# MYCOPHENOLATE MOFETIL

**For up to date version of Shared Care Agreement contact specialist team or latest version on website https://westessexccg.nhs.uk/your-health/medicines-optimisation-and-pharmacy/shared-care-medicines**

## Referral Criteria

- These guidelines are for patients over 16 years of age.
- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patients' GP
- Safe prescribing must be accompanied by effective monitoring
- When transfer is agreed, the patient will be given a supply of mycophenolate sufficient for 4 week maintenance therapy
- **The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.**

From April 2019 West Essex patients under the care of Princess Alexandra Hospital Rheumatology Consultant will be assessed and those patients with stable disease markers and DAS<3.2 after 6 months of consultant led care will be transferred for ongoing case management to a West Essex General Practitioner with Specialist Interest (GPSI) in Rheumatology. Thereafter shared care for the management of DMARD will be between the Consultant/GPSI (further referred to as Specialist) and the GP.

## SHARED CARE RESPONSIBILITIES

**Consultant**

1. Ensure that patient understands risks and benefits of medication and has read appropriate information leaflet.
2. Ensure the patient understands the shared care agreement and has signed the Patient Agreement Letter (page 8-9)
3. Perform baseline tests (see Monitoring section) and provide results to GP
4. Ensure patient has effective contraception in line with MHRA advice December 2015
5. Initiate treatment and prescribe until the patient has been on a stable dose for minimum of SIX weeks
6. Promptly send a letter to the GP requesting shared care for this patient.
7. Review the patient in outpatients as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the specialist.
8. Inform GP, by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.
9. Evaluate any reported adverse effects by GP or patient.
10. Inform GP of patients who do not attend clinic appointments, admin to contact patient to rearrange.
11. Ensure that backup advice is available at all times. (see Contacts section) and respond to any GP queries as soon as practicable.
12. Report any adverse effects to the GP and CHM http://www.mhra.gov.uk/Safetyinformation/Howwemonitorthesafetyofproducts/Medicines/TheYellowCardScheme/Informationforhealthcareprofessionals/index.htm
13. For patients under the care of Princess Alexandra Hospital Rheumatology Consultant refer patients with stable disease markers and DAS<3.2 for ongoing case management after 6 months of consultant led care to General Practitioner with Specialist Interest in Rheumatology; inform the GP.

**General Practitioner with Specialist Interest in Rheumatology** (for West Essex patients under the care of Princess Alexandra Hospital)

- Accept patients with stable disease markers and DAS<3.2 for ongoing case management after 6 months of consultant led care.
- Provide ongoing patient education
- Annual review of all patients as per NICE guidance
- Review the patient annually or as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the Specialist.
- Inform GP, by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Evaluate any reported adverse effects by GP or patient.

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- Inform GP of patients who do not attend clinic appointments and contact patient to rearrange.

**General Practitioner**

1. Monitor patient's overall health and well-being.
2. Consider request to prescribe under shared care arrangements and reply only if you do not agree to share care, in a timely manner within 14 days as outlined on page 7 with clinical reasons and return to Consultant and Pharmacy department.
3. Ensure compatibility with other concomitant medication.
4. Ensure patient has effective contraception in line with MHRA advice December 2015
5. Prescribe at the dose recommended.
6. Monitor U&E, creatinine, FBC and LFTs at recommended frequencies (see Action and Advice) and refer if abnormal.
7. Adjust the dose as advised by the specialist.
8. Stop treatment on advice of specialist or immediately if any urgent need to stop treatment arises.
9. Report any adverse events to the specialist and CHM: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
10. Inform specialist of any change in the medical condition of patient which may have effect on disease / medications.
11. Ensure patient is offered an annual flu vaccination and a one off pneumococcal vaccination

**Patient**

1. Report to specialist or GP if there is not a clear understanding of their treatment and discuss any concerns in relation to treatment
2. Report any adverse effects to their Specialist whilst taking Mycophenolate, especially unexplained bruising/bleeding, fever, infections or mouth ulcers which should be reported immediately.
3. Report any changes in disease symptoms to Specialist whilst taking Mycophenolate.
4. Take effective contraception as advised by Specialist and GP
5. Alert GP immediately should pregnancy occur.
6. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy whilst taking Mycophenolate.
7. Try to avoid contact with chickenpox and shingles if no definite history of chickenpox, and report any such contact to urgently to their GP and/or consultant
8. Inform GP or specialist of any other medicines being taken including over-the-counter products.
9. Attend for regular reviews and blood monitoring tests

## CONTACT NUMBERS FOR ADVICE AND SUPPORT

**Advice and guidance:** Access Advice & Guidance tool via e-RS referral system selecting the relevant specialty for non-urgent queries

| **Princess Alexandra Hospital NHS Trust - Gastroenterology** | |
|---|---|
| Consultant | **For GPs only**: contact Gastroenterologist of the week via switchboard if urgent<br>**Email for GPs only**:<br>tpa-tr.gastroadminclinicalcorrespondence@nhs.net |
| Specialist Gastroenterology Pharmacist:<br>Clare Macpherson | Bleep 272 Direct dial: 01279 278224 (voicemail if not answered)<br>Claremacpherson@nhs.net for medication issues |
| IBD Specialist Nurse | Direct dial:01279 278223 (voice mail only) usual response within 48 hours<br>Paht.ibd@nhs.net |

| **Princess Alexandra Hospital NHS Trust - Rheumatology** |
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| | |
|---|---|
| Consultant: | **For GPs only**: contact Rheumatologist via switchboard if urgent tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net for non-urgent queries. |

| | |
|---|---|
| Rheumatology Specialist Nurse DMARDs | 01279827434 helpline (voice mail only) for non-urgent queries only Lily Robinson |
| Rheumatology Specialist Nurse / Pharmacist - Biologics | 01279827819 helpline (voice mail only) for non-urgent queries only Mona Kamal Zou / Sachini Amarasekera |
| | **Patients can email** tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net for non-urgent queries. |

| **Princess Alexandra Hospital NHS Trust - Dermatology** | |
|---|---|
| Consultant: | **For GPs only**: contact Dermatologist via switchboard if urgent 01279 444455 Ext 7431 / 7421 for non-urgent queries only tpa-tr.dermatologyclinicalcorrespondence@nhs.net |
| Specialist Pharmacist Dermatology | Noemi.corrao@nhs.net |

| **Princess Alexandra Hospital NHS Trust - Pharmacy** | |
|---|---|
| Medicines Information (for medicines related queries) | 01279 827054 |

## CLINICAL INFORMATION

### Prescribed Indications covered by this Shared Care Agreement

The following unlicensed autoimmune disorders:
Severe refractory Eczema[1]
Systemic lupus erythematosus[1]
Lupus nephritis[1]
Dermatomyositis[1]
Polymyositis[6]
Psoriasis[1]
Atopic dermatitis[1]
Autoimmune bullous dermatoses[1]
Rheumatoid arthritis[7]
Scleroderma[2]
Crohns disease and ulcerative colitis[3-5]
Please see tertiary centre shared care agreements for transplant use.

### Therapeutic Summary

Mycophenolate mofetil (MMF) is a pro-drug of mycophenolic acid. It is a reversible inhibitor of inosine monophosphate dehydrogenase and thus inhibits purine synthesis, with potent cytostatic effects on both T- and B-lymphocytes. It does not inhibit production of interleukins as does ciclosporin and tacrolimus.

Different brands and formulations of Mycophenolate have small differences in bioavailability, but this is not a problem in this group of patients. (Transplant patients need to be prescribed the brand specified by the transplant centre)

Time to response is usually between 6 weeks and 3 months.
See SPC for full details http://www.medicines.org.uk/emc/medicine/1680

### Dose and Route of Administration

**Rheumatology**
Starting dose of 500mg daily for the first week, 500mg twice daily for the second week then gradually increased by 500mg each week until the optimal or maximum tolerated dose is reached.
Maximum dose 3g daily in two divided doses.

**Dermatology**
Starting dose of 250-500mg twice a day which can be increased to 1g twice a day.

**Gastroenterology**

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Doses range between 500mg and 2g twice a day

## Adverse Effects and Management

**Gastrointestinal upset** is the most common side effect (e.g. nausea, vomiting, abdominal discomfort, diarrhoea or constipation). If severe or persistent, refer back to specialist.
**Anaemia, leucopenia and thrombocytopenia** are most likely to be discovered through regular monitoring, but prescribers should be alert for any unexplained bruising or bleeding

**Opportunistic infections**
Progressive multifocal leukoencephalopathy (PML) should be considered a differential diagnosis in patients reporting neurological symptoms on treatment with mycophenolate.

## Cautions

**Immunosuppression:** For patients who have not had chicken pox and are in contact with anyone with the virus follow guidance from Public Health England June 2019 https://www.gov.uk/government/publications/varicella-zoster-immunoglobulin
**Cancer risk:** Patients receiving mycophenolate are at increased risk of lymphomas and skin malignancies. Avoiding excessive exposure to the sun and use of high factor sunscreen are recommended.
**Vaccines:** live vaccines should be avoided.
**Genetic deficiencies:** Mycophenolate mofetil is an IMPDH (inosine monophosphate dehydrogenase) inhibitor. On theoretical grounds therefore it should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.

## Contraindications

- Hypersensitivity to mycophenolate, myophenolic acidor to any of the excipients.
- Pregnancy
- Breastfeeding.

## Pregnancy and Lactation

**Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men**
Mycophenolate mofetil and its active metabolite mycophenolic acid are associated with a high rate of serious birth defects and increased risk of spontaneous abortion.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/485099/Drug_Safety_Update_Dec_2015.pdf

- 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.
- Two serum or urine pregnancy tests with a sensitivity of at least 25 mIU/mL are recommended. The second test should be done 8–10 days after the first one and immediately before starting mycophenolate mofetil. Pregnancy tests should be repeated as clinically required (eg, after any gap in contraception is reported). Results of all pregnancy tests should be discussed with the patient.
- 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

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- 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 . UPDATED CONTRACEPTION ADVICE FOR MALE PATIENTS FEB 18.
- 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
- Patients should be instructed not to stop treatment but to consult their physician immediately should pregnancy occur.
- Breast feeding is contra-indicated

## Interaractions with other medications

As mycophenolate metabolites undergo extensive enterohepatic recirculation, any drugs which may interfere with this pathway should be avoided:

- Antacids containing magnesium or aluminum hydroxide – reduces absorption of MMF
- Cholestyramine should not be taken at the same time of day as this will impair the absorption of mycophenolate mofetil.
- Probenicid
- Aciclovir & ganciclovir
- Rifampicin –reduces plasma concentrations of active metabolite of mycophenolate.
- Metronidazole and norfloxacin – possibly reduce bioavailability of mycophenolate.

See current BNF for more information.

## Monitoring Standards for Mycophenolate based on BSR BHPR Standards 2017

The following standards have been agreed for the monitoring of Mycophenolate in all patients at Princess Alexandra Hospital NHS Trust.

| | | |
|---|---|---|
| **Pre-treatment by Specialist** | Height, weight, blood pressure , FBC, U&Es including eGFR, LFTs, chest X-ray fasting lipids.<br>Negative pregnancy test in those of child bearing potential | |
| **Initial monitoring by Specialist** | FBC<br>Creatinine / calculated GFR<br>ALT +/- AST<br>Albumin | Every 2 weeks until on stable dose for 6 weeks. |
| **Ongoing monitoring by GP** | FBC<br>Creatinine / calculated GFR<br>ALT +/- AST<br>Albumin | Then once on stable dose monitor monthly for 3 months. |
| | FBC<br>Creatinine / calculated GFR<br>ALT +/- AST<br>Albumin | At least every 12 weeks. |
| | Lipids | 6 monthly |
| | Pregnancy test | If there is a break in contraception ensure negative pregnancy test in those of child bearing potential |
| **Dose increase** | FBC<br>Creatinine / calculated GFR<br>ALT +/- AST<br>Albumin | Every 2 weeks until on stable dose for 6 weeks, then revert to previous schedule |

## Action and Advice

If a GP has taken blood tests for the general medical management of a patient and blood test results fall into the categories below or the patient reports one of the adverse events below, these are recommendations for considering the withdrawal of Mycophenolate therapy:

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| **Blood Test Results** | |
|---|---|
| WBC < 3.5 x $10^9$/l | Withhold until discussed with specialist team |
| Neutrophils < 2.0 x $10^9$/l | Withhold until discussed with specialist team |
| Platelets < 150 x $10^9$/l | Withhold until discussed with specialist team |
| Unexplained reduction in albumin <30 g/l | Discuss with specialist team |
| Creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min | Withhold until discussed with specialist team |
| Lipids | Discuss abnormal result with specialist team |
| > 2-fold rise in AST, ALT (from upper limit of reference range) | Withhold until discussed with specialist team |
| **Symptoms** | |
| Unexplained rash | Withhold until discussed with specialist team |
| Abnormal bruising or bleeding | Withhold until FBC results available & discuss with specialist team |
| Severe sore throat | Withhold until FBC results available & discuss with specialist team |

## References

1) The Emergence of Mycophenolate Mofetilin Dermatology

2) Scleroderma: oral mycophenolate

3) Mycophenolate mofetil therapy in the management of inflammatory bowel disease – A retrospective caseseries and review MR Smith et al; Journal of Crohn's and Colitis (2014); 8, 890-897

Mycophenolate for IBD.pdf

4) Use of mycophenolate mofetil in inflammatory bowel disease. Tan T1, Lawrance IC. World J Gastroenterol. 2009 Apr 7;15(13):1594-9.

5) Mycophenolate mofetil in refractory inflammatory bowel disease. A. C. Ford et al. Aliment Pharmacol Ther 2003; 17: 1365–1369.

6) Treatment of inflammatory myopathy: emerging therapies and therapeutic targets

7) Mycophenolate mofetil in the treatment of adults with advanced rheumatoid arthritis: three 24-week, randomized, double-blind, placebo- or ciclosporin-controlled trials.

## Further Information

This document does not replace the SPC and BNF and should be read in conjunction with it.
BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs 2017 https://academic.oup.com/rheumatology/article/3053478/BSR-and-BHPR-guideline-for-the-prescription-and?searchresult=1
West Essex Shared Care Guidelines
https://westessexccg.nhs.uk/your-health/medicines-optimisation-and-pharmacy/shared-care-medicines
CKS
http://cks.nice.org.uk/dmards#!scenario
Risk Minimisation Materials
www.medicines.org.uk/emc/.
MHRA and in particular the advice for mycophenolate
https://www.gov.uk/drug-safety-update

# MYCOPHENOLATE MOFETIL

## GP response to Shared Care Agreement

(only complete & send if NOT participating in shared care)

**This shared care agreement has been approved by the Medicines Management Optimisation Programme Board June 2016**

| | |
|---|---|
| Patient Name: | NHS No: |
| Consultant: | Medicine requested for shared care: **Mycophenolate Mofetil** |

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care agreement. My clinical reasons for declining shared care for this patient are listed in the box below:

| |
|---|
| |

Yours sincerely

{GP name}

{Surgery}

**Please send a copy of this response to:**

1. The specialist/consultant requesting shared care
2. **ANONYMISED COPY OF THIS FORM ONLY** to the E-MAIL: **tpa-tr.ClinicalPharmacy@nhs.net**

(sending a copy of this form to the PAH pharmacy will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG Medicines Optimisation Team of the reasons shared care is not being undertaken by GPs allowing for changes to be made in future updates to improve patient safety)

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The Prlncess Alexandra Hospltal NHS
NHS Trust

Information for patients:

# SHARED CARE:
# Agreement information and confirmation

Hamstel Road
Harlow, Essex
CM20 1QX

Tel: 01279 444455

**Patient name:**

.....

**Medicine:**

.....

**We would be grateful if you would take time to read this information as it will help us work with you to manage your condition and ensure safe prescribing of the specific medicine listed above.**

## What is a Shared Care Agreement (SCA)?

A Shared Care Agreement (SCA) enables the care you have for a specific condition to be shared between the hospital and your GP.

The agreement means that the medicine the hospital has started, can be continued by your GP, so you won't have to visit the hospital to collect your medicine.

The SCA gives information on your medicine, guidance on the prescribing and monitoring responsibilities for your consultant (in the hospital), your GP and you. For an SCA, to work everyone involved must understand it and communicate effectively.

Your consultant and your GP will need to sign the agreement and if you agree to this approach, we would ask you to sign this letter, to indicate your agreement to have your care managed in this way.

## How does shared care work?

**Your consultant and GP share responsibility for your care.**

The consultant is a specialist in your condition and will start prescribing your medicine, making sure it is suitable for you. There will come a point in your treatment when you may not need to be monitored by the consultant as often and this monitoring can be done by your GP.

Once your GP has agreed to the SCA, they will be able to prescribe the same medicine for you at the dose recommended by the consultant.

The organisation which regulates GPs, the General Medical Council, says that 'when a GP prescribes a medicine, the GP needs to satisfy themselves that the prescription is needed, appropriate for the patient and within the limits of their competence'.

So, your GP can only issue a prescription if the consultant and you keep to the responsibilities you have agreed (see below). If responsibilities are not kept or if the GP no longer feels it is safe to prescribe the medicine, he/she will explain the reasons to you and your consultant, then prescribing responsibilities will be transferred back to the hospital.

## What do I need to do to ensure the SCA can continue?

- **Attend hospital outpatients**
  You must still attend the hospital for regular reviews as directed by your consultant (these may be less frequent than before and you may be seen by a specialist pharmacist or a specialist nurse). If you do not attend your hospital appointments, your GP will not be able to continue issuing prescriptions for this medication.

- **Attend GP appointments**
  You must attend any appointments you have with your GP in relation to this medicine, so they can look after you effectively

- **Have blood tests as you have been advised to:** Your consultant should have informed you if and how often you need to have blood monitoring tests. You can usually have your blood taken at an appropriate clinic and not need to go to the hospital.

- If you do not have the blood monitoring tests as advised by your consultant, your GP will no longer be able to issue you with prescriptions as it would not be safe to do so.

## What do I do if I am having side-effects to the medicine?

Your consultant should have informed you of the common side-effects to expect and what to do if you experience them. If you think you may be having side-effects from a medicine report these directly to your consultant. Your GP may need to seek advice from your consultant before issuing you with another prescription; this is to ensure it is safe for you to continue on the medication.

## What if my disease symptoms change or get worse?

Report any changes in disease symptoms or circumstances that could affect management of your disease to your consultant.

## What about the other medicines I take?

Inform your GP and the consultant of all other medicines you are taking, including those you may have bought yourself. Do not take new medicines (including those you could buy) until you have discussed this with your pharmacist, GP or consultant.

If you would like to go ahead with a shared care agreement for the specific medication identified on page 1, please sign below to confirm that you:

- Understand the shared care agreement.

- Are happy to have your care for this aspect of your health managed by a shared care agreement.

- You agree to attend regular review appointments as requested.

- You agree to have blood tests as required.

## What happens if I change GP Practice?

If you register at a new GP Practice a new agreement needs to be put in place between your new GP and the specialist team.

The specialist team can start this process if you provide them with information before you move to make sure there is a smooth handover.

Patient's signature .....

Date .....

Print name .....

If at any point in time you would like this shared care agreement to stop, please talk to your GP.