



Which Drugs Are Used to Manage Feline Inflammatory Bowel Disease?

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Profile → Feline idiopathic inflammatory bowel disease (IBD) is a complex, poorly understood chronic enteropathy in which host genetics, mucosal immunity, and environmental factors (eg, diet, intestinal microbiota) all contribute to disease pathogenesis.¹

Data lacking → Strong evidence-based data and clinical trials supporting the superiority of one therapy versus another are sparse. To date, very few randomized controlled drug trials for feline IBD have been reported. Most studies in the veterinary literature provide only weak scientific evidence (ie, grade III-IV) for therapeutic efficacy.²

Basis for therapy → Because there are no reliable means for predicting which cats will respond to which treatments, medical therapy often consists of sequential therapeutic trials using diet, antibiotics, and immunosuppressive drugs.³

Immunosuppressive Drug Therapy (Confirmed Definitive Diagnosis) → **Overview**

Immunosuppressive drug therapy, particularly using glucocorticoids, is the mainstay protocol for cats with IBD that failed to respond to empiric therapy with anthelmintics, hydrolyzed or antigen-restricted diets, and antibiotics. Immunosuppressive drugs are administered with the goal of suppressing antibody and/or cell-mediated immune responses that contribute to chronic intestinal inflammation.

Prednisolone & Prednisone

The glucocorticoids, prednisolone and prednisone, have been shown to be effective for treatment of feline IBD in several case series.⁴⁻⁸ Use oral prednisolone in place of prednisone in cats when possible, as they do not absorb or convert prednisone to prednisolone as well as dogs do.⁹ Both drugs work systemically to induce immunosuppression when administered at appropriate dosages.

Formulation → Oral (tablet or solution), injectable (prednisolone sodium succinate given IV)

Dosage → 1-3 mg/kg PO once a day^{5,7}

- Once patient is in clinical remission, reduce dosage by 25% every 2 weeks, then 0.5 mg/kg every other day.

Key Points

- Generally administered as *induction therapy* for 2 to 4 weeks, then tapered at 25% the starting dose every 2 to 4 weeks based on clinical response^{5,7}
- Dose-dependent side effects include potential adrenal axis suppression and promotion of diabetes mellitus in susceptible cats. Occasionally, polyuria (PU), polydipsia (PD), and polyphagia (PP), along with weight gain, diarrhea, or depression, may be seen.⁹
 - Adverse effects are generally associated with long-term administration of these drugs, especially if given at high doses.
- Contraindicated in patients with bacterial infections, systemic mycotic infections, clinical toxoplasmosis, and retroviral infections, including feline leukemia and feline immunodeficiency viruses⁹

Dexamethasone Sodium Phosphate

Dexamethasone sodium phosphate is an injectable glucocorticoid used in cats with intractable vomiting or when severe enteropathy might interfere with intestinal absorption of orally administered glucocorticoids.

Formulation → Injectable (IM, IV)

Dosage → Typically calculated from prednisolone dose, with dexamethasone administered IM or IV at 10% to 20% of that dose to account for its increased potency¹⁰

Key Point

- Dexamethasone is 5 to 7 times more potent than prednisolone.¹⁰
 - Adjust dosage accordingly.

Budesonide

Budesonide has extensive (90% in humans) first-pass hepatic metabolism¹¹ and thus is associated with fewer side effects as compared with other orally

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IBD = inflammatory bowel disease,
PD = polydipsia, PP = polyphagia,
PU = polyuria



**Immunosuppressive
Drug Therapy
(Confirmed Definitive
Diagnosis)**
(continued)

administered glucocorticoids. This drug works locally in the intestinal tract (15 times more potent than prednisolone) to reduce inflammation.

Formulation → Oral (extended-release capsule)

Dosage → 0.5-1 mg/cat (must be compounded) PO once a day¹²

Key Points

- Anecdotally, budesonide reportedly has a lag effect of 7 to 10 days before positive clinical response is noted.
- Small but separate clinical trials^{13,14} attest to clinical efficacy in treatment of canine IBD; however, similar trials have not been reported in cats.
- May cause pituitary-adrenocortical axis suppression based on pilot observations in dogs¹⁵
- Drugs that inhibit cytochrome P450 3A (CYP3A) can significantly increase the amount of budesonide in systemic circulation.¹¹
- Optimal dosage guidelines have not been established in cats.
- Significantly more expensive than prednisolone

Chlorambucil

Chlorambucil is an alkylating agent used to induce immunosuppression (cross-links cellular DNA to impair both B- and T-cell immune responses) in patients with severe IBD refractory to diet and glucocorticoids. Chlorambucil is also used in cats when intestinal biopsy results fail to conclusively discriminate between severe IBD and alimentary lymphoma.¹⁶

Formulation → Oral (2-mg tablet)

Dosage → Multiple dosing options¹⁷

- Pulse therapy of 20 mg/m² every 2 weeks or 15 mg/m² once a day for 4 days, then repeat every 3-4 weeks
- 2 mg PO every 2 days for cats weighing >4 kg and every 3 days for cats weighing ≤4 kg

Key Points

- May be used with prednisolone as adjunctive therapy for immunosuppression³
- Anecdotally, may be used in patients with steroid-refractory disease¹⁸
- Initially monitor for bone marrow suppression by conducting complete blood count every 2 weeks.^{19,20}
- Recently increased costs make this product expensive to use.

DNA = deoxyribonucleic acid,
GI = gastrointestinal,
IBD = inflammatory bowel disease,
MMF = mycophenolate mofetil

Cyclosporine (Systemic)

Cyclosporine inhibits activation of key transcription factors and decreases production of proinflammatory cytokines (eg, interleukin-2), which promote intestinal inflammation. The immunosuppressive effects of cyclosporine inhibit both B- and T-cell (predominant) host responses. This drug may be used in cats as an adjunct with prednisolone to control gastrointestinal (GI) signs of IBD at a reduced prednisolone dose.

Formulation → Oral (solution, capsule, compounded suspension)

Dosage → 5 mg/kg PO once or twice a day²⁰

- Consider therapeutic drug monitoring, particularly when response is poor or adverse effects occur (ideally, no sooner than 60 hours after starting therapy).
- Trough whole blood levels (12 hours after last dose) have been suggested at 400–600 ng/mL but may not reliably predict clinical response for immunosuppression.
 - Because different methodologies may yield different results, contact the laboratory for recommendations on evaluation of these levels.²¹

Key Points

- More expensive to use as compared with other immunosuppressive drugs
- Anecdotally, may be used in patients with steroid-refractory disease¹⁸
- Adverse effects (eg, anorexia, vomiting) may resolve with 50% reduction in dose.

Other Immunosuppressive Drugs

Both mycophenolate mofetil (MMF) and leflunomide are anecdotally reported to be of benefit in some cats with IBD; however, clinical trial data and accurate dosing schedules have not been reported to date.

Overview

Antibiotics are often used for treatment of IBD because bacterial antigens are hypothesized to initiate and drive host responses, leading to chronic intestinal inflammation. Previous studies^{3,22} have confirmed a potential association involving intestinal microbial imbalances, GI signs, and dysregulated immunity in cats with IBD.

Chlorambucil can be used with prednisolone as adjunctive therapy for immunosuppression³ and (anecdotally) in patients with steroid-refractory disease.¹⁸

Antibiotic Therapy (Confirmed Definitive Diagnosis)

Metronidazole

Metronidazole is a commonly used antibiotic that may reduce intestinal



Antibiotic Therapy → **(Confirmed Definitive Diagnosis)**
(continued)

inflammation via multiple mechanisms, including antibacterial and antiprotozoal actions, and may have immunomodulatory effects on cell-mediated immunity in the intestinal tract.²³⁻²⁵ There is relatively good anecdotal evidence attesting to the efficacy of metronidazole for treatment of feline IBD.^{23,26,27}

Formulation → Oral (solution, tablet, compounded suspension)

Dosage → 10-15 mg/kg PO twice a day²⁷

Key Points

- Reported to be of value as a single drug treatment for feline IBD⁴
- Use cautiously in cats with hepatopathy.²⁸
 - GI signs and neurotoxicity are the most common adverse effects and appear to be dose-dependent.
- Adverse effects include poor palatability (metallic taste); use capsules or flavored compounded suspension.
- Genotoxicity in cats has been reported following a single dose of metronidazole at 20 mg/kg PO.²⁸

Tylosin

Anecdotally, tylosin (a macrolide antibiotic) has been used to treat IBD colitis in cats. Similar to metronidazole, its mechanism(s) of action may include antibacterial and immunomodulatory properties. Clinical evidence is relatively sparse on the efficacy of this drug for treatment of feline IBD.

Formulation → Oral (powder)

Dosage (extralabel) → Anecdotal recommendations range from 10-40 mg/kg PO 2-3 times a day²⁹

- When using tylosin tartrate powder (Tylan Soluble, 100 grams/bottle; Elanco): 1 level teaspoonful (5 mL) of powder contains ≈2.5-2.7 grams of tylosin; one-eighth of a teaspoonful contains ≈325 mg of tylosin.

Key Point

- Because of unpleasant taste, powder must be compounded for oral use

Common → **Adjunctive Therapy**

Micronutrients

Micronutrients, including cobalamin and folic acid, may be deficient in cats with severe enteropathy (poor intestinal absorption in either proximal small intestine [folate] or distal small intestine [ileum with cobalamin]). Reduced dietary intake of these nutrients may also contribute to whole body micro-

nutrient deficiency. Of the two vitamins, cobalamin is more important and may contribute to delayed clinical recovery despite specific dietary and pharmacologic therapy for feline IBD.³⁰

Cyanocobalamin (Vitamin B₁₂)

Cobalamin supplementation as needed is recommended in cats with IBD and severe enteropathy.^{30,31} Clinical signs of chronic small bowel diarrhea and/or significant weight loss should prompt measurement of serum cobalamin concentrations or empiric therapy with parenteral cobalamin if absolute concentrations cannot be determined.

Formulation → Injectable (SC; cyanocobalamin)

Dosage → 250 µg SC once a week for 4-6 weeks, tapered to every other week as needed³²

Key Points

- Failure to diagnose and treat hypcobalaminemia can delay clinical recovery from IBD despite appropriate dietary and pharmacologic therapies.^{33,34}
- Continue therapy until cobalamin concentrations normalize and/or GI signs resolve.³⁵

Folic Acid

Folic acid is a B vitamin needed for nucleoprotein synthesis and normal erythropoiesis. Folic acid deficiency may develop in cats with certain small intestine inflammatory diseases. Folic acid may be used when trimethoprim, ormetoprim, pyrimethamine, and similar reductase inhibitor drugs have been administered for prolonged periods (uncommon).

Formulation → Oral (tablet), injectable (SC)

Dosage → Recommendations vary, with little evidence to support specific dosage³⁶

- Suggested PO dose ranges from 400 µg/cat to 1 mg/cat once a day.³⁶
- When folic acid is used for treatment of IBD, concomitant administration of parenteral cyanocobalamin (vitamin B₁₂) has been anecdotally recommended.³⁶

Key Points

- Safe to use³⁶
- May also be indicated in cats with multiorgan inflammatory GI disease involving the intestines, liver, and/or pancreas³⁶
- In cats, folic acid supplementation is used less frequently than cobalamin supplementation.³⁶

Micronutrients such as cobalamin and folic acid may be deficient in cats with severe enteropathy (ie, poor intestinal absorption in either the proximal or distal small intestine).

GI = gastrointestinal,
IBD = inflammatory bowel disease

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**Common
Adjunctive Therapy**
(continued)

Antiemetics

Antiemetics are administered to inhibit vomiting and improve lack of appetite associated with mucosal inflammation. Excessive vomiting may be attributed to dehydration and electrolyte abnormalities, which can contribute to disease morbidity.

Maropitant

Maropitant, a potent neurokinin-1 (NK₁) receptor antagonist, has proven efficacy in blocking vomiting mediated through the chemoreceptor trigger zone and emetic center. The drug has both central and peripheral antiemetic actions.³⁷

Formulation → Oral (tablet), injectable (SC)

Dosage → 1 mg/kg SC or PO once a day for up to 5 days³⁷

- Labeled dose (ie, 1 mg/kg SC or PO) also used extralabel for prevention of vomiting and motion sickness

Key Points

- May cause pain at injection site
- As an NK₁ receptor antagonist, inhibits substance P (key neurotransmitter involved in vomiting)³⁷
 - May also reduce visceral pain in cats
- Eliminated primarily by the liver³⁷
 - Hepatic metabolism of maropitant involves two cytochrome P450 enzyme systems; thus, use with caution in cats with hepatic dysfunction.
 - Reducing dosage by 50% has been suggested in cats with hepatopathy.

Ondansetron

As a serotonin (5-HT₃) receptor antagonist, ondansetron is used to control intractable vomiting in cats.

Formulation → Oral (tablet, solution), injectable (SC)

Dosage → 0.1-1 mg/kg SC or PO once or twice a day³⁸

Key Point

- May improve lack of appetite associated with nausea

**Additional Oral
Supplementation**

Omega-3 Fatty Acids

Omega-3 fatty acids (ie, eicosapentaenoic acid, docosahexaenoic acid) may reduce intestinal inflammation, based on studies in humans. Doses in cats are extrapolated from those used in humans.

Formulation → Oral (enteric-coated preparation works best in maintaining remission)²⁰

Dosage → Eicosapentaenoic acid, 17-25 mg/kg PO once a day; docosahexaenoic acid, 8-18 mg/kg PO once a day¹⁸

Key Points

- Unpalatable product
- May cause diarrhea²⁰
- No clinical proof of efficacy for treatment of GI disease in cats

Probiotics

In human and animal models of inflammation, there is some evidence for efficacy in patient subsets with IBD.³⁹ The link between microbial imbalances and intestinal inflammation is clear; however, a causal association has not been identified. Clinical trials citing administration or efficacy of probiotics for treatment of feline IBD have not been reported.

Formulation → Single and multistrain commercial products available

- Efficacy varies based on strain and dose.

Dosage → Optimum bacterial composition, dose, or dosing interval has not been established.

- Most products are empirically administered by clinicians.

Key Points

- Administer continuously for beneficial responses.
- One clinical trial demonstrated that shelter cats fed a probiotic had fewer episodes of diarrhea than did controls.⁴⁰
- Avoid use in immunocompromised cats or cats with evidence of severe mucosal damage (ie, bloody diarrhea).^{19,41}

Inflammatory Bowel Disease vs Lymphocytic Lymphoma

Differentiation between severe IBD and lymphocytic lymphoma (LL) is confounded by similarities in patient history, overlapping GI signs, unpredictable clinical course, and even histopathologic findings (H&E stain) in affected cats.

Based on recent studies⁴² → Accurate diagnosis can be realized through assessment and testing.

- Ileal mucosal biopsy assessment (ie, immunophenotyping for clonal expansion of B- or T-lymphocyte populations)
- Molecular testing (ie, PCR for antigen receptor rearrangement [PARR])

These tests may not be available or may be cost prohibitive → Empiric therapy depends on discretion of clinicians.

- Some clinicians recommend using a combination drug protocol that may induce clinical remission in cats with either IBD or LL.

Not all clients can afford the optimum diagnostic workup to confirm IBD. Therefore, clinicians may need to implement treatment if IBD is suspected but not confirmed.⁴

Questionable Diagnosis (Possible Lymphocytic Lymphoma)

GI = gastrointestinal, IBD = inflammatory bowel disease, LL = lymphocytic lymphoma, NK₁ = neurokinin-1, PARR = PCR for antigen receptor rearrangement, PCR = polymerase chain reaction

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**Questionable
Diagnosis
(Possible Lymphocytic
Lymphoma)**
(continued)

Chlorambucil + Prednisolone Chemotherapy

Combined chlorambucil and prednisolone chemotherapy protocols have been established for cats with LL.⁴²

Formulation → Oral (tablet)

Dosage → Prednisolone at 5-10 mg PO once a day; chlorambucil at 2 mg PO every 2-3 days, or 20 mg/m² every 2 weeks^{43,44}

Key Points

- An overall response of 95% with a 56% complete response rate (ie, 100% resolution of clinical signs and detectable tumor) was observed in one study (ie, 2 mg of chlorambucil every 2-3 days, plus prednisolone) with a median remission duration of ≈900 days.⁴³
- A separate investigation using a higher chlorambucil dose (ie, 20 mg/m² every 2 weeks) achieved 95% complete remission response rate, with a median remission time of 26 months.⁴⁴

**Therapeutic
Options**

Biopsy Costs Prohibitive

Not all clients can afford the optimum diagnostic workup with biopsy results confirming IBD. Therefore, clinicians may need to implement treatment measures if the cat is suspected to have IBD.⁴

Key Points

- Consider a dietary trial with an elimination (novel intact protein or hydrolysate) diet for 2 weeks.
 - If incomplete response to dietary therapy occurs, treat next (sequential therapy) with metronidazole as directed below.
- Therapeutic trial with metronidazole (10-15 mg/kg PO twice a day) for 10 to 14 days may also be helpful in reducing mucosal inflammation through multiple mechanisms.
 - Consider abdominal ultrasonography with focus on architecture of the GI (tract) layers; some cats with LL have muscularis thickening, as compared to mucosal thickening in cats with IBD.
- Cats that fail to respond to sequential therapy with diet and metronidazole may do better on a therapeutic trial of prednisolone as a more potent immunomodulator.
- Cats with cachexia and a history of watery, small bowel diarrhea should be considered hypcobalaminemic and treated with parenteral cobalamin supplementation as previously discussed (see **Micronutrients**, page 30).
- Cats with large bowel signs (ie, increased bowel movements, tenesmus, blood/mucus in feces) alone or with enterocolitis may benefit from dietary fiber supplementation (eg, psyllium at one-quarter teaspoon per meal) to reduce colonic inflammation.

GI = gastrointestinal,
IBD = inflammatory bowel disease,
LL = lymphocytic lymphoma

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Rx SOLUTIONS

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