

Post IM administration of the combination Alvegesic vet 10mg/ml Solution for Injection/ medetomidine, recumbency and loss of pedal reflex occurs in approximately 6 minutes and 14 minutes, respectively. Post administration of ketamine, the pedal reflex returns in approximately 53 minutes, followed by sternal recumbency a further 35 minutes later and standing a further 36 minutes later.

CAT

For analgesia

Pre-operative:

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment

IM or SC	0.4	**0.04 ml**	Administer 15-30 minutes prior to the administration of IV induction anaesthetic agents Administer 5 minutes before induction with IM induction anaesthetic agents such as combinations of IM acepromazine/ ketamine or xylazine/ketamine

Preclinical model studies and clinical field trials in cats demonstrated that the analgesic effect of butorphanol tartrate is seen within 20 minutes.

Post-operative

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet. 10 mg/ml ml/kg body weight**	Comment
SC or IM	0.4	**0 04 ml**	Administer 15 minutes before recovery
IV	0.1	**0.01 ml**	Administer 15 minutes before recovery

<u>For sedation when used in combination with other drugs</u>

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine hydrochloride mg/kg body weight	Comment
IM or SC	0.4	**0.04 ml**	0.05	Local anaesthetic infiltration should be used for wound suturing

Route	Dose Butorphanol mg/kg body weight	**Dose Alvegesic vet 10 mg/ml ml/kg body weight**	Dose Medetomidine mg/kg body weight	Dose Ketamine mg/kg body weight	Comments
IM	0.40	**0.04 ml**	0.08	5.0*	Recumbency and loss of pedal reflex occurs within 2-3 minutes and 3 minutes, respectively, post injection. Reversal with atipamezole results in return of the pedal reflex 2 minutes later, sternal recumbency 6 minutes later and standing 31 minutes later.
IV	0.10	**0.01 ml**	0.04	1.25-2.50 (depending on depth of anaesthesia required)	Reversal with atipamezole results in return of the pedal reflex 4 minutes later, sternal recumbency 7 minutes later and standing 18 minutes later.

* Ketamine should be administered 15 minutes after IM administration of the butorphanol/medetomidine combination.

9. Advice on correct administration

Dog: When administering as an intravenous injection, do not inject as a bolus.

10. Withdrawal periods

Horse: Meat and offal: Zero days
Milk: Zero hours

11. Special storage precautions

Keep out of the sight and reach of children. Do not refrigerate or freeze. Keep vial 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 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

Package size:

Cardboard box containing 1 vial of 10 mL.

15. Date on which the package leaflet was last revised

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 and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Belgium

V.M.D. n.v.
Hoge Mauw 900
BE-2370 Arendonk
+32 (0) 14 67 20 51

Local representatives and contact details to report suspected adverse reactions:
[To be completed nationally]

17. Other information

National requirements will be added here.