City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

SHARED CARE GUIDELINE

MYCOPHENOLATE MOFETIL

Treatment of Autoimmune Conditions in Adult Dermatology and Rheumatology Patients

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AND FILED IN NOTES

INTRODUCTION – Indication and Licensing

Mycophenolate mofetil is a pro-drug of Mycophenolic acid. Mycophenolic acid is a potent, selective, uncompetitive and reversible inhibitor of inosine monophosphate dehydrogenase, and therefore inhibits the *de novo* pathway of guanosine nucleotide synthesis without incorporation into DNA. Mycophenolic acid has more cytostatic effect on T- and B-lymphocytes because their proliferation is critically dependent on *de novo* synthesis of purines whereas other cell types can utilise salvage pathways. It may take between 6 weeks to 3 months for the therapeutic effect to be observed.

Licensed indications: not licensed for dermatological and rheumatological conditions.

This guideline does not cover the use of Mycophenolate mofetil for prophylaxis of transplant rejection

Unlicensed indications: systemic lupus erythematosus, vasculitis, scleroderma, dermatomyositis, polymyositis, sarcoidosis, psoriasis, atopic dermatitis, pyoderma gangrenosum and other inflammatory conditions considered appropriate by the hospital specialist.

PATIENT PATHWAY

Clinical Speciality / Indication	Prescribing Initiated by	Prescribing Continued by	Monitored by	Duration of treatment
Dermatology Rheumatology	Dermatologist Rheumatologist	Hospital to transfer the prescribing to GP once patient is on a stable dose and blood results are stable.	Hospital or GP as per shared care agreement letter.	Ongoing if efficacious.

Reviews & dose adjustments

The patient will be reviewed periodically by the hospital specialist team in clinic. Dosing adjustments are to be done by the hospital and this information communicated to the GP in writing within 14 days.

Patients outside of City and Hackney area

It may be more appropriate for blood test monitoring to be done locally if this is more convenient for the patient. The patient should be given a copy of their latest blood results to bring to their clinic appointment (if the hospital specialist team is not able to access this information electronically).

ORAL DOSE AND ADMINISTRATION

- *Initial dose:* 500mg daily and titrate according to tolerability and response (e.g. by 500mg every week).
- *Usual maintenance dose:* 1-2g daily in two divided doses (max. 3g/day in two divided doses).
- Mycophenolate mofetil **must be prescribed by brand.** Mycophenolic acid (Myfortic®) is not interchangeable with Mycophenolate mofetil and should not be prescribed.

Vaccinations

- Annual vaccination against influenza is recommended.
- Pneumococcal vaccination should preferably be given prior to the initiation of Mycophenolate mofetil, however, if this is not possible it should still be administered and repeated every 5 years.
- Concomitant use of a live vaccine could cause a severe antigenic reaction and, therefore, should be avoided. These include: oral polio, oral typhoid, MMR, BCG and yellow fever vaccines.

- Treatment with Mycophenolate is not a contraindication for the shingles vaccine (Zostavax®) for most patients (see JCVI Green Book). Discuss with the specialist team if the shingles vaccine is required.
- Patients who have not been immunised against chicken pox should report to their GP or specialist if they come in to contact with the virus. Passive immunisation should be carried out using varicella zoster immunoglobulin.

Alcohol intake

Patients should be advised to keep alcohol intake well within the government guidelines (maximum 2 units a day or 14 units per week).

CAUTIONS

- Elderly patients (increased risk of infections, possibly gastrointestinal haemorrhage and pulmonary oedema)
- Patients should not donate blood during therapy or for at least 6 weeks following discontinuation of Mycophenolate.
- Men should not donate semen during therapy or for 90 days following discontinuation of Mycophenolate.

CONTRAINDICATIONS

- Hypersensitivity to Mycophenolic acid.
- Pregnancy, breastfeeding, males and females who are trying to conceive.

INTERACTIONS

- Antacid, iron salts and Colestyramine – absorption of Mycophenolate reduced by these drugs.
- Rifampicin – plasma concentration of active metabolite of Mycophenolate reduced by Rifampicin.

MONITORING STANDARDS FOR MEDICATION AT THE ACUTE NHS TRUST

Pre-treatment monitoring (to be done by the specialist team).
FBC, LFTs, U&Es (including eGFR), CRP[#], ESR[#], fasting lipids and BP. Chest X-ray, respiratory examination and check history of respiratory symptoms. *Additional tests to be determined on an individual patient basis:* Pulmonary function tests, varicella zoster, hepatitis B & C serology.
Ongoing monitoring (to be done by specialist team until patient is stable then GP to take over monitoring as per shared care agreement).
FBC, LFTs, U&Es (inc. eGFR) every 2 weeks until on stable dose for 6 weeks, then monthly for 3 months, then every 8-12 weeks thereafter. *Dose increases:* monitor every 4 weeks until on stable dose for 8 weeks then revert back to previous schedule. BP monitoring at each hospital clinic visit.

[#]Monitoring of CRP and ESR may not be applicable in some conditions.

KEY ADVERSE EFFECTS & ACTIONS

- Gastrointestinal (diarrhoea, nausea, vomiting, dyspepsia, abdominal pain, ulceration and bleeding).
- Taste disturbance and gingival hyperplasia.
- Increased susceptibility to infections.
- Blood disorders (leucopenia, thrombocytopenia and anaemia).
- Hepatic and renal impairment.
- Hypertension.
- Metabolic effects (hyperglycaemia, hyperlipidaemia, hypercholesterolaemia, hyperuricaemia and gout).
- Increased susceptibility to skin cancer, lymphomas and other malignancies (avoid use of sunbeds and exposure to strong sunlight).

Laboratory events	Values	Actions (*what action should the GP take if identified in primary care)*
↓ WBC	<3.5 x 10^9/l	Reduction in WBC alone is usually not usually clinically significant. If this is accompanied by a reduction in neutrophil count then **stop drug and seek advice** from the specialist team.
↓ Neutrophil count	<1.6 x 10^9/l	**Stop drug and seek advice** from the specialist team.
↓ Platelet count	<100 x 10^9/l	
↑ MCV	>105fl	Check alcohol intake, B12, folate and TSH and treat any underlying abnormality. If normal, **seek advice** from the specialist team.
↑ ALT/AST	>2 times upper limit of normal	**Stop drug and seek advice** from the specialist team.
↓ eGFR	<30ml/min/1.73	**Seek advice** from the specialist team.

Please note: a rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance. Some patients may have abnormal baseline values (specialist team will advise).

Adverse effects	Actions (*what action should the GP take if identified in primary care)*
Rash	**Seek advice** from the specialist team.
Bruising with or without sore throat	**Stop drug** and check FBC immediately. **Seek advice** from the specialist team.

Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding. A blood count should be performed and the drug stopped immediately if there is suspicion of a blood dyscrasia.

The SCG lists only the key information. Please refer to the current British National Formulary and Summary of Product Characteristics for comprehensive information on cautions, contraindications, interactions and adverse effects.

PREGNANCY AND BREAST FEEDING

- Mycophenolate is a powerful human teratogen and is **contraindicated in pregnancy.**
- Women with childbearing potential should **use two reliable forms of contraception simultaneously** before starting Mycophenolate therapy, during therapy, and for six weeks after stopping the therapy.
- Male patients **or** their **untreated** female partner must use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment.
- Mycophenolate is **contraindicated in breastfeeding** due to lack of information.

Please refer to the <u>current</u> British National Formulary and Summary of Product Characteristics for comprehensive information.

SHARED CARE

<u>Shared care guideline</u>*:* is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets <u>out responsibilities for each party</u>. The intention to shared 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. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use**.**

Consultant

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that the patient understands their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
3. Ensure baseline investigations are normal before commencing treatment.

4. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised).
5. Send a letter to the GP requesting shared care for this patient.
6. Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis.
7. Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated (unless otherwise covered by letter e.g. from the Clinical Nurse Specialist).
8. Where the GP is out of area and is not performing the phlebotomy, the blood test form/EPR request MUST specify that blood results are also copied to the GP. Specialist team to check with pathology IT if unsure on how to do this.
9. Evaluation of any reported adverse effects by GP or patient.
10. Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
11. Inform GP of patients who do not attend clinic appointments.
12. Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
13. Ensure that backup advice is available at all times.
14. Advise that the patient receives appropriate vaccination in primary care either prior to commencing treatment and/or during a treatment that is likely to cause immunosuppression.

General Practitioner

1. Ensure that the patient understands the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA / CHM, where appropriate.
5. Help in monitoring the progression of disease.
6. Prescribe treatment as described. Provide contraception advice and prescription as appropriate.
7. Provide appropriate vaccinations to patients receiving treatments likely to cause immunosuppression.

City and Hackney Medicines Management Team

1. To provide feedback to acute trusts via the Joint Prescribing and Medicines Management Group.
2. To support GPs to make the decision whether to accept clinical responsibility for prescribing.
3. To support acute trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist.
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist.
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
5. Take/ administer the medication as prescribed.
6. Undertake any monitoring as requested by the GP and/or specialist.

Costs

Drug Product	Cost in primary care
Mycophenolate mofetil 250 mg capsules	100-cap pack = £82.26
Mycophenolate mofetil 500 mg tablets	50-tab pack = £9.31

Based on BNF edition 73 (March – September 2017)

RESOURCES AVAILABLE

- Arthritis Research UK website, available at http://www.arthritisresearchuk.org
- British Association of Dermatologists, available at http://www.bad.org.uk
- The Joint Committee on Vaccination and Immunisation (JCVI) Green Book, available at https://www.gov.uk

Relevant contact details	
Consultant or Registrar on-call *via* switchboard	020 8510 5555
Clinical Nurse Specialist (helpline)	**Dermatology** 0208 510 7690 **Rheumatology** 07917 521 117
Generic email	**Rheumatology** huh-tr.rheumliaison@nhs.net (clinical queries) huh-tr.rheumatologyadmin@nhs.net (admin queries)
Trust Homerton University Hospital NHS Foundation Medicines Information	020 8510 7000
City and Hackney Medicines Management Team	0203 816 3224

References

- SCG template adapted from NELMMN and Barts Health NHS Trust.
- BNF edition 73, available at https://ebnf.homerton.nhs.uk (last accessed 26 April 2017).
- Summary of product characteristics. Available at www.medicines.org.uk (last accessed 26 April 2017).
    1. Mycophenolate mofetil 250mg capsules (Actavis UK Ltd).
    2. Cellcept 250mg capsules.
- The British Society for Rheumatology, available at: http://www.rheumatology.org.uk (last accessed 26 April 2017).
    1. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease modifying anti-rheumatic drugs (2017).
    2. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists (2008).
    3. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding – Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids (2016).
- European Medicines Agency. Mycophenolate: updated recommendations for contraception for men and women. Published 15 December 2017. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2017/12/WC500240387.pdf

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