Specialised Medicines Service Guideline ~ Mycophenolate mofetil (Cellcept®) for autoimmune/rheumatology conditions (unlicensed)

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to the BNF and individual product SPC/data sheet for full prescribing data.

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

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. 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.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

Mycophenolate mofetil is a pro-drug of the active metabolite, mycophenolic acid. It is an immunosuppressant drug used in a range of autoimmune diseases such as systemic lupus erythematosus (SLE), scleroderma, vasculitis etc. particularly where other treatments are unsuitable, ineffective or not tolerated.

This guideline refers to the unlicensed use of Cellcept® for the treatment of autoimmune conditions in adults. The use of mycophenolate mofetil for other indications is outside the scope of this guideline.

Specialist responsibilities

Consultants 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 consultant:

- For female patients of child-bearing age, exclude pregnancy prior to initiating treatment
- Where appropriate, for both men and women discuss with the patient (and/or carer) the risks associated with pregnancy, the need for a reliable method of contraception during treatment and for the minimum period following discontinuation (see "Contraception", below)
- Discuss with the patient (and/or carer) the need to immediately consult their physician if there is a possibility of pregnancy
- Undertake pre-treatment assessment, monitoring & follow up as described in "Monitoring" section below
- Discuss with the patient (and/or carer) the benefits, side effects, frequency of dosing and monitoring requirements of mycophenolate mofetil treatment
- Provide chemotherapy record booklet for recording of monitoring and information
- Provide patient (and/or carer) with relevant written information on use, side effects and need for monitoring of medication
- Record the patient's confirmation of understanding of risks and benefits and consent to unlicensed use

- Ascertain immune status by enquiring about history of chicken pox. Measurement of antibodies to varicella-zoster is **not** recommended
- Initiate treatment, supply 28 days' medication
- Send a letter to the GP, asking them whether they are willing to participate in the sharing of care for a particular patient. Include results of any relevant baseline tests, and confirm the frequency of ongoing monitoring
- Advise the GP (in writing) of any dose changes required
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for sharing of care.

If GP has agreed to share care:

- Ensure that women and men taking mycophenolate mofetil understand the need for effective contraception, the risk of harm to the baby, and the need to immediately consult their physician if there is a possibility of pregnancy (see also "Contraception", below)
- Undertake ongoing monitoring and act on results of blood tests/reported side effects as described in "Monitoring" section below
- Ensure that the results of monitoring are recorded in the patients notes
- Continue to prescribe mycophenolate mofetil in accordance with guidelines
- Stop treatment/amend dose and report to and seek advice from a specialist where appropriate
- Report adverse events to specialist and to MHRA via the yellow card scheme
- Offer influenza vaccine annually unless otherwise advised by the initiating specialist
- Check that the patient has had **one dose** of pneumococcal vaccine (revaccination is not recommended, except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia) – see BNF or Green Book.

Monitoring

Baseline assessment to be completed by the specialist service provider:

- At baseline:
  - Height & weight
  - Blood pressure
  - Full blood count (FBC)
  - Creatinine / eGFR
  - ALT and/or AST, and albumin
  - Chest x-ray
  - Immunoglobulin levels
  - Consider patient risk factors for viral infections and screen for occult viral infections (hepatitis B and C and HIV) where appropriate
  - Pregnancy test in women of childbearing age (unless pregnancy has been unequivocally excluded), consider contraception as appropriate

Ongoing monitoring during treatment to be completed by the GP:

Test	Frequency*
FBC	Every two weeks until on stable dose for 6 weeks, then every month for 3 months, then every 12 weeks (Following dose increases, monitor every 2 weeks until on a stable dose for 6 weeks, then as above)
Creatinine/eGFR	
ALT and/or AST and albumin	

* 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).

Other factors that may increase risk of 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.

- Additional FBC for any patient who reports any of the following signs and symptoms: mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, unexplained illness or infection (patient should be seen within 24 hours). Signpost patient to alternative provider if this is not possible e.g. weekend/bank holiday

Action to be taken by GP in response to blood monitoring/side effects:

Blood test results	Action
WCC < 3.5 x 10^9/L	**If blood test 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.
Neutrophils < 1.6 x 10^9/L	
Eosinophils >0.5 x 10^9/L	
Platelets < 140 x 10^9/L	
MCV > 108f/L	
Creatinine increase >30% over 12 months and/or eGFR <60ml/min/1.73m^2	
ALT and/or AST >100 U/L	
Albumin <30g/L	
Symptoms (see also "Adverse effects" section)	**Action**
Any of the following: mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, unexplained illness or infection	See patient within 24 hours of contacting the practice for clinical assessment and urgent FBC. Signpost patient to alternative provider if this is not possible e.g. weekend/bank holiday.
Chickenpox or shingles	In patients suffering from chickenpox or active skin lesions from shingles, **withhold mycophenolate mofetil.** **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).

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 or other treatment is indicated.

During a **serious** infection STOP treatment. During minor infections (e.g. uncomplicated UTI treated with a short antibiotic course) treatment can be continued.

Do not stop treatment prior to surgery unless significant high-risk of infection where an individual patient plan should be made.

Patient/carer responsibilities

- Ensure they understand the importance of monitoring treatment and attend specialist appointments and/ or GP appointments to ensure timely monitoring can be completed (in accordance with the prescribing guideline)
- Understand that treatment will be stopped if they do not attend for monitoring and treatment reviews
- Ensure that the results of monitoring are recorded in their chemotherapy record booklet
- Ensure they have a clear understanding of the treatment, expected benefits and potential side effects
- Take (or support administration of) medication as directed by the prescriber
- Report any of the following to their GP: mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, and any unexplained illness/infection. (Contact out of hours service e.g. NHS 111 if their GP practice is closed for weekend/bank holiday)
- Report any adverse effects to the GP and/or specialist regarding their treatment
- Use a reliable method of contraception during treatment and for the minimum period following discontinuation of mycophenolate mofetil (see “Contraception”, below)
- Advise the GP immediately if pregnancy is suspected
- Store their medicines safely and securely.

Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk

Dosage and administration

Refer to the current BNF or individual product SPCs for Cellcept®.

Usual range: 500mg – 2g per day (max 3g per day) in two divided doses.

Patient specific guidance will be provided to the GP by the specialist.

Contraindications and precautions

Refer to individual product SPCs for Cellcept®.

Patients receiving mycophenolate mofetil must **not** receive immunization with live vaccines. These vaccines include measles, mumps and rubella; BCG; poliomyelitis – oral Sabin vaccine; yellow fever; typhoid – oral.

Shingles vaccination should **not** be given to patients on mycophenolate mofetil

Contraception

Refer to individual product SPCs for Cellcept®.

Women with childbearing potential should use two reliable forms of contraception simultaneously before starting CellCept therapy, during therapy, and for six weeks after stopping the therapy; unless abstinence is the chosen method of contraception.

Sexually active men are recommended to use condoms during treatment and for at least 90 days after cessation of treatment. Condom use applies for both reproductively competent and vasectomised men, because the risks associated with the transfer of seminal fluid also apply to men who have had a vasectomy.

In addition, female partners of male patients treated with CellCept® are recommended to use highly effective contraception during treatment and for a total of 90 days after the last dose of CellCept®.

Pregnancy and lactation

Refer to individual product SPCs for Cellcept®.

Mycophenolate mofetil is a powerful human teratogen and should not be used in pregnancy.

Mycophenolate mofetil should not be given to women who are breastfeeding.

Adverse effects

Refer to individual product SPCs for Cellcept®.

Commonly gastrointestinal effects (vomiting, abdominal pain, diarrhoea, nausea); if severe or persistent, seek specialist advice.

Leucopenia, anaemia and thrombocytopenia: GPs should be alert to any unexplained bruising or bleeding (see “Monitoring” section, above).

Patients receiving mycophenolate mofetil are at increased risk of developing lymphomas and other malignancies, particularly of the skin. To minimise the risk for skin cancer, exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with a high protection factor.

Drug interactions

This list is not exhaustive, for additional information, and further interactions, consult the BNF and individual product SPCs for Cellcept®.

- It is recommended that CellCept® should not be administered concomitantly with azathioprine because such concomitant administration has not been studied.
- Some indigestion remedies and iron preparations may reduce the absorption of mycophenolate. These should not be taken within 2 hours of taking the mycophenolate.
- Colestyramine may decrease absorption of mycophenolate. Mycophenolate should be taken at least 1 hour before or 4–6 hours after colestyramine to reduce possible interference with absorption.

The following drug interactions are classified in the online version of the BNF as **potentially serious;** concomitant administration of the drugs involved should be **avoided** (or only undertaken with caution and appropriate monitoring).

- **Rifampicin:** Plasma concentration of active metabolite of mycophenolate reduced by rifampicin.

Support

Contact details
Specific contact and support details will be provided to the GP by the specialist when requesting the sharing of care. In addition, GPs may use the following generic rheumatology department email*: RD&E rheumatology: rde-tr.rheumatology@nhs.net NDHT rheumatology: ndht.rheumatology@nhs.net Consultants can also be contacted via the individual trusts' switchboards: Northern Devon Healthcare NHS Trust: 01271 322577 Plymouth Hospitals NHS Trust: 01752 202082 Royal Devon and Exeter NHS Foundation Trust: 01392 411611

*** Please do not use** rheumatology department emails for enquiries relating to patients receiving DMARDs under the care of other specialties e.g. dermatology, gastroenterology etc.

Date ratified: May 2017
Partially updated: October 2019

Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

I recommend treatment with the following drug: ……

At the following dosage: ……..……

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Principles:

GPs are invited to participate, 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.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number:**	
Email address:			
Department email:			

Please sign below and return promptly. 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.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Guideline.

Signed: …….. Date: …….

GP name: …… *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: …….. Date: …….

Name: