

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Dolorex 10 mg/ml Solution for Injection for horse, dog and cat.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains

Active substance:

Butorphanol 10 mg (equivalent to butorphanol tartrate 14.6 mg)

Excipients:

Benzethonium chloride 0.1 mg

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for Injection.

Aqueous colourless solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Horse, Dog, Cat.

4.2 Indications for use, specifying the target species

Butorphanol is intended for use where short (horse and dog) and short to medium (cat) duration analgesia is required. For information on the duration of analgesia that can be expected following treatment, see section 5.1.

Horse:

For relief of pain associated with colic of gastrointestinal tract origin

For sedation in combination with certain α_2 -adrenoceptor agonists (see section 4.9).

Dog:

For relief of moderate visceral pain

For sedation in combination with certain α_2 -adrenoceptor agonists (see section 4.9).

Cat:

For the relief of moderate pain associated with soft tissue surgery.

4.3 Contraindications

Do not use in animals with a history of liver or kidney disease.

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

Butorphanol/detomidine 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.

4.4 Special warnings for each target species

In cats, individual response to butorphanol may be variable. In the absence of an adequate analgesic response, an alternative analgesic agent should be used (see section 4.9). Increasing of the dose may not increase the intensity or duration of analgesia.

4.5 Special precautions for use

Special precautions for use in animals

Butorphanol is a morphinan derivative and therefore possesses opioid activity.

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.

Horse, dog, and cat:

Due to its anti-tussive 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.

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 α 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.

The safety of the product in young 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.

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. If accidental self-injection occurs, seek medical advice immediately and show the package leaflet or the label to the physician.

Do not drive.

The effects of butorphanol include sedation, dizziness and confusion. Effects can be reversed with an opioid antagonist such as naloxone.

Wash splashes from skin and eyes immediately.

4.6 Adverse reactions (frequency and seriousness)

Butorphanol may cause the following side effects:

Horse, dog, and cat:

Sedation may be noted in treated animals.

Horse:

- Excitatory locomotor effects (pacing)
- Ataxia
- Reduction in gastrointestinal motility
- Depression of the cardiovascular system.

Dog:

- Depression of the respiratory and cardiovascular system
- Anorexia and diarrhoea
- Reduction in gastrointestinal motility
- Local pain associated with intramuscular injection.

Cat:

- Mydriasis
- Disorientation
- Possible irritation at the injection site in case of repeated administrations
- Mild agitation
- Dysphoria
- Pain on injection

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

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 the product during pregnancy and lactation is not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

Butorphanol may be used in combination with other sedatives such as α 2-adrenoceptor agonists (e.g. romifidine or detomidine in horses, medetomidine in dogs) where synergistic effects can be expected. Therefore, an appropriate reduction in dose is necessary when used concomitantly with such agent (see section 4.9.)

Because of its antagonist properties at the opiate mu (μ) receptor butorphanol may remove the analgesic effect in animals, which have already received pure opioid mu (μ) agonists (morphine/oxymorphone).

4.9 Amounts to be administered and administration route

For analgesia:

Horse:

0.05 to 0.1 mg/kg, intravenous route

(i.e. 2.5 to 5 ml for 500 kg bw)

Dog:

0.2 to 0.4 mg/kg, intravenous route

(i.e. 0.2 to 0.4 ml/10 kg bw)

Rapid intravenous injection should be avoided.

Butorphanol is intended for use where short duration analgesia 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. The need for, and timing of repeat treatment will be based on clinical response. For cases where longer duration analgesia is likely to be required, an alternative therapeutic agents should be used.

Cat:

0.4 mg/kg, subcutaneous route

(i.e. 0.2 ml/5 kg bw)

Cats should be weighed to ensure that the correct dose is calculated. An appropriate graduated syringe must be used to allow accurate administration of the required dose volume (e.g. insulin syringe or 1 ml graduated syringe).

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 (see section 4.4), use of an alternative analgesic agent, such as another suitable opioid analgesic and/or a non-steroidal anti-inflammatory drug, should be considered. Any alternative analgesia should take account of the action of butorphanol on opioid receptors, as described in Section 4.8.

If repeated administrations are required, use different injection sites.

For sedation:

Butorphanol can be used in combination with an α 2-adrenoceptor agonist (e.g. (me)detomidine or romifidine). Adjustment of the dose will then be necessary according to the following recommendations:

Horse:

Detomidine: 0.01 – 0.02 mg/kg intravenous route

Butorphanol: 0.01 – 0.02 mg/kg intravenous route

Detomidine should be administered up to 5 min before butorphanol

Romifidine: 0.05 mg/kg intravenous route

Butorphanol: 0.02 mg/kg intravenous route

Romifidine can be administered concurrently or 4 min before butorphanol

Dog:

Medetomidine: 0.01 – 0.03 mg/kg intramuscular route

Butorphanol: 0.1 – 0.2 mg/kg intramuscular route

Medetomidine and butorphanol can be administered concurrently.

The stopper should not be pierced more than 25 times.

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

The main sign of overdose is respiratory depression, which, if severe, can be reversed with an opioid antagonist (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: Morphinan derivatives, butorphanol.

ATCvet 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 (κ) opioid receptor subtype and antagonist at the mu (μ) receptor subtype. The kappa (κ) 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 properties

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 relative 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

Sodium citrate

Sodium chloride

Citric acid monohydrate

Benzethonium chloride

Water for injection

6.2 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: 3 years.

Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Protect from light.

Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 glass vial (type I) of 10 or 50 ml with a halogenated butyl rubber stopper (type I) and an aluminium cap.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

Intervet Ireland Ltd
Magna Drive
Magna Business Park
Citywest Road
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10996/185/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25th November 2011

10 DATE OF REVISION OF THE TEXT

August 2012