Mycophenolate

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Mycophenolate mofetil is the synthesized prodrug form of mycophenolic acid, a selective and reversible inhibitor of inosine monophosphate dehydrogenase, an enzyme that controls the rate of synthesis of guanine monophosphate in the *de novo* pathway of purine synthesis. Mycophenolate mofetil is a fermentation product derived from fungi in the *Penicillium* group. Mycophenolic acid inhibits B and T cell proliferation, and decreases antibody production. Mycophenolate mofetil is primarily used in human medicine for prevention of rejection of transplanted organs, although it also used to treat immune-mediated diseases such as systemic lupus erythematosus, immune-mediated hemolytic anemia (IMHA), immune-mediated thrombocytopenia and pemphigus vulgaris. Mycophenolate mofetil is often used in the place of azathioprine in human medicine and, since they have similar mechanisms of action, the two drugs should probably not be used together.

The original proprietary mycophenolate mofetil product, CellCept®, and the closely related mycophenolate sodium product, Myfortic®, were expensive, and as a result the products only achieved limited usage in small animal medicine. However, recently, the availability of much cheaper generic alternatives has led to a greatly increased usage of mycophenolate mofetil in small animal patients. A single 250 mg CellCept® capsule currently costs around $7, whereas the equivalent generic 250 mg capsule costs less than 50c. An oral suspension version of mycophenolate mofetil (200 mg/ml) is available for more convenient dosing in smaller patients. Successful usage of mycophenolate mofetil in a small animal patient with naturally-occuring disease was first described in a dog with acquired myasthenia gravis (Dewey). Much of the subsequent anecdotal usage of mycophenolate mofetil for a variety of different immune-mediated diseases was similar to the dosing reported in this original paper (Abelson; Ginel; Yuki). Mycophenolate mofetil is also available in an injectable form, and the intravenous use of the drug has been described during the successful initial stabilization of three dogs with acquired myasthenia gravis that could not tolerate oral medications (Abelson). Ironically, a more recent case report of 15 dogs with acquired myasthenia gravis treated with mycophenolate mofetil reported that the drug was ineffective at attaining clinical remission (Dewey).

A recommended starting dose for mycophenolate mofetil in dogs is 10-20 mg/kg once daily or divided twice daily, although occasionally gastrointestinal signs (particularly vomiting and diarrhea) at the higher end of the dose rate will necessitate dose reductions. Mycophenolate mofetil appears to have variable oral bioavailability in dogs, so variability in response to therapy should probably be expected (Lupu). A pharmacodynamic study in dogs measuring inosine monophosphate dehydrogenase enzyme activity suggested that mycophenolate mofetil would best be dosed three times daily, but this recommendation has not entered common usage (Langman). Mycophenolate mofetil has not been used widely enough in veterinary medicine to establish the frequency of serious side effects but, in people, gastrointestinal signs and, less

commonly, marked myelosuppression and a rare and fatal neurologic disease (progressive multifocal leukoencephalopathy) have been reported. Based on the human side effect profile, complete blood counts should probably be regularly monitored in dogs receiving mycophenolate mofetil. In humans, gastrointestinal side effects can be reduced by replacing mycophenolate mofetil with mycophenolate sodium. Mycophenolic acid in humans is primarily excreted conjugated to glucuronide and, since cats lack the glucuronyl transferases responsible for glucuronidation of drugs such as mycophenolate mofetil, the drug should probably used with caution, if at all, in this species, although the use of mycophenolate mofetil has been described at a dose rate of 10 mg/kg twice daily, with no obvious side effects, in two cats with IMHA (Bacek).

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