THERAPEUTICS SNAPSHOT
PEER REVIEWED

Carprofen

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Carprofen is an NSAID approved in the United States for use in dogs for its analgesic, antiinflammatory, and antipyretic properties.

Clinical Applications

Carprofen is valuable for treatment of pain and inflammation associated with osteoarthritis (OA) and for control of pain after soft tissue or orthopedic surgery.

- PO formulation for OA inflammation/pain
  - —4.4 mg/kg (2 mg/lb) q24h or 2.2 mg/kg (1 mg/lb) q12h (Quellin scored tablets, bayerdvm.com; Rimadyl scored caplets, zoetisus.com).[1-3]
  - —Can be used as long-term maintenance or during acute flare-ups
  - —Anecdotal evidence suggests that carprofen may be clinically more effective when used in conjunction with another pain medication (eg, gabapentin, amantadine, tramadol).
- SC formulation
  - —Although anecdotally clinicians may primarily use sterile injectable carprofen (Rimadyl, zoetisus.com) for short-term postoperative pain control, SC formulation also labeled for OA pain/inflammation
  - —2.2 mg/kg (1 mg/lb) q12h or 4.4 mg/kg (2 mg/lb) q24h (50 mg/mL solution)[4]
    - SC administration 2 hours before procedure has shown greater analgesic effect than administration in early postoperative period.[5]

Peak plasma levels are reached 1–3 hours postadministration, although this does not always correlate with level of analgesia obtained.[5]

- Peak plasma concentrations differ for oral and injectable forms; a single oral dose of 25 mg is rapidly absorbed and reaches a higher maximum plasma concentration than does the same dose administered SC.[6]

Complete mechanisms of action remain unclear.

- Therapeutic action is not believed to be entirely dependent on inhibition of prostaglandin synthesis via cyclooxygenase (COX) inhibition.
- Carprofen is a moderately potent phospholipase A_2 inhibitor and weak reversible COX inhibitor, with preferential activity for COX-2.

Precautionary Measures & Monitoring

Anecdotally, it is generally recommended that most patients be thoroughly screened via the following methods before using carprofen for longer than 2 weeks.

- Thorough physical examination and complete history
- Hematologic and serum chemistry panels
  - —Clinicians may use individual discretion when determining which patients (eg, young & healthy vs geriatric dogs) may benefit from laboratory screening.
- Identification of preexisting conditions, such as
  - —Renal or hepatic disease
  - —Conditions or treatments associated with low effective circulating volume (eg, hypotension, congestive heart failure, ascites, diuretic use)
  - —Coagulopathies or platelet disorders
  - —Evidence of gastric ulceration (eg, melena)
  - —GI disorders
- Determination of concurrent drug use
  - —Because NSAIDs are highly plasma protein bound, carprofen should be used cautiously with other highly protein-bound drugs (eg, benzodiazepines, phenytoin, valproic acid, oral anticoagulants, salicylates, sulfonamides).[1]
    - Displacement of these protein-bound drugs from their binding sites by NSAIDs could alter their metabolism or increase serum levels or durations of action, so it is recommended to use these medications together with caution.
  - —Carprofen should not be combined with other NSAIDs, including aspirin, or with corticosteroids.[1]

There is no consensus on monitoring frequency, but a baseline blood panel followed by renal and hepatic panels 2 weeks after initiating treatment is advised in patients with chronic conditions or in geriatric patients.

- Thereafter, it is unclear whether long-term routine monitoring of hematologic values is efficient for the management of clinical toxicity because of the low incidence of adverse effects in healthy patients.
  - —Clinicians may use clinical judgment when monitoring high-risk patients.

Clinicians should use caution when prescribing carprofen for patients with preexisting renal disease, dehydration, or sodium depletion.

COX = cyclooxygenase

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Cautions

Carprofen appears to be more COX-1 sparing and may cause fewer COX-1–mediated side effects (eg, GI distress or ulceration, platelet inhibition).[7]

- Potential for morbidity and mortality associated with disruption of normal homeostatic mechanisms remains.
- As with other NSAIDs, has been known to unmask occult renal disease or cause renal toxicity (rare)[1]
  - —Clinicians should use caution when prescribing in patients with preexisting renal disease, dehydration, or sodium depletion.
- Although studies conflict, does not seem to significantly alter platelet function in clinically normal dogs[8,9]
  - —It is generally accepted to use with caution in patients with coagulopathies or known platelet disorders.
- Although controversial, carprofen and other NSAIDs may delay or negatively affect healing.
  - —In experimental studies, carprofen was shown to have the potential to affect small intestinal healing after intestinal anastomosis, increasing risk for postoperative intestinal anastomotic leakage in laboratory rats[10,11]; therefore, caution is advised if considered for perioperative analgesia.
- A recent study demonstrated that long-term NSAID use can negatively affect bone healing in dogs.[12]
  - —Numerous rodent and rabbit models also provide evidence that NSAIDs may negatively affect bone healing; however, clinical importance in veterinary patients is unclear.
    - Experimental and clinical trials involving domestic species are needed to guide veterinarian approach to NSAID use after bone injury.

Some dogs receiving carprofen at appropriate dosing have developed idiosyncratic hepatic necrosis during the first month of treatment.[13]

- Patients with preexisting mild elevations in liver enzymes usually do not develop hepatic necrosis.
- In rare cases that do, serum chemistry findings usually reveal hyperbilirubinemia, high ALT and ALP concentrations, and hypoalbuminemia.
  - —Increased ALP alone is not consistent with carprofen hepatotoxicity.
- Clinical signs include anorexia, vomiting, diarrhea, change in urine color, and clinical icterus.
- Clinical course is variable; however, if recognized early, idiosyncratic hepatotoxicity can be reversed with supportive care, drug discontinuation, and possibly addition of glutathione precursors (eg, SAMe, *N*-acetylcysteine).

COX = cyclooxygenase

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