LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE : Carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet. 10 mg/ml
Solution for injection for Horses, Dogs and Cats
Butorphanol (as butorphanol tartrate)

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml contains:

Active substance:	Butorphanol	10.00 mg
	(equivalent to Butorphanol tartrate	14.58 mg)
Excipient:	Benzethonium chloride	0,10 mg

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml

5. TARGET SPECIES

Horse, dog, cat.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

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

8. WITHDRAWAL PERIOD

Withdrawal period:

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

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening: 28 days.
Once opened use by ……...

11. SPECIAL STORAGE CONDITIONS

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

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

Disposal: read package leaflet.

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

For animal treatment only - to be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

V.M.D.n.v.Hoge Mauw 900, 2370 Arendonk, Belgium

16. MARKETING AUTHORISATION NUMBER(S)

Vm 19968/4008

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml white glass vials (type II)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alvegesic vet. 10 mg/ml
Solution for injection for Horses, Dogs and Cats
Butorphanol (as butorphanol tartrate)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

1 ml contains:

Active substance:	Butorphanol	10.00 mg
	(equivalent to Butorphanol tartrate	14.58 mg)
Excipients:	Benzethonium chloride	0.10 mg

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

10 ml

4. ROUTE(S) OF ADMINISTRATION

Horse: IV
Dog and cat: IV, IM, SC

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

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

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

Marketing authorisation holder and manufacturer responsible for batch release:
V.M.D.n.v., Hoge Mauw 900, 2370 Arendonk, Belgium

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

Butorphanol (as butorphanol tartrate)

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

1 ml solution for injection contains:

Active substance:	Butorphanol	10.00 mg
	(equivalent to Butorphanol tartrate	14.58 mg)
Excipients:	Benzethonium chloride	0.10 mg

Clear, colourless solution for injection.

4. INDICATION(S)

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 case of known 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.
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 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. ADVERSE REACTIONS

Local pain associated with intramuscular injection.
Sedation may be noted in treated animals.

Horse:

- The most common side-effect is mild ataxia which may persist for 3 to 10 minutes. An increase in motor activity and ataxia produced by butorphanol lasted 1 – 2 hours in some cases.
- Restlessness, shivering and sedation followed by restlessness were observed in some horses.
- Mild to severe ataxia 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.
- Mild sedation may occur in approximately 15 % of horses following administration of butorphanol as a sole agent.
- A bolus i.v. injection at the maximum label dose (0.1 mg/kg body weight) may result in excitatory locomoter effects (e.g. pacing) in clinically normal horses.
- Butorphanol may also have adverse effects on gastrointestinal tract motility in normal horses, although there is no decrease in gastrointestinal transit time. These effects are dose-related and generally minor and transient.
- Depression of the cardiopulmonary system may occur.

Dog:

- Respiratory and cardiac depression (as evidenced by a decrease in respiratory rate, development of bradycardia and a decrease in diastolic pressure) may occur. The degree of depression is dose dependent. If respiratory depression occurs, naloxone may be used as an antidote.

- Moderate to marked cardiopulmonary depression may occur if butorphanol is given rapidly by intravenous injection.
- Mild sedation may occur.
- Transient ataxia, anorexia and diarrhoea have been reported as occurring rarely.
- Reduction in gastrointestinal motility may occur.
- When using butorphanol as a pre-anaesthetic, the use of an anticholinergic such as atropine, will protect the heart against possible opioid-induced bradycardia.

Cat:

- Mydriasis is likely to occur.
- Mild sedation or occasional periods of mild agitation have also been observed.
- Respiratory depression may occur. If respiratory depression occurs, naloxone may be used as an antidote.
- Butorphanol administration may lead to dysphoria.

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

7. TARGET SPECIES

Horse, dog, cat.

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

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

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 Warning”. 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 Alvegesic vet 10mg/ml Solution for Injection/ medeto-midine, 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.

9. ADVICE ON CORRECT ADMINISTRATION

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

10. WITHDRAWAL PERIOD

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.

EXP: 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 container: 28 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Butorphanol is intended for use where short duration analgesia (horse, dog) or short to medium duration analgesia (cat) is required.
The safety of the product in young puppies and foals has not been established. Use of the product in these groups should be on the basis of a risk: benefit analysis by the responsible veterinarian.

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.

Special precautions for use in animals:
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 *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 product to animals with impaired liver or kidney function.

Horse:
- The use of the 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 administering as an intravenous injection, do not inject as a bolus.

Cat:
- 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:
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.
Use during pregnancy, lactation or lay:
The safety of this veterinary medicinal product has not been established in the target species during pregnancy and lactation. The use of butorphanol during pregnancy and lactation is not recommended.
For use of the product in combination with alpha2-adrenoceptor agonists, see Section 5, contra-indications.

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 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.

Overdose (symptoms, emergency procedures, 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 8.
Other possible signs of overdose in the horse include restlessness/excitability, muscle tremor, ataxia, hypersalivation, decrease of gastrointestinal motility and seizures.

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

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.
Medicines should not be disposed of via wastewater or household waste.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

November 2020

15. OTHER INFORMATION

Package size: 10 ml
To be supplied only on veterinary prescription.
For animal treatment only.

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

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

Approved 06 November 2020