Oxford University Hospitals NHS
NHS Trust

NHS
Oxfordshire
Clinical Commissioning Group

Mycophenolate Mofetil for use in Ocular Inflammation (Ophthalmology) - Adults and Paediatrics
Shared Care Protocol

This protocol provides prescribing and monitoring guidance for mycophenolate mofetil therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF.

Shared Care Responsibilities

Shared care assumes communication between the specialist, GP and patient. The intention to share 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.

Specialist

- Complete pre-treatment assessment (detailed below)
- Initiate treatment and prescribe until the dose is stable and/or the GP formally agrees to shared care. This would normally mean OUHNHSFT would prescribe the first 28 days of treatment.
- Ensure the patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly (supplied by pharmacist in clinic)
- Provide copy of patient information leaflet and drug monitoring card where appropriate (supplied by pharmacist in clinic)
- Send a letter to the GP requesting shared care. Outline shared care protocol criteria
- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments
- Be available to give advice to GP and patient throughout treatment
- Patients will be followed up by telephone call from the clinic pharmacist approx. 4 weeks after starting treatment to confirm they are tolerating the medicine, 2 week blood test has been completed and whether there are any other issues.
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GP

- Prescribe medication once the dose is stable or shared care is agreed
- Ensure all monitoring is completed in accordance to the specific shared care protocol (listed under on-going monitoring).
- Check and record results then advise the specialist of any deteriorations or abnormal results
- Notify the specialist to any changes in patients condition, any adverse drug reactions or failure to attend tests

Patient

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Attend for blood tests and monitoring when required
- Ensure monitoring card is kept up to date and is brought to all appointments
- Report any side effects to the GP or a member of the specialist team

Background for Use
Mycophenolate mofetil is an immunosuppressive drug. It is often referred to as a "steroid sparing agent" or "immunomodulator." Mycophenolate mofetil (MMF) should only be initiated on the recommendation of a specialist. Its uses in this protocol are limited to those mentioned below.

Mycophenolate is used to treat a range of ocular inflammatory diseases. Whilst mycophenolate is not licensed for these indications, its use is supported by a good body of evidence.

Supporting Information
- Mycophenolate may be used alone or in combination with other immunomodulatory drugs e.g. tacrolimus, prednisolone.
- Mycophenolate is used as a second line therapy for those patients who require more than 7.5mg prednisolone/day to control disease, require frequent high dose steroids due to frequently relapsing disease or those with severe disease on presentation.

Contraindications and Precautions

Pregnancy and breastfeeding	Avoid in pregnancy or those trying to conceive. Exercise extreme caution when mycophenolate is used in patients with childbearing potential and in breastfeeding mothers. Only be given to women of childbearing potential who are using highly effective contraception Female patients who can become pregnant must use at least one reliable form of contraception before, during and for 6 weeks after stopping treatment. Two forms of contraception are preferred but no longer mandatory. Avoid in breast feeding.
Family Planning	For male patients, EMA now recommends that either the male patient or his female partner use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment.
Active serious gastro-intestinal disease	Risk of haemorrhage, ulceration and perforation
Elderly	Increase risk of infection, gastro intestinal haemorrhage and pulmonary oedema
Pre-existing bone marrow disorder/cytopaenia	Ask patient to report any new symptoms e.g. infection, bruising or bleeding
Vaccination with LIVE vaccines	Patients receiving mycophenolate must NOT receive immunisation with LIVE vaccines. Inactivated polio is available although sub-optimal response may be seen.
Chicken pox /Shingles	Patients suffering from chickenpox or active skin lesions in shingles withhold mycophenolate and inform specialist team. Exposure to chickenpox or shingles passive immunization should be carried out using VZIG
Alcohol	Limit alcohol intake to 14 units per week
Localised or systemic infections	Withhold mycophenolate if patient has a serious infection, including hepatitis B and C and a history of tuberculosis. Patients being treated with mycophenolate are at increased risk for opportunistic infections, fatal infections and sepsis. These infections are often related to a high total immunosuppressive burden and may lead to serious and fatal conditions that physicians should consider in the differential diagnosis in immunosuppressed patients with deteriorating renal

	function or neurological symptoms.
HGPRT Deficiency	Mycophenolate is an inosine monophosphate dehydrogenase (IMPDH) inhibitor and should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.
Sunlight/UV exposure	Patients receiving MMF are at increased risk of developing lymphomas and other malignancies, particularly of the skin. Give general advice to minimise risk of skin cancer i.e. patients should wear protective clothing and use a sunscreen with a high protection factor.
NSAIDs	May be used unless GFR is low.
Blood donation	Patients must not donate blood whilst on treatment with mycophenolate or for 6 weeks after completion of treatment
Sperm donation	Male patients must not donate sperm whilst on treatment with mycophenolate or for 90 days after completion of treatment

Dosage

Indication	**Dose**
Ocular inflammation/uveitis (Ophthalmology) Adults	The usual dose is up to 2grams per day in two divided doses (orally), however the dose may be increased to a maximum of 3grams per day (1.5g BD) Mycophenolate may be started at full dose or started at a lower dose of 500mg BD for 1-2 weeks if there is concern over intolerance.
Ocular inflammation/uveitis (Ophthalmology) Children	2-18 years: 300mg/metre2 twice daily up to a maximum of 2g daily

Time to Response

It may take up to three months for treatment with mycophenolate to take effect, no action is required during this time. Response to treatment is the responsibility of the specialist but will be communicated to the GP.

Pre-Treatment Assessment

Height
Weight
BP
Baseline FBC, U+E, LFT if nil results available in previous 3 months
Pregnancy test (where applicable)
Hepatitis B/C screening (if risky behaviours identified)
HIV screening (if risky behaviours identified)

Ongoing Monitoring

FBC, U+E, LFTs 2 weeks after starting treatment then
FBC, U+E, LFTs monthly for 3 months then
FBC, U+E, LFTs every 2 months to continue

May be extended further to 3 monthly if results are stable beyond 2 years on therapy
Interval may be shortened if patient is at risk of toxicity

FBC, U+E, LFTs should be repeated 2 weeks after any dose change then revert to previous monitoring schedule.

Where applicable: Pregnancy tests should be repeated as clinically required (e.g. after any gap in contraception is reported)

Actions to be taken

Side Effects	***Action***
WBC < 3.5 X 10^ 9/l	Withhold until discussed with specialist team. Please note that lupus patients and those on steroids often have lymphopenia so often have a normal neutrophil count but total WCC might be low.
Neutrophils < 1.6 X 10 ^ 9/l	Withhold until discussed with specialist team.
Platelets < 140 X 10 ^ 9/l	Withhold until discussed with specialist team.
Unexplained eosinophilia >0.5 x 10 ^ 9/l	Withhold until discussed with specialist team.
Alk Phos, ALT, AST > 2x rise from upper limit of reference range or ALT/AST >100U/L	Withhold until discussed with specialist team.
Albumin < 30g/L	Withhold until discussed with specialist team.
Creatine increase > 30% over 12 months and/or calculated GFR <60ml/min	Withhold until discussed with specialist team.
MCV > 105	Check B12, folate and TFT. If low start appropriate supplementation. Check alcohol status
Sterile haematuria / UTI	Withhold until discussed with specialist team.
Rash	Withhold until symptoms clear. Consider re- challenging at a lower dose. If rash recurs stop MMF and discuss with specialist team
Oral Ulceration	Treat oral ulceration and check FBC. Only stop if neutrophil count is low.
Hypersensitivity reactions	Fever, malaise, rash, vomiting, muscle/bone pain, dizziness. Stop mycophenolate
Nausea, vomiting, diarrhoea	Administer tablets after meals to reduce nausea. An anti-emetic or dose reduction may help. If symptoms persist stop mycophenolate
Abnormal bruising or sore throat	Withhold until FBC result available
Malignancy	Discuss with specialist team.

Please note that in addition to absolute values for haematological indices a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance. NB. Some liver patients with cirrhosis will have pre-existing pancytopenia and lupus patients may have leucopenia because of lymphopenia.

Other side effects include (For a full list refer to BNF and SPC):
Gastrointestinal symptoms (abdominal pain, nausea, diarrhoea, vomiting, ulceration and haemorrhage)
Urogenital (sterile haematuria, urinary tract infection, renal tubular necrosis)
Hyperglycaemia
Psychiatric disorders- agitation, insomnia
Headache
Alopecia

Notable Drug Interactions (Refer to BNF and SPC)

- Antacids and oral magnesium supplements reduce mycophenolate absorption and if required should be separated from mycophenolate by 2-3 hours
- **Mycophenolate may reduce the effectiveness of oral or implant contraception therefore 2 forms of contraception are recommended.**
- Cholestyramine: may decrease the absorption and bioavailability of mycophenolate by 40%.
- Oral iron may reduce absorption
- Metronidazole and norfloxacin may reduce bioavailability.
- Plasma concentration of active metabolites of mycophenolate are reduced by rifampicin.
- Ciclosporin A – Ciclosporin A pharmacokinetics are unaffected by mycophenolate however, if concomitant ciclosporin treatment is stopped, an increase in plasma concentration of MMF of upto 30% is to be expected.
- Aciclovir – mycophenolate increases plasma concentration of aciclovir. Plasma concentration of inactive metabolite of mycophenolateincreased.
- Clozapine – can lead to agranulocytosis
- Phenytoin– reduced absorption of antiepileptic

Back-up Information and Advice

Name, job title, department	Contact Details (phone/email)
Clare Faulkner Specialist Pharmacist-Ocular Inflammation Service	Service email: oeh.uveitis@nhs.net 01865 741166 bleep 8314

References

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