Humber Area Prescribing Committee

# SHARED CARE FRAMEWORK for Mycophenolate mofetil and mycophenolic acid for patients within adult services (non-transplant indications)

HUMBER AREA PRESCRIBING COMMITTEE

DATE APPROVED BY APC: 2ND OCTOBER 2024

REVIEW DATE: OCTOBER 2027

| *PATIENT NAME* | *NHS NUMBER* | *DATE OF BIRTH* |
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| | | |
| *ADDRESS* | | |
| *GP'S NAME* | | |

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Date:……

Specialist Prescriber's Signature……

Professional register name and registration number ……..

Consultant's name (if working under direction of Consultant) ……

Speciality/Department:……..

Primary care prescriber name: …… Date:……

Primary care prescriber Signature ……..... …….

Professional register name and registration number:……

If the primary care prescriber is unable to accept prescribing responsibility for the above patient the specialist prescriber should be informed within two weeks of receipt of this framework and specialist prescriber letter. In such cases the primary care prescriber are requested to update the specialist prescriber, by letter, of any relevant changes in the patient's medication / medical condition.

Humber Area Prescribing Committee

# Shared Care Framework for *Mycophenolate mofetil and mycophenolic acid for patients within adult services (non-transplant indictions)*

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| 1. Introduction: | Mycophenolate mofetil is a pro-drug of the active metabolite mycophenolic acid. Mycophenolic acid is a suppressor of T and B cell proliferation and adhesion and inhibits inosine monophosphate dehydrogenase and eventually blocks the progression to DNA synthesis and proliferation. | |
| 2. Indication: | Off-label use for the treatment of chronic inflammatory conditions where use of mycophenolate mofetil is appropriate, including but not limited to the following specialities and conditions:<br>• Dermatology (e.g. myositis, severe psoriasis, severe atopic dermatitis/eczema, autoimmune bullous dermatoses, SLE)<br>• Gastroenterology (e.g. Crohn's disease, ulcerative colitis)<br>• Haematology (e.g. idiopathic thrombocytopenic purpura)<br>• Hepatology (e.g. auto-immune hepatitis)<br>• Neurology (e.g. inflammatory neuropathies, myasthenia gravis)<br>• Ophthalmology (e.g. uveitis, scleritis)<br>• Oral medicine (e.g. Behçet's disease, refractory inflammatory oral disease)<br>• Renal medicine (e.g. immune-mediated nephritis)<br>• Respiratory disease (e.g. interstitial lung disease)<br>• Rheumatology (e.g. rheumatoid arthritis, systemic lupus erythematosus [SLE], vasculitis)<br>These indications are off-label. The initiating specialist must specify the indication for each patient when initiating shared care and clearly state when use is off-label.<br>This shared care protocol applies to adults aged 18 and over. It does not include use of mycophenolate mofetil for transplant indications. | |
| 3. Licensing Information | Mycophenolate is only licensed for the prevention of acute kidney, heart or liver transplant rejection (in combination with prednisolone or ciclosporin). It is not licensed for all the conditions it is used to treat. However, its use as a disease modifying anti-rheumatic drug (DMARD) and for the indications below are well established and supported by clinical specialists.<br>*All the indications are off label indications for mycophenolate mofetil and mycophenolic acid.* | |
| | Route | Oral |

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| 4. Pharmaceutical Information | Formulation | <u>Mycophenolate mofetil</u><br><br>Mycophenolate mofetil 250 mg capsules<br><br>Mycophenolate mofetil 500 mg tablets<br><br>Mycophenolate mofetil 1g/5mL powder for oral suspension.<br><br>Mycophenolate should be prescribed generically, and not by brand name. Brands include Cellcept® and Myfenax®; generics are available and may be more cost effective.<br><br><u>Mycophenolic acid</u><br><br>Mycophenolic acid gastro-resistant capsules 180 mg and 360 mg tablets<br><br>Mycophenolic acid 720 mg is approximately equivalent to mycophenolate mofetil 1 g but unnecessary switching should be avoided, due to pharmacokinetic differences. Mycophenolic acid should usually be reserved for patients who do not tolerate mycophenolate mofetil. |
| | Administration details | Mycophenolate mofetil can be taken with or without food.<br><br>If a dose is missed it should be taken as soon as remembered, then dosing resumed at the usual times. However, <u>a double dose should not be taken to make up for a missed dose.</u> |
| | Additional information | Capsules and tablets should not be opened crushed, or chewed, to avoid inhalation or direct contact with skin or mucus membranes of the active substance. If such contact occurs, wash thoroughly with soap and water; rinse eyes with plain water. |
| 5. Supporting evidence | *Include links to relevant guidance e.g. NICE TAs, national guidance* | |
| 6. Initiation on ongoing dosage regimen | Transfer of monitoring and prescribing to primary care is normally after at least 12 week, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.<br>The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. | |

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| | All dose or formulation adjustments will be the responsibility of the specialist unless directions have been discussed and agreed with the primary care clinician.<br>Termination of treatment will be the responsibility of the specialist.<br><br>**Initial stabilisation:**<br>To be determined by the specialist based on indication and disease severity. Typically mycophenolate mofetil 250mg or 500mg once or twice daily, increasing in weekly increments.<br>**The loading period must be prescribed by the initiating specialist.**<br><br>**Maintenance dose (following initial stabilisation):**<br>Typically mycophenolate mofetil 1-2 grams daily, in divided doses.<br>Maximum dose: 3 grams daily.<br>**The initial maintenance dose must be prescribed by the initiating specialist.**<br><br>**Mycophenolic acid**<br>Mycophenolic acid 720 mg is approximately equivalent to mycophenolate mofetil 1 g, but unnecessary switching should be avoided due to pharmacokinetic differences. Switches should only be performed by, or with the advice of, the specialist team. Mycophenolic acid should usually be reserved for patients who do not tolerate mycophenolate mofetil.<br><br>**Conditions requiring dose adjustment:**<br>The maximum recommended dose in severe chronic renal impairment (GFR less than 25 mL/min/1.73m$^2$) is:<br>• Mycophenolate mofetil:1 gram, twice daily<br>Mycophenolic acid: 720 mg, twice daily |
| 7. Contraindications and Warnings: | **Contraindications:**<br><br>• Hypersensitivity to mycophenolate mofetil or any excipients<br>• Pregnancy or breastfeeding<br><br>**Cautions:**<br>• Localised or systemic infection.<br>• Very frail or elderly patients.<br>• Patients with suspected lymphoproliferative disorder.<br>• Patients with unexplained anaemia, leukopenia or thrombocytopenia.<br>• Active gastrointestinal disease.<br>• Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever): should usually be avoided in patients taking mycophenolate. Live shingles vaccine should be avoided in |

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| | patients taking mycophenolate 1g/day or more, or lower doses together with prednisolone 7.5 mg/day or more. Please refer to the Green Book Chapter 6 (cautions and contraindications), together with chapters for the specific vaccine under consideration, for current advice. A non-live vaccine can still be used. Contact the specialist if further guidance is required.<br>• Dose reduction or discontinuation should be considered for patients in cases of clinically significant COVID-19.<br>• As there is a potential increased risk of malignancy, any pre-malignant disease should be adequately treated before starting therapy and patients should be up to date with relevant national cancer screening programmes.<br>• Due to the increased risk of skin cancer, exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with a high protection factor<br>• Avoid if previous hepatitis B or C infection, or recurrent shingles<br>• Marked renal failure (eGFR below 25 mL/min).<br>• Paternal exposure. See section 15.<br>• Patients should not donate blood during therapy or for at least 6 weeks following discontinuation of mycophenolate. Men should not donate semen during therapy or for 90 days following discontinuation of mycophenolate.<br>In addition, the MHRA have also issued the following Drug Safety Updates for mycophenolate:<br>• Mycophenolate mofetil: pure red cell aplasia (Dec 2014)<br>• Mycophenolate mofetil (CellCept) and mycophenolic acid: risk of hypogammaglobulinaemia and risk of bronchiectasis (Jan 2015) |
| 8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist | **Baseline investigations**:<br>• Full blood count (FBC)<br>• Urea and electrolytes (U&E), including creatinine and creatinine clearance (CrCl)<br>• Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), and albumin<br>• Height & weight<br>• Blood pressure<br>• Screening for viral infections as per local policy, e.g. HIV and hepatitis B and C, varicella zoster, Epstein Barr virus, cytomegalovirus<br>• Before starting mycophenolate mofetil treatment, people of childbearing potential should have a negative pregnancy test. Two serum or urine pregnancy tests with a sensitivity of at least 25 mIU/mL are recommended. A second test should be done 8-10 days after the first one and immediately before starting mycophenolate mofetil, unless exceptional circumstances exist whereby a delay in the initiation of treatment would cause harm to the patient and the prescriber is satisfied that a single test is adequate to rule out pregnancy. Pregnancy tests should be repeated as clinically required (e.g. after any gap in |

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<tr><td></td><td colspan="2">contraception is reported). See MHRA Drug Safety Update for more detail<br>• Screening for lung disease, including tuberculosis, should be undertaken at clinician discretion on a case by case basis<br>• Provide or request appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19)<br><br>Initial monitoring:<br>To be repeated every 2 weeks until the dose has been stable for 6 weeks, then monthly for 3 months:<br>• FBC<br>• U&Es, including creatinine and CrCl<br>• AST and/or ALT, and albumin<br>Following a dose increase repeat every 2 weeks until the dose has been stable for 6 weeks, then revert to previous schedule.<br>Ongoing monitoring:<br>The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment, and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.</td></tr>
<tr><td rowspan="3">9. Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>• FBC<br>• U&Es including creatinine and CrCl<br>• ALT and/or AST and albumin</td><td>Monthly for three months, unless already completed in secondary care. Thereafter at least every 12 weeks, and more frequently in patients at higher risk of toxicity, as advised by the specialist team.<br><br>The exact frequency of monitoring to be communicated by the specialist in all cases.</td></tr>
<tr><td>• Patients aged 50-79 years old could be eligible for the shingles vaccine (herpes zoster). For patients taking mycophenolate 1g/day or more, or lower doses together with prednisolone 7.5 mg/day or more, a non-live vaccine should be used. Specialist input may be required. If patient is taking additional DMARDs, check advice for all drugs. Please refer</td><td>• Shingles vaccination: one-off.<br>• Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list.<br>• COVID-19 vaccination as per national schedule.</td></tr>
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| | to Green Book Chapter 6 (cautions and contraindications) and Chapter 28a (Shingles) for further details.<br>• Annual influenza (The Green Book, Chapter 19) vaccinations are recommended.<br>• COVID-19 vaccination is safe and recommended (see The Green Book, Chapter 14a). | |
| | **(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.** | |
| 10. Interactions | The following drugs are known or suspected interactions and the GP may wish to discuss with the initiating specialist before commencing: | |
| | Interacting Drug | Advice |
| | **Aciclovir / ganciclovir / valaciclovir / valganciclovir**: | possible increased plasma concentration of antiviral and mycophenolate metabolite especially in patients with renal impairment; possible increased risk of haematological toxicity |
| | **Antacids and proton pump inhibitors** | Magnesium and aluminium containing antacids – reduces absorption of mycophenolate. Best avoided, if concurrent use is unavoidable standard advice is to leave a 2 hour gap.<br>PPIs: Reduced absorption of mycophenolate. Clinical evidence is unclear and no specific advice. |
| | **Further immunosuppression e.g. azathioprine, ciclosporin, sirolimus**: | increased risk of bone marrow suppression. Azathioprine is never used in combination with mycophenolate |
| | **Cholestyramine / colesevelam**: | reduced absorption of mycophenolate - avoid use |
| | **Ciclosporin**: | reduced mycophenolate exposure – higher doses of mycophenolate normally recommended by specialist if used in combination |
| | **Isavuconazole**: | possible increased risk of mycophenolate adverse effects due to increased exposure to mycophenolate or its metabolite |

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| | **Telmisartan**: | may reduce mycophenolate exposure |
| | **Rifampicin**: | decreased plasma concentration of mycophenolate. Monitor concurrent use |
| | **Sevelamer**: | reduced mycophenolate exposure; separate administration by 1-3 hours |
| | Other interacting agents:<br>• **Live vaccines**: Increased risk of generalised infection. Consult the Green Book for the most up to date advice<br>**For full list see SPC at www.medicines.org.uk/emc and BNF** | |
| 11. Adverse effects and management | Adverse effects | Action for GP |
| | • White blood cells less than $3.5x10^9$/L<br>• Lymphocytes less than $0.5x10^9$/L<br>• Neutrophils less than $1.6x10^9$/L<br>• Platelets less than $140x10^9$/L<br>• Eosinophilia greater than $0.5x10^9$/L | Discuss urgently with specialist team, and consider interruption |
| | Mean cell volume >105 fL | Consider interruption in treatment.<br><br>Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal discuss with specialist team urgently. |
| | Signs or symptoms of bone marrow suppression, e.g. unexplained bleeding or bruising with or without sore throat, mouth ulcers | Check FBC immediately and discuss with the specialist team. See haematological monitoring above. |
| | **Infections**:<br><br>Infection requiring antibiotics | Temporarily withhold mycophenolate until the patient has recovered. |

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| | Recurrent or opportunistic infections<br><br>Exposure to chickenpox or shingles | Review for reversible causes. Withhold and discuss with specialist team.<br><br>Contact specialist team for advice. See the Green Book (chapter 34) and PHE guidance for detailed advice on risk assessment and post exposure prophylaxis. |
| | **Liver function tests**:<br><br>ALT or AST > 3 x upper limit of normal (ULN), or any sudden increases (e.g. double of baseline), OR Unexplained fall in serum albumin <30g/L | Withhold and discuss with specialist team.<br><br>Check any other reason for risk of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication. |
| | **Renal function**:<br><br>Creatinine rise >30% over 12 months, or calculated GFR reduces to <60ml/min | Withhold and discuss with specialist team |
| | **Gastrointestinal disorders**:<br><br>Very common adverse effects include nausea and vomiting, abdominal cramps, diarrhoea and dyspepsia. | Review for reversible causes. Advise patient to take with food. If no improvement contact specialist team. |
| | GI ulceration, bleeding and perforation | Review for reversible causes. Withhold and discuss urgently with specialist team. |
| | Suspected pancreatitis | Withhold and discuss with specialist team |
| | **Skin disorders**:<br><br>Skin hypertrophy, acne, alopecia | Review for reversible causes. Discuss with specialist team if symptoms become troublesome. |
| 12. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient | **The patient should be advised to report any of the following signs or symptoms to their GP without delay:**<br>• Rash<br>• Abdominal pain or jaundice (skin or whites of the eyes appear yellow) | |

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| information leaflets on individual medicines. | • Signs and symptoms suggestive of bone marrow suppression e.g. sore throat, oral ulceration, abnormal bruising or bleeding, or signs of infection.<br>• Exposure to chickenpox or shingles or if the patient develops chicken pox or shingles.<br>• Pregnancy or they or their partner are planning to become pregnant.<br><br>**The patient should be advised:**<br>• During a serious infection (requiring antibiotics) mycophenolate mofetil should be temporarily discontinued until the patient has recovered from the infection.<br>• If exposed to chickenpox or shingles patient must alert their primary care prescriber or specialist team and seek advice.<br>• That vaccination in line with current national advice (e.g. for COVID-19, influenza) is safe and recommended.<br>• Tell anyone who prescribes them a medicine that they are taking mycophenolate. Always ask a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.<br>• Patients have a small increased risk of skin cancers so should be advised to wear high factor sunscreen and to wear a hat and protective clothing when in strong sunshine. Sun beds should be avoided. Patients should be advised to carry out regular self-examination of the skin and report if there are any new lesions and/or changes to skin.<br>• Mycophenolate mofetil may cause somnolence, confusion, dizziness, tremor or hypotension, and therefore patients are advised to use caution when driving or using machines.<br>• To use effective contraception, and to take a pregnancy test if they think they could be pregnant. Patients should inform the specialist or GP immediately if they or their partners become pregnant or are planning a pregnancy.<br>• Not to donate blood during treatment or for 6 weeks after stopping, and not to donate semen during treatment or for 90 days after stopping.<br>• To avoid contact with people with chicken pox or shingles and report any such contact urgently to their primary care prescriber. If the patient is exposed, contact the specialist for advice. For detailed advice on risk assessment and post exposure prophylaxis following exposure to chicken pox and shingles, see:<br>  ○ the Green Book (Chapter 34) |

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| | ○ UKHSA guidance: Guidelines on post exposure prophylaxis (PEP) for varicella/shingles.<br><br>Patient information leaflets:<br>• General information: Patient.info<br>• Rheumatology: Versus Arthritis<br>• Dermatology: British Association of Dermatologists<br>• Patient information leaflets are also available from electronic medicines compendium |
| 13. Preconception, Pregnancy, paternal exposure and breast feeding<br>It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist. | **Preconception**<br>**All patients should be informed of the risks and benefits of taking this medicine during pregnancy and breastfeeding. The specialist team should be contacted if a patient becomes pregnant or is planning to become pregnant or breastfeed.**<br><br>**Pregnancy:**<br>**Mycophenolate is contraindicated during pregnancy or breastfeeding. Contraception should be used for 6 weeks after stopping the drug.**<br>Treatment should not be initiated without providing a negative pregnancy test.<br>Because of the genotoxic and teratogenic potential of mycophenolate mofetil, people of childbearing potential must use at least one highly effective form of contraception before and during treatment and for six weeks after stopping mycophenolate unless abstinence is the chosen method of contraception. Two forms of contraception used simultaneously are preferred. See MHRA Drug safety update and letter sent to healthcare professionals. See also more recent advice:<br>• MHRA Drug Safety Update: Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?<br>• Faculty of Sexual and Reproductive Healthcare statement on contraception for women using known teratogenic drugs or drugs with potential teratogenic effects.<br><br>Methods of contraception which are considered 'highly effective' in this context include the long-acting reversible contraceptives (LARC) copper intrauterine device (Cu-IUD), levonorgestrel intrauterine system (LNG-IUS) and progestogen-only implant (IMP) and male and female sterilisation, all of which have a failure rate of less than 1% with typical use. (Note that patients using IMP must not take any interacting drugs that could reduce contraceptive effectiveness).<br>• Information for healthcare professionals: UK Teratology Information Services (UKTIS) |

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| | • Information for patients and carers: Best Use of Medicines in Pregnancy (BUMPs)<br><br>**Breastfeeding:**<br>Mycophenolate should not be prescribed for people who are breastfeeding.<br>Information for healthcare professionals: UK Drugs in Lactation Advisory Service (UKDiLAS)<br><br>**Paternal Exposure**<br>Limited evidence does not indicate an increased risk of malformations or miscarriages in pregnancies where the father is taking mycophenolate. However, mycophenolate is genotoxic and the risk cannot be fully excluded. It is therefore recommended that male patients or their female partners use reliable contraception during treatment, and for at least 90 days after stopping mycophenolate.<br>See MHRA Drug Safety Update: Mycophenolate mofetil, mycophenolic acid, updated contraception advice for male patients (Feb 2018) |
| 14. Specialist contact information | Name: *as per clinic letter*<br>Role and specialty: *as per clinic letter*<br>Daytime telephone number: *as per clinic letter*<br>Email address: *as per clinic letter*<br>Alternative contact: *as per clinic letter*<br>Out of hours contact details: *contact relevant speciality consultant oncall via switchboard* |
| 15. Local arrangements for referral<br>Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change. | Humber Healthcare Partnership – contact relevant speciality via Advice and Guidance on ERS |
| 16. To be read in conjunction with the following documents | • Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/<br>• NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/<br>• General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for- |

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| | doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care<br>NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/. |

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| Document and version control | **This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.** | | |
| | Date approved by Guidelines and SCF Group: | | |
| | Date approved by APC: | | |
| | Review date: | | |
| Version number | Author | Job title | Revision description: |
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