# Mycophenolate Mofetil (MMF)

## SCG: For Transplant patients

*The following guidelines are designed to provide information relating to mycophenolate mofetil and to outline the responsibilities of the primary and secondary care teams in the prescribing of mycophenolate mofetil.*

## AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

### Introduction:

Mycophenolate mofetil is an immunosuppressant which acts by inhibiting the synthesis of guanosine nucleotides in T and B lymphocytes. It is rapidly converted to the active metabolite mycophenolic acid by plasma esterases.

#### Brand versus generic prescribing

Recently generic mycophenolate mofetil has become available for prescribing. Although generic mycophenolate is required to be bioequivalent, these products' bioavailabilities are allowed to vary between 80 and 125% of that of Cellcept®. For this reason Papworth Hospital NHS Trust wish for all patients to remain on a specified generic mycophenolate and not switch between brands to avoid variability in their level of immunosuppression. The generic mycophenolate chosen by Papworth Hospital NHS Trust is the **TEVA** brand (Myfenax®), chosen due to its easy availability in primary care.
Please note that in patients maintained only on dual immunosuppression of mycophenolate and prednisolone the consultant may wish for the patient to continue on branded Cellcept®, you will be informed of this by your patient's consultant.

## RESPONSIBILITIES and ROLES

### Specialist responsibilities (Transplant team):

1. Initially prescribe and stabilise the patient on the treatment regimen and monitor transplant graft function.
2. Monitor efficacy of the treatment and side effects.
3. Provide access to back up and support facilities.
4. Evaluate any adverse events reported by the GP.
5. Provide patients with a current medication record book ("blue book").
6. Educate patients in knowledge of drug therapy to maximise compliance and be aware of when to seek medical attention.

### General Practitioner's responsibilities:

1. Prescribe mycophenolate mofetil once the patient has been stabilised on therapy and side effects have been excluded as far as possible by the hospital.
2. Encourage patients to complete their daily medication record and document any changes to therapy in the "blue book".
3. Check for possible drug interactions when newly prescribing or stopping concurrent medication.

4. Report any suspected adverse events to the Transplant Unit. (All potential adverse events need to be reported).
5. Monitor blood counts and discuss any abnormalities with Transplant Unit.

### Patient's role:

1. Complete daily medication record in their "blue book".
2. Notify GP and Transplant Unit of any suspected adverse events.
3. Notify use or intended use of over the counter (OTC) and herbal medications.

## BACK-UP ADVICE AND SUPPORT

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| Papworth Hospital Main Switchboard | 01480 830541 |
| Transplant Unit Reception | 01480 364455 |
| Transplant Coordinators (on-call) | 01480 830541 (via Hospital Switchboard) |
| Pharmacy Medicines Information Service | 01480 364179 Mon - Fri 9 am to 5 pm |
| Transplant Pharmacist | 01480 830541 ext. 4179 (bleep 931) |
| Consultant Transplant Cardiologist: | Dr J Parameshwar |
| | Dr Clive Lewis |
| Consultant Transplant Pulmonary Physician: | Dr J Parmar |
| Consultant and medical staff are always available to give advice and can be contacted through the main hospital switchboard on: | 01480 830541 |

## SUPPORTING INFORMATION

### Licensed indications:

Mycophenolate mofetil is currently licensed for the prophylaxis of acute transplant rejection in conjunction with ciclosporin and oral corticosteroids in patients receiving renal, cardiac or hepatic transplants. It is not currently licensed for use in lung or heart/lung transplants. However, there are trials in lung transplant patients and it is used in these patients in most centres around the world.

### Dosage and Administration:

The manufacturer's recommended starting dose of mycophenolate mofetil in cardiac transplant patients is 1.5g bd. The 1g bd dose appears to be better tolerated and is the usual dose prescribed at Papworth Hospital.

### Contraindications:

- Hypersensitivity to mycophenolate mofetil or mycophenolic acid
- Breastfeeding
- Not recommended during pregnancy (see "Cautions")

## Cautions:

- Malignancy, especially lymphomas and skin tumours are more common in immunosuppressed patients - advise patient to limit exposure to sunlight by wearing light clothing and using a high factor sunscreen.
- Susceptibility to opportunistic infections is increased in patients receiving immunosuppression.
- Patients should be instructed to report any evidence of bone-marrow depression e.g. infection, bruising, bleeding.
- Due to an increased incidence of digestive system adverse events, including infrequent cases of gastrointestinal tract ulceration, haemorrhage and perforation, mycophenolate should be administered with caution in patients with active serious digestive system disease.
- Effective contraception must be used during therapy and for six weeks following discontinuation of therapy. Patients should contact their physician immediately should pregnancy occur.

## Therapeutic Use:

- Mycophenolate mofetil is prescribed as part of combined therapy (has been used with calcineurin inhibitors e.g. ciclosporin / tacrolimus, corticosteroids and sirolimus) for the prevention of rejection post cardiothoracic transplantation.

## Side Effects:

All immunosuppressive agents are powerful and potentially toxic drugs, and therefore adverse events may be observed. Any adverse effects detected should be reported directly to the Transplant Unit.

The principal adverse reactions associated with the administration of Mycophenolate in combination with ciclosporin/ tacrolimus and corticosteroids include diarrhoea, leucopenia, sepsis and vomiting, and there is evidence of a higher frequency of certain types of infections.

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| **Infection** | Sepsis, gastro-intestinal candidiasis, urinary tract infection, herpes simplex, herpes zoster and others. |
| **Gastrointestinal** | Diarrhoea, vomiting, abdominal pain, nausea |
| **Haematological** | Leucopenia, thrombocytopenia, anaemia, pancytopenia and leukocytosis. |
| **Neoplasms (benign and malignant)** | Skin cancer and benign skin neoplasms. |
| **Cardiovascular** | Hypertension, hypotension, tachycardia |
| **Central Nervous System** | Dizziness, insomnia, tremor, agitation |
| **Metabolic disorders** | Electrolyte disturbances |

The above list of adverse events is not exhaustive but does cover the most frequently reported events to date. A more comprehensive list can be found in SPCs for mycophenolate.

## Monitoring:

**FBC** Complete blood counts should be done **weekly** during the first month, **monthly** for the second and third months of treatment, then 3 **monthly.**. If neutropenia develops (absolute neutrophil count < 1.3 x $10^3$/µl), it may be appropriate to interrupt or discontinue mycophenolate.

## Drug Interactions:

**Aciclovir/ valganciclovir** Increases in both aciclovir and mycophenolic acid plasma concentrations occur with concurrent administration but this interaction is only considered to be of clinical significance in patients with impaired renal function.

**Antacids** With magnesium and aluminium hydroxides, a decrease in the absorption of mycophenolate mofetil may occur.

**Cholestyramine** A significant decrease in the absorption of mycophenolate mofetil may occur with concurrent administration. Use with caution.

**Ciclosporin** May reduce mycophenolic acid levels

**Ganciclovir** Increased ganciclovir and mycophenolic acid concentrations are expected but no dose adjustment of mycophenolate mofetil is required.

**Sirolimus** Potential increase in mycophenolic acid level with increased incidence of adverse effects. Monitor for adverse effects such as leucopenia, diarrhoea and vomiting.

**Live vaccines** are contra-indicated and should not be given to immunocompromised individuals. Other vaccines may be less effective.

**For advice on mycophenolate interactions please do not hesitate to contact the pharmacy Medicines Information Department.**

## Cost:

- PCTs need to ensure that funding for post transplant drug treatment is made available for patients. As soon as a GP is made aware of a patient requiring an expensive medicine, they are advised to discuss the funding mechanisms for it with their PCT prescribing manager.

## Availability:

- Mycophenolate mofetil (Cellcept®) is available from Roche Products Ltd as 250 mg capsules and 500 mg tablets and 1g/5ml suspension (once reconstituted). Community pharmacies can obtain mycophenolate mofetil from local wholesalers within 24 hours.

- Generic mycophenolate (Myfenax®) is readily available from local wholesalers within 24 hours.

## References:


- SPC Cellcept® tablets accessed via emc.medicines.org.uk on 13/07/2011. Last updated 15/04/2011.

- Stockley's Drug Interactions accessed via medicinescomplete.com on 13/07/2011. Last updated May 2011.
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- Product Information Leaflet for Teva brand Mycophenolate (Myfenax®). Last updated February 2011.

- BNF 61 March 2011.


Guidelines:
Reviewed by Transplant Pharmacy
Approved by: Papworth Hospital Drugs and Therapeutics Committee 09/2006
Reviewed by: Transplant Pharmacist (HC)
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