PARTICULARS TO APPEAR ON THE OUTER PACKAGE
CARDBOARD CARTON/ SECONDARY PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetergesic Multidose, 0.3mg/ml solution for injection for dogs, cats and horses
Buprenorphine as buprenorphine hydrochloride

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Buprenorphine (as buprenorphine hydrochloride 0.3 mg/ml) in a 5% glucose solution.
It also contains 1.35 mg/ml chlorocresol as antimicrobial preservative

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml

5. TARGET SPECIES

Dogs, cats and horses

6. INDICATION(S)

For the relief of post-operative pain in the dog, cat and horse and for the potentiation of the sedation in the dog and horse.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Dogs and cats: Intravenous or intramuscular use.
Horses: Intravenous use.
Shake well before use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not authorised for use in horses intended for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Wash hands/affected area thoroughly after any accidental spillage.
As buprenorphine has opioid-like activity, care should be taken to avoid self-injection. In case of accidental self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Following eye contamination or skin contact, wash thoroughly with cold running water. Seek medical advice if irritation persists.

10. EXPIRY DATE

<EXP {month/year}>
Shelf life after first opening the immediate packaging: 28 days
Once broached, use by ,,,,,,,,,,,,,,,,,,,,,,,,

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

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

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
United Kingdom

16. MARKETING AUTHORISATION NUMBER

Vm 15052/4081

17. MANUFACTURER'S BATCH NUMBER

Batch> <Lot> or <BN> {number}.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS TYPE I AMBER GLASS VIAL /PRIMARY PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetergesic Multidose, 0.3mg/ml solution for injection for dogs, cats and horses.
Buprenorphine hydrochloride

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Contains buprenorphine 0.3mg/ml as buprenorphine hydrochloride and 1,35 mg/ml chlorocresol as antimicrobial preservative

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml

4. ROUTE(S) OF ADMINISTRATION

i.m, i.v. (dogs)
i.m, i.v. (cats)
i.v. (horses)
Read the package leaflet before use.

5. BATCH NUMBER

Batch> <Lot> or <BN>

6. EXPIRY DATE

<EXP {month/year}>
Shelf life after first opening the immediate packaging: 28 days.
Once broached, use by:

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

8. SPECIAL STORAGE PRECAUTIONS

Keep container in the outer carton

9. OTHER INFORMATION

Legal category
(Sch-III) POM-V
To be supplied only on Veterinary prescription

10. MARKETING AUTHORISATION NUMBER

Vm 15052/4081

PACKAGE LEAFLET

Vetergesic Multidose, 0.3mg/ml solution for injection for dogs, cats and horses
Buprenorphine (as buprenorphine hydrochloride)

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

Marketing Authorisation Holder:
Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
United Kingdom

Manufacturer responsible for batch release:
LABIANA LIFE SCIENCES, S.A.
C/ Venus, 26 , Pol. Ind. Can Parellada , Terrassa , 08228 Barcelona , Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetergesic Multidose, 0.3mg/ml solution for injection for dogs, cats and horses.
Buprenorphine (as buprenorphine hydrochloride).

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

10 mL solution for injection containing Buprenorphine 0.3 mg/mL (as buprenorphine hydrochloride) in a 5% glucose solution. It also contains 1.35 mg/mL chlorocresol as antimicrobial preservative.

4. PHARMACOLOGICAL EFFECTS

Vetergesic multidose is a trade name for buprenorphine hydrochloride, a potent long-acting analagesic acting at opioid receptor sites in the CNS. Buprenorphine exerts its analgesic effects via high-affinity binding to various sub-classes of opiate receptors, particularly μ, in the central nervous system. Buprenorphine binds to opiate receptors with high affinity and high receptor avidity, such that its dissociation from the receptor is slow, as demonstrated by in vitro studies. This unique property of buprenorphine could account for its longer duration of activity when compared to morphine. Parenteral administration of the product may be by intramuscular (cats and dogs) or intravenous (cats, dogs, horses) injection. Buprenorphine is rapidly absorbed after intramuscular injection in various animal species and in man.
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 ¾ and 6 hours after administration.
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 to dogs at a 20µg/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 intravenous administration in horses, buprenorphine has a mean residence time of approximately 150 minutes, a volume of distribution of approximately 2.5L/kg and a clearance rate of 10L/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.
Buprenorphine is metabolised in the liver and in the major route of excretion is in the faeces, except in the rabbit where urinary excretion predominates. Buprenorphine as little effect on gastro-intestinal motility.

5. INDICATION(S)

Vetergesic Multidose is indicated for the relief of post-operative pain in the dog, cat and horse and for the potentiation of the sedative effects of centrally acting agents in the dog and horse.
When used in horses, an intravenous sedative should be administered within five minutes prior to injection of buprenorphine.

6. CONTRAINDICATIONS

Do not administer by the intrathecal or peridural route.
Do not use pre-operatively for caesarian section.
Not to be used in horses intended for human consumption. Treated horses may never be slaughtered for human consumption. The horse must have been declared as not intended for human consumption under national horse passport legislation.

7. ADVERSE REACTIONS

Salivation, bradycardia, hypothermia, agitation, dehydration and miosis can occur in the dog, and rarely hypertension and tachycardia.
Mydriasis and signs of euphoria (excessive purring, pacing, rubbing) commonly occur in cats and will usually resolve within 24 hours.
Buprenorphine may cause respiratory depression.
When used to provide analgesia in horses, sedation is rarely seen, but may occur at dose levels higher than those recommended. When used in conjunction with sedatives or tranquillisers, excitation is normally minimal, but ataxia may occasionally be marked. Colic is rarely reported.

8. TARGET SPECIES

Dogs, cats and horses.

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

Shake well before use.
An appropriately graduated syringe must be used to allow accurate dosing.

Species	Route of Administration	Post-Operative Analgesia	Potentiation of Sedation
Dog	Intramuscular or intravenous injection	10-20 micrograms per kg (0.3-0.6ml per 10kg). For further pain relief, repeat if necessary after 3-4 hours with 10 microgram per kg or 5-6 hours with 20 microgram per kg.	10-20 micrograms per kg (0.3-0.6ml per 10kg).
Cat	Intramuscular or intravenous injection	10 – 20 microgram per kg (0.3 – 0.6ml per 10kg), repeated if necessary, once, after 1 - 2 hours.	---
Horse	Intravenous injection	10 microgram per kg (3.3 mL per 100 kg), 5 minutes after administration of an iv sedative. The dose may be repeated if necessary, once, after not less than 1 - 2 hours	5 micrograms per kg (1.7mL per 100kg) 5 minutes after administration of an iv sedative. The dose may be repeated if necessary after 10 minutes

10. ADVICE ON CORRECT ADMINISTRATION

In dogs and cats, 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 product should be administered preoperatively as part of premedication. If additional analgesia is required, this may be achieved by administration of further dose(s) of Vetergesic Multidose or concomittant use of a suitable injectable NSAID.
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.

11. WITHDRAWAL PERIOD

Not authorised for use in horses intended for human consumption.

12. SPECIAL STORAGE PRECAUTIONS

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package insert, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.
Keep the vial in the outer carton in order to protect from light.
Shake well before use.
Shelf life after first opening the immediate packaging: 28 days.

13. SPECIAL WARNING(S)

Precautions:
Buprenorphine may cause respiratory depression, although this is generally not clinically significant, care should be taken when treating animals with impaired respiratory function or those being treated with drugs that can cause the condition.
Buprenorphine should be used with caution in animals with impaired liver function, especially biliary tract disease, as the substance is metabolised by the liver and its intensity and duration of action may be affected in such animals. As animals treated with opioids may show variable responses, responses of individual animals should be monitored and subsequent doses should be adjusted accordingly. In some cases repeat doses may fail to provided additional analgesia. In these cases, consideration should be given to using a suitable injectable NSAID. Safety has not been fully evaluated in clinically compromised cats and horses e.g those suffering from renal or hepatic dysfunction, cardiovascular disease or shock. Use in such cases should be based on the risk-benefit assessment of the veterinarian. Repeat administration earlier than the recommended repeat interval suggested is not recommended. Long-term safety of buprenorphine in cats has not been investigated beyond 5 consecutive days of administration or in horses 4 separate administrations on three consecutive days.
The effect of an opioid on head injury is dependent on the type and severity of the injury and the respiratory support supplied. The product should be used in accordance with the benefit-risk assessment of the attending veterinarian.
Safety has not been evaluated in clinically-compromised horses. 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. The safety of buprenorphine has not been demonstrated in horses younger than 10 months old and weighing less than 150kg; therefore, use in such animals should be based on the risk-benefit assessment of the veterinarian.
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.

Pregnancy:
Laboratory studies in rats and rabbits have not produced any evidence of a teratogenic effect. 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 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.

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.

Interactions 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.
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, although 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.
Buprenorphine has been used with successfully with a wide range of premedicant and anaesthetic agents including 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.

User Safety and Warnings
As buprenorphine has opioid-like activity, care should be taken to avoid self-injection. In case of accidental self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Following eye contamination or skin contact, wash thoroughly with cold running water. Seek medical advice if irritation persists.
Wash hands/affected area thoroughly after any accidental spillage.

Overdosage
In cases of overdosage, supportive measures should be instituted, and, if appropriate, naloxone or respiratory stimulants may be used. Because of the prolonged duration of effect of buprenorphine in comparison to such drugs, they may need to be administered repeated or by continuous infusion.
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 effects at up to five times the recommended dosage, but when administered on its own it may cause excitement in pain-free-animals.
Naloxone may be of benefit in reversing reduced respiratory rate and respiratory stimulants such as Doxapram are also effective in man. Because of the prolonged duration of effect of buprenorphine in comparison to such drugs, they may need to be administered repeatedly or by continuous infusion. Volunteer studies in man have indicated that opiate antagonists may not fully reverse the effects of buprenorphine.

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.

14. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

15. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

October 2022

16. OTHER INFORMATION

Presentation:
Vetergesic Multidose is presented in 10 ml amber glass vials, with chlorobutyl rubber stopper, and a 20 mm aluminium collar with flip-off cap, as sterile, clear, colourless, aqueous solution for injection. Each 1ml contains 0.3mg buprenorphine, (as buprenorphine hydrochloride), in a 5% glucose solution. It also contains 1.35mg/ml chlorocresol, as antimicrobial preservative.
Legal category
(Sch-III) POM-V
To be supplied only on Veterinary prescription
For animal treatment only

17. MARKETING AUTHORISATION NUMBER

Vm 15052/4081

Vetergesic is a Trade Mark.

Approved 14 October 2022