THERAPEUTICS SNAPSHOT
PEER REVIEWED

Mycophenolate Mofetil

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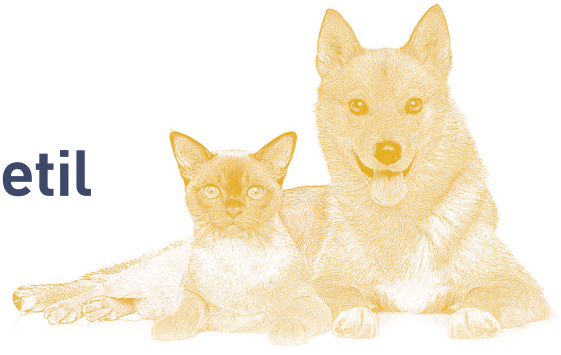

In recent years, the indications and reported frequency of use of mycophenolate mofetil (MMF) in veterinary patients has rapidly expanded.

Clinical Applications

Clinically, MMF is used to suppress the immune system.

- Often used in conjunction with other immunosuppressive medications (eg, glucocorticoids) for the treatment of immune-mediated disease or prevention of tissue rejection following organ transplantation
- Veterinary conditions in which MMF therapy has been investigated include immune-mediated hemolytic anemia, aplastic anemia, immune-mediated thrombocytopenia, glomerulonephritis, myasthenia gravis, inflammatory neurologic disease, and autoimmune dermatologic disease.[1-7]
- Prospective clinical trials are warranted to confirm efficacy and better guide MMF use in veterinary patients.
  —To date, efficacy has primarily been reported retrospectively.

MMF exerts its effect primarily through inhibition of T- and B-lymphocyte proliferation and subsequent reduction in antibody production.

- MMF is the bioavailable prodrug of mycophenolic acid, an inhibitor of the inosine-5'-monophosphate dehydrogenase enzyme necessary for lymphocyte purine production.[8]

Protocol

Commonly, 10 mg/kg PO or IV administered twice a day is used in dogs.

- Reported dose regimens have ranged from 10 mg/kg 2 to 3 times a day to up to 20 mg/kg twice a day, with higher doses often resulting in unacceptable GI toxicity.[9]
  —Dosages at or exceeding 15 mg/kg twice a day generally are not recommended by the authors.

No pharmacokinetic studies have evaluated MMF use in cats.

- A single report has described clinical MMF use at 10 mg/kg PO twice a day with apparent tolerance in 2 cats with immune-mediated hemolytic anemia.[10]

Availability of both oral and parenteral formulations allows MMF to be used in both the intensive and chronic stages of therapy.

- Commercial products include 250-mg capsules, 500-mg tablets, a 200-mg/mL oral suspension, and a powder for IV injection (diluted with 5% dextrose to a final concentration of 6 mg/mL before administration).[11]
- IV administration of MMF is labeled as incompatible with other infusions[11]; the total dose should be administered slowly over a minimum of 2 hours to achieve peak plasma concentrations, similar to oral administration.[12]

MMF can be compounded into an oral liquid without loss of efficacy over time if mixed correctly and handled appropriately.[13,14]

- Storage at room (25°C) or refrigerated (5°C) temperature results in a shelf life of 28 or 210 days, respectively.
- Most solutions should be mixed by gently shaking before withdrawing each dose.[13,14]
- Caution is recommended to ensure compounded products do not contain artificial sweeteners (eg, xylitol) that are unsafe for use in animals.

Pharmacokinetics

Following oral administration, MMF is rapidly absorbed and subsequently undergoes primarily hepatic metabolism with renal excretion.[9,15-17]

- Lesser degrees of renal and intestinal metabolism of administered MMF, as well as biliary excretion of metabolites, have been documented in humans and experimental animal models.[16,18]
- Maximum immunosuppressive effects are typically noted 2 to 4 hours after oral administration.[8]
- Appropriate dose strategy in patients with renal or hepatic insufficiency is unknown, although neither nephrotoxicity nor hepatotoxicity has been reported.

Prospective clinical trials are warranted to confirm efficacy and better guide use of mycophenolate mofetil in veterinary patients, as to date efficacy has primarily been reported retrospectively.

MORE ▶

GI = gastrointestinal,
MMF = mycophenolate mofetil

Veterinary staff and pet owners should wear gloves and wash their hands after being exposed to either the drug itself or the patient's urine.

Adverse Effects & Cautions

GI toxicity is the most commonly reported and anecdotally encountered adverse effect of MMF use in dogs.[1,3,5,6,9]

- Adverse effects include diarrhea, anorexia, vomiting, weight loss, and possible intestinal hemorrhage; mild allergic reactions have been suspected following parenteral use only.[1,3,5,6,9,19,20]
- Dose reduction often resolves adverse effects; however, drug discontinuation may be required.

There is limited experience for safety and efficacy in cats.[21]

Certain drug interactions have been reported in humans[11,22,23]; if possible, these drug combinations should be avoided until they have been evaluated in veterinary patients.

- Fluoroquinolones, metronidazole, and amoxicillin–clavulanic acid may reduce MMF efficacy when administered concurrently, though anecdotally such interactions have not been observed clinically in veterinary patients.[22,23]
- Concurrent use with azathioprine is not recommended based on the similar mechanism of action and therefore likely increased risk for inducing bone marrow suppression.[21]

Efforts should be made to minimize direct human exposure to MMF and prevent possible toxicity.

- Veterinary staff and pet owners should wear gloves when handling MMF and wash their hands following exposure to the drug or a treated patient's urine.
- MMF should be avoided in patients whose owner may be pregnant or nursing, as the drug has shown predisposition to pregnancy loss and birth defects.[11,24]
- To prevent aerosolization of MMF, opening capsules or splitting pills should be avoided.

GI = gastrointestinal, MMF = mycophenolate mofetil

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