1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet. 10 mg/ml, Solution for injection for Horses, Dogs and Cats

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

<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

<u>For anaesthesia in combination with medetomidine & ketamine</u>

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)

VPA16142/002/001

8. DATE OF FIRST AUTHORISATION

04 September 2009

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

21 December 2023

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).