Buprenorphine SR
Injectable

Description
ZooPharm can provide sustained release Buprenorphine HCl by prescription in a proprietary, patent pending, sustained release system.

Buprenorphine SR releases over 72 hours and provides blood levels greater than 1 nanogram/ml in dogs and 0.5 nanogram/ml in cats for post operative analgesia. Buprenorphine SR can be injected subcutaneously through a 22-gauge needle.

Indications
Buprenorphine has produced excellent analgesic results in broad clinical applications for cats, dogs, exotic species and laboratory animals. It provides analgesia for management of perioperative / postoperative pain, as well as painful joint injuries, fractures, tissue inflammation due to infection, tissue necrosis and trauma resulting from wounds. Amelioration of postsurgical pain has been substantiated in a variety of species. Due to its long duration of action, it is one of the most widely used opioid analgesics in veterinary clinical practices.

Chemistry & Pharmacology
Buprenorphine is a thebaine derivative with powerful analgesic approximately twenty-five to forty times as potent as morphine. Its analgesic effect is due to partial agonist activity at -opioid receptors, i.e., when the molecule binds to a receptor, it is only partially activated in contrast to a full agonist such as morphine. Buprenorphine also has very high binding affinity for the µ receptor such that opioid receptor antagonists (e.g. naloxone) only partially reverse its effects.

Its chemical name is 17-[(cyclopropylmethyl)-alpha-(1,1-dimethylethyl)-4,5-epoxy-1819-dihydro-3-hydroxy-6-methoxy-alpha-methyl-6, 14-ethenomorphinan-7-methanol.

Pharmacokinetics
Buprenorphine is metabolized by the liver, via CYP3A4 (also CYP2C8 seems to be involved) isozymes of the cytochrome P450 enzyme system, into norbuprenorphine [by N-dealkylation]. The glucuronidation of buprenorphine is primarily carried out by UGT1A1 and UGT2B7, and that of norbuprenorphine by UGT1A1 and UGT1A3. These glucuronides are then eliminated mainly through excretion into the bile. The elimination half-life of buprenorphine is 20–73 hours (mean 37). Due to the mainly hepatic elimination, there is no risk of accumulation in patients with renal impairment.

Buprenorphine's main active metabolite, norbuprenorphine, is a µ-opioid, δ-opioid, and nociceptin receptor full agonist, with a κ-opioid receptor partial agonist. Buprenorphine antagonizes its effects.

A published study in the Journal of the American Association for Laboratory Animal Science, tested this sustained-release formulation of buprenorphine in rats for analgesic efficacy and plasma concentration over a 72-h time period. Rats were injected subcutaneously with either 1.2 mg/kg sustained-release formulation (Bup-SR), 0.2 mL/kg buprenorphine HCl (Bup-HCl) and tested in a thermal nociception model or a surgical postoperative pain model. In both models, Buprenorphine-SR showed evidence of providing analgesia for 2 to 3 d, reporting plasma concentrations of buprenorphine remaining over 1 ng/mL for 72 h after a single dose.

Another published study compared the efficacy and adverse effects of sustained-release (SR) buprenorphine following SC administration and buprenorphine following oral transmucosal (OTM) administration in cats undergoing ovariohysterectomy. Results indicated that cats undergoing ovariohysterectomy having received a subcutaneous preoperative dose of SR buprenorphine, appeared to have comparable efficacy and adverse events as that of twice-daily OTM administration of buprenorphine before and after surgery.
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**Pharmacokinetics (cont.)**

A laboratory study conducted in domestic cats was designed to determine if the sustained release Buprenorphine SR™ formulation was equivalent to repeated doses of transmucosal administration of the commercial preparation Buprenex™ over a period of 72 hours. Animals received either a single, subcutaneous injection of Buprenorphine SR at a dose rate of 120 µg/kg, or a transmucosal dose of buprenorphine HCl [Buprenex™] every 12 hours for 72 hours. Results from analysis of blood samples [obtained at 1, 4, 8, 12, 18, 24, 36, 48 and 72 hours], reported data showing that only the single-dosed Buprenorphine SR cats maintained therapeutic blood levels for 72 hours.*

No visible injection site irritations or clinical side effects were reported within both test groups.*

**How Supplied**

Buprenorphine hydrochloride is available from ZooPharm upon prescription at a concentration of 10 mg/ml in a 5 ml vial in a sustained release biodegradable matrix.

A concentration of 3 mg/ml is available for use in small dogs and cats, and a 1 mg/ml formulation is available for use in laboratory rats and mice.

**Dosage & Administration**

Recommended Buprenorphine SR™ dose rates are:
- 0.12 mg/kg for Cats
- 0.03 - 0.06 mg/kg for Dogs
- 1.0 - 1.2 mg/kg for Laboratory Rats
- 0.15 – 1.0 mg/kg Laboratory Mice

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**Contraindications & Precautions**

Some patients may exhibit bradycardia and slight sedation associated with opiates.

Veterinarians must rely on their professional knowledge and judgment when prescribing sustained release Buprenorphine. In dogs the dose rate may vary from 0.03 – 0.06 mg/kg body weight. The recommended duration of administration for Buprenorphine SR perioperative and/or postoperative pain control in dogs is a single injection providing therapeutic analgesia for up to 72 hours.

**References**

5. Moody DE; Fang Lin SN; Weyant DM; Strom SC and Omiecinski CJ. Effect of Rifampin and Nelfinavir on the Metabolism of Methadone and Buprenorphine in Primary Cultures of Human Hepatocytes. Drug Metab Dispos December 2009 37:2323-29
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7. Catbagan DL; Quimby JM; Mama KR; Rychel JK; Mich PM Comparison of the efficacy and adverse effects of sustained-release buprenorphine hydrochloride following subcutaneous administration and buprenorphine hydrochloride following oral transmucosal administration in cats undergoing ovariohysterectomy. AJVR, Vol 72, No. 4, April 2011, 461-466
8. Laboratory Study: Comparison of sustained release buprenorphine and transmucosal buprenorphine in cats.

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