

B. PACKAGE LEAFLET

PACKAGE LEAFLET
NALGOSED 10 mg/ml solution for injection

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

Bioveta, a.s.
Komenského 212/12
683 23 Ivanovice na Hané
Czech Republic

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

NALGOSED 10 mg/ml solution for injection
Butorphanol

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

1 ml contains:

Active substances:

Butorphanol	10 mg
(as butorphanol tartrate 14.58 mg)	

Excipients:

Benzethonium chloride	0.1 mg
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Clear, colourless solution for injection.

4. INDICATIONS

The product is indicated for the management of analgesia and sedation in horses, for the management of analgesia, sedation and preanaesthesia in dogs and cats.

HORSE:

As an analgesic: For relief of moderate to severe abdominal pain of gastrointestinal origin including a colic. The product alleviates pain related to a colic or labour.

As a sedative: For sedation after administration of certain alpha2-adrenoceptor agonists (detomidine hydrochloride, romifidine).

Sedation in therapeutic and diagnostic procedures in standing animals.

DOG:

As an analgesic: For relief of moderate to severe pain associated with postoperative procedures, especially after orthopaedic surgery or soft tissue surgery.

As a sedative: In combination with medetomidine hydrochloride.

As a preanaesthetic: Preanaesthetic administration of the product reduces the dose of general anaesthetic, especially sodium thiopental. The product is administered as part of the anaesthesia protocol in combination with medetomidine hydrochloride and ketamine.

CAT:

As an analgesic: For relief of mild to severe pain associated with surgery procedures, especially after castration, orthopaedic surgery or soft tissue surgery.

As a sedative: In combination with medetomidine hydrochloride.

As a preanaesthetic: Preanaesthetic administration of the product reduces the dose of general anaesthetic, especially sodium thiopental. The product is administered as part of the anaesthesia protocol in combination with medetomidine hydrochloride 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 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

As a sole agent and in any combination:

Do not use in horses with a history of liver disease.

Butorphanol/detomidine hydrochloride combination:

Do not use in horses suffering from colic.

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

DOG and CAT

Do not use in dogs and cats with a history of liver disease.

6. ADVERSE REACTIONS

ALL TARGET 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. Safety 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 α_2 -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).

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

Horses, dogs, cats.

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

Route of administration:

HORSE: Strictly intravenous use.

DOG, CAT: Intravenous, subcutaneous or intramuscular use.

Rapid intravenous administration must be avoided. Different injection sites should be used for repeated subcutaneous or intramuscular administration.

Dosage for each species:

HORSE

As an analgesic:

Butorphanol alone:

Administer a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, i.e. 1 ml/100 kg bw, by intravenous injection.

The dose may be repeated as necessary. The analgesic effect is seen within 15 minutes of injection.

As a sedative:

Butorphanol in combination with detomidine hydrochloride:

Administer detomidine hydrochloride at a dose of 0.012 mg/kg bw by intravenous injection. Five minutes later administer butorphanol at a dose of 0.025 mg/kg bw, equivalent to 0.0025 ml of the product/kg bw, i.e. 0.25 ml/100 kg bw, by intravenous injection.

Butorphanol in combination with romifidine:

Administer romifidine at a dose of 0.04-0.12 mg/kg bw by intravenous injection. Five minutes later administer butorphanol at a dose of 0.02 mg/kg bw, equivalent to 0.002 ml of the product/kg bw, i.e. 0.2 ml/100 kg bw, by intravenous injection.

DOG

As an analgesic:

Butorphanol alone:

Administer a dose of 0.2-0.3 mg/kg bw, equivalent to 0.02-0.03 ml of the product/kg bw, i.e. 0.2-0.3 ml/10 kg bw, by intravenous, intramuscular or subcutaneous injection.

Administer the product 15 minutes before the end of anaesthesia to provide an analgesic effect in the recovery phase. The analgesic effect can be observed in 15 minutes. For continuous analgesia the product dose can be repeated as needed.

As a sedative:

Butorphanol in combination with medetomidine:

Administer butorphanol at a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, by intravenous or intramuscular injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.01–0.025 mg/kg bw, by intravenous or intramuscular injection. Both agents should be administered separately, not in a single syringe (see section 12).

Before initiating the therapeutic procedure, wait for 20 minutes after the administration for sufficient sedation.

To reverse the anaesthetic effects, atipamezole should be administered at a dose of 0.05-0.125 mg/kg bw. Sternal recumbency is attained approximately 5 minutes later followed by standing a further 2 minutes later.

As a preanaesthetic:

Butorphanol alone:

Administer a dose of 0.1-0.2 mg/kg bw, equivalent to 0.01-0.02 ml of the product/kg bw, by intravenous, intramuscular or subcutaneous injection.

Administer 15 minutes before inducing anaesthesia.

As a sedative and preanaesthetic – premedication of barbiturate anaesthesia:

Butorphanol in combination with medetomidine:

Administer butorphanol at a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, by intravenous or intramuscular injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.01 mg/kg bw, by intravenous or intramuscular injection. Both agents should be administered separately, not in a single syringe (see section 12).

As part of the anaesthesia protocol:

Butorphanol in combination with medetomidine and ketamine:

Administer butorphanol at a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, by intramuscular injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.025 mg/kg bw by intramuscular injection. Both agents should be administered separately, not in a single syringe (see section 12). Fifteen minutes later administer ketamine at a dose of 5 mg/kg bw by intramuscular injection.

Sedation and the onset of anaesthesia develop approximately in 6 minutes from the first administration. Loss of pedal reflex occurs in approximately 14 minutes. Anaesthesia subsides approximately in 53 minutes from ketamine administration – the pedal reflex returns. Sternal recumbency is attained approximately 35 minutes later followed by standing a further 36 minutes later.

It is not advisable to reverse the butorphanol/medetomidine/ketamine combination with atipamezole.

CAT

As a preoperative analgesic:

Butorphanol alone:

Administer an intramuscular or subcutaneous dose of 0.4 mg/kg bw, equivalent to 0.04 ml of the product/kg bw, i.e. 0.2 ml/5 kg bw.

When intravenous induction of anaesthesia is used, administer butorphanol 15-30 minutes before administering the induction agent.

When intramuscular induction of anaesthesia is used (acepromazine/ketamine or xylazine/ketamine), administer butorphanol 5 minutes before administering the anaesthetic. The use of butorphanol has no distinct effect on the time of recovery.

As a postoperative analgesic:

Intramuscular, subcutaneous administration: Administer a dose of 0.4 mg/kg bw, equivalent to 0.04 ml of the product/kg bw, i.e. 0.2 ml/5 kg bw, by subcutaneous or intramuscular injection.

Intravenous administration: Administer a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, i.e. 0.05 ml/5 kg bw, by intravenous injection.

Administer 15 minutes before the planned end of the anaesthesia.

As a sedative:

Butorphanol in combination with medetomidine:

Administer butorphanol at a dose of 0.4 mg/kg bw, equivalent to 0.04 ml of the product/kg bw, by intramuscular or subcutaneous injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.05 mg/kg bw, by subcutaneous or intramuscular injection. Both agents should be administered separately, not in a single syringe (see section 12).

Local anaesthesia should be used for surgical suturing of wounds.

To reverse the anaesthetic effects of the medetomidine, atipamezole should be administered at a dose of 0.125 mg/kg bw. Sternal recumbency is attained approximately 4 minutes later followed by standing a further 1 minute later.

As part of the anaesthesia protocol:

Butorphanol in combination with medetomidine and ketamine:

Intravenous administration:

Administer butorphanol at a dose of 0.1 mg/kg bw, equivalent to 0.01 ml of the product/kg bw, by intravenous injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.04 mg/kg bw by intravenous injection and ketamine at a dose of 1.25-2.5 mg/kg bw by intravenous injection; ketamine should be titrated to the effect in order to acquire an adequate induction and the depth of the anaesthesia. The agents should be administered separately, not in a single syringe (see section 12).

The patient lies down in 2-3 minutes after, but often almost immediately after induction with the ketamine. Loss of pedal reflex occurs 3 minutes after administration of ketamine. To reverse the anaesthetic effects of the medetomidine, atipamezole should be administered at a dose of 0.2 mg/kg bw. After reversal the pedal reflex returns in approximately 2 minutes, sternal recumbency is attained approximately 6 minutes later followed by standing position a further 18 minutes later.

Intramuscular administration:

Administer butorphanol at a dose of 0.4 mg/kg bw, equivalent to 0.04 ml of the product/kg bw, by intramuscular injection. Immediately thereafter administer medetomidine hydrochloride at a dose of 0.08 mg/kg bw by intramuscular injection and ketamine at a dose of 5 mg/kg bw by intramuscular injection. The agents should be administered separately, not in a single syringe (see section 12 Incompatibilities).

The onset of effect and its subsiding depend on the administered dose of ketamine. The patient lies down in 1 minute including the loss of pedal reflex. If no additional medication is used, anaesthesia may last up to 60 minutes and at that point animal starts to attain the sternal recumbency. The patient stands up in 70–83 minutes. To reverse the anaesthetic effects of the medetomidine, atipamezole should be administered at a dose of 0.1 mg/kg bw. Pedal reflex returns in approximately 4 minutes, sternal recumbency is attained approximately 7 minutes later followed by standing a further 18 minutes later.

9. ADVICE ON CORRECT ADMINISTRATION

To ensure the correct dose is administered, the body weight of an animal should be determined as precisely as possible.

The stopper can be punctured up to 50 times.

10. WITHDRAWAL PERIOD(S)

Horses:

Meat and offal: Zero days.

Milk: Zero hours.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label.

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

12. SPECIAL WARNING(S)

Butorphanol is intended for use where short duration analgesia (horse, dog) or short to medium duration analgesia (cat) is required.

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 the product in combination with any other medicines, the contraindications and warnings stated in the package leaflets of the respective medicines should be taken into account.

Butorphanol is a morphine derivative and thus it exhibits opiate activity. Safety of the product in puppies, kittens and foals has not been established. The use of the product in these groups should be based on 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, 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 α 2-adrenoceptor agonists. 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.

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:

Intravenous application should be slow, not a rapid bolus.

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

CAT:

Apply the accurately calculated dose volume. The dose should be calculated based on the precisely determined body weight of the animal. A syringe with an appropriate scale (e.g. an insulin syringe) should be used for accurate dosing.

Naloxone can be used as an antidote in case of respiratory depression.

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

Care should be taken to avoid accidental self-injection. A guarded needle should preferably be used until the moment of 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 as sedation, dizziness and disorientation may occur. An opioid antagonist may be used as an antidote.

Avoid accidental contact with skin and eyes. In case of accidental spillage on the skin or contact with eyes, rinse immediately with plenty of water.

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.

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 8).

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), if necessary:

Respiratory depression is the most important consequence of overdose. Opioid receptor antagonists (e.g. naloxone) are suitable antidotes.

Atipamazole is a suitable antidote in case of overdose of combinations where butorphanol is used together with α 2-adrenoceptor agonists (e.g. xylazine, medetomidine), with the exception of intramuscular administration of the butorphanol/medetomidine/ketamine combination in dogs.

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

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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

For animal treatment only.

Veterinary medicinal product subject to prescription.

Pack size: 1 x 10 ml.

