DMARDs in Adult Rheumatology –Information for GPs

MYCOPHENOLATE MOFETIL

Clinicians should also refer to the overarching DMARD shared care guideline document for details of the individual responsibilities for each group e.g. e.g. GP / Specialist Rheumatology team under this shared care agreement.

Information for GPs

Indication	• Mycophenolate mofetil is recommended by NICE and National Societies for the treatment of numerous Rheumatological conditions including Vasculitis , connective tissue disorders. • Clinicians should refer to the Summary of Product Characteristics (SPC) for specific licensing information. • Use outside of the licensed indications is regarded as "off label" use.
Drug dose	• Typically, the Specialist Rheumatology team will initiate mycophenolate mofetil therapy at 500mg orally once a day for one week then increase to 500mg twice a day for one week then increase gradually by 500mg every week until optimal or maximum tolerated dose is reached. • Typical maintenance dose is 1-2g / day (in divided doses) • Maximum dose is 3g / day (in divided doses) **VARIATION TO MYCOPHENOLATE DOSING:** Limit maximum dose to 1g twice daily in CKD stages IV or V
Contra-indications / Cautions/ Dose modifications in Special Populations	• **Clinicians should refer to the Summary of Product Characteristics (SPC's) and current electronic BNF for full details** www.medicines.org.uk/emc www.bnf.org/products/bnf-online
Side effects	• Clinicians should refer to the Summary of Product Characteristics (SPC's) and current electronic BNF for full details www.medicines.org.uk/emc www.bnf.org/products/bnf-online

	• **Blood dyscrasias** (e.g. leucopenia and neutropenia) can occur hence the importance of regular blood tests • As mycophenolate mofetil is an immunosuppressant, clinicians should note to inform patients to contact their doctor immediately if they have any side effects , in particular – breathlessness, dry cough, whites of eyes becoming yellow, severe itching of skin, rash, dark urine, infections (including fever, chills or severe sore throats), new unexplained bleeding or bruising, mouth ulcers, vomiting and diarrhoea (particularly at the start of treatment, or if it is severe, at any stage in treatment). • Examples of some common side effects include: o nausea o diarrhoea o vomiting o stomach pain. • **See table 1 for details of when to contact the Specialist rheumatology team with regards blood test results and development of certain side effects etc.**
Drug Interactions	o Mycophenolate mofetil can interact with a variety of drugs, some of which can be **significant.** Examples include: o Antacids o Cholestyramine o Certain antibiotics e.g. metronidazole, co-amoxiclav, norfloxacin and rifampicin o Antiviral agents e.g. aciclovir and valciclovir o Iron salts • **This list is not exhaustive.** Clinicians should refer to the Summary of Product Characteristics (SPC) and the electronic BNF for a **full list** of potential drug interactions before starting any new medication or when stopping any existing medication. www.medicines.org.uk/emc www.bnf.org/products/bnf-online
Pre-treatment Blood Test Monitoring and screening *(To be done by Specialist Rheumatology team)*	• FBC, U+Es, LFT
Blood Test Monitoring requirements *(Typically to be monitored by the GP from week 4 onwards)* **(Ref: Based on British Society of Rheumatology Guidelines , 2017 and current clinical practise)**	• FBC, U+E, LFT **fortnightly until dose and monitoring stable for 6 weeks**, then **monthly for 3 months** then **every 12 weeks* thereafter.** ***More frequent monitoring is appropriate for patients at a higher risk of toxicity.**

	• (**NB: After any dose increase,** blood test monitoring should be carried out every fortnight until on a new stable dose for 6 weeks and then the frequency can revert back to the previous schedule). • CRP / ESR should be monitored every 3-6 months as this can help assess disease activity. • Ensure a prompt two way communication of blood test results between GP and Specialist team is available. (Paper copies should be sent between parties if electronic access via ICE is not available.)
Time to response	• Approx. 6-12 weeks
Infections	• Mycophenolate mofetil is an immunosuppressant and increases the patient's susceptibility to infections, including opportunistic infections. • Initiate prompt anti-infective treatment when indicated on the basis that the patient may be immunosuppressed to some degree. • During a serious infection*, mycophenolate mofetil should be temporarily discontinued until the patient has recovered from the infection. (* Serious infection: warrants admission to hospital or requires parenteral anti-microbial therapy.) • <u>If exposed to measles and / or chickenpox</u> : Check immunity to measles and varicella-zoster; if non-immune and exposed to measles or chickenpox contact the Specialist Rheumatology team ASAP for consideration of appropriate immunoglobulin therapy. • <u>If patient develops shingles or chickenpox</u>, stop the drug and treat with aciclovir.
Vaccinations	• The immune response to vaccination may be impaired. • Pneumovax and annual flu vaccination are recommended. • **Live vaccines should be avoided** e.g. yellow fever, varicella • GPs should contact the Specialist Rheumatology team for advice in situations where a live vaccine may be required.
Alcohol	• As both alcohol and mycophenolate mofetil can affect the liver, patients should be advised to only drink alcohol in small amounts and stay within government guidelines, which state that adults should not drink more than 14 units per week and should have alcohol free days without 'saving units up' to drink in one go.
Elective surgery	• **Contact the Specialist Rheumatology team for advise:-** Generally, mycophenolate mofetil should not routinely be stopped in the peri- operative period, although individualised decisions should be made for high-risk procedures (e.g. 'contaminated', or duration over 60 minutes), in which case it can be stopped 2 weeks prior to surgery and then restarted once wound healing is satisfactory. • Caution for early detection of infections.

Contraceptive advice (males and females)	• The Specialist Rheumatology team should discuss family planning before initiating treatment with mycophenolate mofetil • Patients should be advised that mycophenolate mofetil is contraindicated in pregnancy and that they should contact their GP and Specialist Rheumatology team if they wish to start a family. • In female patients, mycophenolate mofetil should be stopped at least 6 weeks before planned pregnancy. • Female patients should continue to use effective contraception for 6 weeks after stopping mycophenolate mofetil. • **Male patients** – to discuss with Specialist Rheumatology team.
Pregnancy and breast feeding	• Mycophenolate mofetil is teratogenic and contra-indicated in pregnancy and breast feeding. • Patients should be advised to stop taking mycophenolate mofetil and contact their GP and Specialist Rheumatology team as soon as possible if they become pregnant.
Photosensitivity	• Encourage use of sunscreens / protective covering to reduce sunlight exposure.
Malignancies	• Possible increases risk of lymphomas due to oncogenic viruses (e.g. EBV) and skin tumours.)
Drug Formulations	**Oral** • Available as 250mg capsules, 500mg tablets, oral suspension 200mg/ml. • NB: A gastro-resistant tablet is also available, however this tablet contains mycophenolate acid and **not** mycophenolate mofetil and a dose conversion is required (See BNF for details.)
Practical Points for GPs to note:	• Advise patients to attend for a blood test a week before their next prescription is due to ensure that the results can be reviewed before the next prescription is requested for issue. • Check the results of recent blood test **before** issuing a prescription. (Refer to table 1 for actions to take in the event of blood test abnormailities and side effects - page 5). • Increase blood test monitoring after a dose increase as detailed above. • Prescribers should note that whilst absolute blood test values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance. • Advise patients to contact their doctor immediately if they experience any side effects, in particular – breathlessness, dry cough, whites of eyes becoming yellow, severe itching of skin, rash, dark urine, infections (including fever, chills or severe sore throats), new unexplained bleeding or bruising, mouth ulcers, vomiting and diarrhoea (particularly at the start of treatment, or if it is severe, at any stage in treatment).

	• Advise any patients who wish to consider starting a family to contact their GP and Specialist Rheumatology team as soon as possible for advice. • Advise that any patient who becomes pregnant should stop taking mycophenolate mofetil and contact their GP and Specialist Rheumatology team as soon as possible. • Provide a maximum of 4 weeks supply at a time.
Patient Information Leaflets	• Patients should be advised to read the Arthritis Research UK patient information leaflet and the package insert. • The current Arthritis Research UK leaflet can be downloaded from: http://www.arthritisresearchuk.org/arthritis-information/drugs/mycophenolate.aspx

Table 1:

Actions to be taken

Prescribers should note that whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance and urgent discussion with Specialist Rheumatology team.

WBC <3.5 x 10^9/L	**Withhold and contact Specialist Rheumatology team urgently if any of the results opposite develop.**
Neutrophils <1.6 x 10^9/L	
Unexplained eosinophilia >0.5 x 10^9/L	
Platelet count <140 x 10^9/L	
MCV > 105 f/L	
Creatinine >30% above baseline and/or calculated GFR <60	
ALT and/or AST >100 units/L	
Unexplained fall in serum albumin	
Any rapid fall or consistent downward trend in any indices	

Abnormal bruising with or without sore throat	**Immediate FBC and withhold until result available and contact the Specialist Rheumatology team.**
Nausea, vomiting, abdominal pain, diarrhoea, dyspepsia	**Withhold until discussed with Specialist rheumatology team.**

BACK-UP ADVICE AND SUPPORT

- **GP queries should be directed to the Rheumatology consultants.**
- **Patient queries should be directed to the Rheumatology Specialist Nurses**

All urgent requests should be answered within one working day.

Contact Details:

The Luton & Dunstable Hospital

Consultants

Dr Daniel Fishman, Dr Muhammed Nisar, Dr Tanya Baqai

Dr Balaji Ramabhadran, Dr Vanessa Quick, Dr Marian Chan

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Specialist Nurses

Nicki Wood, Julie Begum, Sue O'Connor : **Nurse Advice Line**: 01582 718305

Bedford Hospital

Consultants :

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References:

- BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with British Association of Dermatologists. Rheumatology.2008 K Chakravarty et al. www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/diseasemodifying_antirheumatic_drug_dmard_therapy.pdf
- BSR/BHPR Non-biologic DMARD guidelines ((2017) https://academic.oup.com/rheumatology/article/56/6/865/3053478
- SPC (Summary of product characteristics) www.electronicmedicinescompendium.com
- BNF (electronic) www.bnf.org/products/bnf-online