Oxford University Hospitals NHS
NHS Foundation Trust

NHS
Oxfordshire
Clinical Commissioning Group

# MYCOPHENOLATE FOR USE IN ADULT RHEUMATOLOGY
## Shared Care Protocol

**This protocol provides prescribing and monitoring guidance for mycophenolate mofetil therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF**

## Shared Care Protocol – Responsibilities

Shared care assumes communication between the rheumatology specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. See Rheumatology Shared Care Responsibilities document for further information.

***Rheumatology Specialist Team***

**At the start of treatment:**

- Complete pre-treatment assessments, including baseline tests, in accordance to the specific shared care protocol
- Initiate treatment by prescribing the first 56 days
- Supply the patient with 3 blood cards (for FBC, U&E and LFTs) and inform patients to book and attend blood tests at 2, 4 and 6 weeks after starting treatment
- Ensure that patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly, as part of obtaining informed agreement to shared care
- Provide a copy of the drug-specific patient information leaflet (or direct patient to Versus Arthritis website https://www.versusarthritis.org/about-arthritis/treatments/drugs/)
- Provide a copy of OUHFT 'Rheumatology Shared Care Monitoring Card' to the patient and/or carer, which includes contact details for the rheumatology advice line
- Send a letter to the GP requesting shared care once dose is stable, confirming the above has been completed. Include any results from pre-treatment assessments if appropriate. Provide details of the dose to be continued. Outline shared care protocol criteria and/or direct them to the relevant document on the Oxfordshire CCG website

**After 2-6 weeks of treatment:**

- Check blood test results from week 2, week 4 and week 6 (available on EPR for Oxfordshire patients/contact GP practice for blood results if patient's GP practice is not in Oxfordshire)
- Ensure any abnormal results are acted upon promptly

**After 4-6 weeks of treatment:**

- Conduct a consultation with the patient and/or to check that the patient is not experiencing any issues or side effects.
- Confirm that the patient is stable (no side effects, tolerating the drug and established on monthly blood tests). Communicate this information in a shared care handover letter to the GP. Shared care can now commence.
- If the patient is not stable requiring change in the treatment regime, the patient will remain under the care of the specialist until they become stable, as above.



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**Unless any concerns are raised by the GP within 14 days, shared care will be assumed and the patient will collect the next prescription from the GP. [6]**

**During treatment:**

- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments
- Be available to give advice to GP and patient
- If the dose is increased, patient's bloods will be monitored as above
- If dose is decreased, additional monitoring may not be required at discretion of the rheumatology specialist - this will be clearly communicated in the clinic letter and the existing monitoring schedule should continue

***GP***

- Ensure that provision has been made for the patient to have blood monitoring as per local arrangements
- Prescribe medication once the dose is stable or shared care is agreed
- Ensure all monitoring is completed in accordance to 'Recommended monitoring schedule for patients taking disease-modifying anti-rheumatic drugs (DMARDs)'
- Check results then advise the specialist of any deteriorations or abnormal results. Results should be recorded on the monitoring card if the GP practice is outside of Oxfordshire.
- Notify the specialist to any changes in patient's condition, any adverse drug reactions or failure to attend tests
- If a patient fails to attend for monitoring:
  - Only issue a 28 day prescription and book them in for the next available appointment for a blood test
  - If they fail to attend a second blood test then contact the specialist team for advice and to discuss suitability for continuing treatment before supplying further prescriptions

***Patient and/or carer***

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Ensure that they are booked in for blood test monitoring as per local arrangements and attend as required
- Attend all hospital and GP appointments as scheduled
- Ensure monitoring card is kept up to date and is brought to all appointments (especially patients whose GPs are out of Oxfordshire)
- Report any side effects to the GP or a member of the specialist team

## BACKGROUND

Mycophenolate mofetil (MMF) is an immunosuppressive drug. It is often referred to as a "steroid sparing agent" or "immunomodulator." Mycophenolate mofetil should only be initiated on the recommendation of a specialist.

In rheumatology, it is used for:

- Used for systemic lupus erythematosus (SLE), vasculitis and related inflammatory conditions (unlicensed indication but supported by British Society of Rheumatology guidelines)

## DOSAGE

- Usual oral starting dose is 500mg daily, increasing by 500mg weekly until optimum or maximum tolerated dose is reached.

Week 1: 500mg each morning
Week 2: 500mg bd
Week 3: 1g each morning and 500mg each evening
Week 4: 1g bd (usual maintenance dose)

- The typical dose is 1-2g daily in divided doses, up to a maximum dose of 3g per day.
- The therapeutic benefit will often be seen after 3 months of therapy.
- Available as 250mg capsules, 500mg tablets or 1g/5ml oral suspension. There is no clinical difference in generic or branded preparations of MMF. It should therefore be prescribed **generically**.
- The tablets or capsules should be swallowed whole and not crushed or broken, with or after food.

## PRE-TREATMENT ASSESSMENT

FBC, including platelets and differential, U&Es, LFTs, CRP and urinalysis, Chest X-ray.

Pregnancy testing must be carried out for women of childbearing age, as mycophenolate is teratogenic. Treatment should not be initiated without providing a negative pregnancy test to rule out unintended use in pregnancy. Women of child bearing age should use highly effective contraception if prescribed mycophenolate.

## ONGOING MONITORING

More information available in separate guideline, 'Recommended Monitoring Schedule for patients taking disease-modifying anti-rheumatic drugs (DMARDs)'

Pregnancy tests should be repeated as clinically required (e.g. after any gap in contraception is reported)[5].

Baseline assessments should include height, weight, blood pressure, FBC, U&Es, LFTs and CRP.

**Standard Monitoring Schedule as per British Society of Rheumatology Guidelines[1]:**

- Following initiation or dose change: Check FBC, U+Es and LFTs **every 2 weeks** until on stable dose for **6 weeks**
- Once on stable dose, check FBC, U+Es and LFTs **monthly** for **3 months**
- Thereafter, check FBC, U+Es and LFTs **every 3 months**.
- More frequent monitoring is appropriate in patients at higher risk of toxicity (extremes of body weight, CKD3 or above, pre-existing liver disease, significant other medical co-morbidity, age over 80 years and previous DMARD toxicity)

**Exceptions and Additions to the Monitoring Schedule:**

| Drug | Laboratory monitoring | Other monitoring |
|---|---|---|
| Mycophenolate | Standard monitoring schedule | In women of childbearing age: pregnancy testing should be repeated as clinically required (e.g. after any gap of contraception is reported) |

**Abnormal Laboratory Results and Action to be Taken:**

Please note that in addition to absolute values for haematological indices a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance.
Some patients may have abnormal baseline values; specialist will advise if so. e.g. some patients with cirrhosis will have pre-existing pancytopenia and lupus patients may have leucopenia because of lymphopenia.

| Laboratory Result | Action |
|---|---|
| WBC less than 3 x $10^9$/l | Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly. |
| Neutrophils less than 1.6 x $10^9$/l | Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly. |
| Platelets less than 140 x $10^9$/l | Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly. |
| MCV greater than 110 fl | Withhold and discuss with Rheumatology. May be able to continue if chronic increase.<br>Check folate and $B_{12.}$ If level low, start appropriate supplementation. |
| Creatinine increase greater than 30% over 12 months and/or calculated GFR less than 60ml/min/1.73$m^2$ | Discuss with Rheumatology as dose adjustments or further investigations may be required. |
| **Adult** liver function<br>ALT greater than 2.5 x upper limit of normal or over 100U/l | Withhold and discuss with adult rheumatology. |

**CONTRAINDICATIONS AND PRECAUTIONS**

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| Renal impairment (CKD 4 or 5) | Maximum dose of MMF is 1g BD |
| Chicken pox /Shingles | Patients suffering from chickenpox or active skin lesions in shingles withhold MMF and inform specialist team.<br><br>Exposure to chickenpox or shingles passive immunization should be carried out using VZIG |
| Localised or systemic infections | Withhold MMF if patient has a serious infection, including hepatitis B and C and a history of tuberculosis. Patients being treated with MMF are at increased risk for |

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|---|---|
| | opportunistic infections, fatal infections and sepsis. These infections are often related to a high total immunosuppressive burden and may lead to serious and fatal conditions that physicians should consider in the differential diagnosis in immunosuppressed patients with deteriorating renal function or neurological symptoms. |
| HGPRT Deficiency (Lesch-Nyhan and Kelly-Seegmiller syndrome) | MMF is an inosine monophosphate dehydrogenase (IMPDH) inhibitor and should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome. |
| Sunlight/UV exposure | Patients receiving MMF are at increased risk of developing lymphomas and other malignancies, particularly of the skin. Give general advice to minimise risk of skin cancer i.e. patients should wear protective clothing and use a sunscreen with a high protection factor. |
| Blood donation | Patients must not donate blood whilst on treatment with mycophenolate or for 6 weeks after completion of treatment |
| Gastro-intestinal disease | MMF should be used in caution in patients with active serious digestive disease due to an association with gastrointestinal tract ulceration, haemorrhage and perforation. |
| Sperm donation | Male patients must not donate sperm whilst on treatment with mycophenolate or for 90 days after completion of treatment |

**SIDE EFFECTS AND ACTIONS TO BE TAKEN**

| **Side Effects** | **Action** |
|---|---|
| Sterile haematuria / UTI | Withhold until discussed with specialist team. |
| Rash | Withhold until symptoms clear. Consider re-challenging at a lower dose. If rash recurs stop MMF and discuss with specialist team |
| Oral Ulceration | Treat oral ulceration and check FBC. Only stop if neutrophil count is low. |
| Hypersensitivity reactions | Angioneurotic oedema, anaphylactic reaction, fever, malaise, rash, vomiting, muscle/bone pain, dizziness. Stop MMF |
| Nausea, vomiting, diarrhoea | Administer tablets after meals to reduce nausea. An anti-emetic or dose reduction may help. If symptoms persist stop MMF |

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| Abnormal bruising or sore throat | Withhold until FBC result available |
| Malignancy | Discuss with specialist team. |

## NOTABLE DRUG INTERACTIONS

**(Please note that this is not an extensive list. Refer to BNF and SPC for any specific drug interaction queries)**

| Drug | Interaction |
|---|---|
| Aluminium/magnesium hydroxide antacids and oral magnesium supplements | Reduce MMF absorption and if required should be separated from MMF by 2-3 hours |
| Aciclovir, valaciclovir, ganciclovir, valganciclovir | Increased risk of haematological toxicity when used in combination especially if renal impairment is present |
| Colestyramine | May decrease the absorption and bioavailability of MMF by 40%. If considered essential, confirm that the immunosuppressant effects of MMF remain adequate. |
| Rifampicin | Reduces plasma concentration of active metabolites of MMF. Monitor closely during concurrent use and adjust dose of MMF as required. |

## FAMILY PLANNING

**Females**: Avoid in pregnancy. Treatment should be stopped at least 6 weeks before trying to conceive. Female patients with childbearing potential must use at least one reliable form of contraception before, during and for 6 weeks after stopping treatment. Two forms of contraception are preferred but no longer mandatory.[5] Avoid in breastfeeding.

**Males**: EMA now recommends that either the male patient or his female partner use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment. For further advice on paternal exposure, please discuss with secondary care.

## VACCINATIONS

Check Department of Health Green Book guidance and if not covered, discuss with secondary care

## BACK-UP INFORMATION AND ADVICE

| Contact Details | Oxford University Hospitals NHS Foundation Trust | |
|---|---|---|
| Rheumatology | Rheumatology Helpline (Adult and Paediatric)<br><br>Monday to Friday 8am - 2pm (answerphone service)<br><br>Closed on weekends and bank holidays | Tel: 01865 737656<br><br>Email: rheumatology.noc@nhs.net |
| | Rheumatology Registrar/Consultant on call<br><br>Monday to Friday 9am-8pm<br><br>Weekends and bank holidays 9am-5pm | OUH switchboard number: 0300 304 7777, ask for Rheumatology on call |
| Medicines Information | Tel: 01865 221505 (Monday to Friday 9am - 5pm)<br><br>Email: Medicines.information@ouh.nhs.uk | |

## REFERENCES


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