South West Yorkshire Area Prescribing Committee

Mycophenolate Mofetil Shared Care Guideline

Introduction	
General Statements	• The patient will receive supplies of the drug from the hospital until the transfer of shared care is agreed between the Consultant and GP • The GP must reply in writing to the request for shared care as soon as practicable if unwilling to participate. • Responsibility for prescribing and monitoring must be clearly documented in the patient's hospital and GP notes • The agreement to consider the use of a shared care guideline is only considered when the patient's clinical condition is stable or predictable
Indication	**Unlicensed indications** • Systemic Lupus Erythematosus (SLE), particularly lupus nephritis, other connective tissue diseases and systemic vasculitis. • Treatment of Myasthenia Gravis in patients intolerant or non-responding to azathioprine. Please note mycophenolate mofetil can be prescribed generically for the above indications.

Individual's Responsibilities	
Hospital Specialist's Responsibilities	➢ Record patient consent to unlicensed use in medical notes. ➢ Baseline monitoring and initial prescribing until the patient is established on treatment (minimum of 8 weeks). ➢ Monitoring disease progression and response to treatment-4 weeks after starting therapy and continue monitoring monthly until stable then 3 monthly for first year and yearly thereafter. ➢ Supporting and advising GPs. ➢ Monitoring booklets are available and may be beneficial in certain circumstances, for example if the patient receives blood monitoring at a location where results are inaccessible to the clinician. In these situations the Hospital Specialist will communicate this fact to the GP at the point when prescribing and monitoring is transferred
General Practitioner's Responsibilities	➢ Ensure hospital is notified if unwilling to undertake monitoring when requested ➢ Prescribing following written request from specialist care. ➢ Prescribe mycophenolate mofetil (not mycophenolic acid – *Myfortic*) ➢ Ensure monitoring is undertaken according to shared care guideline and only continue prescription if compliance with monitoring and results satisfactory. ➢ Follow guidance in the event of reaction or abnormality ➢ Update patient's monitoring booklet as appropriate (including test dates & results, when available) ➢ Encourage influenza and pneumococcal vaccination
Monitoring Required	**Baseline** (undertaken by Hospital Specialist)– FBC, U&E's, serum creatinine (use with caution if eGFR <25ml/min), LFTs, BP, lipids The Hospital Specialist must confirm to the GP which stages of the

	maintenance monitoring have already been completed at the point when prescribing and monitoring are transferred to the GP **Maintenance** (undertaken by Hospital specialist for initial two months, then by GP) Repeat FBC, U&E's, serum creatinine, LFTs & BP at 1 week then, 2 weekly for 2 months, monthly for 4 months then 3 monthly.
When and How to Discontinue Treatment	Loss of efficacy, intolerability, abnormal blood monitoring Please see 'Recommended action for abnormal results or adverse effects' for detailed guidance as regards stopping treatment. In any other circumstances the decision to stop treatment should be discussed and agreed with the specialist. Discontinue 6 weeks prior to conception – effective contraception needed during this time. In case of a Severe Adverse Effect Mycophenolate Mofetil must be stopped immediately. In any other cases (lack of response, poor tolerance, planning to conceive) Mycophenolate should be discontinued slowly, usually reducing 250mg bd every week.
Information given to the patient	For Systemic Lupus Erythematosus (SLE),other connective tissue diseases and systemic vasculitis indications-Patient information leaflet and monitoring booklet will be provided. For Myasthenia Gravis patients -Verbal information during clinical interview, written letter summarising treatment and risks will be provided. Patients should be warned to report any signs or symptoms of bone marrow suppression eg. infection or unexplained bleeding or bruising.
Contact Details	Documented in letter from specialist care to GP

Product Information

The information in this Shared Care Guideline should be used in conjunction with the latest edition of the BNF and Summary of Product Characteristics

Dosage	<u>Systemic Lupus Erythematosus (SLE),other connective tissue diseases and systemic vasculitis indications</u> Commence with **250-500mg bd**, increasing to a maximum of **1.5g bd*** <u>Myasthenia Gravis:</u> Commence with **250mg bd**. In some cases of aggressive Myasthenia Gravis, it may be appropriate to commence with 500mg bd*. Titrate at a rate not faster than 250mg bd every 2-4 weeks. The appropriate rate will be determined individually depending on the severity of the symptoms and the tolerability. The process of titration may be slower in patients who were previously using other immunosupressing drugs such as Azathioprine. The usual maintenance dose in Myasthenia Gravis is between **1g bd** and **1.5 g bd.** The maximum dose is **1.5g bd.*** * The hospital specialist will confirm the dosage at the point prescribing is transferred to the GP.
Adverse Effects	**Gastrointestinal upset** most common side effect – eg. diarrhoea, abdominal cramps, nausea and vomiting.

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	Bone Marrow toxicity - particularly neutropenia Possible increased risk of lymphoma associated with oncogenic viruses and skin tumours. **Teratogenic** – effective contraception required during treatment and for 6 weeks after discontinuation of treatment. Refer to the current BNF and www.medicines.org.uk/emc/ for complete and up to date information.
Precautions and Contra-indications	**Contraindications** – pregnancy and breast feeding, recurrent herpes or shingles, previous hepatitis B or C **Precautions** –recurrent infection, suspected lymphoproliferative disorder. renal impairment with eGRF less than 25ml/min **Avoid live vaccines** - passive immunisation with VZIG may be required if exposed to chickenpox or shingles. Please consult the Green Book for complete and up to date information: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/148515/Green-Book-Chapter-34-v2_0.pdf
Clinically relevant Drug Interactions and their management	**Antacids**, **cholestyramine** – decrease absorption of mycophenolate. **Probenecid** – may prevent renal excretion and increase mycophenolate levels **Aciclovir/ganciclovir** may increase mycophenolate levels **Rifampicin** – may reduce levels of active metabolite but also increase risk of toxicity. Refer to the current BNF and www.medicines.org.uk/emc/ for complete and up to date information.

Recommended action for abnormal results or adverse events

Investigation	Action
WBC <3.5 x10^9/L Neutrophils < 2 x10^9/L Platelets < 150 x10^9/L -for Myasthenia gravis Platelets <100 x10^9/L	Stop and contact rheumatology /neurology department
Hb fall >1g in 4 weeks or below 10g	Check for increased disease activity Ask about NSAID use and symptoms of GI blood loss or dyspepsia and stop NSAIDS if implicated. Check MCV and iron studies Consider endoscopy Monitor FBC weekly and contact neurology if changes persist in Myasthenia Gravis patients
ALT above normal range but below 3x upper limit ALT > 3x upper limit	Repeat bloods every 2 weeks Ask patient about viral/bacterial infections Check that it is not due to another drug or NSAID particularly diclofenac and stop this first Consider dose reduction Stop and contact rheumatology department For myasthenia gravis- If patient is asymptomatic, initiate slow reduction and contact Neurology. If

	patient has symptoms (jaundice, abdominal pain, and confusion), **STOP immediately and contact Neurology**.

Recommended action for adverse events

Adverse effect	Action
Bruising, bleeding	Check FBC, clotting screen
GI side effects	Try splitting dose to QDS regime Reduce dose if persistent and intolerable
Rash	Contact hospital specialist