NHS LINCOLNSHIRE in association with
UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE:
Mycophenolate mofetil or mycophenolic acid for Maintenance of Immunosuppression after Kidney Transplantation in Adults

General Principles

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF* 63, March 2012, pg.1)

Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and , if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further Copies

Further copies of any guidelines in this series are available from NHS Lincolnshire Prescribing Advisers.

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Drug Details

Approved Name: Mycophenolate mofetil
Brand Name: non-proprietary (generic)
Or CellCept®
or Mycophenolic acid - Myfortic®
Form and Strength: capsules 250mg , tablets 500mg (non- proprietary)
capsules 250mg or tablets 500mg (CellCept®)
capsules 360mg (Myfortic®)

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

The Leicester based renal transplant centre have stated that the dosing of mycophenolate mofetil is less critical and for this reason switching between brands is not believed to be detrimental. This allows for mycophenolate mofetil to be prescribed generically.

Mycophenolic acid (Myfortic) is used in those who cannot tolerate the gastrointestinal side effects which are commonly associated with mycophenoate mofetil. Patients should not be switched to or from mycophenolic acid (Myfortic) except on the advice of a transplant specialist.

Specialist Responsibilities

The specialist secondary/tertiary care service will:

All patients eligible for treatment under this protocol will have received their renal transplant at least one year ago and will now be transferred to the care of the Lincoln based renal services.

1. Send a letter to the GP notifying them of the changes to the ongoing care of the patient and asking them if they are willing to accept share care, and confirm that they will continue to provide regular prescriptions for myclophenolate mofetil or mycophenolic acid.
2. Ensure that the patient receives supplies of mycophenolate mofetil or mycophenolic acid until the GP formally agrees to share care, except in those circumstances where the patient already receives these medications from the GP under a prior arrangement.
3. Measure biochemistry including U&Es and Full Blood counts in line with local and national guidelines/protocols.
4. Titrate the dose of mycophenolate mofetil or mycophenolic acid as necessary to the optimum level according to local/national guidelines.
5. Advise the GP when the dose should be changed.
6. Provide patient with treatment information leaflet.
7. Communicate promptly any changes in monitoring and modification of mycophenolate mofetil or mycophenolic acid dose to the GP.
8. Communicate promptly any changes in test results to the GP.
9. Periodically (at six-monthly intervals in clinic) review the patient's clinical condition.
10. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.

11. Follow up any adverse drug reactions reported by the GP and report back to the GP.
12. Advise the GP on related issues such as drug interactions.
13. Respond to issues raised by the GP after the care of the patient has been transferred.

GP Responsibilities

The GP will:

1. Notify the consultant in writing, within two weeks, if they agree to share care.
2. Provide repeat prescriptions after achievement of a stable dose regime according to recommendations by the Nephrology department, Lincoln County Hospital.
3. Monitor the patients overall health and wellbeing.
4. Ensure advice is sought from the secondary care clinician if there is any significant change in the patient's physical health status.
5. Monitor the patient for adverse drug reactions and abnormalities and remain vigilant to the risk of potential drug interaction, and raise these issues with the secondary care clinician if necessary.
6. Carry out any investigations that are communicated and deemed appropriate.
7. Change the dose or stop treatment in line with instructions from the secondary care clinician.
8. Consult promptly with the specialist when test results are abnormal or when patient defaults from blood test appointments undertaken by primary care.

Referral Criteria

1. Patients will have been stabilized on their immunosuppressants, and other specialist medications.
2. Patients will have received their renal transplant at least 12 months ago and their ongoing supervision and care will have been transferred to the Lincoln based renal services.
3. The specialist will have carried out an assessment of efficacy.

Licensed Indications

Mycophenolate mofetil non-proprietary brands or CellCept®) or mycophenolic acid (Myfortic®) are licensed for the maintenance of immunosuppression following kidney transplantation in adults.

Recommended Dosage and Administration

Mycophenolate mofetil

Starting dose 1g twice daily (local practice- 500mg twice daily in combination with tacrolimus)

Mycophenolic acid (Myfortic®)

Starting dose: 720mg twice daily (local practice- 360mg twice daily in combination with tacrolimus)

Background Pharmacology

Mycophenolate mofetil/mycophenolic acid are potent, selective, uncompetitive inhibitors of the de novo pathway of guanosine nucleotide synthesis without incorporation into DNA. Because T- and B-lymphocytes are critically dependent for their proliferation on the de novo synthesis of purines, mycophenolate mofetil/mycophenolic acid have more potent cytostatic effects on lymphocytes than on other cells.

Mycophenolate mofetil or mycophenolic acid are used in combination with other immunosuppressants to reduce risk of side effects and to optimise immunosuppression.

Preparations Available

250mg and 500mg tablets non-proprietary Mycophenolate Mofetil. 500mg tablets (Arizip)

250mg capsules and 500mg tablets, 1g in 5ml oral suspension of mycophenolate mofetil (CellCept®)

180mg and 360mg capsules of mycophenolic acid (Myfortic®)

Adverse Effects

Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding.

Gastrointestinal disturbances including taste disturbance, gingival hyperplasia, nausea, vomiting, abdominal pain, constipation,flatulence, anorexia, weight loss, gastrointestinal ulceration and bleeding, abnormal liver function tests, hepatitis, jaundice, pancreatitis,stomatitis, oedema, tachycardia, hypertension, hypotension, vasodilatation,tachycardia, cough, dyspnoea, insomnia, agitation, confusion, depression , anxiety, convulsions, paraesthesia, myasthenic syndrome, tremor, dizziness, headache, influenza-like syndrome, infections, hyperglycaemia, renal impairment, increased risk of malignancy particularly of the skin, blood disorders, disturbances of electrolytes and blood lipids, arthralgias, alopecia, acne, skin hypertrophy and rash; also reported intestinal villious atrophy, progressive multifocal leucoencephalopathy, interstitial lung disease and pulmonary fibrosis (in combination with other immunosupressants).

Drug Interactions

a) Levels of mycophenolate are increased by: acyclovir and possibly ganiciclovir.
b) Levels of mycophenolate are decreased by: antacids, rifampicin, oral iron, colestyramine. Levels possibly reduced by metronidazole, norfloxacin, and sevelamer.
c) Mycophenolate possibly reduces the absorption of phenytoin, and digoxin.
d) Avoid concomitant use with clozapine as may increase the risk of agranulocytosis.

e) Avoid use of live attenuated vaccines.

Precautions and Contraindications

Precautions

Active gastrointestinal disease (risk of haemorrhage, ulceration and perforation).
Increased susceptibility to skin cancer, patients should be advised to avoid exposure to strong sunlight. Patients should be advised to wear protective clothing and use a sunscreen with a high protection factor.
Use with caution in elderly patients due to increased risk of infection, gastrointestinal haemorrhage and pulmonary oedema.
Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding.

Because of pharmacokinetic differences patients should not unnecessarily be switched between CellCept® and Myfortic®

Contraindications

Pregnancy, breast feeding
Hypersensitivity to mycophenolate mofetil or mycophenolic acid

Monitoring

Full blood counts, U and Es and Liver Function Tests every 6 months or more frequently. Monitoring remains the responsibility of the secondary care service although some testing may be devolved to the primary care setting.

Treatment should be reviewed and advice from the supervising specialist sought if:

- if neutrophils <1.5 x 10^9 /litre advise interrupting or discontinuing treatment and seek urgent advice.
- there is deterioration in the clinical condition and/or the patient experiences major side-effects.
- serum creatinine levels rise by >20% in 3 months.

Indication of Likely Cost of Therapy in Primary Care

June 2012

mycophenolate mofetil 500mg	500mg £14.95 for 50 tablets
Mycophenolate mofetil (CellCept®)	250mg £82.26 for 100 capsules
	500mg £82.26 for 50 tablets
Mycophenolic acid (Myfortic®)	180mg £96.72 for 120 capsules
	360mg £193.43 for 120 capsules

Information Given to the Patient

Patient information leaflet available with each container of Mycophenolate mofetil (CellCept®) or mycophenolic acid (Myfortic®).

Contact Details

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References

1. BNF 63 March 2012.
2. SPC Arizip Winthrop Pharmaceuticals UK ltd. . Last updated 12th January 2011. eMC website accessed 19th June 2012
3. SPC Myfortic Novartis Pharmaceuticals UK ltd. Last updated 10th May 2012. eMC accessed 19th June 2012
4. SPCs CellCept® Roche, Last updated 27th October 2009. eMC accessed 19th June 2012.
5. MIMS June 2012
6. Leicester Medicines Strategy Group – Leicestershire statement on the use of generic immunosuppressants. March 2011.

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