LINCOLNSHIRE Clinical Commissioning Groups in association with
UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE:
Mycophenolic acid for Maintenance of Immunosuppression after Kidney Transplantation in Adults

THERE IS A SEPARATE SHARED CARE PROTOCOL COVERING THE USE OF MYCOPHENOLATE MOFETIL

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* 70, September - March 2016, pg.4)

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 members of the Arden and GEM commissioning Support Unit – Lincolnshire Prescribing & Medicines Optimisation Team.

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Principles of shared care

The General Medical Council published their Good Practice in Prescribing and Managing Medicines and which came into effect 25th February 2013. A section of the guidance provides recommendations for the sharing of care which applies to any instance when care is shared between different services.

Good practice recommendation 35.

- Decisions about who should take responsibility for continuing care or treatment after initial diagnosis or assessment should be based on patients best interest rather than on convenience or the cost of the medicine and associated monitoring or follow-up

Good practice recommendation 36.

- Shared care requires the agreement of all parties including the patient. Effective communication and continuing liaison between all parties to a shared care agreement is essential.

Good practice recommendation 37.

- If you prescribe at the recommendation of another doctor, nurse or other healthcare professional, you must satisfy yourself that the prescription is needed, appropriate for the patient and within the limits of your competence.

Good practice recommendation 38.

- If you delegate assessment of a patients' suitability for a medicine, you must be satisfied that the person to whom you delegate has the qualifications, experience, knowledge and skills to make the assessment. You must give them enough information about the patient to carry out the assessment required

Good practice recommendation 39.

- In both cases, you will be responsible for any prescription you sign.

Good practice recommendation 40.

- If you recommend that a colleague, for example a junior doctor or general practitioner, prescribes a particular medicine for a patient, you must consider their competence to do so. You must satisfy yourself that they have sufficient knowledge of the patient and the medicine, experience (especially in the case of junior doctors) and information to prescribe. You should be willing to answer their questions and otherwise assist them in caring for the patient, as required

Good practice recommendation 41

- If you share responsibility for a patient's care with a colleague, you must be competent to exercise your share of clinical responsibility.

You should:

a) Keep yourself informed about the medicines that are to be prescribed for the patient
b) Be able to recognise serious and frequently occurring adverse side effects
c) Make sure appropriate clinical monitoring arrangements are in place and that the patient and the healthcare professionals involved understand them
d) Keep up to date with relevance guidance on the use of the medicines and on the management of the patient's condition

Good practice recommendation 42

- In proposing a shared care arrangement, specialists may advise the patient's general practitioner which medicine to prescribe. If you are recommending a new or rarely prescribed medicine you should specify the dosage and means of administration and agree a protocol for treatment. You should explain the use of unlicensed medicines and departures from authoritative guidance or recommended treatments and provide both the general practitioner and the patient with sufficient information to permit the safe management of the patient's condition.

Good practice recommendation 43

- If you are uncertain about your competence to take responsibility for the patients continuing care you should seek further information or advice from the clinician with whom the patient's care is shared or from another experienced colleague. If you are still not satisfied you should explain this to the other clinician and to the patient and make appropriate arrangements for their continuing care.

Drug Details

Approved Name: Mycophenolic acid - Myfortic gastro resistant tablets.
Brand Name: Myfortic®
Form and Strength: tablets 180mg or 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.

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.

The use of mycophenolate mofetil is covered in a separate shared care protocol.

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 six months 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 mycophenolic acid. Either enclose a copy of the shared care protocol or the GP should be signposted to where they can find a copy of the shared care protocol e.g. the PACEF website http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef
2. Inform all patients (male and female) of the risks of serious birth defects associated with mycophenolate treatment. Patients should be advised of the

need for effective contraception, the need to plan for pregnancy and change treatment if necessary and the need to immediately consult a doctor if there is a possibility of pregnancy. Female patients should be advised to use 2 forms of effective contraception during treatment and for 6 weeks after stopping treatment. Male patients including those who have had a vasectomy should use condoms during treatment and for at least 90 days after stopping treatment.

3. Women of child bearing potential should have a negative pregnancy test result to exclude unintended exposure of the embryo to mycophenolate. Two serum or urine pregnancy tests with a sensitivity of at least 25mIU/ml are recommended. The second test should be done 8-10 days after the first one and immediately before starting mycophenolate. Pregnancy tests should be repeated as clinically required (e.g. after any gap in contraception is reported). Results of all pregnancy tests should be discussed .Patients should be instructed not to stop treatment but to consult their physician immediately should pregnancy occur.
4. Ensure that the patient receives supplies of 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.
5. Measure biochemistry including U&Es and Full Blood counts in line with local and national guidelines/protocols.
6. Titrate the dose ofr mycophenolic acid as necessary to the optimum level according to local/national guidelines.
7. Advise the GP when the dose should be changed.
8. Provide patient with treatment information leaflet.
9. Communicate promptly any changes in monitoring and modification of mycophenolic acid dose to the GP.
10. Communicate promptly any changes in test results to the GP.
11. Periodically (at six-monthly intervals in clinic) review the patient's clinical condition.
12. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
13. Follow up any adverse drug reactions reported by the GP and report back to the GP.
14. Advise the GP on related issues such as drug interactions.
15. 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 that the patient (both males and females) is aware of the importance of effective contraception and the need to immediately consult a physician if there is a possibility of pregnancy.(See precautions/contraindications page 7)
5. Ensure advice is sought from the secondary care clinician if there is any significant change in the patient's physical health status.

6. 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.
7. Carry out any investigations that are communicated and deemed appropriate.
8. Change the dose or stop treatment in line with instructions from the secondary care clinician.
9. 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 six 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

Mycophenolic acid (Myfortic®) is licensed for the maintenance of immunosuppression following kidney transplantation in adults.

Recommended Dosage and Administration

Mycophenolic acid (Myfortic®)

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

In order to retain the integrity of the enteric coating, Myfortic tablets should not be crushed.

Myfortic can be taken with or without food. Patients may select either option but must adhere to their selected option

Patients with severe renal impairment (glomerular filtration rate <25 $ml \cdot min^{-1} \cdot 1.73\ m^{-2}$) should be carefully monitored and the daily dose of Myfortic should not exceed 1,440 mg.

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

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

Adverse Effects

Please refer to BNF and the summary of product characteristics (SPC) for a full list.

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

Common or very common

Gastrointestinal disturbances including taste disturbance, gingival hyperplasia, nausea, vomiting, abdominal pain, constipation, flatulence, anorexia, weight loss, gastrointestinal inflammation, 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,leucopenia,pancytopenia,red cell aplasia, anaemia,thrombocytopenia disturbances of electrolytes and blood lipids, hyperglycaemia, arthralgias, alopecia, acne, skin hypertrophy and rash;

There have been published reports of bronchiectasis who receive mycophenolic acid in combination with other immunosupressants. Risk of bronchiectasis may be linked to hypogammaglobulinaemia or to a direct effect on the lung. Also isolated reports of interstitial lung disease and pulmonary fibrosis. It is recommended that patients who develop persistent pulmonary symptoms such as cough and dyspnoea are investigated.

Frequency not known

intestinal villious atrophy, progressive multifocal leucoencephalopathy, interstitial lung disease and pulmonary fibrosis

Drug Interactions

a) bioavailability of mycophenolate possibly reduced by metronidazole and norfloxacin,plasma concentration of mycophenolate possible reduced by co-amoxiclav. Plasma concentration of active metabolite of mycophenolate reduced by rifampicin.

b) Levels of mycophenolate and the plasma concentration of inactive metabolite are increased by: acyclovir and valaciclovir and possibly increased by ganiciclovir and valganciclovir.

c) Levels of mycophenolate are decreased by: antacids, oral iron and colestyramine. Levels possibly reduced by sevelamer.

d) Mycophenolate possibly reduces the absorption of phenytoin, and digoxin.

e) Avoid concomitant use with clozapine as may increase the risk of agranulocytosis.

f) Avoid use of live attenuated vaccines.

g) Colestilan, the manufacturers of colestilan advise against giving mycophenolate at least one hour before or 3 hours after colestilan.

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.
Increased risk of opportunistic infections (bacterial,fungal,viral and protozoal) , fatal infections and sepsis cases of hepatitis due to reactivation of hepatitis B or C have been reported in carrier patients treated with immunosupressants.
Use with caution in elderly patients, they have an increased risk of adverse events such as certain infections (including cytomegalovirus tissue invasive disease), gastrointestinal haemorrhage and pulmonary oedema, compared to younger patients.
Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding.(See monitoring section)
Patients with severe renal impairment should be carefully monitored and the daily dose of Myfortic should not exceed 1440mg.
No dose adjustments are needed for renal transplant patients with severe hepatic impairment.

Contraindications
Hypersensitivity to mycophenolate mofetil or mycophenolic acid
Mycofortic contains lactose. Patients with rare hereditary problems with galactose intolerance, the lapp lactase deficiency or glucose-galactose malabsorption should not take this product.
Pregnancy, breast feeding
Risk of serious birth defects associated with mycophenolate
Medicines and Healthcare Regulatory Agency (MHRA) have highlighted the associated high rate of serious birth defects and spontaneous abortions in the December 2015 edition of their Drug safety Update.
The MHRA have issued the following advice for health care professionals

- **Mycophenolate mofetil or mycophenolic acid should not be used in pregnancy unless there is no suitable alternative treatment to prevent transplant rejection**
- **Physicians should ensure that women and men taking mycophenolate mofetil and mycophenolic acid understand: the risk of harm to a baby; the need for effective contraception; the need to plan for pregnancy and change treatment as necessary; and the need to immediately consult a physician if there is a possibility of pregnancy**
- **Mycophenolate mofetil or mycophenolic acid treatment should only be initiated in women of child bearing potential when there is a negative pregnancy test result to rule out unintended use in pregnancy**
- **Mycophenolate mofetil or mycophenolic acid should only be given to women of childbearing potential who are using highly effective contraception**
- **Women should use 2 forms of effective contraception during treatment and for 6 weeks after stopping treatment**
- **Men (including those who have had a vasectomy) should use condoms during treatment and for at least 90 days after stopping treatment. This advice is a precautionary measure due to the genotoxicity of these products**
- **Female partners of male patients treated with mycophenolate mofetil or mycophenolic acid should use highly effective**

contraception during treatment and for 90 days after the last dose.

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.
- Patients report any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding
- Patients develop a cough and/or dyspnoea
- patients present with signs symptoms of an infection (bacterial,fungal,viral and protozoal)

Indication of Likely Cost of Therapy in Primary Care

January 2016

Mycophenolic acid (Myfortic®)	180mg £96.72 for 120 tablets
	360mg £193.43 for 120 tablets

Information Given to the Patient

Patient information leaflet available with each container of mycophenolic acid (Myfortic®).

Contact Details

Lincoln Renal Unit: 01522 573961

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Renal Pharmacist
County Hospital

References

1. BNF 70 September 2015 - March 2016.
2. SPC Myfortic Novartis Pharmaceuticals UK ltd. Last updated 2nd June 2015. eMC accessed 12th February 2016
3. MIMS February 2016
4. Leicester Medicines Strategy Group – Leicestershire statement on the use of generic immunosuppressants. March 2011.
5. MHRA Drug Safety Update . December 2016. Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men.

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