

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Torphadine 10 mg/ml solution for injection for dogs, cats and horses
butorphanol



2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains:
Butorphanol 10.0 mg
Equivalent to 14.58 mg of butorphanol tartrate

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml
20 ml

5. TARGET SPECIES

Dogs, cats and horses

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Dog and cat: For intravenous, intramuscular and subcutaneous use.
Horse: For intravenous use.

8. WITHDRAWAL PERIOD

Withdrawal periods:
Meat and offal: zero days.
Not authorised for use in mares producing milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Shelf life after first opening the container: 28 days

Once broached use by...

11. SPECIAL STORAGE CONDITIONS

12. SPECIFIC 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

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

16. MARKETING AUTHORISATION NUMBER

Vm 41821/4037

17. MANUFACTURER’S BATCH NUMBER

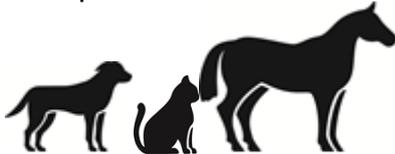
Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10, 20 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Torphadine 10 mg/ml injection
butorphanol



2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

10 mg/ml

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

10 ml

20 ml

4. ROUTE(S) OF ADMINISTRATION

Dog, Cat: IV, SC, IM
Horse: IV

5. WITHDRAWAL PERIOD

Withdrawal period: read package leaflet.

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use by

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

Torphadine 10 mg/ml solution for injection for dogs, cats and horses

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

Marketing authorisation holder:

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

Manufacturer responsible for batch release:

Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Torphadine 10 mg/ml solution for injection for dogs, cats and horses
butorphanol

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENT

Each ml contains:

Active substance:

Butorphanol 10.0 mg
Equivalent to 14.58 mg butorphanol tartrate

Excipient:

Benzethonium chloride 0.10 mg

Clear, colourless solution.

4. INDICATIONS

Dog

As an analgesic:

- For relief of mild to moderate visceral pain.

As a sedative:

- For sedation, when used in combination with certain alpha2-adrenoceptor agonists (medetomidine).

As a premedicant prior to general anaesthesia:

- For use in combination with acepromazine to provide analgesia and sedation prior to induction of general anaesthesia. A dose-related reduction in the dose of induction-anaesthetic agent (propofol or thiopentone) is also provided.

- For premedication, give as the sole pre-anaesthetic agent.

As an anaesthetic:

- For anaesthesia, when used in combination with medetomidine and ketamine.

Cat:

As an analgesic for the relief of moderate pain:

- For pre-operative use to provide analgesia during surgery.
- For post-operative analgesia after small surgical procedures.

As a sedative:

- For sedation, when used in combination with certain alpha2-adrenoceptor agonists (medetomidine).

As an anaesthetic:

- For anaesthesia, when used in combination with medetomidine and ketamine, suitable for short painful anaesthetic procedures.

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Horse:

As an analgesic:

- For the relief of moderate to severe abdominal pain associated with colic of gastrointestinal origin.

As a sedative:

- For sedation, given after the administration of certain alpha2-adrenoceptor agonists (detomidine, romifidine).

5. CONTRAINDICATIONS

All target species:

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

Do not use in animals with severe dysfunction of the liver or kidneys.

Do not use in animals with cerebral injury or organic brain lesions.

Do not use in animals with obstructive respiratory disease, heart dysfunction or spastic conditions.

Horse:

Butorphanol/detomidine hydrochloride combination:

Do not use in horses with a pre-existing cardiac dysrhythmia or bradycardia.

Do not use in cases of colic associated with impaction as the combination will cause a reduction in gastrointestinal motility.

Do not use in horses with emphysema due to a possible depressive effect on the respiratory system.

Do not use in pregnant mares.

Butorphanol/romifidine combination:

Do not use during the last month of pregnancy.

6. ADVERSE REACTIONS

All target species:

There may be some pain on intramuscular injection.

Sedation may be noted in treated animals.

Dog:

Respiratory and cardiovascular depression (as evidenced by a decrease in respiratory rate, development of bradycardia and a decrease in diastolic pressure) may occur (see 'Special warnings - Special precautions for use in animals'). 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.

When using butorphanol as a pre-anaesthetic, the use of an anticholinergic such as atropine, will protect the heart against possible narcotic-induced bradycardia.

Transient ataxia, anorexia, and diarrhoea have been reported as occurring rarely.

Reduction in gastrointestinal motility may occur.

Cat:

Respiratory depression may occur. If respiratory depression occurs, naloxone may be used as an antidote.

Mydriasis is likely to occur.

Butorphanol administration may cause excitation, anxiety, disorientation and dysphoria.

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

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, and shivering and sedation followed by restlessness have both been observed in some horses.

A bolus i.v. injection at the maximum label dose (0.1 mg/kg body weight) may result in excitatory locomotor effects (e.g. pacing) in clinically normal horses.

Mild to severe ataxia may be encountered in combination with detomidine, but horses are unlikely to collapse. Normal precautions should be observed to prevent injury (see 'Special warnings - Special precautions for use in animals').

Mild sedation may occur in approximately 15% of horses following administration of butorphanol as a sole agent.

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. When used in combination with alpha2-adrenoceptor agonists, cardiopulmonary system depression may be fatal in rare cases.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Dogs, cats and horses

8. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Horse: Intravenous use.

Dog and cat: Intravenous, intramuscular and subcutaneous use.

Animals should be weighed to establish an accurate body weight prior to calculation of the appropriate treatment dose.

Dog:

For analgesia:

Route	Dose butorphanol	Dose product
IV, IM or SC	0.20-0.30 mg/kg bw	0.02-0.03 ml/kg bw
Comment	IV injection should be slow. Analgesic effects are seen within 15 minutes of injection. Administer 15 minutes before terminating anesthesia to provide analgesia in the recovery phase. For continuous analgesia repeat dose as required.	

For sedation in combination with medetomidine hydrochloride:

Route	Dose butorphanol	Dose product	Dose medetomidine hydrochloride
IM or IV	0.1 mg/kg bw	0.01 ml/kg bw	0.01*-0.025**mg/kg bw
Comment	Allow 20 minutes for profound sedation to develop before commencing the procedure. Where compatibility is accepted, products containing medetomidine and butorphanol may be combined and administered in the same syringe (see section 'special warnings – incompatibilities').		

*Depending on degree of sedation required: 0.01 mg/kg: For sedation and as a premedicant to barbiturate anaesthesia

**Depending on degree of sedation required 0.025 mg/kg: For profound sedation and as a premedicant to ketamine anaesthesia

For use as a premedicant/pre-anaesthetic:

- When the product is used as the sole agent:

Route	Dose butorphanol	Dose product
IV, IM or SC	0.1-0.20 mg/kg bw	0.01-0.02 ml/kg bw
Comment	15 minutes prior to induction	

- When the product is used together with 0.02 mg/kg acepromazine:

Route	Dose butorphanol	Dose product
IV or IM	0.10 mg/kg bw*	0.01 ml/kg bw*
Comment	Allow at least 20 minutes before the onset of action but the time between pre-medication and induction is flexible from 20-120 minutes. Where compatibility is accepted, products containing butorphanol and acepromazine may be combined and administered in the same syringe (see section 'special warnings – incompatibilities').	

* 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 and ketamine:

Route	Dose butorphanol	Dose product	Dose medetomidine	Dose ketamine
IM	0.10 mg/kg bw	0.01 ml/kg bw	0.025mg/kg bw	5.0mg/kg bw*
Comment	Reversal with atipamezole is not recommended Where compatibility is accepted, products containing medetomidine and butorphanol may be combined and administered in the same syringe (see section 'special warnings – incompatibilities').			

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

Cat:

For pre-operative analgesia:

Route	Dose butorphanol	Dose product
IM or SC	0.4 mg/kg bw	0.04 ml/kg bw
Comment	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	

For post-operative analgesia:

Route	Dose butorphanol	Dose product
SC or IM	0.4 mg/kg bw	0.04 ml /kg bw
IV	0.1 mg/kg bw	0.01 ml /kg bw
Comment	Administer 15 minutes before recovery	

For sedation in combination with medetomidine hydrochloride:

Route	Dose butorphanol	Dose product	Dose medetomidine hydrochloride
IM or SC	0.4 mg/kg bw	0.04 ml/kg bw	0.05 mg/kg bw
Comment	Local anaesthetic infiltration should be used for wound suturing. Where compatibility is accepted, products containing medetomidine and butorphanol may be combined and administered in the same syringe (see section 'special warnings – incompatibilities').		

For anaesthesia in combination with medetomidine and ketamine:

Route	Dose butorphanol	Dose product	Dose medetomidine	Dose ketamine
IM	0.40 mg/kg bw	0.04 ml/kg bw	0.08 mg/kg bw	5.0 mg/kg bw*
IV	0.10 mg/kg bw	0.01 ml/kg bw	0.04 mg/kg bw	1.25-2.50 mg/kg bw (depending on depth of anaesthesia required)
Comment	Where compatibility is accepted, products containing medetomidine, butorphanol and ketamine may be combined and administered in the same syringe (see section 'special warnings – incompatibilities').			

Horse:

For analgesia:

Route	Dose butorphanol	Dose product
IV	0.10 mg/kg bw	1 ml/100 kg bw
Comment	Analgesic effects are seen within 15 minutes of injection. Dose may be repeated as required.	

For sedation in combination with detomidine hydrochloride:

Route	Dose of detomidine hydrochloride	Dose butorphanol*	Dose product
IV	0.012 mg/kg bw	0.025 mg/kg bw	0.25 ml/100 kg bw
Comment	Detomidine should be administered up to 5 minutes before the butorphanol dose.		

*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.

For sedation in combination with romifidine:

Route	Dose of romifidine	Dose butorphanol	Dose product
IV	0.04-0.12 mg/kg bw	0.02 mg/kg bw	0.2 ml/100 kg bw
Comment	Romifidine should be administered up to 5 minutes before the butorphanol dose.		

Before this product is combined and administered in the same syringe as another veterinary medicinal product always refer to the section on 'Special warnings – Incompatibilities'.

The maximum number of vial punctures when using needle sizes 21G and 23G should not exceed 100 and when using a 18G needle, the maximum should not exceed 40.

9. ADVICE ON CORRECT ADMINISTRATION

Not applicable

10. WITHDRAWAL PERIOD

Meat and offal: zero days.

Not authorised for use in mares producing milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions. 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 WARNINGS

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. In cases where longer duration analgesia is likely to be required, an alternative therapeutic agent should be used.

Marked sedation does not occur when butorphanol is used as a sole agent in cats. 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

For all target species:

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, butorphanol should only be used according to a benefit-risk assessment by the responsible veterinary surgeon.

Prior to use of the product in combination with α 2-adrenoreceptor agonists routine cardiac auscultation should be performed and the concurrent use of anticholinergic drugs, e.g. atropine should be considered.

The combination of butorphanol and an α 2-adrenoceptor agonists should be used with caution in animals with mild to moderate dysfunction of the liver or kidney.

Take care when administering butorphanol to animals concurrently treated with other central nervous depressants (see section on 'interaction with other medicinal products and other forms of interaction').

The safety of the product in puppies, kitten and foals has not been established and therefore in these animals the product should only be used according to a benefit-risk assessment by the responsible veterinary surgeon.

Dog:

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

In dogs with MDR1 mutation reduce dose by 25-50%

Cat:

Use of either insulin syringes or 1 ml graduated syringes is recommended.

Horse:

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

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

Butorphanol has opioid activity. The most frequent adverse effects of butorphanol in humans are drowsiness, sweating, nausea, dizziness and vertigo, and these may occur following unintended self-injection. Care should be taken to avoid accidental injection/self-injection. If accidental self-injection occurs, seek medical advice

immediately and show the package leaflet or the label to the physician. Do not drive. An opioid antagonist (e.g. naloxone) may be used as an antidote.

Wash any splashes from skin and eyes immediately.

Pregnancy and lactation:

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. See also the section on 'Contraindications'.

Interaction with other medicinal products and other forms of interaction:

When butorphanol is used in combination with certain α_2 -adrenoceptor agonists (romifidine or detomidine in horses; medetomidine in dogs and cats) synergistic effects occur, requiring a butorphanol dose reduction (see section on 'Dosage for each species, routes and method of administration').

Butorphanol is antitussive and should not be used in combination with an expectorant as it may lead to an accumulation of mucous in the airways.

Butorphanol has antagonist properties at the opiate mu (μ) receptor which may remove the analgesic effect of pure opioid mu (μ) agonists (e.g. morphine/oxymorphone) in animals that have already received these agents.

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 butorphanol dose should be used when administering these agents concurrently

Overdose (symptoms, emergency procedures, antidotes):

The main sign of overdose is respiratory depression, which can be reversed with naloxone.

To reverse the sedative effect of butorphanol/alpha 2 adrenoceptor agonist combinations, atipamezole may be used. To reverse adverse cardiopulmonary effects of these combinations, higher atipamezole doses may be required. Atipamezole should not be used in dogs treated with a combination of butorphanol, medetomidine, and ketamine used intramuscularly to produce anaesthesia.

Other possible signs of overdose in the horse include restlessness/excitability, muscle tremor, ataxia, hypersalivation, decrease of gastrointestinal motility and seizure. In the cat, the main signs of overdose are incoordination, salivation, and mild convulsions.

Incompatibilities:

Butorphanol must not be mixed with other veterinary medicinal products in the same syringe with the exception of the following combinations: butorphanol/medetomidine, butorphanol/medetomidine/ketamine and butorphanol/acepromazine.

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

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

July 2021

15. OTHER INFORMATION

Clear type I glass vials closed with a coated bromobutyl rubber stopper and aluminium cap in a carton box.
Pack sizes: 10 ml and 20 ml.

Not all pack sizes may be marketed.

Approved: 08/10/21

