Specialised Medicines Service (SMS) Guideline ~
Mycophenolate mofetil and mycophenolic acid for patients within adult dermatology, ophthalmology and neurology services (Devon Wide)

This guideline details the responsibilities for the ongoing prescribing and monitoring required to enable a shared care agreement to be arranged between the primary and secondary care interface. Refer to the online British National Formulary (BNF), Summary of Product Characteristics (SmPCs) or the Medicines and Healthcare products Regulatory Agency (MHRA) for full and up-to-date prescribing data.

Specialist: Please complete the shared care agreement letter at the end of this document and send together with the guideline to the GP.

GP: GPs are invited to participate. Please indicate whether you wish to share patient's care by completing the relevant letter at the end of this document and returning to the specialist.

Responsibilities remain with the specialist service until formally accepted by the GP. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

If the GP agrees to share the care of the patient, the patient should not be discharged from the care of their specialist, but rather the care of the patient is shared between the patient, GP and specialist in accordance with the responsibilities outlined in this guideline.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

Introduction and aims of treatment

This SMS guideline covers the use of mycophenolate mofetil and mycophenolic acid for the treatment of the following **unlicensed** indications in patients within adult dermatology, ophthalmology and neurology services. Although unlicensed, the indications listed below are well established and supported by local specialists. The specialist must specify the indication for each patient when initiating shared care and clearly state when use is off-label.

Dermatology
- Severe refractory eczema
- Bullous pemphigoid

Ophthalmology
- Uveitis
- Ocular pemphigoid
- Thyroid eye disease / Graves' orbitopathy

Neurology
- Myasthenia gravis
- Autoimmune neuropathies including chronic inflammatory demyelinating polyneuropathy (CIDP)
- Inflammatory myopathies including immune mediated myositis
- Neuromyelitis optica spectrum disorder (NMOSD)
- Autoimmune encephalitis
- Neurosarcoidosis

Use of mycophenolate mofetil or mycophenolic acid for other indications, including transplant, falls outside the scope of this guideline.

For shared care / SMS guidelines on the use of mycophenolate mofetil or mycophenolic acid for other indications, refer to the NHS Devon website (https://onedevon.org.uk/our-work/services-and-support/medicines-and-treatments/clinical-guidancefor-prescribers/) or the Devon Formulary website (https://devonformularyguidance.nhs.uk/).

Important safety information

MHRA Drug Safety Update (February 2018): Mycophenolate mofetil, mycophenolic acid: updated contraception advice for male patients

Male patients – review of risks associated with pregnancies exposure via the father

- Available clinical evidence does not indicate an increased risk of malformations or miscarriage in pregnancies where the father was taking mycophenolate medicines, however mycophenolate mofetil and mycophenolic acid are genotoxic and a risk cannot be fully excluded.
- It is recommended that male patients or their female partner use reliable contraception during treatment and for at least 90 days after stopping mycophenolate medicines
- Discuss with male patients planning to have children the implications of both immunosuppression and the effect of prescribed medications on the pregnancy

Female patients – reminder of pregnancy-prevention advice

- Mycophenolate medicines remain contraindicated in women of childbearing potential who are not using reliable contraception and in pregnant women unless there are no suitable alternatives to prevent transplant rejection
- Female patients of childbearing potential must use at least one reliable form of contraception before and during treatment and for 6 weeks after stopping mycophenolate medicines; 2 forms of contraception are preferred
- Mycophenolate treatment should only be initiated in women of childbearing potential when there is a negative pregnancy test result to rule out unintended use in pregnancy. Two pregnancy tests 8–10 days apart are recommended.

MHRA Drug Safety Update (January 2015): Mycophenolate mofetil (CellCept) and mycophenolic acid: risk of hypogammaglobulinaemia and risk of bronchiectasis

When using mycophenolate mofetil or any other medicine containing mycophenolic acid as its active ingredient:

- Measure serum immunoglobulin levels if recurrent infections develop
- In cases of sustained, clinically relevant hypogammaglobulinaemia, consider appropriate clinical action. Take into account the potent cytostatic effects of mycophenolic acid on B-lymphocytes and T-lymphocytes
- Consider bronchiectasis or pulmonary fibrosis if patients develop persistent respiratory symptoms, such as cough and dyspnoea

MHRA Drug Safety Update (December 2014): Mycophenolate mofetil: pure red cell aplasia

Consideration of a dose reduction or discontinuation of mycophenolate mofetil if patients develop pure red cell aplasia - changes to treatment should only be done under specialist supervision to minimise the risk of graft rejection.

Specialist responsibilities

Specialists may decide to delegate some of these tasks to members of their team, however the responsibility for ensuring they are undertaken remains with the named specialist overseeing the care of the individual patient:

- Assess the patient, establish diagnosis and the need for treatment with mycophenolate mofetil or mycophenolic acid. Ensure the diagnosis is within scope of this SMS guideline.
- Provide appropriate counselling to ensure the patient and/ or the patient's carer is involved in making an informed choice about their treatment.
- Provide the patient and/ or the patient's carer with suitable written and verbal information about the medication prior to starting treatment, including benefits and risks, side effects, cautions, frequency of dosing, monitoring requirements and treatment reviews (timing and by whom).
- Inform the patient and/or the patient's carer if the indication being treated is unlicensed. Outline any associated risks and benefits with treatment; document patient consent in the patient's medical records.
- Confirm patient and/or the patient's carer understands the treatment and record consent and agreement to associated patient responsibilities in the patient's medical records.

- Update records with list of existing drugs from available resources and ensure there are no drug interactions of clinical significance with current medication, recreational drugs, or over the counter (OTC) drugs or herbal remedies. Recommend the patient and/ or the patient's carer consults a pharmacist before using OTC treatments or herbal remedies.
- Ensure the patient is on appropriate contraception **(refer to important safety information above, and maternal exposure or paternal exposure in pregnancy section below)**. Explain the risks of pregnancy to individuals on initiation and at each review; the ongoing responsibility for providing this advice rests with both the specialist and the GP. Manufacturer education materials are available (here) in order to assist patients in avoiding foetal exposure to mycophenolate and to provide additional important safety information regarding risks.
- **Exclude pregnancy prior to starting treatment**. Mycophenolate treatment should only be initiated in women of childbearing potential when there is a negative pregnancy test result to rule out unintended use in pregnancy. Two pregnancy tests 8–10 days apart are recommended.
- Advise the patient and GP regarding the need for appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19). Refer to The Green Book for latest vaccination schedules and guidance.
- Ensure the patient and/ or the patient's carer understands that treatment may be stopped if they do not attend for monitoring & treatment review.
- Undertake pre-treatment screening and required baseline monitoring before initiating mycophenolate.
- **Initiate, prescribe and optimise mycophenolate mofetil or mycophenolic acid and monitor the patient.** The condition should be stable with satisfactory blood results and the dose optimised with no anticipated further changes expected in the immediate future, before transfer to GP; this is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks.
- Once treatment is optimised, ask the GP in writing whether they are willing to participate in shared care for a particular patient using the shared care agreement letter below. Include all relevant test results (GPs may not have access to these results in primary care). Prescribing and monitoring will remain in secondary care until the GP agrees to share care.
- Ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued by the specialist if, for unforeseen reasons, arrangements for shared care are not in place at the end of this period.
- Retain responsibility for monitoring the patient's ongoing response to treatment. Review the patient at agreed specified clinically appropriate intervals - assess patient's ongoing response to treatment. NHS England recommends that this should usually be undertaken annually.
- Ensure prompt written summary is sent to the GP whenever the patient is reviewed including any changes in treatment or monitoring requirements, results of monitoring undertaken, assessment of adverse events, or guidance on when to stop treatment if indicated. Confirm ongoing dose.
- Communicate urgent changes to treatment electronically and directly to the GP surgery (and followed up by telephone as required) to ensure prompt and immediate update.
- Provide the GP with relevant contact information and clear arrangements for back-up advice and support (including weekend and bank holidays).
- Ensure that the GP is informed in writing of any changes to the patient's specialist or their contact details.
- Where patient care is transferred from one specialist service to another, and/or the patient is initiated on a different treatment with associated SMS guidelines a new shared care agreement must be completed between the specialist, the GP and the patient.
- Respond promptly to GP or patient queries and advise on action required when abnormal monitoring results are identified or adverse effects signs or symptoms are detected and flagged.
- Any individual who becomes pregnant or wishes to become pregnant will be referred back to the specialist for an individualised review and discussion of ongoing management plans to provide the best outcome for the individual patient. The specialist will reassume prescribing responsibility, ending the shared care agreement.
- Report suspected side effects to MHRA via yellow card scheme.

General practitioner responsibilities

GPs may decide to delegate some of these tasks to members of their team; however, the responsibility for ensuring the following are undertaken remains with the GP overseeing the care of the individual patient:

- Ensure a timely reply is sent to the specialist in response to the request for shared care using the shared care agreement letters below. Where possible this should be undertaken within 14 days of the request being made.

If GP has agreed to share care:

- Continue to prescribe mycophenolate mofetil or mycophenolic acid and continue to monitor treatment in accordance with these guidelines.
- Ensure the patient is vaccinated in accordance with national vaccination programmes – seek guidance from initiating specialist where required e.g. where treatment has already commenced:
  - Influenza vaccination (The Green Book Chapter 19)
  - Pneumococcal vaccination (The Green Book Chapter 25)
  - COVID-19 vaccination (The Green Book Chapter 14a)
  - Shingles (herpes zoster) (The Green Book Chapter 28a)
- Review monitoring results and take any necessary action (see monitoring requirements below).
- Be alert to the possibility of interactions when initiating new medicines, recommending over the counter (OTC) treatments or herbal remedies, or disclosure of the use of recreational drugs.
- It is the responsibility of the specialist to provide advice on the need for contraception to individuals on initiation and at each review. GPs should re-enforce contraceptive advice **for both men and women** during routine reviews (see supporting information below).
- Be alert to the possibility of adverse effects at every contact. Manage patient in accordance with guidance below. Ensure prompt action in the case of a severe adverse effect or signs or symptoms.
- **Stop mycophenolate mofetil or mycophenolic acid and discuss urgently with the specialist if the patient develops gastrointestinal bleeding or perforation is suspected.** See monitoring guidance below for further details.
- Ensure advice sought promptly from the specialist if there is a change in the patient's physical or mental health status which is of concern to the GP and may affect treatment.
- Any individual who becomes pregnant should be referred back to the specialist. The specialist will reassume prescribing responsibility, ending the shared care agreement.
- Discuss with the specialist if the patient plans to become pregnant.
- Respond promptly to advice from specialist regarding any changes in treatment or monitoring requirements.
- Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.
- Where patient care is transferred from one GP practice to another a new shared care agreement must be completed.
- Report suspected side effects to specialist and to MHRA via yellow card scheme.

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Patient and/ or carer responsibilities

- Understand the importance of monitoring treatment and attend specialist and GP appointments to ensure timely monitoring and reviews can be completed in accordance with the guideline.
- Understand that treatment will be stopped if they do not attend for monitoring and treatment review.
- Ensure contact details are kept up to date with both the GP and the Specialist.
- Read the medication patient information leaflet. Request information in different format(s) if required to aid understanding. Understand treatment, expected benefits and potential side effects. Links to patient information resources can be found in the Supporting Information section below.
- Take (or support administration of) mycophenolate mofetil or mycophenolic acid as directed by the prescriber.
- Patients wishing to reduce their dose or stop treatment should discuss with their specialist before doing so. Avoid abrupt withdrawal unless advised by the GP or specialist.
- Tell anyone who prescribes them a medicine that they are taking mycophenolate mofetil or mycophenolic acid.
- Seek guidance from a pharmacist, GP or specialist on medication safety and potential interaction with mycophenolate mofetil or mycophenolic acid if engaging in recreational drug use, or using herbal remedies or over the counter (OTC) treatments.
- Report any adverse effects or newly presenting signs or symptoms to the GP and/or specialist.
- **Report the following signs and symptoms to the GP without delay (out of hours contact NHS 111):**
  - Symptoms of chickenpox or shingles, or contact with a person with chickenpox or shingles.
  - Persistent cough, shortness of breath, or any other problems with breathing.
  - Signs or symptoms of bone marrow suppression e.g. sore throat, mouth or throat ulcers, abnormal bruising or bleeding, high temperature, skin rash, swollen glands, or any other signs or symptoms of infection
  - Signs or symptoms of liver problems e.g. yellow skin or eyes (jaundice), itching all over, nausea or vomiting, abdominal pain or discomfort, dark urine
  - Diarrhoea or weight loss
  - Diffuse alopecia
  - Peripheral neuropathy
- Inform the specialist or GP immediately if they or their partners become pregnant or are planning a pregnancy
- **Contraception for male patients (including those who have had a vasectomy) or their female partner**
  - Individuals must use reliable contraception during treatment and for at least 90 days after stopping mycophenolate medicines
- **Contraception for female patients of childbearing potential**
  - Individuals must use at least one reliable form of contraception before and during treatment and for 6 weeks after stopping mycophenolate medicines; 2 forms of contraception are preferred
- Individuals should take a pregnancy test if they think there is a possibility they or their partner may be pregnant and inform the GP or specialist immediately if they become pregnant or wish to become pregnant. During treatment pregnancy tests should be repeated as clinically required (e.g. after any gap of contraception).
- Do 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.
- Due to the increased risk of skin cancer avoid exposure to intense sunlight especially between 11am and 3pm, and avoid UV rays (e.g. sunbeds and sunlamps). Purchase and use a sunscreen with a high sun protection factor (SPF) of at least 30 and a star rating of at least 4; wear a hat and clothes that cover your arms and legs when in the sun.
- Carry out regular self-examination of the skin and report if there are any new lesions, swellings, lumps and/or changes to skin which last more than two weeks.
- Use caution when driving or using machines (mycophenolate mofetil may cause somnolence, confusion, dizziness, tremor or hypotension).
- Store medicines safely and securely; it must not be shared with anyone else. Dispose of any unused medication appropriately.
- Report suspected side effects to the GP or specialist and the MHRA via yellow card scheme.

Monitoring requirements

Baseline assessment to be completed by the specialist before initiating mycophenolate mofetil or mycophenolic acid in adults:

Full history and physical examination and laboratory tests to include:

- Medical history and current medication
- Height, weight, blood pressure
- Consideration of cautions and contraindications associated with treatment
  - Confirm to GP that any underlying blood dyscrasias have been considered
- Chest x-ray and additional screening for lung disease, including interstitial lung disease and tuberculosis, will be undertaken at clinician discretion on a case-by-case basis
- Assessment of renal function, liver function, U&Es and FBC.
- Ascertain immune status by enquiring about history of chickenpox. If chicken pox immune status is unclear then consider checking antibodies to varicella zoster.
- Any infections should be attended to before initiation of treatment.
- Ensure patient is vaccinated in line with recommendations in The Green Book.
- Discuss contraception in all patients and the risks of pregnancy (see patient responsibilities above for further information).
- Exclude pregnancy prior to starting treatment. Mycophenolate treatment should only be initiated in women of childbearing potential when there is a negative pregnancy test result to rule out unintended use in pregnancy. Two pregnancy tests 8–10 days apart are recommended. The manufacturer recommends “serum or urine pregnancy tests with a sensitivity of at least 25 mIU/ml”.
- Screening for viral infections as per local policy, e.g. HIV and hepatitis B and C, varicella zoster, Epstein Barr virus, cytomegalovirus

Specialist should copy all baseline results to GP.

Monitoring Requirements:

The requirements outlined in the table below will be **completed by the specialist until the GP takes over prescribing and monitoring.**

The transfer to primary care is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks. The condition should be stable and the dose optimised (with no anticipated further changes expected in the immediate future).

The exact frequency of monitoring to be communicated by the specialist in all cases.

Where abnormal results are identified during routine monitoring consider the actions in the table below, seeking advice from specialist for further support and guidance where required. **As well as responding to absolute values, a rapid change or a consistent trend in any value should prompt caution and extra vigilance**.

If monitoring results are forwarded to the specialist team, include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

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<table>
<tr><th>Tests</th><th>Frequency of monitoring</th><th>Threshold for action</th><th>Action to be taken by GP</th></tr>
<tr><td>FBC</td><td rowspan="3">Every 2 weeks until on a stable dose for 6 weeks, then every month for 3 months, then at least every 12 weeks thereafter.

Following dose increases, monitor every 2 weeks until on a stable dose for 6 weeks, then revert to previous schedule.

Patient factors where continued monthly monitoring is recommended (unless otherwise specified)*:
• Previous toxicity or deranged FBC or LFTs while on DMARDs
• Chronic kidney disease (CKD 3 or worse)
• Pre-existing liver disease

Additional urgent monitoring tests should be carried out within 24 hours for any patient with acute kidney injury (AKI).</td><td>WCC < 3.5 x 10^9/L
Neutrophils < 1.6 x 10^9/L
Eosinophils >0.5 x 10^9/L
Platelets < 140 x 10^9/L
Lymphocytes < 0.5x10^9/L
MCV > 105fl (if samples are being analysed by Derriford Hospital lab, MCV >108fl)</td><td rowspan="3">If results meet specified criteria, stop treatment and refer to specialist.
If isolated MCV rise, check for other causes (B12, folate, thyroid function and alcohol consumption). If results are normal, refer to specialist.

If concerned about sequential drops in FBC indices (possibly still within normal range), consider an early re-test/seek specialist advice.

If deterioration in renal function, dose adjustment may be necessary; if toxicity suspected or dosing advice required refer to specialist team.

Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including over the counter (OTC) treatments or complementary medication.</td></tr>
<tr><td>U&Es including creatinine / eGFR</td><td>Creatinine increase >30% over 12 months and/or eGFR <60ml/min/1.73m^2</td></tr>
<tr><td>ALT and/or AST and albumin</td><td>ALT and/or AST >100 U/L

Albumin unexplained reduction to <30g/L</td></tr>
<tr><td>Adverse effects</td><td>At every contact</td><td colspan="2">See table below</td></tr>
<tr><td colspan="4">*Other factors that may increase risk of DMARD toxicity include moderate renal impairment, extremes of body weight, polypharmacy (especially other haematotoxic / hepatotoxic / nephrotoxic drugs), comorbidities, age > 80 years. Where more frequent ongoing monitoring is required due to a combination of patient factors this will be advised by the specialist prescriber.</td></tr>
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Presentation of the following adverse effects, signs or symptoms and associated actions should be noted. Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. See also adverse effects in supporting information below.

Adverse effects, signs and symptoms	Action to be taken by GP
Infections	During a serious infection **withhold mycophenolate medicines** until the patient has recovered. Discuss with specialist if required and consider additional investigations e.g. FBC if clinically appropriate. During minor infections (e.g. uncomplicated UTI treated with a short antibiotic course) treatment can be continued. If patient requires antibiotics ensure potential interaction risk has been considered. If recurrent or opportunistic infection review for reversible cause. Measure serum immunoglobulin levels. Withhold mycophenolate medicines and discuss with specialist team. In cases of sustained, clinically relevant hypogammaglobulinaemia, appropriate clinical action should be considered taking into account the potent cytostatic effects that mycophenolic acid has on T- and B-lymphocytes. Consider bronchiectasis or pulmonary fibrosis if persistent respiratory symptoms such as cough and dyspnoea develop.
Fatigue, lethargy, pallor, breathing problems, dizziness, headaches	Review for possible causes. If pure red cell aplasia seek specialist advice; dose reduction or discontinuation may be required.
Bone marrow suppression Symptoms may include: unexplained bleeding or bruising with or without sore throat, purpura, mouth ulcers	**Withhold mycophenolate medicines**. Check FBC and discuss with the initiating specialist immediately. See also haematological monitoring advice above.
Nausea and vomiting, abdominal cramps, diarrhoea and dyspepsia	Review for reversible causes. Advise patient to take with food. If no improvement contact initiating specialist.
GI ulceration, bleeding and perforation	Review for reversible causes. **Withhold mycophenolate medicines** and discuss urgently with initiating specialist.
Suspected pancreatitis Symptoms may include: abdominal pain/swelling, nausea or vomiting, diarrhoea, indigestion, jaundice fever	**Withhold mycophenolate medicines** and discuss with initiating specialist.
Skin hypertrophy, acne, alopecia	Review for reversible causes. Discuss with initiating specialist if symptoms become troublesome.
Skin rash	Review for possible causes. If cause of rash thought to be mycophenolate or immune-mediated, **withhold mycophenolate medicines** and discuss with initiating specialist.
Neurological symptoms, psychiatric disorders, sudden onset or worsening of shortness of breath, cough or dyspnoea	Review for reversible causes. **Withhold mycophenolate medicines** and discuss with initiating specialist.
Suspicion of malignancy	Discuss with initiating specialist. Refer for diagnosis and treatment of malignancy in accordance with local pathways.

Pregnancy	In pregnant patients **withhold mycophenolate medicines** immediately and discuss with initiating specialist urgently. In pregnancies with paternal exposure, discuss with initiating specialist.
Chickenpox or shingles	**Post exposure prophylaxis** Contact microbiology if a patient, not known to be immune to chickenpox, comes into contact with shingles or chickenpox, for advice on whether varicella-zoster immune globulin (VZIG) or other treatment is indicated. For detailed advice on risk assessment and post exposure prophylaxis following exposure to chicken pox and shingles, see: • the Green Book (Chapter 34) • UKSHA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles, January 2023 **In patients suffering from chickenpox or active skin lesions from shingles** **Withhold mycophenolate medicines**. **Patients with chickenpox**: contact microbiologist for consideration of admission to hospital for IV antivirals. **Patients with shingles**: if any vesicles are still present (regardless of the time of onset), treat with aciclovir (800mg five times a day for 7 days).

Supporting Information

This section provides additional information regarding mycophenolate medicines. Refer to the online BNF, SmPCs, the MHRA or NICE websites for up-to-date information on any medicine.

Formulation

Refer to Devon formulary for list of oral preparations approved for use locally. Brand-name prescribing is no longer considered necessary for mycophenolate.

Mycophenolic acid should usually be reserved for patients who do not tolerate mycophenolate mofetil.

Administration

Mycophenolate mofetil can be taken with or without food; patients may select either option but must adhere to their selected option.

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.

Dosage and administration

Specialist Pharmacy Service: Specific medicine switches for solid dose and liquid formulations (2023).

Mycophenolate mofetil is a pro-drug of the active metabolite mycophenolic acid. Mycophenolic acid 720mg is approximately equivalent to mycophenolate mofetil 1g; avoid unnecessary switching because of pharmacokinetic differences.

Mycophenolic acid should usually be reserved for patients who do not tolerate mycophenolate mofetil.

No dose adjustment is required when switching between mycophenolate mofetil solid dose formulations and mycophenolate mofetil oral suspension.

All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the GP.

There is a wide dose range depending on the indication and disease severity.

Initial stabilisation: Typically mycophenolate mofetil 250mg or 500mg once or twice daily, increasing in weekly increments.

Maintenance dose: Typically mycophenolate mofetil 1-2 grams daily, in divided doses. Maximum dose: 3 grams daily.

Switches between mycophenolate mofetil and mycophenolic acid should only be performed by, or with the advice of, the specialist team.

Renal impairment

Refer to SmPCs for full guidance. The maximum recommended dose in severe chronic renal impairment (GFR <25 mL/min/1.73m^2) is:

- Mycophenolate mofetil:1 gram, twice daily
- Mycophenolic acid: 720 mg, twice daily

Treatment review and discontinuation

Termination of treatment will be the responsibility of the specialist with exceptions due to adverse effects detailed in the table above. Treatment duration will be based on clinical response and tolerability.

Contraindications

- Hypersensitivity to mycophenolate mofetil, mycophenolate sodium, mycophenolic acid or any excipients
- Pregnancy
- Treatment should not be initiated to women of childbearing potential:
  - in the absence of a pregnancy test result to rule out unintended use in pregnancy
  - who are not using highly effective contraception
- Breastfeeding

Precautions

In addition to the points listed below, refer to the monitoring section above for further cautions to be noted during treatment depending on patient medical history and actions to take in the case of a severe adverse effect or patient reported signs or symptoms.

- Localised or systemic infection.
- Patients with suspected lymphoproliferative disorder.
- Patients with unexplained anaemia, leukopenia or thrombocytopenia.
- Pure red cell aplasisa
- Active gastrointestinal disease (risk of haemorrhage, ulceration and perforation)
- Mycophenolate is an IMPDH (inosine monophosphate dehydrogenase) inhibitor; avoid in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.
- Very frail or elderly (increased risk of infection, gastro-intestinal haemorrhage and pulmonary oedema)
- 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 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. If patient is taking additional DMARDs, check advice for all drugs. Contact the specialist if further guidance is required.
- Dose reduction or discontinuation should be considered for patients in cases of clinically significant COVID-19.
- Increased risk of skin cancer
- Increased risk of lymphoma and other malignancies
- Any pre-malignant disease should be adequately treated before starting therapy and patients should be up to date with relevant national cancer screening programmes.

- Risk of hypogammaglobulinaemia or bronchiectasis when used in combination with other immunosuppressants
- Interstitial lung disease, pulmonary fibrosis
- Avoid if previous hepatitis B or C infection, or recurrent shingles
- Marked renal failure (eGFR below 25 mL/min).
- Paternal exposure

Adverse effects

The data below has been taken from the online BNF. **The list is not exhaustive.** Refer to the online BNF and SmPCs for full prescribing data. Seek specialist advice where necessary. See also adverse effects, signs and symptoms in monitoring requirements section above.

Very common (≥1/10) or common (≥1/100 to <1/10): Acidosis; alopecia; anaemia; anxiety; appetite decreased; arthralgia; asthenia; bone marrow disorders; burping; chills; confusion; constipation; cough; depression; diarrhoea; dizziness; drowsiness; dyslipidaemia; dyspnoea; electrolyte imbalance; fever; gastrointestinal discomfort; gastrointestinal disorders; gastrointestinal haemorrhage; gout; headache; hepatic disorders; hyperbilirubinaemia; hyperglycaemia; hypertension; hyperuricaemia; hypotension; increased risk of infection; insomnia; leucocytosis; leucopenia; malaise; nausea; neoplasms; neuromuscular dysfunction; oedema; oral disorders; pain; pancreatitis; paraesthesia; renal impairment; respiratory disorders; seizure; sepsis; skin reactions; tachycardia; taste altered; thinking abnormal; thrombocytopenia; tremor; vasodilation; vomiting; weight decreased

Uncommon (≥1/1000 to <1/100): Agranulocytosis

Frequency not known: Endocarditis; hypogammaglobulinaemia; malignancy; meningitis; neutropenia; polyomavirus-associated nephropathy; progressive multifocal leukoencephalopathy (PML); pure red cell aplasia

Hypersensitivity reactions (including anaphylaxis) and de novo purine synthesis inhibitors-associated acute inflammatory syndrome characterised by fever, arthralgia, arthritis, muscle pain and elevated inflammatory markers have been reported post-marketing.

Interactions

The following lists are not exhaustive. Consider interaction with prescription and recreational drugs. Refer to the online BNF and SmPCs for full prescribing data. Seek specialist advice where necessary and / or refer to specialist Medicines Information services for additional support (and reference to Stockley's Drug Interactions where paid subscription available) if concomitant administration of interacting medicines clinically indicated.

The following interactions are classified in the online BNF as **severe** (the result may be a life-threatening event or have a permanent detrimental effect):

- **Live vaccines (e.g. cholera, dengue, herpes zoster, influenza, rotavirus, varicella zoster, yellow fever, MMR, BCG, oral polio and typhoid):** Increased risk of generalised infection (possibly life-threatening). Avoid. Consult Green Book for the most up to date advice
- **Rifampicin**: Rifampicin decreases the concentration of mycophenolate. Manufacturer advises monitor and adjust dose.

The following interactions have been highlighted by the NHS England shared care protocol, SmPC and the British Association of Dermatology (BAD):

- **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. Manufacturer advises monitor
- **Antibiotics e.g. co-amoxiclav, ciprofloxacin, norfloxacin, metronidazole**: potential to reduce the plasma level of mycophenolate
- **Azathioprine**: the manufacturer recommends that mycophenolate should not be administered concomitantly with azathioprine because such concomitant administration has not been studied.
- **Antacids and proton pump inhibitors**: reduced absorption of mycophenolate
- **Cholestyramine / colesevelam:** reduced absorption of mycophenolate
- **Ciclosporin:** reduced mycophenolate exposure

- **Clozapine:** Both clozapine and mycophenolate might cause blood dyscrasias and therefore serious adverse effects. The manufacturer contraindicates the concurrent use of clozapine with other drugs that have substantial potential to cause agranulocytosis and suppress the bone marrow.
- **Immunosuppressants e.g. azathioprine, ciclosporin, sirolimus:** increased risk of bone marrow suppression
- **Isavuconazole:** possible increased risk of mycophenolate adverse effects due to increased exposure to mycophenolate or its metabolite. Manufacturer advises monitor adverse effects
- **Tacrolimus:** Mycophenolate might increase tacrolimus exposure. Monitor closely, particularly if changing from ciclosporin to tacrolimus or vice versa. Consider adjusting the mycophenolate dose if adverse effects (such as diarrhoea, vomiting and leucopenia) occur.
- **Telmisartan:** may reduce mycophenolate exposure
- **Sevelamer**: reduced mycophenolate exposure; separate administration by 1-3 hours

Pregnancy, lactation and paternal exposure

Before prescribing in this area seek specialist advice and check up-to-date sources of information.

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.

MHRA Drug Safety Update (February 2018): Mycophenolate mofetil, mycophenolic acid: updated contraception advice for male patients

Devon Formulary signposts to resources for contraception for drugs with teratogenic potential, and prescribing in pregnancy and lactation including MHRA Drug Safety Update (March 2019): Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?

Pregnancy (Maternal exposure)

The UK Teratology Information Service (UKTIS) provides a national service on all aspects of the toxicity of drugs and chemicals in pregnancy (Tel: 0344 892 0909), and provides the 'best use of medicines in pregnancy' (bumps) website for supportive patient information relating to individual treatments. A UKTIS abstract on the use of mycophenolate is available here. A patient information leaflet from bumps is available here.

Mycophenolate medicines are **contra-indicated during pregnancy**. Pregnancy should be excluded with a negative pregnancy test prior to starting treatment; two pregnancy tests 8–10 days apart are recommended. The UKTIS reports that there is an increased risk of first trimester pregnancy loss and confirmed human teratogenic effects, including craniofacial anomalies (cleft lip and/or palate, microtia, external auditory canal atresia, micrognathia); microphthalmia, coloboma of iris and retina, and hypertelorism; complex congenital cardiac anomalies, including septal defects, conotruncal and outflow tract anomalies; oesophageal atresia, diaphragmatic hernia, and various vertebral and skeletal anomalies.

Patients of reproductive potential must be counselled regarding pregnancy prevention and planning. During treatment pregnancy tests should be repeated as clinically required (e.g. after any gap of contraception).

Female patients of childbearing potential:

- Must use at least one reliable form of contraception* before and during treatment and for 6 weeks after stopping mycophenolate medicines; 2 forms of contraception are preferred
- Should take a pregnancy test if they think there is a possibility they or their partner may be pregnant, and inform the GP or specialist immediately if they become pregnant or wish to become pregnant.

** Highly effective methods of contraception have typical-use failure rates of less than 1% and include male or female sterilisation and long-acting reversible contraceptive (LARC) methods (intrauterine devices and implants).*

The MHRA has published an aide-memoire table to provide guidance to prescribers of medicines with teratogenic potential on the frequency of pregnancy testing needed to avoid exposure in pregnancy during treatment, depending on the chosen contraceptive method.

Women exposed to mycophenolate medicines during early pregnancy should be counselled about the risks to the foetus and offered detailed anomaly scans focussing on the craniofacial structures, the heart, abdomen and

skeletal system. Clinicians should also be aware that case-specific assessment of risk could also be affected by other factors that may independently increase the risk of adverse pregnancy outcome.

Paternal exposure

Available clinical evidence does not indicate an increased risk of malformations or miscarriage in pregnancies where the father was taking mycophenolate medicines, however mycophenolate mofetil and mycophenolic acid are genotoxic and a risk cannot be fully excluded.

Sexually active male patients or their female partners are recommended to use reliable contraception during treatment of the male patient and for at least 90 days after cessation of mycophenolate mofetil. Male patients of reproductive potential should be made aware of and discuss with a qualified healthcare professional the potential risks of fathering a child.

Lactation

UK Drugs in Lactation Advisory Service (UKDILAS) provides evidence-based information on the use of drugs during the breastfeeding period to all UK healthcare professionals.

Mycophenolic acid is excreted in human milk; mycophenolate medicines are therefore **contraindicated in breast-feeding** because of the potential for serious adverse reactions in breast-fed infants.

Patient Information Resources

General information	https://patient.info/medicine/mycophenolate-mofetil-cellcept-myfenax
Dermatology	https://www.bad.org.uk/for-the-public/patient-information-leaflets/mycophenolate-mofetil
Additional patient information leaflets (manufacturer specific)	https://www.medicines.org.uk/emc/search?q=mycophenolate

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Support

Dermatology Services Contact Details	
Royal Devon and Exeter Hospital Email: rduh.dermsec@nhs.net Telephone: 01392 405510	**North Devon District Hospital** Email: d-icb.dermatology@nhs.net Telephone: 01271 312850
University Hospitals Plymouth NHS Trust Contact initiating specialist using contact details provided at outset or via hospital switchboard, telephone: 01752 202082	**Torbay and South Devon NHS Foundation Trust** Email: sdhct.dermatology@nhs.net Reception telephone: 01803 654754 Dermatology Team leader telephone: 01803 656532 Secretary telephone: 01803 654869

Ophthalmology Services Contact Details	
Royal Devon and Exeter Hospital Email: rduh.exeteriritis@nhs.net Telephone: 01392 406002	**North Devon District Hospital** Email: rduh.failsafe-eyes@nhs.net Telephone: 01271 322461 (Emergency Dr Line) or 01271 370263 (Ophthalmology Failsafe Officers)
University Hospitals Plymouth NHS Trust Email: Plh-tr.ophthalmologyadmin@nhs.net Telephone: 01752 439956	**Torbay and South Devon NHS Foundation Trust** Email: tsdft.ophthalmology@nhs.net Telephone: 01803 655141

Neurology Services Contact Details	
Royal Devon and Exeter Hospital Telephone: 01392 404950 (Neuro secretary) or 01392 411611 (Hospital switchboard)	**North Devon District Hospital** Telephone: 01271 311585 (Neuro secretary) or 01271 322577 (Hospital switchboard)
University Hospitals Plymouth NHS Trust Email: 01752 431201 Telephone: plh-tr.neuroreferrals@nhs.net	**Torbay and South Devon NHS Foundation Trust** Email: tsdft.neurologyadvice@nhs.net Telephone: 01803 614567 (switchboard)

For further support and information in relation to individual shared care agreements please contact your practice pharmacist or alternatively please contact the Medicines Optimisation Team.

Email: D-ICB.medicinesoptimisation@nhs.net

Version 1

Date ratified: 29th January 2025

This guideline has been reviewed by stakeholders across Devon and is intended for use in accordance with locally commissioned services.

This guideline has been developed with consideration and local adaptation of the national shared care protocol; “Mycophenolate mofetil and mycophenolic acid for patients within adult services (non-transplant indications)” 4 July 2022 Version 1 (available here). Development of the national guideline was led by the Regional Medicines Optimisation Committee (RMOC) (north) with approval for publication on the NHS England website.

Shared Care Agreement Letter - Specialist Request to GP

To	**GP name**	
	Practice address	
Patient name		
Hospital number		
NHS number		
Date of birth		
Address		

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

This patient is now suitable for prescribing to move to primary care. The patient fulfils criteria for shared care therefore I am writing to request your agreement to continue the care of this patient according to the Specialised Medicines Service (SMS) Guideline.

In accordance with the SMS Guideline the transfer of monitoring and prescribing to the GP is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks. The condition should be stable with satisfactory blood results and the dose optimised (with no anticipated further changes expected in the immediate future).

I have discussed and agreed the following treatment with the patient:

	Specialist to complete
Mycophenolate mofetil or **mycophenolic acid**	*<Specify medication, formulation and dose to be administered>*
Indication	*<state indication>*
Treatment start date	*<insert date>*
Patient has been on the optimised dose stated for	*<insert duration>*
Sufficient medication has been provided to last until	*<insert date>*
GP to undertake prescribing and monitoring in line with the SMS Guideline from	*<insert date>*
Next monitoring due date	*<insert date>*
Follow up due date	*<insert date>*

I can confirm that the following have occurred with regard to this treatment:

	Specialist to complete (YES/NO)
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	
The roles of the Specialist / GP / Patient have been explained and agreed	
The risks and benefits of treatment have been explained to the patient	
Pregnancy has been excluded in female patients with a negative pregnancy test prior to starting treatment (two pregnancy tests 8–10 days apart recommended)	
Baseline investigation and monitoring as set out in the SMS Guideline have been completed and were satisfactory	
Female patients of childbearing potential are using at least one reliable form of contraception (2 forms preferred). *Provide details of contraception in supporting information box below.*	
Male patients (including those who have had a vasectomy) or their female partner are using reliable contraception during treatment. *Provide details of contraception in supporting information box below.*	
I have enclosed a copy of the SMS Guideline which covers this treatment. The guideline can also be found here	
I have included with this letter copies of the information the patient has received	

The results of baseline tests, early monitoring and any additional supportive information are included below and/or attached. Highly effective methods of contraception have typical-use failure rates of less than 1% and include male or female sterilisation and long-acting reversible contraceptive (LARC) methods (intrauterine devices and implants). Please detail contraception in use and insertion date where applicable.

GP please sign response letter and return promptly (where possible this should be within 14 days of the request being made).

Specialist signature		**Date**	
Specialist name, role, speciality			
Daytime telephone number			
Email address			
Alternative contact **e.g. clinic or specialist nurse**			
Out of hours contact details **e.g. duty doctor**			

Remember to keep a copy of this letter for the patient's records.

Shared Care Agreement Letter – GP Acceptance Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment:

Mycophenolate mofetil or **mycophenolic acid** (Delete as required. State formulation and dose to be administered)

……

I can confirm that **I am willing to take on this responsibility** from …….. and will maintain the prescribing and monitoring responsibilities as set out in the Specialised Medicines Service (SMS) Guideline.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

Shared Care Agreement Letter – GP Refusal Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

In the interest of patient safety NHS Devon, in conjunction with local acute trusts have classified mycophenolate mofetil and mycophenolic acid as a "shared care" drugs which require a number of conditions to be met before transfer can be made to primary care.

Thank you for your request for me to accept prescribing responsibility for this patient. I regret to inform you that in this instance **I am unable to take on responsibility** due to the following:	**Tick all applicable**
The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care. As the patients GP I do not feel clinically confident to manage this patient's condition. I have consulted with other GPs in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given below.**	

The condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement. As the condition requested to be treated is not included on the locally recognised list of indications for shared care for mycophenolate mofetil and mycophenolic acid I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this condition is identified locally as requiring shared care with mycophenolate mofetil or mycophenolic acid the responsibility for providing this patient with their medication remains with you.**	
A minimum duration of supply by the initiating specialist. As the patient has not had the minimum supply of medication to be provided by the initiating specialist (28 days) I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.**	
Initiation and optimisation by the initiating specialist. Transfer of monitoring and prescribing to the GP is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks. The condition should be stable with satisfactory blood results and the dose optimised (with no anticipated further changes expected in the immediate future). As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.**	
Other (GP to complete if there are other reasons why shared care cannot be accepted):	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records.