Mycophenolate mofetil

Post Solid Organ Transplant Shared Care Guideline

Specialist Details	Patient Identifier
Name: _____	
Location: _____	**Date:** _____
Tel: _____	

Introduction

Use of generic mycophenolate mofetil post transplant.

Bioavailability: Different formulations of the same immunosuppressant may vary in bioavailability and to avoid reduced effect or excessive side effects, it is important not to change formulation except on the advice of a transplant specialist.

In Northern Ireland patients established on the innovator brand of mycophenolate mofetil (Cellcept®) may be selected by transplant specialists as being suitable for transfer to a generic mycophenolate mofetil. It is known that it will not be possible to provide a consistent brand of generic to these patients.
Selection and follow up of patients will be undertaken by transplant teams, and GPs should not switch patients established on the Cellcept brand except on the specific advice of the specialist who will provide specific advice around any planned change.

Licensed indication: immunosuppression post organ transplant.

- **Post renal transplant**: Mycophenolate mofetil is usually prescribed initially as part of a triple therapy immunosuppressive regimen, along with ciclosporin or tacrolimus, and prednisolone. For maintenance, it is usually prescribed in a dual-regimen with prednisolone or tacrolimus. Mycophenolate mofetil is never prescribed concurrently with azathioprine. (Renal transplant patients are initiated on Cellcept at Belfast City Hospital).
  - **Adult dosage and administration:** The initial recommended dose is up to 1g twice daily. Patients may be on a lower dose in due time after transplantation or if they have not tolerated the higher dose. Gastro-intestinal adverse-effects (most commonly diarrhoea and nausea) may be limited by increasing dose frequency (e.g. 500mg four times daily).
- **Post liver transplant:** Mycophenolate mofetil is not routinely used for immunosuppression in liver transplant patients. It is reserved for use in cases where chronic rejection develops, and also in combination with prednisolone for patients who have experienced nephrotoxicity with tacrolimus or ciclosporin. Mycophenolate mofetil may occasionally be used in combination with tacrolimus.
- **Adult dosage and administration:** The initial recommended dose is up to 1g twice daily. Patients may be on a lower dose in due time after transplantation or if they have not tolerated the higher dose. Gastro-intestinal adverse-effects (most commonly diarrhoea and nausea) may be limited by increasing dose frequency (e.g. 500mg four times daily).

Available as: Mycophenolate mofetil (Cellcept®) tablets 500mg, capsules 250mg and oral suspension 1g/5ml. A number of generics are also available. See notes above relating to use of generic formulations of mycophenolate mofetil in Northern Ireland.

Hospital Specialist Responsibilities

- Agree shared care with the patient's GP
- Send a copy of this guideline to the GP.
- Provide patient/carer with relevant information on use, side effects and the need for Monitoring of medication
- Baseline tests and ongoing safety monitoring:
  - FBC
  - LFT
  - U&E
  - Urinalysis
  - Lipids
  - Blood glucose
  - Blood pressure
- Drug monitoring and mycophenolate mofetil dose adjustments.
- Review results of safety monitoring and request additional tests as necessary.
- Investigate, as appropriate, where symptoms suggest viral or fungal infections or possible tumours.
- Provide any other information or advice for the GP if required.
- **If a patient is selected for a change from Cellcept to a generic, the transplant clinic will manage this switch, and communicate with the GP on a patient specific basis.**

GP Responsibilities

- Prescribe mycophenolate mofetil as Cellcept®. Caution: a number of brands are available.
  - **If a patient is selected for a change from Cellcept to a generic, the transplant clinic will manage this switch, and communicate with the GP on a patient specific basis.**
- Monitor patient's overall health and wellbeing.
- The Liver Unit may occasionally request tests to be repeated at the GP practice but will provide specific advice on this and the process to follow. HRA/CHM).
- Ensure no drug interactions with other medicines.
- Administer i**nactivated** influenza vaccine annually unless otherwise advised by the initiating specialist
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia.) - see BNF or Green Book.
- Passive immunization using Varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact Regional Virus Laboratory, Royal Group of Hospitals for advice if exposure is suspected.
- **Suspected non-compliance** with immunosuppression is serious and can lead to loss of the graft - refer to the specialist urgently

Adverse Effects, Precautions and Contraindications

Gastrointestinal upset is the most common side effect (e.g. nausea, vomiting, abdominal discomfort, diarrhoea or constipation). If severe or persistent, refer to specialist.
Acute Kidney Injury (AKI): Transplant patients are at increased risk of developing AKI. ACEI, ARBs, and NSAIDs should be withheld in situations of hypotension/hypovolaemia (GAIN,2014)
Infection: immunosuppressants can increase susceptibility to infection.
Blood disorders; Leucopenia, anaemia, thrombocytopenia, pancytpopenia, pure red cell aplasia, neutropenia, and leucocytosis have been reported are most likely to be discovered at outpatient appointments. GPs should be alert to any oral ulceration / sore throat, unexplained rash or abnormal bruising or bleeding.
Hepatic dysfunction and **hyperlipidaemia** are screened for at outpatient appointments. Statin therapy is recommended for hyperlipidaemic patients.
Cancer risk Patients receiving long-term immunosuppressive drugs are at increased risk of developing a malignancy. The most frequently occurring types are lymphoma and skin malignancy. The avoidance of excessive exposure to the sun, and the use of high factor sunscreen and protective clothing are advised.

Adverse Effects, Precautions and Contraindications (continued)

Pregnancy / contraception. There is evidence of increased risk of teratogenicity by maternal exposure to mycophenolate. Women of childbearing potential receiving mycophenolate mofetil should be advised to use two reliable forms of contraception simultaneously before starting therapy, during, and for six weeks after stopping the therapy. There is not similar evidence of paternal teratogenicity although men are also advised to use contraception during and up to 90 days after cessation of mycophenolate.
As there is risk of precipitating acute rejection with a change in immunosuppression regimen, women taking mycophenolate who are contemplating pregnancy, or who become pregnant, should be referred back to their transplant specialist for advice. Men whose partners are contemplating pregnancy, or who become pregnant, should also be referred back to their transplant specialist for advice.
Breastfeeding: women being treated with mycophenolate mofetil should not breastfeed.
Vaccines. Live vaccines should be avoided, except on the advice of initiating specialist.

Common Drug Interactions

The interactions listed below relate to mycophenolate mofetil. Consideration should be given to the other agents used as part of a regime.
The degree of renal function should be taken into consideration when co-prescribing for renal transplant patients.
The following drugs should not be initiated by a GP unless discussed with the specialist:

Antibacterials: Rifampicin reduces mycophenolate plamsa levels

Aciclovir is widely used for the prevention and treatment of viral infections in immunosuppressed patients. Although it may cause small increases in mycophenolate mofetil plasma levels, these are not considered clinically significant. If patient has significant renal impairment contact the specialist for advice.

Antacids & colestyramine: should not be taken at the same time of day, as they will impair the absorption of mycophenolate mofetil.

Communication

Renal Units

Altnagelvin Hospital: Renal Unit	028 7161 1162
Antrim Hospital: Renal Unit	028 9442 4894 or 028 9442 4472
Belfast City Hospital: Renal Unit	028 9504 0719
Daisy Hill Hospital: Renal Unit	028 3083 5036
Omagh hospital and primary care complex (OHPCC): Renal Unit	028 8283 3350
Royal Belfast Hospital for Sick Children: Dialysis Unit	028 9063 6621
Ulster Hospital: Renal Unit	028 9056 4839

Liver Unit

Royal Victoria Hospital	028 9063 3182