LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Buprecare 0.3 mg/ml Solution for Injection for Dogs and Cats
Buprenorphine as Buprenorphine hydrochloride

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Buprenorphine 0.3 mg/ml as buprenorphine hydrochloride.

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

5 ampoules, each 1 ml.

5. TARGET SPECIES

Dogs and cats.

6. INDICATION(S)

Dog
Post-operative analgesia.
Potentiation of the sedative effects of centrally-acting agents.

Cat
Post-operative analgesia.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intramuscular use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP DD/MM/YY

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Protect from light.
Do not refrigerate or freeze.
Keep the container in the outer carton.
Use immediately after opening the ampoule. Discard any solution remaining following withdrawal of the required dose.

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

Disposal: read package leaflet.

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

For animal treatment only – to be supplied only on veterinary prescription.

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

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Animalcare Ltd
10 Great North Way
York
YO26 6RB
UK

16. MARKETING AUTHORISATION NUMBER

Vm 10347 / 4024

17. MANUFACTURER'S BATCH NUMBER

BN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

AMPOULES

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Buprecare
Buprenorphine 0.3 mg/ml Injection for Dogs and Cats

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

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

4. ROUTE(S) OF ADMINISTRATION

i.m.

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

BN:

7. EXPIRY DATE

EXP :DD/MM/YY

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

Ad us. vet.

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Buprecare 0.3 mg/ml Solution for Injection for Dogs and Cats

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

Marketing Authorisation Holder:
Animalcare Limited
10 Great North Way
York
YO26 6RB
UK

Manufacturer responsible for batch release:
Haupt Pharma Livron,
1 rue Comte de Sinard,
26250 LIVRON SUR DROME,
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Buprecare 0.3 mg/ml Solution for Injection for Dogs and Cats
Buprenorphine as Buprenorphine hydrochloride

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

Active substance:

Each ampoule contains:
Buprenorphine 0.3 mg/ml as buprenorphine hydrochloride.
Clear, colourless solution.

4. INDICATIONS

Dog
Post-operative analgesia.
Potentiation of the sedative effects of centrally-acting agents.

Cat
Post-operative analgesia.

5. CONTRAINDICATIONS

The product should not be used pre-operatively for caesarean section.

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

6. 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 occasionally cause significant respiratory depression; care should be taken in animals with impaired respiratory function or those being treated with drugs that can cause the condition.

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

7. TARGET SPECIES

Dogs and cats.

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

For intramuscular use.

Dog:
Post-operative analgesia: 10–20 µg buprenorphine per kg (0.3–0.6 ml Buprecare per 10 kg), repeated if necessary after 3–4 hours with 10 µg and 5–6 hours with 20 µg doses.
Sedation: 10–20 µg buprenorphine per kg (0.3–0.6 ml Buprecare per 10 kg).

Cat:
Post-operative analgesia: 10–20 µg buprenorphine per kg (0.3–0.6 ml Buprecare per 10 kg), repeated if necessary, once after 2 hours.

While sedative effects are present by 15 minutes after administration, analgesic activity becomes apparent after approximately 30 minutes. To ensure that analgesia is present during surgery and immediately on recovery, the 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 responses 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.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Do not store above 25 °C
Protect from light.
Do not refrigerate or freeze.
For single use only.
Do not use after the expiry date stated on the carton.
Keep the container in the outer carton.
The product does not contain an antimicrobial preservative. Use immediately after opening the ampoule. Any solution remaining in the ampoule following withdrawal of the required dose should be discarded.

12. SPECIAL WARNINGS

Special precautions for use in animals
Buprenorphine may occasionally cause significant 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.

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 some animals.

In case of renal, cardiac or hepatic dysfunction, or shock, there may be greater risk associated with the use of the product. The benefit:risk ratio for using the product should be made by the attending vet. Safety has not been fully evaluated in clinically compromised cats.

The safety of buprenorphine has not been demonstrated in animals less than 7 weeks of age, therefore use in such animals should be based on the benefit:risk assessment by the veterinarian.

Repeated administration earlier than the recommended repeat interval suggested in the Dosage and Administration table above is not recommended.

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.

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 accidental 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. Naloxone should be available in case of accidental parenteral exposure.

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

Use during pregnancy or lactation
Laboratory studies in rats have not produced any evidence of a teratogenic effect. 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 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 section on lactation below).

Studies in lactating rats have shown that, after intra-muscular administration of buprenorphine, concentrations of unchanged buprenorphine in 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.

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 buprenorpine should not be used in conjunction with morphine or other opioid-type analgesics e.g. etorphine, fentanyl, pethidine, methadone, papaveretum and butorphanol.

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

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

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.

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

many times higher than those indicated in the Dosage and Administration table have been used without serious side effects.

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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIAL, 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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

April 2008

15. OTHER INFORMATION

Buprenorphine is a potent long-acting analgesic acting at opioid receptor sites in the central nervous system (CNS). Buprenorphine exerts its analgesic effect via high-affinity binding to various subclasses of opiate receptors, particularly μ, in the CNS.

At clinical dose levels for analgesia, buprenorphine demonstrates high efficacy and binds to opiate receptors with high affinity, such that its dissociation from the receptor is slow, as demonstrated in *in vitro* studies. This 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 is rapidly absorbed after intra-muscular injection in various animal species and in man. In the cat, pharmacological effects occur within 30 minutes after injection and peak effects are usually observed at about 1–1.5 hours. Following intramuscular injection 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.

Combined pharmacokinetic and pharmacodynamic studies in cats have demonstrated a marked delay between plasma concentrations and analgesic effect. Plasma concentrations of buprenorphine should not be used to formulate individual animal dosage regimes, which should be determined by monitoring of the patient's response.

Presented in 1 ml clear glass, snap ampoules, in boxes of five.

Approved: 11 October 2018