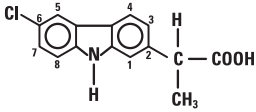
PRESCRIPTION ANIMAL REMEDY
KEEP OUT OF REACH OF CHILDREN
FOR ANIMAL TREATMENT ONLY

CARPRIEVE 20 mg Tablets for Dogs
CARPRIEVE 50 mg Tablets For Dogs
CARPRIEVE 100 mg Tablets For Dogs

INDICATIONS
The active ingredient in CARPRIEVE Tablets for Dogs, carprofen, is a non-steroidal, anti-inflammatory drug for the relief of pain and inflammation in dogs.

PRODUCT DESCRIPTION
Carprieve 20 mg and 50 mg Tablets are presented as circular, white/off-white tablets for oral administration to dogs.
Carprieve 100 mg Tablets are presented as circular, yellow tablets for oral administration to dogs. Each tablet contains either 20 mg, 50 mg or 100mg carprofen in a palatable base.
CARPRIEVE Tablets contain carprofen, a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class.
The chemical name for carprofen, a substituted carbazole, is (±)-6-chloro-α-methylcarbazole-2-acetic acid. The structural formula is:



carprofen

Carprofen is a white, crystalline compound with an empirical formula of C15H12NO2Cl and a molecular weight of 273.72. It is freely soluble in ethanol, but practically insoluble in water at 25°C.

CLINICAL PHARMACOLOGY:
Carprofen is a non-narcotic, non-steroidal, anti-inflammatory drug with characteristic analgesic and antipyretic activity, approximately equipotent to indomethacin in animal models[1].
As with other NSAIDs, the exact mode of action of carprofen has not been established; however, inhibition of prostaglandin synthesis accounts for at least part of its mechanism of action[2].
Carprofen is a moderately potent inhibitor of phospholipase A2 and a reversible inhibitor of cyclooxygenase[3]. Two unique cyclooxygenases have been described in mammals[4]. The constitutive cyclooxygenase, COX-1, synthesises prostaglandins necessary for normal gastrointestinal and renal function. The inducible cyclooxygenase, COX-2, generates prostaglandins involved in inflammation. Inhibition of COX-1 is thought to be associated with gastrointestinal and renal toxicity while inhibition of COX-2 provides anti-inflammatory activity. The specificity of a particular NSAID for either COX-2 or COX 1 may vary from species to species. In an *in vitro* study using canine cell cultures, carprofen demonstrated a greater than 100-fold selective inhibition of COX-2 compared with COX-1[1].
Carprofen has also been shown to inhibit the release of several prostaglandins in two inflammatory cell systems: rat polymorphonuclear leukocytes (PMN) and human rheumatoid synovial cells, indicating inhibition of acute (PMN system) and chronic (synovial cell system) inflammatory reactions[1].
In mice, carprofen has been shown to be a much weaker blocker of castor oil induced diarrhoea and arachidonic acid-induced toxicity than indomethacin[5].
This decreased effect of carprofen on prostaglandin synthesis in the gastrointestinal tract may explain its relatively low ulcerogenic activity compared to other drugs in its class[1,6].
Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses[7,8,9,10]. Data also indicate that carprofen inhibits the production of osteoclast-activating factor (OAF), PGE^1, and PGE^2 by its inhibitory effects on prostaglandin biosynthesis[1].
Whole blood clotting times were evaluated in dogs given carprofen at a dose rate of 9 mg/kg once daily for 14 days. At all observations both prior to and during treatment, the mean clotting times remained within the range of normal values[11].
Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (more than 90% bioavailable) when administered orally[11,12].
The mean terminal half-life of carprofen is approximately 8 hours (range 4.5 – 9.8 hours) after single oral doses varying from 1-25 mg/kg of bodyweight.
After a 100 mg single intravenous bolus dose, the mean elimination half-life was approximately 11.7 hours in the dog[12].
Carprofen is more than 99% bound to plasma protein and exhibits a very small volume of distribution[12]. Carprofen is eliminated in the dog primarily by biotransformation in the liver followed by rapid excretion of the resulting metabolites (the ester glucuronide of carprofen and the ether glucuronides of 2 phenolic metabolites, 7-hydroxy carprofen and 8-hydroxy carprofen) in the faeces (70-80%) and urine (10-20%)[13].
Some enterohepatic circulation of the drug has been observed.
Studies have not revealed any evidence of chiral inversion of carprofen enantiomers[14,15].

DIRECTIONS FOR USE:
For oral administration only.

CONTRAINDICATIONS:
This product is contraindicated for use in the cat. The elimination time of NSAIDs, including carprofen, in the cat is longer than in the dog, and the therapeutic index is narrower. In the absence of specific data, the use of CARPRIEVE Tablets in the cat is contraindicated.
This product is contraindicated for use in dogs suffering from cardiac, hepatic or renal disease, where there is a possibility of gastrointestinal ulceration or bleeding, or where there is evidence of a blood dyscrasia or hypersensitivity to the product.
This product is contraindicated for use in dogs exhibiting previous hypersensitivity to carprofen.

PRECAUTIONS:
DO NOT exceed the stated dose. All dogs should undergo a thorough clinical examination and appropriate laboratory tests before introduction of NSAID therapy. During extended administration, appropriate re-evaluation and laboratory tests should be undertaken periodically.
Use in dogs less than 6 weeks of age, or in aged animals, may involve additional risk. If such use cannot be avoided, such dogs may require a reduced dosage and careful clinical management.
Avoid use in any dehydrated, hypovolaemic or hypotensive dog, as there is a potential risk of increased renal toxicity.
Avoid administration concurrently with other NSAIDs or corticosteroids. Appropriate 'washout' time should be allowed when changing therapy. If changing anti-inflammatory products, take into account the pharmacokinetic properties of the drugs used previously when considering the delay period between individual drugs. Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs, which can lead to toxic effects.
Concurrent administration of potential nephrotoxic drugs should be avoided. Specific studies to establish the safety of this product in breeding, pregnant or lactating bitches have not been undertaken, therefore use in these classes of dogs is not recommended or should be done with caution.
NSAIDs can cause inhibition of phagocytosis and hence in the treatment of inflammatory conditions associated with bacterial infection, appropriate concurrent antimicrobial therapy should be instigated.
As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. Effects may result from decreased prostaglandin production and inhibition of the enzyme cyclooxygenase, which is responsible for the formation of prostaglandins from arachidonic acid. When NSAIDs inhibit prostaglandins that cause inflammation they may also inhibit those prostaglandins which maintain homeostatic function. These anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease more often than in healthy patients. Sensitivity to drug-associated adverse effects varies with the individual patient. NSAID therapy could unmask occult disease, which has previously been undiagnosed due to the absence of clinical signs.

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CARPRIEVE Tablets should be used with caution in dogs with bleeding disorders (eg. Von Willebrand's disease), as safety has not been established in dogs with these disorders. The safe use of CARPRIEVE Tablets in pregnant and lactating bitches and dogs used for breeding purposes has not been established.
Studies to determine the activity of CARPRIEVE Tablets when administered concurrently with other protein-bound drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring additional therapy.

SIDE EFFECTS:
Carprofen is an NSAID, and as with others in the class, adverse reactions may occur with its use. Typical adverse reactions of NSAIDs include loss of appetite, vomiting, diarrhoea, melaena or faecal occult blood and lethargy.
Events involving suspected renal, haematological, neurological, dermatological and hepatic effects have also been reported. Symptomatic treatment may be necessary. In rare cases death has been reported. In most cases, side effects are transient and disappear following termination of treatment. Owners should be advised to discontinue therapy and contact their veterinary surgeon immediately if signs of intolerance are observed.

DOSAGE AND ADMINISTRATION:
For oral administration only

Dosage: 2 to 4 mg/kg bodyweight per day. Dose, frequency and duration of treatment will be dependent upon clinical response of the condition under treatment. Initial therapy at 4 mg/kg bodyweight per day given in 2 equally divided doses is generally recommended. Subject to clinical response, the dose may be reduced to 2 mg/kg bodyweight per day administered as a once daily dose.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre, *Phone Australia 131126.*

Disposal:
Dispose of empty containers or expired product by wrapping with paper and putting in garbage.

Presentation:
CARPRIEVE 20 mg Tablets:
100 tablets per securitainer, 500 tablets per securitainer, 10 Blister strips containing 10 tablets per strip, 50 Blister strips containing 10 tablets per strip.

CARPRIEVE 50 mg Tablets:
100 tablets per securitainer, 250 tablets per securitainer, 500 tablets per securitainer, 5 Blister strips containing 10 tablets per strip, 10 Blister strips containing 10 tablets per strip, 25 Blister strips containing 10 tablets per strip, 50 Blister strips containing 10 tablets per strip.

CARPRIEVE 100mg Tablets:
14 tablets per securitainer, 30 tablets per securitainer, 100 tablets per securitainer, 1 Blister strips containing 10 tablets per strip, 2 Blister strips containing 10 tablets per strip, 3 Blister strips containing 10 tablets per strip, 5 Blister strips containing 10 tablets per strip, 6 Blister strips containing 10 tablets per strip, 7 Blister strips containing 10 tablets per strip, 10 Blister strips containing 10 tablets per strip, 14 Blister strips containing 10 tablets per strip, 18 Blister strips containing 10 tablets per strip, 20 Blister strips containing 10 tablets per strip, 25 Blister strips containing 10 tablets per strip, 30 Blister strips containing 10 tablets per strip, 50 Blister strips containing 10 tablets per strip, 100 Blister strips containing 10 tablets per strip.

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Storage:
Store below 25°C (Air conditioning) in a dry place out of direct sunlight.

APVMA Approval Numbers:
CARPRIEVE 20 mg Tablets for Dogs 54885/1209
CARPRIEVE 50 mg Tablets for Dogs 548841209
CARPRIEVE 100mg Tablets for Dogs 63022/1209

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