M120167AB

buprecare® Multidose 0.3mg/ml

Solution for Injection for Dogs and Cats

Buprenorphine (as buprenorphine hydrochloride)

Statement of the active substance(s) and other ingredient(s)

Each 1ml of solution contains:

Active substance: Buprenorphine 0.3mg
(as buprenorphine hydrochloride)

Excipient: Chlorocresol 1.35mg

Clear, colourless solution.

Indications

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

Contra-indications

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

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

Target species

Dogs and cats.

Dosage route and method of administration

For intramuscular or intravenous use.

Species	Post-Operative Analgesia	Potentiation of Sedation
Dog	10–20µg per kg (0.3–0.6ml per 10kg) For further pain relief, repeat if necessary after 3–4 hours with 10µg per kg or 5–6 hours with 20µg per kg.	10–20µg per kg (0.3–0.6 ml per 10kg).
Cat	10–20µg per kg (0.3–0.6ml per 10kg), repeated if necessary, once, after 1-2 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 pre-operatively 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 administration of the required dose volume. This is particularly important when injecting small volumes.
The vial seal may be punctured up to a maximum of 30 times.

Special storage precautions

Keep out of the reach and sight of children. Do not store above 25°C. Keep the vial in the outer carton in order to protect from light. Do not refrigerate or freeze. Shelf life after first opening the vial: 28 days. Do not use after the expiry date stated on the label and the carton. 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 carton.

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 cases 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 veterinarian. 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 attending veterinarian. Repeated administration earlier than the recommended repeat interval suggested in the

dosage section is not recommended. Long-term safety of buprenorphine in cats has not been investigated beyond 5 consecutive days of administration. 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

Wash hands/affected area thoroughly after any accidental spillage. 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.

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. Although post-implantation losses and early peri-natal deaths were observed, 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 of the attending 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 intramuscular administration of buprenorphine, concentrations of unchanged buprenorphine in the milk equalled or exceeded that in the plasma. It is likely that buprenorphine will be excreted in the milk of other species: use only according to the benefit-risk assessment of the attending 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, 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

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

Special precautions for the disposal of unused product or waste material, if any

Dispose of any unused product in accordance with the Misuse of Drugs Regulations 2001 (UK). Dispose of part-used product and empty containers in accordance with guidance from your local waste regulation authority.

Date on which the package leaflet was last approved: 28 September 2011

Other information

For animal treatment only. Buprenorphine is a potent long-acting analgesic acting at opioid receptor sites in the central nervous system (CNS). 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 CNS.

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 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. Analgesic effects appear around 30 minutes after injection with peak effects usually being observed at about 1–1.5 hours.

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.

Buprenorphine has little effect on gastro-intestinal motility.

Pack sizes

1 vial with 10ml solution for injection.

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

Manufacturer for the batch release: Recipharm Monts, 18 Rue de Montbazon, 37260 Monts, France

UK only

POM-V

CD Sch III

To be supplied only on veterinary prescription

Vm: 10347/4031

IE only

VPO

Veterinary Practitioner Only

VPA: 10778/001/002