Sussex MSK Partnership

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OPT-OUT SHARED CARE GUIDELINE

It is assumed that shared care **will** be accepted unless the specialist is informed otherwise within 28 days of receipt of the request at the end of this document.

MEDICATION NAME: **Myophenolate Mofetil oral**

INDICATIONS COVERED: Rheumatoid Arthritis and other inflammatory conditions in Adults

NHS Brighton and Hove CCG, Crawley CCG and Horsham and Mid-Sussex CCG
Traffic Light System Classification: Amber

NOTES to the general practitioner (GP) or primary care prescriber

For medicines which require specialist initiation and/or dose titration and specific ongoing monitoring. For initiation, dose stabilisation and prescribing (including monitoring) by a specialist until the patient is stabilised (usually for 3 months) after which the GP may be asked to work under shared care through the use of approved shared care guidelines.
The expectation is that these guidelines should provide sufficient information to enable GPs or primary care prescribers to be confident to take clinical and legal responsibility for prescribing these medicines.

The questions below will help you confirm this:

- Is the patient currently under your care (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge)?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. It is assumed that shared care will be accepted unless the specialist is informed otherwise within 28 days of receipt of this request.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should inform the consultant or specialist within 28 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust or specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your CCG medicines management pharmacist will assist you in making decisions about shared care if you are unsure.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The GP or primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant or specialist.

Reason for update: New	**Prepared by:** SCT Medicines Management Team	**Updated by:** N/a
Approved by (Specialist or Consultant):		
Approved by (Chief Trust Pharmacist):		
Approved by (CCG Medicines Management Pharmacist): `		
Approved by Brighton and Hove CCG on: April 2017		
Approved by Crawley CCG, Horsham and Mid-Sussex CCG on: June 2017		

Information

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SPC website**: http://www.medicines.org.uk/emc/ .

2. **Background to use for the indication(s), including licence status:**

Mycophenolate is an immunosuppressive medicine; it is used for various indications including rheumatoid arthritis and other autoimmune diseases.

Mycophenolate is a licensed medicine with marketing authorisation for use in transplantation. Evidence exists for the use of this agent in some autoimmune diseases (see reference section).

3. **Dose & administration:**

Starting dose is usually 500mg daily for the 1st week, 500 mg twice daily for the 2nd week and then increased gradually by 500 mg each week until the optimal or maximum tolerated dose is reached. The typical dose is 1g to 2 g per day taken in two divided doses. The maximum dose is up to 3 g per day. Gastrointestinal adverse effects (most commonly diarrhoea and nausea) may be limited by increasing dose frequency (e.g. 500mg four times daily).

Time to response is usually 6 weeks to 3 months.

4. **Cautions:**

- Avoid excessive unprotected sun exposure and advise the patient to use a high factor sunscreen.
- Localized or systemic infection. Patients may have a decreased resistance to infection, including opportunistic infections.
- Patients with suspected lymphoproliferative disorder or unexplained anaemia, leucopenia and thrombocytopenia. Progressive multifocal leukoencephalopathy (PML) should be considered as a differential diagnosis in patients reporting neurological symptoms on treatment with mycophenolate.
- Patients with active serious digestive system disease.
- The very frail and elderly.
- In severe chronic renal impairment (glomerular filtration rate < 25 mL per min per1.73 m^2), doses greater than 1 g administered twice a day should be avoided.
- The capsules / tablets should not be opened or crushed to avoid inhalation or direct contact with skin or mucous membranes of the powder. If such contact occurs, wash thoroughly with soap and water; rinse eyes with plain water.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

5. **Contraindications:**

- Pregnancy. Any patient contemplating becoming pregnant must be seen by the specialist at the earliest opportunity to discuss the complex issues surrounding therapy with mycophenolate. Mycophenolate mofetil and its active metabolite mycophenolic acid are associated with a high rate of serious birth defects and increased risk of spontaneous abortion.
- Breastfeeding mothers. Any patient contemplating breast feeding must be seen by the specialist at the earliest opportunity to discuss the complex issues surrounding therapy with mycophenolate mofetil.
- Localised or systemic infections.
- Live vaccines (see drug interaction section).
- Hypersensitivity to mycophenolate or the excipients.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

6. Side effects:

The principal adverse reactions include diarrhoea, leucopenia, sepsis and vomiting, and there is evidence of a higher frequency of infections, including opportunistic infections.

Table 1. Side effects and actions to take for abnormal results

Contact Rheumatology and consider interruption of treatment if any of the following develop:

White Cell Count $<3.5x10^9$/l	Mean cell volume >105 f/l
Neutrophils $<1.6\ 10^9$/l	Creatinine increase >30% over 12 months and/or calculated GFR
Unexplained eosinophilia $>0.5\ 10^9$/l	ALT and/or AST >100 U/l
Platelet count $<140\ 10^9$/l	Unexplained reduction in albumin <30 g/l

Whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

7. Notable drug interactions:

- Aciclovir: Causes increase in the concentration of both mycophenolate mofetil and aciclovir (the increase is significant in renal impairment).
- Antacids, such as magnesium and aluminium hydroxides, and proton Pump Inhibitors (PPIs), including lansoprazole and pantoprazole cause a decrease in the absorption and bioavailability of mycophenolate mofetil.
- Cholestyramine: May decrease the absorption and bio-availability of mycophenolate mofetil.
- Probenecid: Prevents renal tubular secretion and causes an increase in plasma concentration of mycophenolate mofetil.
- Rifampicin: Plasma concentration of the active metabolite of mycophenolate is reduced.

Vaccines:

- Patients must not receive immunisation with live vaccines. **AVOID LIVE VACCINES**.
- Inactivated vaccines such as influenza vaccine are safe to use although they may elicit a lower response.
- In patients exposed to chickenpox or shingles, passive immunisation should be carried out using immunoglobulin.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

8. Criteria for use:

Chronic inflammatory conditions as determined by the appropriate specialist according to this shared care guideline. Specialist has initiated and dose stabilised (usually for a minimum 3 months).

GP or Primary Care Prescriber confident to take clinical and legal responsibility for prescribing this drug.

9. Any further information (e.g. supporting therapies):

Mycophenolate mofetil 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 should use highly effective contraception during treatment and for 90 days after the last dose. See MHRA Drug Safety Update in reference section.

10. References:

British Society for Rheumatology, Immunisation against shingles in people with inflammatory rheumatic disease. Available at http://www.rheumatology.org.uk/includes/documents/cm_docs/2013/i/immunisation_with_zostavax_for_people_with_inflammatory_rheumatic_disease.pdf (accessed 13/3/17).

BSR/BHPR Non biologic DMARD guidelines 2017 Ledingham, J et al. Available at http://www.rheumatology.org.uk/includes/documents/cm_docs/2016/f/full_dmards_guideline_and_the_executive_summary.pdf

Immunisations against infectious diseases (Green Book online), Chapter 34: Varicella. Updated Aug 2015. Available at https://www.gov.uk/government/publications/varicella-the-green-book-chapter-34 (accessed 24/1/2017)

Joint Formulary Committee. British National Formulary; Mycophenolate mofetil, Sep 2015, British Medical Association and Royal Pharmaceutical Society. London. Available at: https://www.medicinescomplete.com/mc/bnf/current/ (accessed 13/3/17).

Medicines and Healthcare products Regulatory Agency (MHRA): Drug Safety Update Volume 9, Issue 5, December 2015.Mycophenyolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/485099/Drug_Safety_Update_Dec_2015.pdf (accessed 13/3/17).

Summary of Product Characteristics, Cellcept® 250mg & 500mg Capsules. Roche Products Limited. Available at: http://www.medicines.org.uk/emc/ (accessed 13/3/17)

Summary of Product Characteristics, Mycophenolate Mofetil 250 mg & 500mg Capsules. Accord Healthcare Limited. Available at: http://www.medicines.org.uk/emc/ (accessed 13/3/17).

Summary of Product Characteristics, Mycophenolate Mofetil 500mg Tablets. Wockhardt UK Ltd. Available at: http://www.medicines.org.uk/emc/ (accessed 13/3/17).

Surrey and Sussex Healthcare NHS Trust, Shared Care Prescribing Guideline: Mycophenolate Mofetil for non-transplant indications. Available at: http://www.horshamandmidsussexccg.nhs.uk/intranet/clinical/programmes/medicines-management/ (accessed 13/3/17).

UKMI. *Suggestions for Drug Monitoring in Adults in Primary Care.* February 2014. Available at http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug%20monitoring%20document%20Feb%202014.pdf (accessed 13/3/17)

RESPONSIBILITIES and ROLES

Consultant or specialist responsibilities	
1	Confirm diagnosis and indication for treatment with mycophenolate mofetil.
2	To discuss fully the aims, benefits, risks and side effects of treatment and a treatment plan with the patient and/or carer and written information to be supplied to the patient and/or carer.
3	Prior to treatment ask GP whether patient has had pneumococcal vaccination and flu vaccination and, if not, immunise (unless contra-indicated).
4	Inform GP when initiating treatment so the GP is aware what is being prescribed and can add to GP clinical record.
5	Undertake baseline monitoring as required (specific to the medication).
6	Record other medications and address potential medicine interactions before starting therapy.
7	Discuss the potential implications of pregnancy and breastfeeding in women of child bearing potential and agree a risk minimisation strategy. Treatment should only be initiated in women of child bearing potential when there are negative pregnancy test results to rule out unintended use in pregnancy. Ensure that women and men 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
8	To initiate treatment by prescribing and monitoring usually for a minimum of 3 months.
9	Undertake monitoring if dose changed.
10	Monitor and prescribe according to guidelines until handover is appropriate (including when dose changes are made).
11	Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment.
12	Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to, or a copy of, the shared care guideline when requesting transfer of prescribing to GP or primary care prescribers.
13	Advise GP if treatment dose changes or treatment is discontinued.
14	Inform GP if patient does not attend planned follow-up.

GP or primary care prescriber responsibilities	
1	Continue prescribing of mycophenolate mofetil at the dose recommended and undertake monitoring requirements.
2	Undertake all relevant monitoring as outlined in the monitoring requirements section below, and take appropriate action as set out in this shared care guideline.
3	Monitor for adverse effects throughout treatment and check for medicine interactions on initiating new treatments.
4	Add information about the medicine to the patient record, initially as "hospital prescribed", and highlight the importance that this medicine is only to be prescribed under a shared care guideline in primary care.
5	Inform the consultant or specialist of any issues that may arise.
6	Refer patient back to the Consultant/Specialist if any concerns.
7	Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline (e.g. ensuring the patient record is correct in the event of a patient moving surgery).

Monitoring requirements and appropriate dose adjustments

Commencing therapy:
Two negative pregnancy test results with a sensitivity of at least 25 milli-international units per millilitre (mIU/mL) to rule out unintended use in pregnancy. The second test should be done 8–10 days after the first one and immediately before starting mycophenolate mofetil.
Best practice should include documentation of height, weight and blood pressure prior to commencing therapy
• FBC, creatinine/ calculated GFR, ALT, and / or AST and albumin every:
  ○ 2 weeks until on stable dose for 6 weeks; then
  ○ Once on stable dose, monthly FBC, creatinine/ calculated GFR, ALT and / or AST and albumin for 3 months and thereafter,
  ○ FBC, creatinine/ calculated GFR, ALT and / or AST and albumin at least every 12 weeks*.

* More frequent monitoring is appropriate in patients at higher risk of toxicity.

1 Monitor for adverse drug reactions throughout treatment.
2 Check for drug interactions on initiating new treatments.
3 Provide patient with pneumococcal vaccination and flu vaccination unless contra-indication
4 Pregnancy tests should be repeated as clinically required (e.g., after any gap in contraception is reported).
5 Whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance.

Patient and/or carer role
1 Make sure that you understand the treatment and ask for more information, if needed.
2 Share any concerns in relation to treatment with whoever is prescribing this medicine for you.
3 Tell the prescriber of this medication about any other medication being taken, including over-the-counter products.
4 Read the patient information leaflet included with your medication and report any side effects or concerns you have to whoever is prescribing this medicine for you.
5 Report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding.
6 Attend any follow up appointments with the consultant or specialist.
7 Attend any monitoring appointments (e.g. blood tests).

SHARED CARE GUIDELINE

MEDICATION NAME: Mycophenolate mofetil

INDICATION: Rheumatoid Arthritis and other inflammatory conditions in Adults

DATE OF REQUEST:

Agreement to transfer prescribing to general practice or primary care prescriber:

Patient details:

Name:
Address:
DoB:
NHS No:
Hospital No:

Medication name, form and strength: Mycophenolate mofetil

The following tests and investigations have been carried out:

Date treatment initiated:

At the last patient review the medication appeared to be effectively controlling symptoms or providing benefit:
Yes/No

The patients has now been stabilised on a dose of:

The patient has been given written information about their medication:
Yes/No

The patient understands that this medication is being prescribed under a shared care agreement between their GP and specialist and that they have responsibilities under the agreement to ensure they attend their GP to be regularly monitored.
Yes/No

The patient has been informed that the GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient persistently does not attend for monitoring:
Yes/No

Date of next clinic appointment:

If the practice declines shared care, then the named consultant or specialist should be informed within 28 days of receipt of this request. Forms used to decline prescribing can be found here:

Brighton and Hove CCG:
http://www.gp.brightonandhoveccg.nhs.uk/prescribing/joint-formulary-supporting-information
Crawley CCG, Horsham and Mid Sussex CCG:
http://www.horshamandmidsussexccg.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=415216

BACK-UP ADVICE AND SUPPORT

	Name and position	Telephone	Email
Specialist or Consultant			
Alternative specialist (e.g. departmental contact)			

Specialist pharmacist			
Out of hours (e.g. medical team on call)			

Link to full SCG: http://