NORTH AND EAST DEVON HEALTHCARE COMMUNITY SHARED CARE PRESCRIBING GUIDELINE

http://www.devonpct.nhs.uk/Treatments/NE_Devon_Shared_Care_Guidelines.aspx#M

https://nww.devonpctinfo.nhs.uk/Prescribing/SCG/

MYCOPHENOLATE (ORGAN TRANSPLANT PATIENTS)
(MYCOPHENOLATE MOFETIL - CELLCEPT® OR MYCOPHENOLIC ACID - MYFORTIC®)

This shared care guideline sets out details for the sharing of care of adults with **RENAL TRANSPLANTS** prescribed **MYCOPHENOLATE**. These guidelines provide additional limited information necessary to aid in the treatment of patients with **RENAL TRANSPLANTS**. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and ***do not*** replace them.

INTRODUCTION/BACKGROUND INFORMATION

Mycophenolate is licensed in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in adult patients receiving allogeneic renal, cardiac or hepatic transplants. This Shared Care Guideline should only be used in reference to renal transplants.

It is a reversible antagonist of inosine monophosphate dehydrogenase, inhibiting the guanosine nucleotide synthesis pathway on which T- and B-lymphocytes are dependent for proliferation. Its mode of action is similar to that of azathioprine but has greater specificity.

Mycophenolate is available as the mofetil salt (CellCept®) and as the acid (Myfortic®). **These products are not bioequivalent and are not recommended to be interchangeable**.

Some transplant patients may receive mycophenolate only to avoid renal toxicity of ciclosporin or tacrolimus.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

Mycophenolate is used post-transplant for the prevention of rejection in combination with other immunosuppressants, when patients are at increased risk of rejection.

It may also replace azathioprine in patients who have resistant rejection while on the standard immunosuppressive regimen.

It is considered to decrease nephrotoxicity when added to the immunosuppression regimen as doses of more nephrotoxic drugs e.g. ciclosporin may be reduced.

DOSAGE AND ADMINISTRATION

Initiation and stabilisation of the immunosuppressant drug regime will take place at the renal clinic.

Mycophenolate mofetil (CellCept®)**:**

Adult dose normally 500mg to 1g orally twice daily.

Dose is dependant on concomitant immunosuppression prescribed and renal function.

Mycophenolic acid (Myfortic®): 720mg twice daily.

Note Tablets and capsules are not appropriate for dose titration in young children.

Splitting the daily dose into four divided doses may alleviate gastrointestinal side effects.

CONTRAINDICATIONS

- Hypersensitivity to mycophenolate.
- Pregnancy. Mycophenolate should not be initiated until a negative pregnancy test has been obtained. This drug is contra-indicated in pregnancy as it has the potential to affect the development of the unborn child. Patients should be advised to use a reliable method of contraception during treatment.
- Breastfeeding.
- Lesch-Nyhan syndrome.
- Kelley-Seegmiller syndrome.

PRECAUTIONS

- Elderly (increased risk of infection, gastro-intestinal haemorrhage and pulmonary oedema).
- Children (higher incidence of side-effects may call for temporary reduction of dose or interruption).
- Active serious gastro-intestinal disease (risk of haemorrhage, ulceration and perforation).
- Delayed graft function.
- Use of sunbeds and unprotected exposure to sunlight are not recommended due to potential risk of skin malignancy.
- Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection and inexplicable bruising or bleeding.
- As there are potential teratogenic effects, mycophenolate capsules / tablets should not be opened or crushed to eliminate risk of inhalation.
- Direct contact with skin or mucous membranes should be avoided.
- Immunosupressed patients reporting neurological symptoms should consider progressive multifocal leucoencephalopathy.

SIDE EFFECTS

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

Very common:

- Sepsis, gastrointestinal candidiasis.
- Vomiting, abdominal pain, diarrhoea, nausea, sepsis, gastrointestinal candidiasis.
- Urinary tract infection, herpes simplex, herpes zoster.
- Leucopenia, thrombocytopenia, anaemia.

Common:

- Pneumonia, influenza, respiratory tract infection, respiratory moniliasis,, gastroenteritis, gastrointestinal infection, bronchitis, pharyngitis, sinusitis, fungal skin infection, skin candida, vaginal candidiasis, rhinitis.
- Skin cancer, benign neoplasm of skin.
- Pancytopenia, leucocytosis.
- Agitation, confusional state, depression, anxiety, thinking abnormal, insomnia.

- Convulsion, hypertonia, tremor, somnolence, myasthenic syndrome, dizziness, headache, paraesthesia, dysgeusia.
- Tachycardia, Hypotension, hypertension, vasodilatation.
- Pleural effusion, dyspnoea, cough.
- Gastrointestinal haemorrhage, peritonitis, ileus, colitis including cytomegalovirus colitis, gastric ulcer, duodenal ulcer, duodenal ulcer, gastritis, oesophagitis, stomatitis, constipation, dyspepsia, flatulence eructation.
- Pancreatitis, hepatitis, jaundice, hyperbilirubinaemia.
- Skin hypertrophy, rash, acne, alopecia.
- Renal impairment.
- Oedema, pyrexia, chills, pain, malaise, asthenia, arthralgia.
- Hepatic enzyme increased, blood creatinine increased, blood lactate dehydrogenase increased, blood urea increased, blood alkaline phosphatase increased, weight decreased.

Uncommon:

- Intestinal villous atrophy, Infections including meningitis, endocarditis, tuberculosis, atypical mycobacterial infection and progressive multifocal leukoencephalopathy (PHL).

Rare:

- Agranulocytosis, Neutropenia. Hypersensitivity reactions, including angioneurotic oedema and anaphylactic reaction.

Increased risk of malignancies including lymphoma, skin and other tumours appear to be linked to degree and duration of immunosuppression. The incidence is similar to that of other immunosuppressive agents or therapies.

MONITORING

- A full blood count should be performed weekly during the first month, twice monthly during the 2nd and 3rd months then monthly thereafter.
- Monitoring of mycophenolate blood levels is not considered necessary.

STOP AND REFER TO THE SPECIALIST TEAM IF

Patient exhibits signs of Neutropenia or absolute neutrophil count <1.3 x 10^9/L.

COMMON/SIGNIFICANT DRUG INTERACTIONS

- Azathioprine administration concurrently with mycophenolate has not been studied should be avoided.
- Antacids and cholestyramine may decrease the absorption of mycophenolate.
- Aciclovir or ganiciclovir may impair the excretion of mycophenolate leading to increased blood levels of both drugs. This may be of greater significance in renally impaired patients.
- Drugs which interfere with enterohepatic recirculation may also have the potential to reduce the efficacy of mycophenolate.
- Iron preparations – may lead to reduction in absorption of mycophenolate.
- Sevelamer – may moderately reduce mycophenolate absorption.
- Vaccinations: may not give full protection against disease and live vaccines need to be avoided.

NOTES

- Live vaccines include: measles, mumps and rubella; BCG; poliomyelitis – oral Sabin vaccine; yellow fever; typhoid – oral.
- Patients require counselling on the potential skin malignancy risks of exposure to UV light including not using sunbeds and covering exposed skin with clothes or sunscreen SPF of at least 25.
- Dose equivalence: Mycophenolic acid 720mg is approximately equivalent to mycophenolate mofetil 1g. Unnecessary switching should be avoided because of pharmacokinetic differences.

PRODUCT INFORMATION

Prescribing of mycophenolate must be **BY BRAND**.

CellCept® -Mycophenolate mofetil is available as 250mg and 500mg caplet-shaped tablets.
Capsules 250mg 100 = £87.33
Capsules 500mg 50 = £87.33
Oral suspension, 1 g/5mL when reconstituted with water 175mL = £122.25
Intravenous infusion 500mg vial = £9.69.

Myfortic® - Tablets, e/c 180mg 120-tab = £122.49; 360mg 120-tab = £244.97. Must be swallowed whole not chewed.

REFERENCES:

- Summary of Product Characteristics: CellCept® and Myfortic® accessed at http://emc.medicines.org.uk
- BNF 55 March 2008

AUTHORS:

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Please note: The prescribing of mycophenolate mofetil for the prevention of rejection in renal transplant patients has been repatriated to secondary care. This shared care guideline has been archived.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients that are prescribed **MYCOPHENOLATE (CellCept® or Myfortic®)** for the **PREVENTION OF RENAL TRANSPLANT REJECTION** can be shared between the specialist and the general practitioners. GPs are **invited** to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event the total clinical responsibility for the patient for the diagnosed condition remains with the specialist**. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Specialist responsibilities:

- ❑ Prescribing **mycophenolate** is retained for 3 months or until the patient's condition/dose is stabilised and the GP agrees to take over responsibility for prescribing. **Brand of mycophenolate needs to be communicated to the GP.**
- ❑ Provide the patient or patient's parents/guardians/carers with suitable written and verbal information about the drug prior to starting medication and discuss the benefits and side effects of treatment.
- ❑ Monitoring of treatment as described in the Shared Care Guideline will normally be the responsibility of secondary care and will include full blood counts and renal function.
- ❑ Prompt communication of test results and any treatment changes in therapy at least 3 monthly and whenever a significant change in monitoring parameters occurs or ANY change in drug therapy.
- ❑ Ensure monitoring of full blood counts and renal function where they are not taken in renal clinic.
- ❑ As appropriate, liaison with other members of the multidisciplinary team e.g. renal pharmacist, transplant nurse.
- ❑ Ask the GP whether they are willing to participate in shared care.
- ❑ Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- ❑ Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- ❑ Reporting adverse events to the CSM.

General Practitioner responsibilities:

- ❑ Reply to request for shared care as soon as practical.
- ❑ Prescribing of **mycophenolate by specified brand** after communication with the specialist regarding the need for treatment.
- ❑ Undertake monitoring of full blood counts and renal function tests (unless carried out in the renal clinic).
- ❑ Prompt referral to a specialist if there is a change in the patient's status.
- ❑ Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- ❑ Reporting adverse events to specialist and CSM.
- ❑ Immediate referral in the case of a severe adverse event or as per shared care guideline.

Patient responsibilities:

- ❑ Take **mycophenolate** as prescribed.
- ❑ Report any adverse effects to their GP and/or specialist regarding their treatment.
- ❑ Ensure that they have a clear understanding of their treatment.
- ❑ Ensure they attend for monitoring requirements as per shared care guideline.
- ❑ Aware of the necessity of attendance for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No:	E-mail address
Dr R D'Souza	(01392) 402587	Richard.DSouza@rdeft.nhs.uk
Dr C Bingham	(01392) 406366	Coralie.Bingham@rdeft.nhs.uk
Dr. H. Clarke	(01392) 406367	Helen.Clarke@rdeft.nhs.uk
Dr.M.Bello-Villalba	(01392) 402191	Maria.Bello@rdeft.nhs.uk
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Dr. C Mulgrew	(01392) 403535	Chris.Mulgrew@rdeft.nhs.uk

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Shared Care Agreement Letter - Consultant Request

To: Dr.....

Practice Address: .....

.....

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Patient Name:
Hospital number:
Date of birth:
Address:

DIAGNOSED CONDITION: **.....**

I recommend treatment with the following drug: **.....**

I am requesting your agreement to sharing the care of this patient according to the Devon Primary Care Trust North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

Signed:	
Consultant name:	
Department:	
Contact telephone number:	
Date:	

GP RESPONSE

I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: ..... Date: .....

GP name: ..... ***Delete as appropriate**