

## Mycophenolate for rheumatoid arthritis and other rheumatological diseases (Adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between consultants and general practitioners (GPs).

This guideline reinforces the basic premise that:

When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the “sharing of information with the individual GP and their mutual agreement to the transfer of care.”

These are not rigid guidelines. On occasions, consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

### Indications:

Unlicensed indications: severe rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus and other rheumatological conditions.

### Dosage and administration:

Week one: 500mg orally in the morning. If tolerated:  
Week two: 500mg orally twice daily  
Week three: 1g orally in the morning, 500mg in the evening  
Week four onwards: 1g orally twice daily.  
Further increase by 500mg each week until optimal or maximum tolerated dose is reached to maximum 3g/day.

### Additional Information

- Patients should be instructed to report immediately any evidence of infection, unexpected bruising, bleeding or any other manifestation of bone marrow depression
- Increase susceptibility to skin cancer – avoid exposure to strong sunlight
- Mycophenolate should not be given to women who are pregnant, or likely to become pregnant. Effective contraception must be used before starting therapy, during therapy, and for six weeks following discontinuation of therapy. Men should use reliable contraception during treatment and for 13 weeks after completion.

### Monitoring requirements:

Before treatment:

- Full blood count (FBC) including platelets, urea and electrolytes (U&Es), creatinine, liver function tests (LFTs), Chest X-ray

During treatment:

- FBC, LFTs, U/Es and creatinine weekly for the first month then if stable twice monthly for 3 months then every 2 months thereafter if stable
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)
- ESR monthly for disease monitoring purposes

### Responsibility for monitoring, once stable, rests with the GP

### Action to be taken if abnormal results/adverse effects:

- WBC <  $3.5 \times 10^9/l$       Check neutrophil count
- Neutrophils <  $2.0 \times 10^9/l$       Monitor weekly. If it falls below  $1.5 \times 10^9/l$  STOP DRUG and contact helpline.
- Platelets <  $150 \times 10^9/l$       Monitor weekly. If drop below  $100 \times 10^9/l$  contact helpline
- Abnormal bruising      Repeat FBC and act on results as above
- Sore throat      Repeat FBC and act on results as above

- Recurrent infections associated with hypogammaglobulinaemia: Measure serum immunoglobulin levels and contact helpline
  - Development of persistent respiratory symptoms, such as cough, dyspnoea: contact helpline
- Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.**

#### **Contraindications:**

- Mycophenolate should not be given to women who are pregnant, or likely to become pregnant. Effective contraception must be used before beginning therapy, during therapy, and for six weeks following discontinuation of therapy
- Mycophenolate is contraindicated in women who are breastfeeding.
- Live vaccines are contra-indicated in patients with impaired immune response.
- Hypersensitivity to mycophenolate mofetil or mycophenolic acid.

#### **Drug interactions: Check appendix 1 of current BNF before co-prescribing any medicines**

- Rifampicin-reduces plasma concentration of active metabolite of mycophenolate
- Antacids – absorption of mycophenolate reduced
- Metronidazole possibly reduces bioavailability of mycophenolate
- Norfloxacin possibly reduces bioavailability of mycophenolate
- Cholestyramine should not be taken at the same time of day as it will impair the absorption of Mycophenolate
- Oral Iron should not be taken at the same time of day as it will impair the absorption of Mycophenolate -
- Aciclovir – mycophenolate increases aciclovir plasma levels (significant only in renal impairment)
- Ganciclovir: mycophenolate possible increases plasma concentration of ganciclovir, also plasma concentration of inactive metabolite of mycophenolate possibly increased
- Sevelamer: plasma concentration of mycophenolate possibly reduced

#### **Cautions:**

- Active serious digestive system disease (risk of haemorrhage, ulceration and perforation).
- Elderly (increased risk of infection, gastrointestinal haemorrhage and pulmonary oedema)
- Patients with suspected lymphoproliferative disorder or unexplained anaemia, leucopenia and thrombocytopenia.
- Patients receiving immunosuppressive therapy are at slightly increased risk of developing lymphomas and other malignancies, notably skin cancers – exposure to sunlight and UV light should be limited and patients should be advised to wear protective clothing and use a sunscreen with a high protection factor.

#### **Adverse Effects:**

taste disturbance, gingival hyperplasia, nausea, constipation, flatulence, anorexia, weight loss, vomiting, abdominal pain, gastro-intestinal inflammation, ulceration, and bleeding, hepatitis, jaundice, pancreatitis, stomatitis, oedema, tachycardia, hypertension, hypotension, vasodilatation, cough, dyspnoea, insomnia, agitation, confusion, depression, anxiety, convulsions, paraesthesia, myasthenic syndrome, tremor, dizziness, headache, influenza-like syndrome, infections, hyperglycaemia, renal impairment, malignancy (particularly of the skin), blood disorders (including leucopenia, anaemia, thrombocytopenia, pancytopenia, and red cell aplasia), disturbances of electrolytes and blood lipids, arthralgia, alopecia, acne, skin hypertrophy, and rash, intestinal villous atrophy, progressive multifocal leucoencephalopathy, interstitial lung disease, pulmonary fibrosis

#### **Specialist responsibilities:**

- Confirm the diagnosis of rheumatoid arthritis, psoriatic arthritis or systemic lupus erythematosus

- Discuss with the patient the benefits and side effects of treatment with mycophenolate
- If the patient is a woman of child bearing potential or male – ensure that they are aware of the importance of effective contraception and the need to discuss with their consultant if they wish to become pregnant
- Ensure baseline monitoring of full blood count and biochemical profile.
- Discuss how the patient/carer can be aware of possible signs of mycophenolate toxicity or intolerance
- Ensure that the patient understands and accepts their responsibilities (see section below)
- Seek consent for treatment and document in the patient's notes. Informed consent for 'off-label' use should be obtained and documented. This consent should be communicated to the GP.
- Provide written instruction to the GP for initiation and escalation of mycophenolate.
- Provide the patient with a monitoring booklet and enter the blood results into the booklet.
- Review the patient at the intervals specified below to monitor the patient's disease activity, the efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
- Discontinue if no response or patient has a significant adverse effect.
- Promptly communicate with the GP via a clinic letter any changes in treatment, results of monitoring undertaken, and assessment of adverse events. The clinic letter should clearly state if the dose has remained the same or if a dose adjustment had been made – specifically highlighting the new dose in comparison with the preceding one.
- Advise GPs when to stop treatment.
- Provide clear arrangements for back-up, advice and support.
- Report serious adverse events at <https://yellowcard.mhra.gov.uk/>

#### **GP's responsibilities:**

- Initial referral to Consultant Rheumatologist raising the possibility of rheumatological disease
- Provide the patient with monthly repeat prescriptions of medication following written instructions for initiation and escalation by the specialist. The patient should allow at least 48 hours for the prescription from the GP to be generated.
- Continue monitoring as outlined on the first page and document the results in the shared care booklet.
- Ensure patient's shared care booklet and practice computer system are updated with any dose changes.
- Refer promptly to the specialist if there is a change in the patient's status or concerns regarding compliance. In most cases, do not stop treatment without discussion with the Rheumatology Helpline.
- If patient fails to attend more than 2 monitoring visits it is not safe to continue treatment – contact the Rheumatology Helpline for advice.
- Report serious adverse events to the specialist and at <https://yellowcard.mhra.gov.uk/>
- Administer Pneumococcal Vaccine/ Pneumovax® II and annual influenza vaccines.
- Consider passive immunisation with Varicella zoster immunoglobulin in non-immune patients exposed to chicken pox or shingles.

#### **Patient responsibilities:**

- Read the written patient information provided about the drug and have a clear understanding of the risks / benefits of mycophenolate treatment.
- Attend for blood tests.
- Report any adverse effects to their GP and/or specialist whilst treated with mycophenolate.
- Limit alcohol to national safe weekly limits

- Take monitoring booklet every time the patient sees the GP, has a hospital appointment or visits the pharmacist.

**Secondary care review: During initiation:** 4 – 6 weekly until controlled

**Once disease controlled:** Annual review by consultant

Availability: 250mg capsule: 100 = £82.26 500mg tablet: 50 = £9.31

(*Online Drug Tariff February 2016*)

**Back up advice and support:**

Rheumatology Helpline

**Telephone:** 0151 604 7505

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