IRISH MEDICINES BOARD ACT 1995

EUROPEAN COMMUNITIES (ANIMAL REMEDIES) (No. 2) REGULATIONS 2007

(S.I. No. 786 of 2007)

VPA:**10799/011/001**
Case No: 7004091

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

Dechra Ltd

Dechra House, **Jamage Industrial Estate**, **Stoke-on-Trent ST7 1XW**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

Buprenodale 0.3 mg/ml Solution for Injection for Dogs and Cats

The particulars of which are set out in Part 1 and Part 2 of the said Schedule. The authorisation is also subject to any special conditions as may be specified in Part 2 of the said Schedule.

This authorisation,unless previously revoked, shall continue in force from **06/02/2009** to **05/02/2014**.

Signed on behalf of the Irish Medicines Board

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Buprenodale 0.3 mg/ml solution for injection for dogs and cats

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains:

Active Substance

Buprenorphine 0.3 mg as buprenorphine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs and cats

4.2 Indications for use, specifying the target species

Post-operative analgesia in the cat and dog.
Potentiation of the sedative effects of centrally acting agents in the dog.

4.3 Contraindications

The product should not be used pre-operatively for caesarian section (see section 4.7).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals

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.

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

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 of the veterinarian.

Repeated administration earlier than the recommended repeat interval suggested in Section 4.9 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.

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

4.6 Adverse reactions (frequency and seriousness)

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; refer to section 4.5 i).
When used to provide analgesia, sedation may appear as an adverse reaction.

4.7 Use during pregnancy, lactation or lay

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.
As reproductive studies have not been conducted in target animals, 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).

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.

4.8 Interaction with other medicinal products and other forms of interaction

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, halothane, isoflurane, ketamine, medetomidine, propofol, sevoflurane, thiopentone and xylazine without any observed adverse effects.

Buprenorphine may cause some drowsiness, which may be potentiated by other centrally-acting agents, including tranquillisers, sedatives and hypnotics.

4.9 Amounts to be administered and administration route

For intramuscular use.

Species	Post-Operative Analgesia	Potentiation of sedative effects
Dog	10 – 20 microgram per kg (0.3 – 0.6mL per 10kg) repeated if necessary after 3 – 4 hours with 10 microgram or 5 – 6 hours with 20 microgram doses.	10 – 20 microgram per kg (0.3 – 0.6mL per 10kg).
Cat	10 – 20 microgram per kg (0.3 – 0.6mL per 10kg), repeated if necessary, once, after 2 hours.	

To ensure that analgesia is present immediately on recovery, the product can be administered preoperatively (see section 5.2). Pharmacological effects occur within 30 minutes after injection. If additional analgesia is subsequently required, this may be achieved by administration of a further dose of Buprenorphine or concomitant use of a suitable injectable NSAID.
An appropriately graduated syringe must be used to allow accurate dosing. This is particularly important when injecting small volumes.
When administered pre-operatively in conjunction with other premedicants, it may be possible to reduce the amount of premedicant, such as acepromazine or medetomidine, and also 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 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.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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

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 above 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.

Please also refer to Sections 4.5.i) and 4.6 of this SPC.

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Opioid analgesics, oripavine derivatives

ATC vetcode QN02AE01

5.1 Pharmacodynamic properties

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

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 demonstrates high efficacy and 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.

5.2 Pharmacokinetic properties

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

No relevant pharmacokinetic data are available in the dog.

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 regimens, which should be determined by monitoring of 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 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucose anhydrous
Sodium hydroxide (pH adjustment)
Hydrochloric acid (pH adjustment)
Water for injection

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years

The product does not contain an antimicrobial preservative. Any solution remaining in an ampoule following withdrawal of the required dose should be discarded.

6.4 Special precautions for storage

Do not store above 25°C. Keep the ampoule in the outer carton in order to protect from light.
Do not refrigerate or freeze**.**

6.5 Nature and composition of immediate packaging

Cardboard carton containing five 1 ml colourless Type I glass 'snap' top ampoules.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Any unused product or waste material should be disposed of in accordance with national requirements.

7 MARKETING AUTHORISATION HOLDER

Dechra Limited
Dechra House
Jamage Industrial Estate
Talke Pits
Stoke-on-Trent
ST7 1XW
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10799/011/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

6th February 2009

10 DATE OF REVISION OF THE TEXT