MMF 500 mg

Mycophenolate mofetil 500 mg

FORM AND PRESENTATION:
• MMF 500 mg : pink coated tablet : Box of 56 tablets, blister.
COMPOSITION PER TABLET:

	MMF 500 mg
Mycophenolate mofetil	500 mg
Excipients : microcristallin cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, anhydrous colloidal silica, Opadry pink ..... q.s.f. one tablet List of active excipients : Lactose	

PHARMACOLIGICAL PROPRIETIES:
Mycophenolate mofetil is the 2-morpholinoethyl ester of mycophenolic acid (MPA).
MPA is a selective, noncompetitive, reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH) and therefore inhibits the de novo pathway of guanosine nucleotide synthesis. Because T-and B-lymphocytes are critically dependent for their proliferation on de novo synthesis of purines whereas other cell types can utilize salvage pathways, MPA has more potent cytostatic effect on lymphocytes than on other cells.
THERAPEUTIC INDICATIONS:
MMF 500 mg is indicated in combination with cyclosporine and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants.
CONTRAINDICATIONS:
- Hypersensitivity to mycophenolate mofetil or to mycophenolic acid,
- Pregnancy and lactation.

DOSAGE AND MODE OF ADMINISTRATION:
MMF 500 mg should be used only by transplant specialist doctor.
Renal transplantation :
Adult :
by oral intake, **MMF 500** must be initiate up to 72 hours after the transplant. The recommended dose is 1 g twice a day (daily dose of 2 g).
Children and adolescents: (2 to 18 years)
MMF 500 mg tablets must be used only in patient who body area exceeded 1.5 m2 .the dose is than like adult 2 g daily.
Heart transplantation :
Adults :
the recommended dose for heart transplant patients is 1.5 g twice daily (daily dose 3 g) and initiated up to 5 days after transplant.
Children :
no data are available for pediatric cardiac transplant patients.
Elderly patients :
Elderly patients should be given the normal adult dose. In general, the risk of side effects may be increased in patients in this age group.
Hepatic transplantation:
Adults :
the recommended dose for hepatic transplant patients is 1.5 gtwice daily (daily dose : 3 g). No pharmacokinetic data are available for hepatic transplant rejection.
Children and adolescents:
no data are available for pediatric hepatic transplant patients.
Elderly patients (>= 65 ans):
The recommended dosages of 1 g twice per day among renal persons receiving a transplant and of 1,5 g twice per day among cardiac or hepatic persons receiving a transplant are adapted for the old patients.
Renal failure :
Renal transplant patients with severe chronic renal impairment (glomerular filtration rate < 25 ml/min/1.73 m2. such renal transplant patients should not be given doses of **MMF 500 mg** greater than 1 g and should be carefully monitored.
In heart or hepatic transplant patients with severe chronic renal failure, **MMF 500 mg** should be used only if the expected benefit outweighs the potential risk. No data are available for these patients.
Hepatic failure:
Dose adjustment is unnecessary in renal transplant patients with severe parenchymal liver disease. No data are available on heart transplant patients with severe parenchymal liver disease.
WARNING AND PRECAUTIONS OF USE:
- As in patients receiving immunosuppressant regimes involving combinations of drugs, patients receiving **MMF 500 mg** as part of an immunosuppressant regime are at increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent. As in all patients at increased risk of skin cancer, sun and ultraviolet exposure should be limited by wearing protective clothing and using a sunscreen with a high protection factor.
- Patients treated with **MMF 500 mg** must be told to report immediately any evidence of infection, unexpected bruising, bleeding or other symptoms of bone marrow aplasia.
- Oversuppression of the immune system can also increase susceptibility to infection, e.g. opportunistic infections, fatal infections and sepsis.
- In patients receiving **MMF 500 mg** the neutrophil count should be monitored and if necessary **MMF 500 mg** should be interrupted or the dose reduced. Complete blood counts should be performed weekly during the first month, twice monthly during the second and third months of treatment, then monthly through the first year.
- Because **MMF 500 mg** has been associated with an increased incidence of gastrointestinal ulcers, hemorrhage and perforations – it should be administered with caution to patients with severe active disease of the digestive tract.
- As **MMF 500 mg** is an inosine monophosphate dehydrogenase (IMPDH) inhibitor, on theoretical grounds it should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl- transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.

Pregnancy and lactation:
An evident teratogenic effect was observed in animals.
MMF 500 mg is contraindicated in pregnancy.
Women of childbearing age must have a negative serum or urine pregnancy test within 1 week before the start of treatment. It is recommended that the doctor should not initiate **MMF 500 mg** therapy until a report of a negative pregnancy test has been obtained.
Effective contraception must be used before the start of **MMF 500 mg** therapy.
MMF 500 mg is contraindicated in nursing women.
Users and drivers machines:
No specific studies have been performed. The pharmacodynamic profile and the reported adverse reactions indicate that an effect of **MMF 500 mg** is unlikely.
DRUG INTERACTIONS:
- Aciclovir and its prodrugs, probenecid and other drugs that undergo active tubular secretion may compete with MPAG for tubular secretion. Higher MPAG (8.6%) and acyclovir (17.4%) AUCs were observed after coadministration of mycophenolate mofetil and aciclovir than after administration of each drug alone. In the presence of renal impairment there may be a further increase in the concentration of both drugs.
- Antacids with magnesium and aluminium hydroxides: absorption of mycophenolate mofetil was reduced when administered concomitantly with antacids.
- Cholestyramine and other drugs that interfere with enterohepatic circulation : reduced absorption associated with interference with enterohepatic circulation by cholestyramine reduces the AUC of MPA by 40%. MPA levels should be closely monitored during use of cholestyramine and other drugs, that interfere with enterohepatic circulation because of the potential of these drugs to reduce the efficacy of **MMF 500 mg**.
- Cyclosporin A : Cyclosporin A pharmacokinetics were unaffected by mycophenolate mofetil.
- Ganciclovir : based on the results of a single-dose administration study of recommended doses of oral mycophenolate and ganciclovir and known effects of renal impairment on the pharmacokinetics of mycophenolate mofetil and ganciclovir, it is to be expected that coadministration of these agents (which compete for renal tubular secretion) will result in increase in MPAG and ganciclovir concentration. No substantial alteration of MPA pharmacokinetics is to be expected and MMF dose adjustment is not required. Patients with renal impairment who receive mycophenolate mofetil and Ganciclovir concomitantly should be monitored carefully.
- Oral contraceptives : the pharmacokinetics of oral contraceptives are not influenced by concomitant administration of **MMF 500 mg**.
- Tacrolimus : stable renal transplant patients receiving cyclosporine and **MMF 500 mg** (1 g twice daily) showed an approximately 30% increase in MPA plasma AUC and an approximately 20% decrease in MPAG plasma AUC when cyclosporine was replaced with tacrolimus . MPA Cmax was not affected. While MPAG Cmax was reduced by approximately 20%. When switching from the combination cyclosporine plus **MMF 500 mg** to tacrolimus plus **MMF 500 mg**. MPA level should be monitored and if necessary the dose of **MMF 500 mg** should be adjusted. For patients on tacrolimus, the dose of **MMF 500 mg** should exceed 1 g twice daily. In another study in renal transplant patients it was found that tacrolimus concentration does not appear to be altered by **MMF 500 mg**.
In hepatic transplant patients: very limited pharmacokinetic data on MPA AUC are available in hepatic transplant patients treated with **MMF 500 mg** in combination with tacrolimus. In a study designed to evaluate the effect of **MMF 500 mg** on the pharmacokinetics of tacrolimus in stable hepatic transplant patients, there was an increase of approximately 20% in tacrolimus AUC when **MMF 500 mg** was administered repeatedly (1,5 g twice daily) to patients taking tacrolimus.
- Live vaccines: Live vaccines should not be given to patients with an impaired immune response, since the antibody response to other vaccines may be diminished.

ADVERSE EFFECTS:
- The principal adverse reactions associated with the prophylactic use of **MMF 500 mg** in renal, cardiac and hepatic transplant patients in combination with cyclosporine and corticosteroids are diarrhea, leukopenia, sepsis and vomiting, and there is evidence of a higher frequency of certain types of infection, opportunistic infections.
In controlled trials on the prevention of rejection after renal transplantation daily doses of 2 g mycophenolate mofetil were generally better tolerated than daily doses of 2 g.
- Malignant tumours: as in patients immunosuppressant regimes involving combinations of drugs, patients receiving **MMF 500 mg** as part of an immunosuppressant regime are at increased risk of developing lymphomas and other malignancies, particularly of the skin.
- Opportunistic infections: all transplant patients are at increased risk for opportunistic infections. The risk increases with total immunosuppressive load.
The most common opportunistic infections in renal, cardiac and hepatic transplant patients receiving **MMF 500 mg** (2 g or 3 g daily) who were followed for at least 1 year were mucocutaneous candida, CMV viremia/syndrome and herpes simplex infections. The proportion of patients with CMV viremia/syndrome was 13.5%.
- Elderly patients (>= 65 ans) : elderly patients may be at greater risk of developing certain infections (including tissue-invasive cytomegalovirus [CMV] disease), and possibly gastrointestinal hemorrhage and pulmonary edema than younger patients, especially if they take MMF 500 mg as part of an immunosuppressive combination therapy.

OVERDOSAGE :
Experience with overdose of **MMF 500 mg** in humans is very limited. The cases of reported overdose fall within the known safety profile of the drug.
MPA and MPAG cannot be removed by hemodialysis. However, at high MPAG plasma concentrations (> 100 μg/ml), small amounts of MPAG are removed. Bile acid sequestrants such as cholestyramine can remove MPA.
DELIVERY CONDITIONS:
List I – Only on medical prescription.
SPECIAL PRECAUTIONS OF STORAGE:
Store at a temperature below 25° C.
PRESENTATION AND M.A. NUMBER :

Specialities	**M.A. numbers**	**Presentation**
MMF 500 mg	923 346 1 H	Box of 56 tablets

This is a drug

- A drug is a specific product agent.
- A drug is a product acting on your health and its use, contrary to prescriptions may be dangerous for you.
- Strictly respect the doctor's prescription and the instructions of use he has prescribed.
- Follow your pharmacist's kmow this drug ; its indiations and contra-indications.
- Do not discontinue the drug intake by yourself during the prescription period.
- Do not repeat the prescription or increase the dosage without consulting your doctor.

KEEP ANY DRUG OUT OF THE REACH OF CHILDREN.

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MédiS

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