NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT

Shared care guidelines for Mycophenolate Mofetil for the treatment of autoimmune conditions
Monitoring level – Amber 2 – perform more intense level of monitoring, eg 3-monthly review

Generic and Proprietary/Brand Name	
Mycophenolate mofetil - prescribe generically	
Indications for shared care	
Second or third line immunosuppressant in: • **Dermatology**: psoriasis, atopic dermatitis and autoimmune bullous dermatoses such as pemphigus • **Gastroenterology:** autoimmune hepatitis • **Haematology:** immune cytopenias (e.g. immune thrombocytopenia ITP) • **Neurology:** myasthenia gravis, cerebral vasculitis, autoimmune or limbic encephalitis, or other refractory autoimmune disorders resistant to conventional immunotherapy • **Respiratory:** interstitial lung disease (ILD). • **Rheumatology**: rheumatoid arthritis, systemic lupus erythematosus and lupus nephritis, and inflammatory myopathy such as dermatomyositis and polymyositis and scleroderma, vasculitis and Behcet's disease • **Renal:** renal lupus, vasculitis, Goodpasture's disease, glomerulonephritis and nephrotic syndrome	
Specialist Prescribing and Monitoring Responsibilities – summary. Full details in main body of document	**GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities – summary. Full details in main body of document**
• Each medical team is responsible for the initiation period plus six weeks' prescription of MMF at a stable dose. • Patient education **Pre-treatment assessment:** • Check FBC, Liver Function Tests (ALT) and albumin, and creatinine / eGFR. • Record baseline **Height** and **Weight** • Check **BP**. **Initial monitoring:** Check FBC, eGFR, ALT and albumin every 2 weeks, until a stable dose has been achieved and tolerated for 6 weeks. Monitoring and prescription supply will be covered by the relevant consultant team during this period. Once on a stable dose, check FBC, eGFR, ALT and albumin every month. **Specialist ongoing monitoring:** • Review efficacy of treatment at regular intervals and ensure any drug treatment changes are communicated to the GP. • Perform annual review monitoring.	• After 6 weeks of the patient being on a stable dose, to prescribe and monitor MMF, communicating adverse events to the appropriate consultant • After the patient has been on a stable dose for 6 weeks, monitor FBC, eGFR, ALT and albumin every month for at least 3 months and thereafter. • Where there is a low risk of toxicity, the frequency of monitoring may be reduced in some patients to 3-monthly as a minimum, but only after discussion with the relevant consultant, and usually not in children or those at high risk of toxicity. **Risk factors for toxicity include:** A history of adverse drug events; medical comorbidities including renal and liver impairment (e.g. NAFLD) and malignancy; patients at the extremes of weight (BMI <18 or >30 kg/m^2), and old age (>80 years). Patients on concomitant DMARDs, should have monthly monitoring
Patient Information	
Contact GP or the relevant clinical team in the event of side effects. The contact number will be given at the time of patient education.	

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment

MMF is an immunosuppressant which reduces the signs and symptoms in a number of autoimmune diseases. MMF is a pro-drug of the active metabolite of mycophenolic acid. It is a suppressor of T and B cell proliferation and adhesion and inhibits inosine monophosphate dehydrogenase that eventually blocks the progression to DNA synthesis and proliferation.

MMF has routinely been used in organ transplantation for many years and this remains the licensed indication for its use.

Licensed use and agreed local off-label use

Mycophenolate mofetil 250mg capsules are indicated in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants. There is wide experience in off-label use with its place in therapy recognised in national guidelines.

Criteria for Patient Selection

Mycophenolate has been used as a general immunosuppressant in a number of conditions with good effect. See Indications for Shared Care listed above.

Form and strength of preparation

Standard dose is 1–2 g/day. Maximum dose: Up to 3 g/day.
Paediatric dosing: paediatric doses will be advised on an individual patient basis.
Oral: 500mg tablets, 250mg capsules and 1g/5mL suspension available.
Other than in renal transplantation, the generic form should be used preferentially.

Please refer to the manufacturers' SPCs for current prescribing and administration information - http://www.medicines.org.uk/emc/

Side Effects and Management

Link to BNF

Link to SPC

Drug Interactions

Link to BNF

Link to SPC

Vaccines and Immunisation:

- Patients receiving MMF must not receive immunization with live vaccines. Inactivated polio is available although suboptimal response may be seen.
- Annual flu and pneumococcus vaccinations are recommended.

- In patients receiving MMF exposed to chickenpox or shingles, passive immunization should be carried out using VZIG.
- Shingles vaccine – The Green Book Chapter 28a v3_0 regarding the shingles vaccine, states "*Long term stable low dose corticosteroid therapy (defined as <20mg prednisolone per day for more than 14 days), either alone or in combination with low dose non-biological oral immune modulating drugs (e.g. methotrexate less than or taking 25mg/week), are not considered sufficiently immunosuppressive and these patients can receive the vaccine. Patients on higher doses should be discussed with the consultant*".

Cautions and Contraindications

Link to BNF

Link to SPC

Initiation of therapy and ongoing dose regimen

The relevant consultant team will prescribe until the patient has been on a stable dose for 6 weeks.

Starting adult dose:
500mg daily for the 1st week, 500 mg twice daily for the 2nd week, and increase gradually by 500mg each week until 1g bd is reached or to the maximum tolerated dose.

Paediatric dosing:
Doses will be advised on an individual patient basis.

Escalation beyond 1g bd should only be on the recommendation by the supervising consultant.

Administration Information

MMF should be taken 1-2 hours before food. The half-life is approximately 18 hours.

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

Time to response: 6 weeks to 3 months. Treatment is likely to be long term.

Baseline assessment and ongoing monitoring – by Specialist

Pre-treatment assessment:

Check FBC, Liver Function Tests (ALT) and albumin, and creatinine / eGFR.

Lung disease:

Routine CXR are no longer undertaken but clinical assessment of coexisting pulmonary disease may result in pulmonary function tests to assess lung reserve and CT assessment being undertaken. Pre-existing lung disease is not a contraindication to DMARD use but prescription is undertaken with caution, and chest x-ray (excluding paediatrics).

Liver disease:

In patients with deranged liver biochemistry, hepatotoxic DMARDs should be used with caution, with careful attention to trends in test results. In patients with impaired liver synthetic function (e.g. cirrhosis), DMARD therapy should be used with extreme caution. Patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to DMARD initiation.

Occult viral infections:

Screening for occult viral infections such as HIV and hepatitis B and C should be offered and Varicella status recorded. GP to be advised of any abnormal results.

Record baseline **Height** and **Weight**

Check **BP**.

Pregnancy testing & Contraception:

Prior to treatment, two serum or urine pregnancy tests with a sensitivity of at least 25 mIU/mL are recommended where this is indicated. The second test should be done 8 to 10 days after the first, and immediately before starting mycophenolate mofetil. Pregnancy tests should be repeated as clinically required (e.g. after any gap in contraception is reported). Patients should be instructed not to stop treatment but to consult their physician immediately should pregnancy occur.

Initial monitoring:

Check FBC, eGFR, ALT and albumin every 2 weeks, until a stable dose has been achieved and tolerated for 6 weeks. Monitoring and prescription supply will be covered by the relevant consultant team during this period.

Once on a stable dose, check FBC, eGFR, ALT and albumin every month.

See **GP monitoring section** *for subsequent monitoring*.

Specialist ongoing monitoring:

- Review efficacy of treatment at regular intervals and ensure any drug treatment changes are communicated to the GP.
- Perform annual review monitoring.

GP / Community Team or other Primary Care monitoring responsibilities

- After the patient has been on a stable dose for 6 weeks, monitor FBC, eGFR, ALT and albumin every month for at least 3 months and thereafter.
- Where there is a low risk of toxicity, the frequency of monitoring may be reduced in some patients to 3-monthly as a minimum, but only after discussion with the relevant consultant, and usually not in children or those at high risk of toxicity.
  Risk factors for toxicity include:
  A history of adverse drug events; medical comorbidities including renal and liver impairment (e.g. NAFLD) and malignancy; patients at the extremes of weight (BMI <18 or >30 kg/m^2), and old age (>80 years).
- Patients on concomitant DMARDs, should have monthly monitoring.

Haematology patients:

Monitoring as directed by the supervising consultant.

Consultant / Specialist prescribing responsibilities

Each medical team is responsible for the initiation period plus six weeks' prescription of MMF at a stable dose.

Patient education will be undertaken within the relevant multidisciplinary team.

GP prescribing responsibilities

After 6 weeks of the patient being on a stable dose, to prescribe and monitor MMF, communicating adverse events to the appropriate consultant

Pregnancy, Paternal Exposure and Breastfeeding

- Mycophenolate mofetil or mycophenolic acid are teratogenic and should *not* be used in pregnancy or in women who are breastfeeding.
- 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 where this may be possible.
- 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. Men should not donate semen during treatment or for 90 days following discontinuation of MMF. 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.

Indications for referral back to Specialist

Look for trends in the monitoring e.g. rapidly falling WCC

If the patient's:

- WBC <3.5 x 10^9/L
- Neutrophils <1.6 x 10^9/L
- Platelets <140 x 10^9/L
- Unexplained eosinophilia >0.5x10^9/l
- ALT > twice upper limit of normal or
- Unexplained falling albumin <30g/l
- MCV >105fl
- Creatinine increase >30% over 12 months and/or eGFR <60ml/min/1.73m^2

Haematology patients will have individual plans.

Bruising with or without sore throat:

- check FBC immediately and discuss with specialist team
- Temporary suspension of MMF for 10–14 days usually results in recovery of the cell count.
- Once the cell count recovers, the drug can be re-administered at *half the previous dose* and *gradually increased* until a stable dose is attained without any toxic effect.

Severe neutropenia:

- Occurs in 0.5% patients receiving MMF in the full dose.
- STOP the drug.
- Check FBC immediately and also discuss with specialist team.

Abdominal pain, GI disturbances, rash or shortness of breath:

- please contact the relevant department

Pre-surgery: There is no indication to stop mycophenolate at the time of surgery

Infection:

- Mycophenolate should be stopped in the event of a severe infection e.g. requiring hospitalisation.

The decision to restart mycophenolate where the patient has had a break from therapy e.g. of more than one month, should be undertaken by the hospital specialist team.

Specialist Contact Details

Consultant and medical staff and nurse practitioners are available to give advice and can be contacted either through the main hospital switchboard or direct

NNUH Department / Specialist	Contact Telephone Number
Hospital switchboard – ask for specialist or on-call specialist (rheumatology/dermatology) out-of-hours	(01603) 286286
Rheumatology	
Rheumatology Practitioners	(01603) 287801
Dr De Silva's secretary	(01603) 288623
Dr Gaffney's secretary	(01603) 289670
Professor MacGregor's secretary	(01603 288677
Dr Marshall's secretary	(01603) 288677
Dr Merry's secretary	(01603) 287003
Dr Mukhtyar`s secretary	(01603) 286766
Dermatology	
Dr Garioch's secretary	(01603) 288210
Dr Grattan's secretary	(01603) 288265
Dr Levell's secretary	(01603) 288225
Dr Millington's secretary	(01603) 288209
Dr Shah's secretary	(01603) 288850
Dr Skellett's secretary	(01603) 288379
Dr Tan's secretary	(01603) 288208
Samantha Browne – Dermatology Sister	(01603) 288385
Hepatology	
Dr Simon Rushbrook	(01603) 286227
Dr Martin Phillips	(01603) 287117
Dr Arun Shankar	(01603) 287345
Dr Syed Alam	(01603) 288363
Haematology	
Haematology consultant	(01603) 286286 ext 6744
Haematology secretary	(01603) 286286 ext 6750
Haematology specialist nurse	(01603) 286286 ext 6753
Paediatrics	
Paediatric rheumatology nurse specialist	(01603) 287911
Dr Armon's secretary	(01603) 287534
Dr Morris' secretary	(01603) 289936
Respiratory	
Professor Andrew Wilson	(01603) 289802
Dr Ajay Kamath	(01603) 289642
Sandra Olive (ILD Nurse Specialist)	(01603) 289654
Pharmacy	
Medicines Information Helpline	(01603) 287139 or Bleep 500 via switchboard (01603) 286286

QEH Department/Specialist	Contact Telephone Number	
Rheumatology		
Dr Pradeep and Dr Riaz (via secretary)	01553 613726	
Dermatology		
Dr Dootson and Dr Stefanescu (via secretary)	01553 613040	
Gastroenterology		
Dr Douds and Dr Bagewadi (via secretary)	(01553) 613989	
Dr Karanth and Dr Mathialagan (via secretary)	(01553) 613708	
Dr Wiles and Dr Hariraj (via secretary)	(01553) 613004	
Paediatrics		
Dr Reeve and Dr Rewitzky (via secretary)	(01553) 613678	
Dr Piel, Dr Grabowska-Wnuk and Dr Wnuk (via secretary)	(01553) 613687	
Dr Adiga and Dr Nair (via secretary)	(01553) 613882	
Dr Ibrahim and Dr Fawi (via secretary)	(01553) 613718	

Further information and supporting documents

BSR/BHPR guidelines for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs (February 2017) - https://www.rheumatology.org.uk/Knowledge/Excellence/Guidelines/ArtMID/1262/ArticleID/94/Prescription-and-monitoring-of-non-biologic-DMARDs

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Document history:

Version	Date	Author / Editor	Status	Comment
1.0	Nov / Dec16	Dr Tarnya Marshall (NNUH) / Fiona Marshall, NEL CSU	Draft	For consideration by the Therapeutics Advisory Group (TAG) – January 2017.
1.1	Jan 2017	Dr Tarnya Marshall (NNUH) / Fiona Marshall, NEL CSU	Superseded	Link to Papworth Hospital shared care document inserted regarding patients with interstitial lung disease. Supported by the TAG and the N&W D&TCG.
2.	May to July 2017	Dr Tarnya Marshall (NNUH) / Fiona Marshall, NEL CSU	Current	Reviewed and updated following publication of revised British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) guidance for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs Feb 2017 - ***Link*** Circulated by the authors across all stakeholder specialisms and to the JPUH and the QEH for consultation. Changes made to monitoring requirements and responsibilities, side-effects, available products, advice to GPs regarding thresholds and responsibilities regarding referral back to specialists. Advice regarding shingles vaccination updated in line with the Green Book. Revised version supported by the TAG – July 2017. Final version approved by the D&TCG August 2017.
3.0	Dec 2018 – Jan 2019	As per 2.	Draft - final	CSU logos updated. Clarification of use in ILD as recommended by local specialists. NNUH respiratory consultants' contacts added.

				Supported by the TAG – January 2019
4.0	Aug 2021	Jen Carroll, TAG Lead Technician	FINAL	Discussed at August 2021 TAG meeting. Review dates extended for a year from meeting due to covid pressures
5.0	Feb 2024	Jen Carroll, TAG Lead Technician	FINAL	Content not reviewed. Existing SCA transferred to new template ready for move to KNoW.