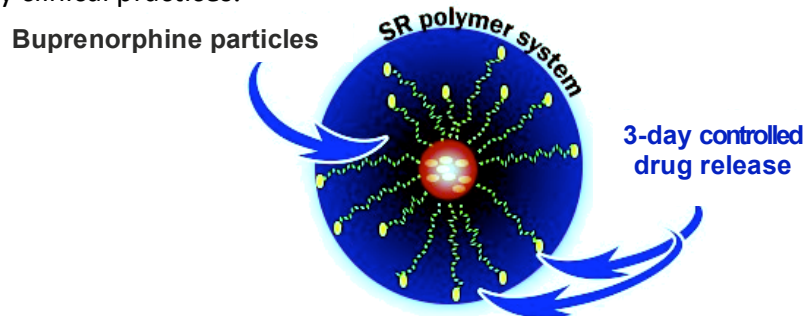


Description

Buprenorphine SR™ is an injectable, proprietary, sustained-release polymer system designed to release Buprenorphine over a 72-hour period.

Indications

Buprenorphine has produced excellent analgesic results in broad clinical applications for cats, dogs, exotic species and laboratory animals. This thebaine derivative 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 species¹. Due to its long duration of action, it is one of the most widely used opioid analgesics in veterinary clinical practices.^{2,3,4}



1. Roughan JV and Flecknell PA. 2002. Buprenorphine: a reappraisal of its antinociceptive effects and therapeutic use in alleviating post-operative pain in animals. *Lab Anim* 36:322-343.

2. Capner CA, Lascelles BD and Waterman-Pearson AE. 1999. Current British veterinary attitudes to peri-operative analgesia for dogs. *Veterinary Record* 458 145:95-99.

3. Dohoo SE and Dohoo IR1996 Factors influencing the postoperative use of analgesics in dogs and cats by Canadian veterinarians. *CanVetJ* 37:552-56

4. Watson AD, Nicholson A, Church DB and Pearson MR. 1996. Use of anti-inflammatory and analgesic drugs in dogs and cats. *Aust Vet J* 74:203-210.

Key Features of Buprenorphine SR™

- Provides sustained release delivery of Buprenorphine in a fully biodegradable liquid polymer matrix
- Provides a consistent 72-hour release profile with consistent drug absorption
- Provides blood levels greater than 1 nanogram/mL for post operative analgesia
- Formulation can be injected subcutaneously through a 22-gauge needle

Chemistry and Pharmacology

Common Name: Buprenorphine Hydrochloride

Chemical Name: 6,14-Ethenomorphinan-7-methanol, 17-(cyclopropylmethyl)-alpha-(1,1-dimethylethyl)-4,5-epoxy-18,19-dihydro-3-hydroxy-6-methoxy-alpha-methyl-, hydrochloride, [5alpha, 7alpha (S)]

Buprenorphine is a thebaine derivative with powerful analgesia approximately twenty-five to forty times as potent as morphine, and its analgesic effect is due to partial agonist activity at μ -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.

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Buprenorphine SR™ Injectable

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.⁵

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.

In an unpublished study, three dogs administered 270 $\mu\text{g}/\text{kg}$ subcutaneously had plasma concentrations that rose rapidly reaching average C_{max} of 2.14 ng/mL at an average T_{max} of 1 hour. Notably average plasma concentration remained over 1.0 ng/mL from under 1 hour to over 72 hours post injection.

A recently 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.⁶

A pilot 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 $\mu\text{g}/\text{kg}$, 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.⁷

No visible injection site irritations or clinical side effects were reported within both test groups.⁷

How Supplied

Buprenorphine hydrochloride in a sustained release biodegradable matrix is available in **5 mL vials** at concentrations of:

- 10 mg/mL [for use in dogs]
- 3 mg/mL [for use in small dogs and cats]
- 1 mg/mL [for use in laboratory rats]

Dosage/Administration

- 0.12 mg/kg for Cats
- 0.12 - 0.27 mg/kg for Dogs
- 1.2 mg/kg for Laboratory Rats

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.

Precautions and Contraindications

Some patients may exhibit bradycardia and slight sedation associated with opiates. Veterinarians must rely on their professional knowledge and judgment when prescribing Buprenorphine SR. In dogs, the dose rate may vary from 0.12- 0.27 mg/kg body weight. Large dogs dosed at highest dose rate occasionally experience prolonged depression and inappetence beyond 72 hours.

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

6. Foley PL; Liang H; Crichlow AR Evaluation of a sustained release formulation of buprenorphine for analgesia in rats. *JAALAS* Vol 50, No 2, March 2011, 198–204

7. Pilot Study: Comparison of sustained release buprenorphine and transmucosal buprenorphine in cats

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