

Parvovirus Myocarditis in Young Dogs

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In the Literature

Ford J, McEndaffer L, Renshaw R, Molesan A, Kelly K. Parvovirus infection is associated with myocarditis and myocardial fibrosis in young dogs. *Vet Pathol.* 2017;54(6):964-971.

FROM THE PAGE ...

Canine parvovirus is typically caused by canine parvovirus type 2, a single-stranded, nonenveloped DNA virus. Dogs 6 weeks to 6 months of age are at the highest risk for infection; however, infection can occur earlier. Puppies infected within 2 weeks of birth are at a high risk for the virus invading the cardiac myocytes, which can result in fatal necrotizing myocarditis. Some dogs will survive the acute infection but may later develop heart failure secondary to lymphocytic myocarditis and fibrosis. Although parvovirus infection has been less commonly seen since the development of a vaccine, the authors of this study hypothesized that parvoviral infection of myocardial cells is underrecognized as a cause of cardiac damage in dogs younger than 2 years.

Brief Summary: Before using please consult the product insert, a summary of which follows.

ANADA 200-595, Approved by FDA

Carprieve® (carprofen) Chewable Tablets

Non-steroidal anti-inflammatory drug

For oral use in dogs only

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS: Carprieve is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs.

CONTRAINDICATIONS: Carprieve should not be used in dogs exhibiting previous hypersensitivity to carprofen.

WARNINGS: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. **For use in dogs only.** Do not use in cats. The safe use of Carprieve in animals less than 6 weeks of age, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered. **Owners should be advised to observe for signs of potential drug toxicity.**

PRECAUTIONS: As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity.

The most frequently reported effects have been gastrointestinal signs. Events involving suspected renal, hematologic, neurologic, dermatologic, and hepatic effects have also been reported. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be approached cautiously, with appropriate monitoring. Concomitant use of carprofen with other anti-inflammatory drugs, such as other NSAIDs or corticosteroids, should be avoided because of the potential increase of adverse reactions, including gastrointestinal ulcerations and/or perforations.

Carprieve 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. The safe use of Carprieve in animals less than 6 weeks of age, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. Due to the liver flavoring contained in Carprieve chewable tablets, store out of the reach of dogs and in a secured area.

INFORMATION FOR DOG OWNERS:

Carprieve, like other drugs of its class, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include decreased appetite, vomiting, diarrhea, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. **Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue Carprieve therapy and contact their veterinarian immediately if signs of intolerance are observed.**

ADVERSE REACTIONS: During investigational studies for the caplet formulation with twice daily administration of 1 mg/lb, no clinically significant adverse reactions were reported. Some clinical signs were observed during field studies (n=297) which were similar for carprofen caplet- and placebo-treated dogs. Incidences of the following were observed in both groups: vomiting (4%), diarrhea (4%), changes in appetite (3%), lethargy (1.4%), behavioral changes (1%), and constipation (0.3%). The product vehicle served as control. There were no serious adverse events reported during clinical field studies with once daily administration of 2 mg/lb. The following categories of abnormal health observations were reported. The product vehicle served as control.

Percentage of Dogs with Abnormal Health Observations Reported in Clinical Field Study (2 mg/lb once daily)

Observation	Carprofen (n=129)	Placebo (n=132)
Inappetence	1.6	1.5
Vomiting	3.1	3.8
Diarrhea/Soft stool	3.1	4.5
Behavior change	0.8	0.8
Dermatitis	0.8	0.8
PUJ/PD	0.8	--
SAP increase	7.8	8.3
ALT increase	5.4	4.5
AST increase	2.3	0.8
BUN increase	3.1	1.5
Bilirubinuria	16.3	12.1
Ketonuria	14.7	9.1

Clinical pathology parameters listed represent reports of increases from pre-treatment values; medical judgment is necessary to determine clinical relevance. During investigational studies of surgical pain for the caplet formulation, no clinically significant adverse reactions were reported. The product vehicle served as control.

Percentage of Dogs with Abnormal Health Observations Reported in Surgical Pain Field Studies with Caplets (2 mg/lb once daily)

Observation*	Carprofen (n=148)	Placebo (n=149)
Vomiting	10.1	13.4
Diarrhea/Soft stool	6.1	6.0
Ocular disease	2.7	0
Inappetence	1.4	0
Dermatitis/Skin lesion	2.0	1.3
Dysrhythmia	0.7	0
Apnea	1.4	0
Oral/Periodontal disease	1.4	0
Pyrexia	0.7	1.3
Urinary tract disease	1.4	1.3
Wound drainage	1.4	0

* A single dog may have experienced more than one occurrence of an event.

During investigational studies for the chewable tablet formulation, gastrointestinal signs were observed in some dogs. These signs included vomiting and soft stools. Post-Approval Experience:

Although not all adverse reactions are reported, the following adverse reactions are based on voluntary post-approval adverse drug experience reporting. The categories of adverse reactions are listed in decreasing order of frequency by body system.

Gastrointestinal: Vomiting, diarrhea, constipation, inappetence, melena, hematemesis, gastrointestinal ulceration, gastrointestinal bleeding, pancreatitis.

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

Neurologic: Ataxia, paresis, paralysis, seizures, vestibular signs, disorientation. **Urinary:** Hematuria, polyuria, polydipsia, urinary incontinence, urinary tract infection, azotemia, acute renal failure, tubular abnormalities including acute tubular necrosis, renal tubular acidosis, glucosuria.

Behavioral: Sedation, lethargy, hyperactivity, restlessness, aggressiveness.

Hematologic: Immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, blood loss anemia, epistaxis.

Dermatologic: Pruritus, increased shedding, alopecia, pyotraumatic moist dermatitis (hot spots), necrotizing panniculitis/vasculitis, ventral ecchymosis. **Immunologic or hypersensitivity:** Facial swelling, hives, erythema.

In rare situations, death has been associated with some of the adverse reactions listed above.

To report a suspected adverse reaction call 1-866-591-5777.

DOSE AND ADMINISTRATION: Always provide Client Information Sheet with prescription. Carefully consider the potential benefits and risk of Carprieve and other treatment options before deciding to use Carprieve. Use the lowest effective dose for the shortest duration consistent with individual response. The recommended dosage for oral administration to dogs is 2 mg/lb of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb twice daily. For the control of postoperative pain, administer approximately 2 hours before the procedure.

See product insert for complete dosing and administration information.

STORAGE: Store 25 mg and 75 mg Carprieve chewable tablets at 59-86°F (15-30°C). Store 100 mg Carprieve chewable tablets at controlled room temperature, 68-77°F (20-25°C). Use half-tablet within 30 days.

HOW SUPPLIED: Carprieve chewable tablets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per tablet. Each tablet size is packaged in bottles containing 30, 60, or 180 tablets.

Made in the UK.

Manufactured by:
Norbrook Laboratories Limited, Newry, BT35 6PU,
Co. Down, Northern Ireland

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This retrospective study examined tissue archives of dogs 2 years of age or younger from June 2007 to November 2015. Forty dogs with a diagnosis of myocardial necrosis, inflammation, or fibrosis were identified, along with 41 age-matched controls. Histopathology of the samples was graded based on severity of myocardial necrosis, inflammation, and fibrosis on a scale of 0 to 3, with 0 indicating normal tissue and 3 being most severe ($\geq 25\%$ area of total tissue affected). In addition, PCR and reverse transcription quantitative PCR (RT-qPCR) were used to identify parvoviral DNA in the tissue samples. Immunohistochemistry and in situ hybridization (ISH) were performed on any case or control sample that tested positive with PCR or RT-qPCR.

PCR identified parvoviral DNA in 12/40 cases and 2/41 controls; RT-qPCR identified the same cases. Immunohistochemistry identified parvoviral material in 7/12 positive PCR cases, whereas ISH signal was detectable in 9 of these 12 cases. Immunohistochemistry and ISH were negative in both PCR-positive control cases.

... TO YOUR PATIENTS

Key pearls to put into practice:

- 1** Parvoviral myocardial infection appears to be a more common cause of myocardial damage in young dogs than previously thought, despite widespread vaccination.
- 2** PCR-based detection of canine parvovirus type 2 is a reliable, inexpensive, and rapid method to presumptively identify parvoviral myocarditis; ISH can provide an alternative for diagnosis, with higher sensitivity than immunohistochemistry.

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IMPORTANT SAFETY INFORMATION: As a class, NSAIDs may be associated with gastrointestinal, kidney and liver side effects. These are usually mild, but may be serious. Dog owners should discontinue therapy and contact their veterinarian immediately if side effects occur. Evaluation for pre-existing conditions and regular monitoring are recommended for dogs on any medication, including Carprieve. Use with other NSAIDs or corticosteroids should be avoided. See full product labeling for full product information. Norbrook logo and Carprieve are registered trademarks of Norbrook Laboratories Limited. Rimadyl is a registered trademark of Zoetis, Inc. 0518-595-1018