ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

10 ml printed carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Buprenorphine 0.3 mg/ml (as buprenorphine hydrochloride 0.324 mg/ml)
Preservative: Benzethonium chloride

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml

5. TARGET SPECIES

Dogs, cats and horses

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Administration:
Read the package leaflet before use.
Dog, Cat – intramuscular or intravenous injection
Horse – intravenous injection

8. WITHDRAWAL PERIOD

Not authorised for use in horses intended for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP (month/year)
Once broached, use by…....

11. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.
Keep the vial in the outer carton in order to protect from light.

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

Dispose of waste material in accordance with local requirements.
Any unused product must be disposed of in accordance with the Misuse of Drugs Regulations (2001).

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 SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Jurox (UK) Limited
Second Floor, Richmond House
105 High Street
Crawley
West Sussex
RH10 1DD

16. MARKETING AUTHORISATION NUMBER(S)

Vm 25296/4002

17. MANUFACTURER'S BATCH NUMBER

Batch:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml vial label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

0.3 mg/ml

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

10 ml

4. ROUTE(S) OF ADMINISTRATION

Administration:
Read the package leaflet before use.
Dog, Cat – intramuscular or intravenous injection; Horse – intravenous injection

5. WITHDRAWAL PERIOD

Not authorised for use in horses intended for human consumption.

6. BATCH NUMBER

Batch:

7. EXPIRY DATE

EXP: month/year
Once broached, use by…...

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Buprelieve Multidose 0.3 mg/ml solution for injection for dogs, cats and horses

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

Marketing authorisation holder and manufacturer responsible for batch release:
Jurox (UK) Limited
Second Floor, Richmond House
105 High Street
Crawley
West Sussex
RH10 1DD

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

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

A clear, colourless solution for injection containing buprenorphine 0.3 mg/ml as the active substance, and benzethonium chloride 0.100 mg/ml as preservative.

4. INDICATION(S)

Post-operative analgesia in the dog, cat and horse.
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.

5. CONTRAINDICATIONS

Do not administer by the intrathecal or peridural route.
Do not use pre-operatively for Caesarean section.
Do not use in cases 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 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.

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

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).

7. TARGET SPECIES

Dogs, cats and horses

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

Administration:

Dog: intramuscular or intravenous injection
Cat: intramuscular or intravenous injection
Horse: intravenous injection

Species	Route of Administration	Post-Operative Analgesia	Potentiation of Sedation
Dog	Intramuscular or intravenous injection	10 - 20 micrograms per kg (0.3 - 0.6 ml per 10 kg). 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 - 0.6 ml per 10 kg).
Cat	Intramuscular or intravenous injection	10 - 20 microgram per kg (0.3 - 0.6 ml per 10 kg). 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 (1.7 ml per 100 kg), 5 minutes after administration of an iv sedative. The dose may be repeated if necessary after 10 minutes

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 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.

9. ADVICE ON CORRECT ADMINISTRATION

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

10. WITHDRAWAL PERIOD

Not authorised for use in horses intended for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25ºC.
Keep the vial in the outer carton in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month. Shelf life after first opening the container: 28 days.

When the container is broached (opened) for the first time, using the in-use shelf life which is specified on this package leaflet, the date on which any product remaining in the carton should be discarded should be worked out. This discard date should be written in the space provided.

12. SPECIAL WARNING(S)

Special warning for each target species
None

Special precautions for use in animals

Buprenorphine may 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.

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 assessment for using the product should be made by the attending vet. Safety has not been fully evaluated in clinically compromised cats.

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.

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

Repeat administration earlier than the recommended repeat interval suggested in <<Dosage for each species, route(s) and method of administration>> is not recommended.

Long-term safety of buprenorphine has not been investigated beyond five consecutive days of administration in cats or four 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. The product should be used in accordance with the benefit-risk assessment of the responsible 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 benefit-risk assessment of the responsible 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.

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

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. Naloxone should be available in case of accidental self-injection. Buprenorphine may be absorbed systemically on exposure to mucous membranes. The product may cause skin or eye irritation if contact occurs.Avoid contact with skin and eyes. In case of accidental spillage onto the skin or eyes, wash the affected area thoroughly with running water. Seek medical advice if irritation persists.

Pregnancy:

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. These may have resulted from a reduction in parental body condition during gestation and in post-natal care owing to sedation of the mothers.

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 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 according to the 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 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, alfaxalone/alfadolone, 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.

Overdose (symptoms, emergency procedures, 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 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.

Incompatibilities:

This veterinary medicinal product can be mixed in the same syringe with aqueous solutions for injection containing acepromazine as maleate and medetomidine and dexmedetomidine as hydrochlorides. Syringes with these mixtures should be used as soon as practicable. Any unused mixed solution remaining in the syringe should be disposed appropriately.
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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.
Any unused product must be disposed of in accordance with the Misuse of Drugs Regulations (2001).

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

June 2021

15. OTHER INFORMATION

Pack sizes: 10 ml amber glass vials

For any information about this veterinary medicinal product, please contact the marketing authorisation holder:

Jurox (UK) Limited
Second Floor, Richmond House
105 High Street
Crawley
West Sussex
RH10 1DD
Tel: +44 (0) 1293 510 681

Approved 15 February 2022