1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Torbuphanol 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
(as butorphanol tartrate 14.58 mg)

Excipients:
Benzethonium chloride 0.1 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Horse, dog and cat.

4.2 Indications for use, specifying the target species

HORSE
As an analgesic
For relief of pain associated with colic of gastrointestinal tract origin.
As a sedative
For sedation when given after the administration of certain alpha2-adrenoreceptor agonists (detomidine, romifidine).
For therapeutic and diagnostic procedures such as minor standing surgery.

DOG
As an analgesic
For relief of mild to moderate visceral pain and pain associated with post-surgical procedures.
As a sedative

In combination with medetomidine hydrochloride.

As a pre-anaesthetic

Pre-anaesthetic use of the product has resulted in a dose related reduction in the dose of induction anaesthetic agents, such as thiopentone sodium.

As an anaesthetic: For anaesthesia in combination with medetomidine and ketamine.

CAT

As an analgesic

For relief of mild to moderate visceral pain. For pre-operative use to provide analgesia during surgery. For post-operative analgesia after a variety of surgical procedures.

As a sedative

In combination with medetomidine hydrochloride.

As anaesthetic: For anaesthesia in combination with medetomidine and ketamine.

4.3 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 diseases, heart dysfunction or spastic conditions.

HORSE

Butorphanol/detomidine hydrochloride combination

The combination should not be used in horses with a 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.

See also section 4.7

4.4 Special warnings for each target species

Butorphanol is intended for use where short duration analgesia (dog, horse) is required. For information on the duration of analgesia that can be expected following treatment see section 5.1. However, repeat treatments of butorphanol may be administered. For cases where longer duration analgesia is likely to be required, an alternative therapeutic agent should be used.

In the cat, butorphanol is intended for use where short to medium duration analgesia is required. For information on the duration of analgesia that can be expected

following treatment see section 5.1. Depending on the clinical response, product administration may be repeated within six hours. In the absence of an adequate analgesic response, use of an alternative analgesic agent, such as another suitable opioid analgesic and/or a non-steroidal anti-inflammatory drug, should be considered. Increasing of the dose may not increase the intensity or duration of analgesia. Any alternative analgesia should take account of the action of butorphanol on opioid receptors, as described in Section 4.8.

Mild sedation may occur in all species when the product is used as a sole agent.

4.5 Special precautions for use

Special precautions for use in animals
FOR ALL TARGET SPECIES

The safety of the product in puppies, kitten 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.

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 after a risk-benefit evaluation by the responsible veterinarian.

Routine cardiac auscultation should be performed prior to use in combination with α2-adrenoceptor agonists. 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.

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.

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
Cats should be weighed to ensure that the correct dose is calculated. 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.

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 splashes from skin and eyes immediately.

4.6 Adverse reactions (frequency and seriousness)

ALL SPECIES
In very rare cases, pain on intramuscular injection may be observed.

HORSE
The most commonly side effect is mild ataxia which may persist for 3 to 10 minutes.
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.
In very rare cases, butorphanol may also have adverse effects on gastrointestinal tract motility in horses, although there is no decrease in gastrointestinal transit time. These effects are dose-related and generally minor and transient.
Very rarely, butorphanol may cause excitatory locomotor effects (pacing).
When used in combination with α2-adrenoceptor agonists, cardiopulmonary system depression may occur very rarely. In these cases, fatality may occur rarely

DOG
Transient ataxia, anorexia, and diarrhoea have been reported as occurring rarely.
In very rare cases, 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.
In very rare cases, reduction in gastrointestinal motility may occur.

CAT
In very rare cases, respiratory depression may occur.
Very rarely, butorphanol may cause excitation, anxiety, disorientation, dysphoria and mydriasis.

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)

4.7 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.

4.8 Interaction with other medicinal products and other forms of interaction

When butorphanol is used in combination with certain α2-adrenoceptor agonists (romifidine or detomidine in horses, medetomidine in dogs and cats) synergistic effects occur requiring a butorphanol dose reduction (see section 4.9). 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/oxymorphine) 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.

4.9 Amounts to be administered and administration route

Horse: Intravenous use (IV).
Dog and Cat: Intravenous (IV), subcutaneous (SC) and intramuscular (IM) use.
When administering as an intravenous injection, do no inject as a bolus.
If repeat SC or IM administrations are required, use different injection sites.
Rapid intravenous injection should be avoided.
Number of broachings should be limited to ≤ 40.
For information on the duration of analgesia that can be expected following treatment, see section 5.1.

HORSE

As an analgesic

Monotherapy:

0.1 mg/kg (1 ml/100 kg bw) IV. The dose may be repeated as required. Analgesic effects are seen within 15 minutes of injection.

As a sedative

With detomidine:

Detomidine hydrochloride: 0.012 mg/kg IV, followed within 5 minutes by
Butorphanol: 0.025 mg/kg IV.

With romifidine:

Romifidine: 0.04 - 0.12 mg/kg IV, followed within 5 minutes by

Butorphanol: 0.02 mg/kg IV.

DOG

As an analgesic
Monotherapy:
0.2-0.3 mg/kg (0.02-0.03 ml/kg bw) IV, IM or SC injection.
Administer 15 minutes before terminating anaesthesia to provide analgesia in the recovery phase. Repeat dose as required.

As a sedative
With medetomidine:
Butorphanol: 0.1 mg/kg (0.01 ml/kg bw) IV or IM
Medetomidine: 0.01-0.025 mg/kg IV or IM.
Allow 20 minutes for sedation to develop before commencing the procedure.

As a premedicant/pre-anaesthetic
For sedation and as a premedicant to barbiturate anaesthesia.
Butorphanol : 0.1 mg/kg (0.01 ml/kg bw) IV or IM
Medetomidine: 0.01 mg/kg IV or IM

As a pre-anaesthetic
Monotherapy for canine analgesia.
Butorphanol: 0.1-0.2 mg/kg (0.01-0.02 ml/kg bw) IV, IM or SC given 15 minutes prior to induction.

As an anaesthetic
In combination with medetomidine and ketamine:
Butorphanol: 0.1 mg/kg (0.01 ml/kg bw) IM
Medetomidine: 0.025 mg/kg IM, followed after 15 minutes by
Ketamine: 5 mg/kg IM.
It is not advisable to reverse this combination in the dog with atipamezole.

CAT

As an analgesic
Pre-operative:
Butorphanol: 0.4 mg/kg (0.04 ml/ kg bw) IM or SC
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. See also section 5.1. for duration of analgesia.

Post-operative:

Administer 15 minutes before recovery:
either Butorphanol: 0.4 mg/kg (0.04 ml/kg bw) SC or IM
or: 0.1 mg/kg (0.01 ml/kg bw) IV

As a sedative
With medetomidine:
Butorphanol: 0.4 mg/kg (0.04 ml/ kg bw) IM or SC.
Medetomidine: 0.05 mg/kg SC.
Additional local anaesthesia should be used for wound suturing.
As an anaesthetic
In combination with medetomidine and ketamine:

IM administration:
Butorphanol: 0.4 mg/kg (0.04 ml/ kg bw) IM
Medetomidine: 0.08 mg/kg IM
Ketamine: 5 mg/kg IM.

IV administration:
Butorphanol: 0.1 mg/kg (0.01 ml/ kg bw) IV
Medetomidine: 0.04 mg/kg IV
Ketamine: 1.25-2.50 mg/kg IV (depending on depth of anaesthesia required).

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

The most important result of overdosage is respiratory depression. This can be reversed with an opioid antagonist (e.g. naloxone).

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.

4.11 Withdrawal period(s)

Horse: Meat and offal: zero days.
Milk: zero hours.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Analgesics, morphinan derivatives.
ATC vet code: QN02AF01

5.1 Pharmacodynamic properties

Butorphanol tartrate (R(-) enantiomer) is a centrally acting analgesic. Its action is agonist-antagonist at the opiate receptors in the central nervous system; agonist at the kappa (?) opioid receptor subtype and antagonist at the mu (μ) receptor subtype. The kappa (?) receptors control analgesia, sedation without depression of cardiopulmonary system and body temperature, whereas the mu (μ) receptors control supraspinal analgesia, sedation and depression of cardiopulmonary system and body temperature. The agonist component of butorphanol activity is ten times more potent than the antagonist component.

Onset and duration of analgesia:
Analgesia generally occurs within 15 minutes following administration in horse, dog and cat. After a single intravenous dose in the horse, analgesia usually lasts for 15 – 60 minutes. In the dog, it lasts for 15 - 30 minutes after a single intravenous administration. In cats with visceral pain, analgesic effect for 15 minutes up to 6 hours after butorphanol administration has been demonstrated. In cats with somatic pain, the duration of analgesia has been considerably shorter.

5.2 Pharmacokinetic particulars

In the horse, butorphanol has a high clearance (on average 1.3 L/h.kg) after intravenous administration. It has a short terminal half-life (mean < 1 hour), indicating that 97% of a dose will be eliminated after intravenous administration in, on average, less than 5 hours.
In the dog, butorphanol administered by the intramuscular route has a high clearance (around 3.5 L/h.kg). It has a short terminal half-life (mean < 2 hours), indicating that 97% of a dose will be eliminated after intramuscular administration in, on average, less than 10 hours. Repeated dose pharmacokinetics and the pharmacokinetics following intravenous administration have not been studied.
In the cat, butorphanol administered by the subcutaneous route has a low clearance (< 1320 mL/kg.h). It has a relatively long terminal half life (around 6 hours) indicating that 97% of the dose will be eliminated in approximately 30 hours. Repeated dose pharmacokinetics have not been studied.
Butorphanol is metabolised extensively in the liver and excreted in the urine. The volume of distribution is large, suggesting wide distribution into tissue.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzethonium chloride

Citric acid monohydrate
Sodium citrate
Sodium chloride
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Keep the vial in the outer carton in order to protect from light

6.5 Nature and composition of immediate packaging

Cardboard box with 1 amber glass type I vial of 10 or 50 ml with a chlorobutyl stopper and aluminium over seal.
Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Zoetis Belgium S.A.
2nd Floor, Building 10
Cherrywood Business Park
Loughlinstown
Co Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA10387/080/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th November 2012
Date of last renewal: 9th November 2017

10 DATE OF REVISION OF THE TEXT

November 2017