RIMADYL® CHEWABLE 25

RIMADYL® CHEWABLE 75

RIMADYL® CHEWABLE 100

Chewable Tablets

Veterinary medicine

SCHEDULING STATUS:

Schedule 3

PROPRIETARY NAMES (and dosage forms):

Rimadyl Chewable 25 chewable tablets

Rimadyl Chewable 75 chewable tablets

Rimadyl Chewable 100 chewable tablets

COMPOSITION:

Rimadyl Chewable 25: Each tablet contains 25 mg Carprofen

Rimadyl Chewable 75: Each tablet contains 75 mg Carprofen

Rimadyl Chewable 100: Each tablet contains 100 mg Carprofen

PHARMACOLOGICAL CLASSIFICATION:

C 3.1.2.2 NSAIDs, Selective COX2 inhibitors

PHARMACOLOGICAL ACTION:

Carprofen is a non-narcotic, non-steroidal anti-inflammatory agent with characteristic analgesic and antipyretic activity.

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. Carprofen is a moderately potent inhibitor of phospholipase A_2 and a reversible inhibitor of cyclo-oxygenase (COX). In *in-vitro* cell-culture of canine origin, carprofen displayed selectivity for COX-2, the inducible form of the enzyme upregulated in damaged and inflamed tissue, compared with its inhibition of COX-1, the iso-enzyme which is involved in normal gastric function.

Carprofen has also been shown to inhibit the release of prostaglandins in acute polymorphonuclear leukocytes and chronic inflammatory reactions.

Carprofen has modulatory effects on both humoral and cellular immune responses. It inhibits the production of osteoclast-activating factor (OAF), PGE_1 and PGE_2 by its inhibitory effects on prostaglandin biosynthesis.

Following repeat therapeutic dosing for eight weeks, carprofen has shown to have no detrimental effect on canine arthritic cartilage. In addition, therapeutic concentraions of carprofen have been shown in vitro to increase glycosaminoglycan (GAG) synthesis in chondrocytes derived from canine arthritic cartilage.
Stimulation of GAG synthesis will narrow the difference between the rate of degeneration and regeneration of cartilage matrix, resulting in a slowing of the process of cartilage loss.

Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (more than 90 % bioavailable) when administered orally. Peak blood plasma concentrations are achieved in 1-3 hours after oral administration of 1, 5 and 25 mg/kg to dogs. The mean terminal half-life of carprofen is approximately 8 hours after single oral doses varying from 1 – 35 mg/kg of body weight. After a 100 mg single intravenous bolus dose, the mean elimination half-life was approximately 11.7 hours in the dog. **Rimadyl** is more than 99 % bound to plasma protein and exhibits a very small volume of distribution.

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 faeces (70 %) and urine (10 to 20 %). Some enterohepatic circulation of the drug is observed.

INDICATIONS:

Rimadyl is indicated for the relief of pain and inflammation associated with musculoskeletal disorders in dogs. **Rimadyl** was shown to be clinically effective for the relief of signs associated with osteoarthritis in dogs.

CONTRA-INDICATIONS:

Rimadyl should not be used in dogs exhibiting previous hypersensitivity to carprofen.
Rimadyl is not recommended for use in dogs with bleeding disorders (e.g. Von Willebrand's Disease), as safety has not been established in dogs with these disorders.

WARNINGS:

The ulcerogenic oral dosage in dogs was determined to be 30 mg/kg.

The safe use of **Rimadyl** in pregnant bitches, dogs used for breeding purposes or in lactating bitches has not been established. Studies to determine the activity of **Rimadyl** when administered with other protein-bound drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring additional therapy.

All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish haematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered. Owners should be advised to watch for signs of drug intolerance

For use in dogs only. Do not use in cats.

DOSAGE AND DIRECTIONS FOR USE:

The recommended dosage for oral administration to dogs is 4.4 mg carprofen per kg of body weight daily. The total daily dose should be administered as 4.4 mg/kg of body weight once daily or divided and administered as 2.2 mg/kg twice daily. Tablets are scored and dosage should be calculated in half-tablet increments.

Tablets can be halved by placing the tablet on a hard surface and pressing down on both sides of the score. **Rimadyl** Chewable tablets are palatable and willingly consumed by most dogs when offered by the owner. Therefore, they may be fed by hand or placed on food. Care should be taken to ensure that the dog consumes the complete dose.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

As a class, cyclo-oxygenase inhibitory non steroidal anti-inflammatory drugs may be associated with gastro-intestinal and renal toxicity. The most frequently reported effects have been mild gastro-intestinal signs. Events involving suspected renal, haematologic, neurologic, dermatologic and hepatic effects have also been reported. Patients at greatest risk for renal toxicity are those on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction.

Dogs receiving **Rimadyl** should be observed for signs of drug intolerance, such as inappetence, vomiting, diarrhoea, melaena, polyuria, polydypsia, anaemia, jaundice, lethargy, ataxia, seizure or behavioural changes. Susceptibility to drug-associated adverse effects varies with the individual patient. The side-effects of this drug class, in rare situations, may be serious and if corrective action is not taken may result in hospitalization or even fatal outcomes.

Side-effects include:

Gastro-intestinal: Vomiting, diarrhoea, inappetance, melaena, haematemesis, gastro-intestinal ulceration.

Behavioral: Sedation, lethargy, hyperactivity, restlessness.

Hepatic: Inappetence, vomiting, jaundice, acute hepatic toxicity, hepatic enzyme elevation, abnormal liver function test(s), hyperbilirubinemia, hyperbilirubinuria, hypoalbuminemia. Approximately one-third of hepatic reports were in Labrador Retrievers.

Renal: Haematuria, polyuria, polydypsia, urinary incontinence, urinary tract infection, azotaemia, acute renal failure, tubular abnormalities including acute tubular necrosis, renal acidosis, glucosuria.

Neurological: Ataxia, paresis, paralysis, seizures, vestibular signs, disorientation.

Haematological: Immune-mediated haemolytic anaemia, immune-mediated thrombocytopaenia, blood loss anaemia.

Dermatological: Pruritus, increased shedding, alopecia, pyotraumatic moist dermatitis (hot spots), necrotizing panniculitis/vasculitis, ventral ecchymosis.

Immunological or hypersensitivity: Facial swelling, hives, erythema.

INTERACTIONS: Since many NSAIDs possess the potential to induce gastro-intestinal ulceration, concomitant use of **Rimadyl** with other anti-inflammatory drugs, such as corticosteroids and other NSAIDs, should be avoided or very closely monitored.

KNOWN SIGNS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See “Side-effects and Special Precautions”

Treatment is symptomatic and supportive.

IDENTIFICATION:

Rimadyl Chewable 25: A light brown rounded square tablet, debossed “R” on one side and bisected with “25 mg” on the opposite side.

Rimadyl Chewable 75: A light brown rounded square tablet, debossed “R” on one side and bisected with “75 mg” on the opposite side.

Rimadyl Chewable 100: A light brown rounded square tablet, debossed “R” on one side and bisected with “100 mg” on the opposite side.

PRESENTATION:

Rimadyl Chewable 25: Packaged in white high density polyethylene square bottles with child-resistance closure. Packs of 60 or 180 chewable tablets.

Rimadyl Chewable 75: Packaged in white high density polyethylene square bottles with child-resistance closure. Packs of 60 or 180 chewable tablets.

Rimadyl Chewable 100: Packaged in white high density polyethylene square bottles with child-resistance closure. Packs of 60 or 180 chewable tablets.

STORAGE INSTRUCTIONS:

Store below 25ºC in a dry place, protected from light. Keep out of reach of children and uninformed persons.

REGISTRATION NUMBERS:

Rimadyl Chewable 25: C 01/3.1.2.2/1

Rimadyl Chewable 75: C 01/3.1.2.2/2

Rimadyl Chewable 100: C 01/3.1.2.2/3

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

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