Basingstoke,Winchester and Southampton District Prescribing Committee

Shared Care Guideline: **Mycophenolate Mofetil**

Name of patient treated under this guideline: | |

This shared care guideline has been produced to support the seamless transfer of prescribing and patient monitoring from secondary to primary care, and provides an information resource to support clinicians providing care to the patient. It does not replace discussion about sharing care on an individual patient basis.

This guideline was prepared using information available at the time of preparation, but users should always refer to the manufacturer's current edition of the Summary of Product Characteristics (SPC or "data sheet") for more details.

1.0 Status of the Drug

Mycophenolate mofetil is an ester pro-drug of mycophenolic acid, an active immunosuppressant. It inhibits the proliferation of T and B lymphocytes by blocking the enzyme inosine monophosphate dehydrogenase. Mycophenolate mofetil is licensed for acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants.

Shared-care will only be considered once the patient has been stabilised on an immunosuppressant regimen and the patient is at least three months post transplant. In addition if the patient has any related conditions e.g. infection then these will be treated before shared care is requested.

Mycophenolate Mofetil is an "amber" drug using our local traffic light system. This means that treatment will be initiated in secondary care. When the patient is stabilised on the medication shared care arrangements can be considered. The key principle is that the GP is provided with information and given the opportunity to accept (or decline) prescribing responsibility before the transfer occurs. In accepting prescribing responsibility the GP also accepts responsibility for undertaking the activities outlined in this shared care guideline. Shared care arrangements should be definitive and agreed between the consultant, GP and patient

2.0 Licensed Indications and Dose

Mycophenolate Mofetil is licensed in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. At Southampton University Hospitals NHS Trust we follow guidance from the Addenbrookes transplant team and use mycophenolate mofetil if a patient has had a second biopsy proven rejection episode or are intolerant of azathioprine, in combination with other immunosuppressants.

The recommended oral dose of mycophenolate mofetil is 1.5g twice a day. Sometimes this dose is not tolerated and patients will be given a lower dose. The range seen for liver transplant patients is 500mg to 1.5g twice a day. Mycophenolate mofetil should be taken orally, on an empty stomach. Gastro-intestinal adverse-effects can be limited by splitting doses (e.g. 250mg four times daily), or by taking with food. If renal impairment is present specialist literature should be consulted.

Mycophenolate mofetil is available as 250mg capsules, 500mg tablets and a 1g in 5ml suspension.

It is important to note that there is another formulation of mycophenolate now available which has a different molar equivalent strength. Enteric-coated mycophenolate sodium (Myfortic®) 720mg is approximately equivalent to mycophenolate mofetil 1g. This shared care guideline is not related to Myfortic®.

THE TWO FORMULATIONS ARE NOT INTERCHANGEABLE. GPs are requested not to switch between brands.

3.0 Referral Criteria

Mycophenolate mofetil will be considered as an immunosuppressant for adult liver transplant patients who are intolerant of azathioprine or who have had a second biopsy proven rejection episode

4.0 Patient Selection

Patients will be selected according to their status pre and post transplant with regards to concurrent disease states, blood results and response to immunosuppression.

5.0 Safety Issues

5.1 Contra-indications (see BNF or SPC)

- Patients with a hypersensitivity to mycophenolate mofetil or mycophenolic acid.
- Women who are breastfeeding.
- Not recommended in pregnancy.

5.2 Cautions (see BNF or SPC)

- Patients receiving immunosuppressant regimens are at increased risk of lymphomas and skin malignancies. Avoiding excessive exposure to the sun and the use of high factor sunscreens are advised.
- Bone marrow suppression is a serious adverse effect associated with mycophenolate mofetil. Patients receiving mycophenolate mofetil should be instructed to report immediately any evidence of infection, unexpected bruising, bleeding or any other manifestation of bone marrow depression.
- Mycophenolate mofetil has been implicated in neutropenia; patients should be monitored for neutropenia as cessation of therapy may be indicated.
- Patients treated with mycophenolate mofetil will be immunocompromised and have an increased susceptibility to infection (including bacterial, protozoal, fungal and viral).
- Progressive multifocal leukoencephalopathy (PML) should be considered a differential diagnosis in patients reporting neurological symptoms on treatment with mycophenolate.
- Reports exist of mycophenolate causing pure red cell aplasia via an unknown mechanism. Reduction in dose or cessation of therapy can lead to reversal of the condition.
- Patients treated with mycophenolate should avoid the use of “live” vaccines; the response to vaccinations may be altered in immunocompromised patients. Specialist advice should be sought if wishing to vaccinate this group of patients.
- Gastrointestinal upset is the most common side effect (e.g. nausea, vomiting, abdominal discomfort, diarrhoea or constipation). If it is severe or persistent then refer to the consultant as mycophenolate mofetil has been associated with infrequent cases of gastrointestinal tract ulceration, haemorrhage and perforation. Mycophenolate mofetil should be used with caution in patients with active serious digestive system disease.
- Women of childbearing potential receiving mycophenolate mofetil should be advised to use effective contraception prior to, during and for six weeks following discontinuation of therapy. Patients discovered or planning to become pregnant should be referred to the initiating consultant at the earliest opportunity and be prescribed folic acid tablets.

5.3 Common Side Effects (See BNF or SPC)

Any adverse effects detected should be reported directly to the Consultant - it is vital that drug doses are not changed without consultation. See the manufacturer’s SPC & BNF for full details.

Very Common (≥ 1/10**)**: Sepsis, Gastrointestinal candidiasis, Urinary tract infection, Herpes simplex, Herpes zoster, Leucopenia, Thrombocytopenia, Anaemia, Vomiting, Abdominal pain, Diarrhoea, nausea.

Common (≥ 1/100, <1/10): Pneumonia, Influenza, Respiratory tract infection, GI infection, Candidiasis, Gastroenteritis, Infection, Bronchitis, Pharyngitis, Sinusitis, Fungal skin infection, Skin cancer, Pancytopenia, Leucocytosis, Acidosis, Hyperkalaemia, Hypokalaemia,

Hyperglycaemia, Hypomagnesaemia, Hypocalcaemia, Hypercholesterolemia, Hyperlipidaemia, Hypophosphataemia, Hyperuricaemia, Gout, Anorexia, Agitation, Confusion, Depression, Anxiety, Insomnia, Convulsion, Hypertonia, Tremor, Headache, , araesthesia, Tachycardia, hypo/hypertension, Pleural effusion, Dyspnoea, Cough, GI haemorrhage, , peritonitis, , Ileus, Colitis, Gastric ulcer, Duodenal ulcer, Gastritis, Oesophagitis, Stomatitis, Constipation, Dyspepsia, Flatulence, Eructation, Hepatitis, Jaundice, Hyperbilirubinaemia, Skin hypertrophy, Rash, Acne, Alopecia, Arthralgia, Renal impairment, Oedema, Pyrexia, Chills, Pain, Malaise, Asthemia, Hepatic enzyme increased, Blood creatinine increased, Blood lactate dehydrogenase increased, Blood urea increased, Blood alkaline phosphatase increased, Weight decreased

5.4 Drug Interactions (see BNF or SPC)

- *Aciclovir* – potential for higher aciclovir and mycophenolic acid glucoronide (MPAG - glucoronide of mycophenolic acid) when the two medications are given concurrently.
- *Antacids* with magnesium and aluminium hydroxides - a decrease in the absorption of mycophenolate mofetil may occur with concurrent administration.
- *Colestyramine* - a decrease in the absorption of mycophenolate mofetil may occur with concurrent administration and so there is the potential for reduced efficacy of mycophenolate mofetil.
- *Ciclosporin* – mycophenolic acid levels may be reduced with concurrent administration of ciclosporin.
- *Ganciclovir* - increases in both ganciclovir and MPAG plasma concentrations have been shown to occur with concomitant administration.
- *Iron preparations* – decreases in the absorption of mycophenolate mofetil have occurred with dual administration.
- *Probenecid* - prevents renal tubular secretion and hence causes an increase in MPAG plasma concentrations with concurrent administration.
- *Sevelamer* – moderately reduces mycophenolic acid levels. Mycophenolate should be taken 1-3 hours after sevelamer.
- *Valganciclovir* - increases in both ganciclovir and the inactive mycophenolic acid glucuronide (MPAG) plasma concentrations have been shown to occur with concurrent administration.
- *Rifampicin* may reduce the levels of mycophenolic acid.
- *Vaccines* may be less effective in immunosuppressed patients. Live vaccines should be avoided.

5.5 Pre-treatment Assessment

- Liver function and clotting
- Renal Function
- Full blood count
- Lipid profile

5.6 Routine Safety Monitoring

- The patient will be seen in hospital outpatient clinics: weekly for the first month post transplant, then monthly for the next 2 months, then every 3 months until the patient is two years post transplant and then every 6 months thereafter.
- Liver function tests & clotting, creatinine, urea &electrolytes, full blood count, blood pressure and weight will initially be performed/checked by the hospital. This will be taken over by the GP when they agree to shared care. These bloods will need to be checked every month for the first year of treatment by the GP.
- A Full blood count (FBC) will need to be checked weekly for the first month post transplant then fortnightly for the 2nd and 3rd months post transplant. After the first 3 months the FBC should then be checked on a monthly basis for the rest of the year then every 3 months thereafter.
- If any unusual or serious adverse effect is detected by the GP or if a full blood count/liver function test is found to be abnormal the GP must contact the hospital specialist for further advice.

6.0 Role of Consultant

The decision to use mycophenolate mofetil will be made by a specialist Hepatology consultant.

1. To assess the suitability of the patient for treatment with mycophenolate mofetil.
2. To discuss relevant safety issues with the patient, and to make them aware of cautions and side effects.
3. To initially prescribe and stabilise the patient on treatment. Prescribing should continue until at least 3 months post transplant.
4. To provide the patient with a current medication card for monitoring and/or to alert other clinical staff to the treatment they are receiving (or update the one they already hold).
5. To monitor liver function tests & clotting, creatinine, urea &electrolytes, full blood count, blood pressure and weight every 1-3 months as clinically needed, whilst prescribing remains in secondary care.
6. To take responsibility for ensuring FBC is conducted as appropriate until prescribing taken over by GP.
7. To monitor for treatment efficacy, for side effects and the patient's general condition every 3-6 months in clinic.
8. To ask the GP in writing whether they are willing to participate in shared care, this should include a copy of the shared care guideline.
9. To evaluate and answer any adverse events or concerns reported by the GP or patient.
10. To ensure prompt communication in writing with the GP of any changes to treatment, of assessment of response and any occurrence of adverse effects.
11. To advise the patient of arrangements being made to share care with their GP, including information of who will be monitoring each aspect of therapy and what side effects and concerns to report (and to whom).
12. Inform the GP of information given to the patient and if they have been given a medication card.
13. Inform the GP if the patient misses any clinic appointments.

7.0 Role of GP

1. To ensure all practice staff are aware of this shared care guideline.
2. To prescribe oral mycophenolate mofetil maintenance treatment according to dosage instructions from the hospital consultant. This will be at least 3 months post transplant and in accordance with this shared care guideline.
3. To monitor liver function tests & clotting, creatinine, urea &electrolytes, full blood count, blood pressure and weight every 1-3 months, once shared care has been agreed and prescribing has been taken over.
4. To take responsibility for ensuring a FBC is conducted as appropriate once shared has been accepted.
5. To contact the consultant if there are any concerns based on blood test results for advice.
6. Encourage patients to carry an up to date medication card.
7. To report any suspected adverse effects to the hospital consultant and MHRA as needed.
8. To ask the patient to report if they experience any unexplained rashes, oral ulceration/sore throat or unusual bruising.
9. Bone marrow suppression is a serious adverse effect associated with mycophenolate mofetil. If a patient presents with unexplained bruising, bleeding or signs of infection, request an urgent FBC and contact the hospital consultant for advice.
10. To check for possible drug interactions when newly prescribing or stopping concurrent medication.
11. Report to and seek advice from the consultant on any aspect of patient care that is of concern and may affect treatment.
12. If exposure to measles or chickenpox occurs consider the use of an appropriate preparation of immunoglobulin (varicella zoster immunoglobulin (VZIG) or human normal immunoglobulin (HNIG)). If exposed to chickenpox it may be beneficial to give prophylactic aciclovir in addition to VZIG or as an alternative when VZIG is not indicated. Please discuss with the hospital consultant before taking any action.
13. Ensure that the 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.
14. Administer the influenza vaccine annually.

15. Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.

8.0 Role of Patient

1. To take medications as prescribed.
2. Report any adverse effects to their GP or hospital consultant whilst taking the mycophenolate mofetil.
3. Ensure they have a clear understanding of their treatment and raise any outstanding queries.
4. Hold a medication record card and ensure it is updated. Alert other clinical staff to the treatment they are receiving.
5. Ensure correct administration and storage of the mycophenolate mofetil.
6. To attend hospital clinic and GP appointments as necessary and have blood tests at the appropriate time intervals.

9.0 Further Information

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