SHARED CARE GUIDELINE FOR MYCOPHENOLATE MOFETIL FOR RHEUMATOLOGY INDICATIONS

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription of mycophenolate mofetil when used in Rheumatology.

2. The Guidance

2.1. See below for the Shared Care Guideline.

MYCOPHENOLATE MOFETIL IN RHEUMATOLOGY

This shared care guideline sets out details for the sharing of care of patients prescribed **mycophenolate mofetil in Rheumatology**. These guidelines provide additional limited information necessary to aid in the treatment of IBD and AIH patients. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the BNF, ABPI summary of product characteristics and ***do not*** replace them.

BACKGROUND INFORMATION

Mycophenolate mofetil is licensed for prophylaxis of acute rejection in renal, hepatic, and cardiac transplant recipients in combination with other agents. It can also be used off-license as an alternative to azathioprine in patients with conditions such as systemic lupus erythematosus, glomerulonephritis, and connective tissue diseases on hospital advice if unresponsive or allergic to azathioprine.

The use of mycophenolate mofetil is now accepted within Rheumatology but it is acknowledged that this is relatively new to primary care. **The initiation and early prescribing remain the responsibility of the Rheumatology team.** After three months treatment and if the patient is on a stable dose, the Rheumatology team will continue to monitor the patient, but primary care are requested to take over the routine prescribing of mycophenolate mofetil. This shared care guideline gives a summary of clinical information, and highlights the potential side effects and drug interactions. These are monitored at hospital clinic visits, but the primary care team should be aware. Any potential interactions or other concerns can be discussed with the Rheumatology team.

DOSAGE

Mycophenolate mofetil: 250mg to 1.5g twice daily.

CONTRAINDICATIONS

- Pregnancy. This drug is contra-indicated in pregnancy as it has the potential to affect the development of the unborn child. Patients should be advised to use a reliable method of contraception during treatment.
- **Female patients of childbearing potential** must be using two reliable form of contraception before, during and for six weeks after stopping treatment unless abstinence is the chosen method of contraception.
- **Male patients** should use condoms during treatment and for at least 90 days after stopping treatment. This also applies to vasectomized males with female partners of child-bearing potential as the drug can be transferred into the seminal fluid in sufficient amounts to affect the developing foetus.
- **Female partners of male patients** should use highly effective contraception while their partner is on treatment and for 90 days after the last dose.
- Breast-feeding.
- Hypersensitivity to the parent compound or metabolites.

PRECAUTIONS

- **Elderly** – increased risk of infection, gastro-intestinal haemorrhage, pulmonary oedema.
- **Active serious Gastro-intestinal disease** – risk of haemorrhage, ulceration and perforation.
- **Increased susceptibility to skin cancer** – avoid exposure to sunlight and UV light with protective clothing and a high protection sun cream.
- **Bone Marrow Suppression** – Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection and inexplicable bruising or bleeding.

MONITORING – INITIAL AND ONGOING:

Pre-treatment blood tests will be carried out in secondary care as dictated by the patient's condition.

FBC, LFTs, Electrolytes fortnightly until stable dose for 6 weeks, then monthly for three months, then at least once every 12 weeks. Routine blood tests will be performed at the GP surgery as this is more convenient for patients. Interim bloods should be taken in the event of infection, new side effect or after the introduction of a potentially interacting drug.

Rheumatology patients are usually seen for counselling in clinic before commencing treatment, after the first month to check tolerance and discuss dose escalation and then at three months with further follow-up as dictated by the patient's clinical condition (but at least once every six months).

Mycophenolate levels are not performed routinely but are sometimes useful. Such levels are requested in secondary care. Secondary care physicians will adjust the dosage to the individual patient requirements.

ONGOING MONITORING – PRIMARY CARE

There are no specific monitoring requirements for General Practice, other than blood tests as discussed above

IF ANY OF THE FOLLOWING OCCUR, REPEAT THE TEST, CONSIDER INTERRUPTING TREATMENT AND IF REQUIRED CONTACT THE SPECIALIST TEAM FOR ADVICE:

- WCC < 3.5 x 10^9/L – particularly if falling trend
- Neutrophils < 1.6 x 10^9/L – particularly if falling trend
- Mean Cell Volume > 105 – particularly if rising trend
- Unexplained eosinophilia > 0.5 x 10^9/L
- Platelet count < 140 x 10^9/L
- ALT and/or AST > 100
- Unexplained reduction in albumin (below 30 g/L)
- Creatinine increased > 30% over 12 months
- eGFR decreases < 60mL/min/1.73m² and there is a significant falling trend.
- ***Severe*** nausea or diarrhoea
- ***Severe*** mouth or genital ulceration

SIDE EFFECTS

Below are some of the more common side effects please note that this list is **NOT exhaustive** and it is recommended that the SPC and BNF should be consulted for a more comprehensive list.

- **Gastrointestinal disturbances** e.g. diarrhoea, gastritis, nausea, abdominal discomfort, vomiting and constipation. GI side effects may be transient.
- **CVS effects**: Hypertension, oedema and tachycardia
- **CNS effects**: headache, insomnia, anxiety
- **Metabolic effects**: Increased glucose, increased cholesterol
- **Infections:** increased risk (viral, bacterial and fungal)
- **Increased blood creatinine**
- **Blood dyscrasias** - leucopenia, anaemia and thrombocytopenia
- **Malignancy**: Risk of malignancies increased including lymphoma, skin and other tumours appear to be linked to degree and duration of immunosuppression. The incidence is similar to that of other immunosuppressive agents or therapies.
- **Less commonly** – gastro-oesophageal reflux, gastro-intestinal ulceration and bleeding, cough, influenza-like syndrome, pancreatitis, abnormal liver function tests, hepatitis, tachycardia, blood pressure changes, oedema, dyspnoea, tremor, insomnia, dizziness, hyperglycaemia, disturbances of electrolytes and blood lipids, renal tubular necrosis, arthralgia, alopecia, acne, rash.

COMMON/SIGNIFICANT DRUG INTERACTIONS

- Absorption of Mycophenolate reduced by antacids, colestyramine, metronidazole, norfloxacin, and sevelamer.
- Mycophenolate level reduced by rifampicin
- Mycophenolate increases plasma concentration of aciclovir and ganciclovir
- Mycophenolate possibly reduces the absorption of phenytoin
- Mycophenolate level increased by aciclovir
- Increased risk of agranulocytosis with clozapine – avoid concomitant use
- Vaccines may be less effective in immunocompromised patients. Live vaccines (which include measles, mumps and rubella; BCG; herpes zoster – Zostavax; poliomyelitis – oral Sabin vaccine; yellow fever; typhoid – oral) should be avoided. Annual influenza vaccine is advised, though less effective.

PRODUCT INFORMATION

Prescribing must be BY BRAND: Mycophenolate mofetil products should not be indiscriminately interchanged or substituted because of their different pharmacokinetic profiles. This is less likely to be problematic in patients who are receiving mycophenolate mofetil for non-transplant indications.

Mycophenolate Mofetil is available as 250mg capsules, 500mg tablets, 1g in 5ml oral suspension and as an intravenous infusion. The intravenous infusion should not be prescribed in primary care. The RCHT preferred brand to use is Myfenax.

Tablets should be kept in original packaging to protect from moisture, light and degradation. Tablets/capsules should be swallowed whole and not crushed or opened.

REFERENCES

Summary of Product Characteristics
https://www.medicines.org.uk/emc/

CONTACT

- For urgent advice, contact on the on-call Consultant Rheumatologist via RCHT switchboard 01872 252000
- RCHT Medicines Information: 01872 252587
- RCHT Rheumatology Secretaries:
  Dr Endean & Dr Jenkinson: 01872 253792
  Dr Davis & Dr Hutchinson: 01872 53978

- RCHT Rheumatology Pharmacists: via Consultant Secretaries or email rch-tr.rheumpx@nhs.net

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AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients who are prescribed **mycophenolate mofetil in Rheumatology** can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs**.** Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

In its guidelines on responsibility for prescribing (circular EL(91)127) between hospitals and GPs, the DH has advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

Specialist:

- Decision to prescribe mycophenolate mofetil. Discuss with the patient the benefits of treatment, the cautions and side effects associated with treatment, especially recommendations for contraception, the monitoring requirements and the timing of re-assessment and by whom.
- Initiate oral mycophenolate mofetil and stabilise patient on a therapeutic dose before referral to the GP. Prescribing will remain in secondary care for at least 3 months.
- Ask the GP whether they are willing to participate in shared care.
- Prompt communication with GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events. If a dose change is required, to communicate this to the patient and the GP by letter.
- Specify review dates at clinically relevant time intervals for both the patient and the consultant.
- Advice to GPs on when to stop treatment.
- Ensure clear arrangements for back-up advice and support.
- Reporting adverse events to the MHRA.

General Practitioner:

- Reply to request for shared care as soon as practical.
- Prescribing of mycophenolate mofetil after communication from specialists regarding the need for treatment and confirmation that the patient's dose is stabilised.
- Clinical patient monitoring as outlined in the shared care guideline.
- To be aware of side effects of treatment, and seek urgent advice as necessary. Reporting adverse events to specialist and MHRA
- Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prompt referral to a specialist if there is a change in the patient's situation and / or if there is : Bone Marrow suppression on interim tests; Suspected allergy or reaction; Sepsis – bacterial infections requiring antibiotics; Deranged LFTs
- To check for possible drug interactions when newly prescribing or stopping concurrent medication
- Stopping treatment in the case of a severe adverse event or as per shared care guideline.

Patient:

- Report any adverse effects to their GP and/or specialist whilst being treated with mycophenolate mofetil
- Ensure that they have a clear understanding of their treatment, recommendations for contraception, and ensure they attend for monitoring requirements as per shared care guideline.
- Aware that treatment may be stopped if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RHEUMATOLOGY DEPARTMENT

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Medicines Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Relevant Clinical Staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Shared Care Guideline for mycophenolate mofetil in Rheumatology					
Date Issued/Approved:	January 2018					
Date Valid From:	January 2018					
Date Valid To:	January 2021					
Directorate / Department responsible (author/owner):	Rheumatology Dept M Wilcock, Head of Prescribing Support Unit, Pharmacy Department, RCHT					
Contact details:	01872 253548					
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists					
Suggested Keywords:	Shared care					
	RCHT		CFT		KCCG	
	✓				✓	
Executive Director responsible for Policy:	Medical Director					
Date revised:	January 2018					
This document replaces (exact title of previous version):	Shared Care Guideline for mycophenolate mofetil in Rheumatology					
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee					
Divisional Manager confirming approval processes	Not required					
Name and Post Title of additional signatories	, Governance Lead CSSC					
Signature of Executive Director giving approval	{Original Copy Signed}					
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only			
Document Library Folder/Sub Folder	Clinical / Pharmacy					
Links to key external standards	None					
Related Documents:	None					
Training Need Identified?	No					

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
Jan'18	V1.1	Some modifications to content – contraception advice and monitoring advice	M Wilcock, Head of Prescribing Support Unit

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.

This document is only valid on the day of printing

Controlled Document

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Appendix 2.Initial Equality Impact Assessment Screening Form

Name of service, strategy, policy or project (hereafter referred to as *policy)* to be assessed: Shared care guideline for mycophenolate mofetil in Rheumatology	
Directorate and service area: Pharmacy	Is this a new or existing Procedure? Existing
Name of individual completing assessment: Dan Thomas, Pharmaceutical Services Contracting Team, NHC Kernow	Telephone:01726 627953
1. Policy Aim*	To provide information on prescribing of mycophenolate mofetil in Rheumatology to enable General Practitioners to take over prescribing responsibility from secondary care.
2. Policy Objectives*	To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)
3. Policy – intended Outcomes*	Confident and competent prescribers, enabling medicines to be access in a primary care setting.
5. How will you measure the outcome?	If the guideline is not well received, publicised and adopted, then some GPs may not enter into shared care arrangements.
5. Who is intended to benefit from the Policy?	General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.
6a. Is consultation required with the workforce, equality groups, local interest groups etc. around this policy? b. If yes, have these groups been consulted? c. Please list any groups who have been consulted about this procedure.	No Cornwall & IoS Area Prescribing Committee

7. The Impact Please complete the following table.			
Are there concerns that the policy **could** have differential impact on:			
Equality Strands:	Yes	No	Rationale for Assessment / Existing Evidence
Age		✓	
Sex (male, female, trans-gender / gender reassignment)		✓	

Race / Ethnic communities /groups		✓	
Disability - learning disability, physical disability, sensory impairment and mental health problems		✓	
Religion / other beliefs		✓	
Marriage and civil partnership		✓	
Pregnancy and maternity		✓	
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		✓	

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**	**No** ✓

9. If you are not recommending a Full Impact assessment please explain why.

Signature of policy developer / lead manager / director	Date of completion and submission

Names and signatures of members carrying out the Screening Assessment	1. Dan Thomas 2. Mike Wilcock	

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead, c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

A summary of the results will be published on the Trust's web site.

Signed _____ Dan Thomas and Mike Wilcock _____

Date _____ July16 _____