Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Morphasol 10 mg/ml solution for injection for horses

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substance
Butorphanol 10 mg
(as Butorphanol tartrate 14.7 mg/ml)

Excipients
Benzethonium chloride 0.1 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Horses

4.2 Indications for use, specifying the target species

For short term relief of pain associated with colic of gastrointestinal tract origin. For information on the onset and duration of analgesia that can be expected following treatment, see section 5.1.
For sedation in combination with certain α2-adrenoceptor agonists (see section 4.9).

4.3 Contraindications

Butorphanol – as a sole agent and in any combination:
Do not use in horses with a history of liver or kidney disease.
Do not use in case of known hypersensitivity to the active substance or to any of the excipients.
Do not use in cases of cerebral injury or organic brain lesions (e.g. lesions following cranial trauma) and in animals with obstructive respiratory diseases, heart dysfunction or spastic convulsions.

Butorphanol / detomidine hydrochloride combination:
The combination should not be used in pregnant animals.
Do not use the combination in horses with a pre-existing cardiac dysrhythmia or bradycardia.
Do not use in horses with emphysema due to a possible depressive effect in the respiratory system.

Butorphanol / romifidine combination:
Do not use during the last month of pregnancy

Butorphanol / xylazine combination:
The combination should not be used in pregnant animals.

Any reduction in gastrointestinal motility caused by butorphanol (see section 4.6) may be enhanced by the concomitant use of α2-adrenoceptor agonists. Consequently, such combinations should not be used in cases of colic associated with impaction.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Safety and efficacy of butorphanol in foals have not been established. In foals use the product only according to the benefit/risk assessment 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 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 use of the product at the recommended dose may lead to transient ataxia and/or excitement. Therefore, to prevent injuries in patient and people, the location for the treatment should be chosen carefully.

Butorphanol / detomidine hydrochloride combination:
Routine cardiac auscultation should be performed prior to use in combination with detomidine.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Direct contact with skin or eye of the user should be avoided since the product might induce irritation and sensitization. Accidental spillage on the skin should be washed immediately with soap and water. When the product comes into contact with the eyes, rinse immediately with plenty of water.
Care should be taken when handling the product to avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package insert or the label to the physician, and DO NOT DRIVE, since drowsiness, nausea and dizziness may occur. Effects can be reversed by the administration of an opioid antagonist.

4.6 Adverse reactions (frequency and seriousness)

Butorphanol may cause the following side-effects:
- Excitatory locomotor effects (pacing)
- Mild sedation (may occur following the administration of butorphanol as a sole agent)
- Ataxia
- Reduction in gastrointestinal motility
- Depression of cardiovascular system

4.7 Use during pregnancy, lactation or lay

The safety of this product has not been investigated in the target species during pregnancy and lactation. The use of butorphanol during pregnancy and lactation is not recommended.
For information on use in combination with α2-adrenoceptor agonists, see section 4.3.

4.8 Interaction with other medicinal products and other forms of interaction

See section 4.5
Butorphanol may be used in combination with other sedatives such as α2-adrenoceptor agonists (e.g. romifidine, detomidine, xylazine) where synergistic effects can be expected. Therefore, an appropriate reduction in dose is necessary when used concomitantly with such agents.
Because of its antagonist properties at the opiate mu receptor, butorphanol may inhibit the analgesic effect in animals, which have already received pure opioid mu agonists (morphine/oxymorphine).
Because of the antitussive properties of butorphanol, it should not be used in combination with an expectorant, as this may lead to an accumulation of mucous in the airways.
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.

4.9 Amounts to be administered and administration route

For intravenous administration only.

For analgesia:
Dose rate: 100 µg butorphanol per kg bodyweight (BW) (equivalent to 1 ml for 100 kg BW), by intravenous injection. Butorphanol is intended for use where short duration analgesia is required. The dose may be repeated as required. The need for and timing of repeat treatment will be based on clinical response. For information on the onset and duration of analgesia see section 5.1. For cases where longer duration analgesia is likely to be required, an alternative therapeutic agent should be used.

For sedation in combination with detomidine hydrochloride:
A dose rate of 12 µg detomidine hydrochloride per kg BW should be given intravenously followed within 5 minutes by a dose rate of 25 µg butorphanol per kg BW (equivalent to 0.25 ml for 100 kg BW) intravenously.

For sedation in combination with romifidine:
A dose of 40-120 µg romifidine per kg BW followed within 5 minutes by a dose rate of 20 µg butorphanol per kg BW (equivalent to 0.2 ml for 100 kg BW) should be administered intravenously.

For sedation in combination with xylazine:
A dose rate of 500 µg xylazine per kg BW followed immediately by a dose of 25-50 µg butorphanol per kg BW (equivalent to 0.25-0.5 ml per 100 kg) should be administered intravenously.

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

The main sign of overdose is respiratory depression which 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.

4.11 Withdrawal Period(s)

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

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Synthetic opioid (morphinan derivatives), centrally acting analgesic.
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 opioid receptor subtype and antagonist at the mu receptor subtype. The kappa receptors control analgesia, sedation without depression of cardiopulmonary system and body temperature, whereas the mu 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 intravenous administration. After a single intravenous dose in the horse, analgesia usually lasts for 15-90 minutes.

5.2 Pharmacokinetic properties

Following intravenous injection, butorphanol is well distributed in tissue. Butorphanol is metabolised extensively in the liver and excreted in the urine. In horses, butorphanol administered by intravenous route has a high clearance (21ml/kg/min) and a short terminal half-life (44 minutes), indicating that 97% of a dose will be eliminated after intravenous administration in, on average, less than 5 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzethonium chloride
Citric acid monohydrate
Sodium citrate
Sodium chloride
Water for injections

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

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 clear glass vial (type I) of 20 ml with a grey butyl rubber stopper and an aluminium cap.

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

aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
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8 MARKETING AUTHORISATION NUMBER(S)

VPA 10826/009/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th October 2010
Date of last renewal: 19th June 2015

10 DATE OF REVISION OF THE TEXT