

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bupredine Multidose 0.3 mg/ml solution for injection for dogs, cats and horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Buprenorphine 0.3 mg
(equivalent to 0.324 mg buprenorphine hydrochloride)

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Chlorocresol	1.35 mg
Glucose monohydrate	
Hydrochloric acid dilute (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injection	

Clear, colourless aqueous solution

3. CLINICAL INFORMATION

3.1 Target species

Dogs, cats and horses.

3.2 Indications for use for each target species

Cats: post-operative analgesia.

Dogs: post-operative analgesia, potentiation of the sedative effects of centrally acting agents.

Horses: post-operative analgesia, in combination with sedation, potentiation of the sedative effects of centrally acting agents.

3.3 Contraindications

Do not administer by the intrathecal or peridural route.

Do not use pre-operatively for Caesarean section (see section 3.7).

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

3.4 Special warnings

As buprenorphine is metabolised by the liver, its intensity and duration of action may be affected in animals with impaired liver function.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The safety of buprenorphine has not been demonstrated in kittens or puppies less than 7 weeks of age, nor in horses younger than 10 months old and weighing less than 150 kg: therefore use in such animals should be based on the benefit-risk assessment of the veterinarian.

Safety has not been fully evaluated in clinically compromised cats or horses.

Long-term safety of buprenorphine has not been investigated beyond 5 consecutive days of administration in cats or 4 separate administrations on three consecutive days in horses.

The effect of an opioid on head injury is dependent on the type and severity of the injury and the respiratory support supplied. In case of renal, cardiac or hepatic dysfunction, or shock, there may be greater risk associated with the use of the veterinary medicinal product. In all of these cases the veterinary medicinal product should be used in accordance with the benefit-risk assessment of the attending veterinarian.

Buprenorphine may occasionally cause respiratory depression and as with other opioid drugs, care should be taken when treating animals with impaired respiratory function or animals that are receiving drugs that can cause respiratory depression.

Repeat administration earlier than the recommended repeat interval suggested in Section 3.9 is not recommended.

In horses, use of opioids has been associated with excitation, but effects with buprenorphine are minimal when administered in conjunction with sedatives and tranquilisers such as detomidine, romifidine, xylazine and acepromazine.

Ataxia is a known effect of detomidine and similar agents; consequently it may be seen after administration of buprenorphine with such substances. Occasionally, ataxia may be marked. To ensure ataxic horses sedated with detomidine/buprenorphine do not lose their balance, they should not be moved or otherwise handled in any way that would compromise their stability.

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

As buprenorphine has opioid-like activity, care should be taken to avoid self-injection or ingestion. In case of accidental self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

The veterinary medicinal product may cause skin or eye irritation or hypersensitivity reactions if contact occurs. Following eye, skin or mouth contact, wash the affected area thoroughly with water. Seek medical advice in case of hypersensitivity reactions or if irritation persists. Wash hands after use.

To the physician:
Naloxone should be available in case of accidental self-injection.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10 000 animals treated):	Hypertension, tachycardia
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Hypersalivation Bradycardia Hypothermia Agitation Respiratory depression ^a
Undetermined frequency (cannot be estimated from the available data)	Dehydration Miosis

^a See also Section 3.5.

Cats:

Common (1 to 10 animals / 100 animals treated):	Mydriasis ^a Euphoria (excessive purring, pacing, rubbing) ^a
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Respiratory depression ^b

^a Usually resolves within 24 hours.

^b See also Section 3.5.

Horses:

Rare (1 to 10 animals / 10 000 animals treated):	Colic
Undetermined frequency (cannot be estimated from the available data)	Excitation ^{a,d} , restlessness ^{a,b} Respiratory depression ^c Ataxia ^d Digestive tract hypomotility

^a When buprenorphine is used without the prior use of a sedative agent.

^b Spontaneous locomotor activity.

^c See also Section 3.5.

^d When buprenorphine is used as directed in conjunction with sedatives or tranquillisers, excitation is minimal but ataxia may occasionally be marked.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:

Laboratory studies in rats have not produced any evidence of a teratogenic effects. However, these studies have shown post-implantation losses and early foetal deaths. As reproductive toxicity studies have not been conducted in the target species, use only according to the benefit-risk assessment by the responsible veterinarian.

The veterinary medicinal product should not be used pre-operatively in cases of Caesarean section, due to the risk of respiratory depression in the offspring periparturiently, and should only be used post-operatively with special care (see below).

Lactation:

Studies in lactating rats have shown that, after intramuscular administration of buprenorphine, concentrations of unchanged buprenorphine in the milk equalled or exceeded that in the plasma. As it is likely that buprenorphine will be excreted in the milk of other species, use is not recommended during lactation. Use only accordingly to benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Buprenorphine may cause some drowsiness, which may be potentiated by other centrally-acting agents, including tranquillisers, sedatives and hypnotics. There is evidence in humans to indicate that therapeutic doses of buprenorphine do not reduce the analgesic efficacy of standard doses of an opioid agonist, and that when buprenorphine is employed within the normal therapeutic range, standard doses of opioid agonist may be administered before the effects of the former have ended without compromising analgesia. However, it is recommended that buprenorphine is not used in conjunction with morphine or other opioid-type analgesics, e.g. etorphine, fentanyl, pethidine, methadone, papaveretum or butorphanol.

Buprenorphine has been used with acepromazine, alphaxalone/alphadalone, atropine, detomidine, dexmedetomidine, halothane, isoflurane, ketamine, medetomidine, propofol, romifidine, sevoflurane, thiopentone and xylazine. When used in combination with sedatives, depressive effects on heart rate and respiration may be augmented.

3.9 Administration routes and dosage

Species and route	Post-Operative Analgesia	Potential of Sedative Effects
Dog: Intramuscular or intravenous use	10 - 20 µg/kg* (0.3 - 0.6 ml product per 10 kg) repeated if necessary after 3 - 4 hours with 10 µg/kg or 5 - 6 hours with 20 µg/kg doses	10 - 20 µg/kg (0.3 - 0.6 ml product per 10 kg)
Cat: Intramuscular or intravenous use	10 - 20 µg/kg (0.3 - 0.6 ml product per 10 kg) repeated once if necessary after 1 – 2 hours	--
Horse: Intravenous use	10 µg/kg (3.3 ml product per 100 kg) 5 minutes after administration of an iv sedative. The dose may be repeated once, if necessary, after not less than 1 – 2 hours, in combination with intravenous sedation.	5 µg/kg (1.7 ml product per 100 kg) 5 minutes after administration of an iv sedative, repeated if necessary after 10 minutes.

*) The dosages expressed in µg/kg in the table above refer to buprenorphine (as hydrochloride). The kg in the table refers to body weight.

When used in horses, an intravenous sedative must be administered within five minutes prior to injection of buprenorphine.

In dogs, sedative effects are present by 15 minutes after administration.

Analgesic activity may not develop fully until 30 minutes. To ensure that analgesia is present during surgery and immediately on recovery, the veterinary medicinal product should be administered preoperatively as part of premedication. When administered for potentiation of sedation or as part of premedication, the dose of other centrally-acting agents, such as acepromazine or medetomidine, should be reduced. The reduction will depend on the degree of sedation required, the individual animal, the type of other agents included in premedication and how anaesthesia is to be induced and maintained. It may also be possible to reduce the amount of inhalational anaesthetic used.

Animals administered opioids possessing sedative and analgesic properties may show variable responses. Therefore, the response of individual animals should be monitored and subsequent doses should be adjusted accordingly. In some cases, repeat doses may fail to provide additional analgesia. In these cases, consideration should be given to using a suitable injectable NSAID.

An appropriately graduated syringe must be used to allow accurate dosing.

The closure must not be punctured more than 100 times (with a 21G or 23G needle).

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In cases of overdosage, supportive measures should be instituted, and, if appropriate, naloxone or respiratory stimulants may be used.

When administered at overdose to dogs, buprenorphine may cause lethargy. At very high doses, bradycardia and miosis may be observed.

Studies in horses where buprenorphine has been administered with sedatives have shown very few side effects at up to five times the recommended dosage, but when administered on its own it can cause excitement.

When used to provide analgesia in horses, sedation is rarely seen, but may occur at dose levels higher than those recommended.

Naloxone may be of benefit in reversing reduced respiratory rate.

In toxicological studies of buprenorphine hydrochloride in dogs, biliary hyperplasia was observed after oral administration for one year at dose levels of 3.5 mg/kg/day and above. Biliary hyperplasia was not observed following daily intramuscular injection of dose levels up to 2.5 mg/kg/day for 3 months. This is well in excess of any clinical dose regimen in the dog.

Please also refer to Sections 3.5 and 3.6 of this SPC.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not authorised for use in horses intended for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QN02AE01

4.2 Pharmacodynamics

In summary buprenorphine is a potent, long-acting analgesic acting at opiate receptors in the central nervous system.

Buprenorphine can potentiate the effects of other centrally-acting agents, but unlike most opiates, buprenorphine has, at clinical doses, only a limited sedative effect of its own.

Buprenorphine exerts its analgesic effect via high affinity binding to various subclasses of opiate receptors, particularly μ , in the central nervous system. At clinical dose levels for analgesia, buprenorphine binds to opiate receptors with high affinity and high receptor avidity, such that its dissociation from the receptor site is slow, as demonstrated in *in vitro* studies.

This unique property of buprenorphine could account for its longer duration of activity when compared to morphine. In circumstances where excessive opiate agonist is already bound to opiate receptors, buprenorphine can exert a narcotic antagonistic activity as a consequence of its high-affinity opiate receptor binding, such that an antagonistic effect on morphine equivalent to naloxone has been demonstrated. Buprenorphine has little effect on gastro-intestinal motility.

4.3 Pharmacokinetics

Buprenorphine is rapidly absorbed after intramuscular injection in various animal species. The substance is highly lipophilic and the volume of distribution in body compartments is large.

Pharmacological effects (e.g. mydriasis) may occur within minutes of administration and signs of sedation normally appear by 15 minutes. Analgesic effects in dogs and cats appear around 30 minutes with peak effects usually being observed at about 1 – 1.5 hours. In pain-free horses, antinociceptive effects appear during the first 15 - 30 minutes; peak antinociceptive effects occur between $\frac{3}{4}$ and 6 hours after administration.

Following intravenous administration to dogs at a 20 µg/kg dose, the mean terminal half-life was 9 hours and the mean clearance was 24 ml/kg/min, however, there is considerable inter-dog variability in pharmacokinetic parameters.

Following intramuscular administration to cats, the mean terminal half-life was 6.3 hours and the clearance was 23 ml/kg/min; however, there was considerable inter-cat variability in pharmacokinetic parameters.

Following intravenous administration in horses, buprenorphine has a mean residence time of approximately 150 minutes, a volume of distribution of approximately 2.5 l/kg and a clearance rate of 10 l/minute.

Combined pharmacokinetic and pharmacodynamic studies have demonstrated a marked hysteresis between plasma concentration and analgesic effect. Plasma concentrations of buprenorphine should not be used to formulate individual animal dosage regimens, which should be determined by monitoring the patient's response. The major route of excretion in all species except the rabbit (where urinary excretion predominates) is the faeces. Buprenorphine undergoes N-dealkylation and glucuronide conjugation by the intestinal wall and the liver and its metabolites are excreted via the bile into the gastro-intestinal tract.

In tissue distribution studies carried out in rats and rhesus monkeys the highest concentrations of drug-related material were observed in liver, lung and brain. Peak levels (C_{max}) occurred rapidly and declined to low levels by 24 hours after dosing. Protein binding studies in rats have shown that buprenorphine is highly bound to plasma proteins, principally to alpha and beta globulins.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Clear type I glass vials closed with a coated bromobutyl rubber stopper and aluminium cap in a carton box.

Pack sizes: 5 ml, 10 ml, 20 ml, 50 ml and 100 ml.

Not all pack sizes may be marketed.

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

Any unused product must be disposed of in accordance with the Misuse of Drugs Regulations 2001.

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.

7. MARKETING AUTHORISATION NUMBER

Vm 41821/5025

Vm 41821/3019

8. DATE OF FIRST AUTHORISATION

04 November 2015

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

June 2026

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Approved 24 June 2026
Gavin Hall