Ref: APCSCG2017/014 **South East London Shared Care Prescribing Guideline for Mycophenolate Mofetil for the prevention of Organ Rejection in Adult Liver Transplant Recipients in EXISTING patients only (i.e. those already being prescribed this drug in primary care)**
Date approved: June 2017 **Review date:** June 2018 (or sooner if evidence or practice changes)

SHARED CARE PRESCRIBING GUIDELINE Mycophenolate Mofetil for the prevention of Organ Rejection in Adult Liver Transplant Recipients in existing patients only (i.e. those already being prescribed this drug in primary care)

Continuation of Mycophenolate Mofetil for the prevention of Organ Rejection in Adult Liver Transplant Recipients already being prescribed this drug in primary care
NOTES to the GP

The information in the shared care guideline has been developed in consultation with CCGs in South East London and it has been agreed that it is suitable for shared care in line with the criteria outlined in this document.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing mycophenolate mofetil for the prevention of organ rejection in adult liver transplant recipients.

Due to a planned repatriation of immunosuppressants in the future, shared care is **not** appropriate for new patients. Shared care will only be requested for existing patients who are already being prescribed this drug in primary care by their GP practice. Having a shared care agreement in place will help support safer prescribing in primary care and clarify responsibilities of clinicians and patients.

The questions below will help you confirm this:

- Is the patient already being prescribed mycophenolate mofetil for this clinical indication by your practice?
- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to continue to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept continuing prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local CCG Medicines Management Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email (preferred) or fax back to the requesting clinician if you are in agreement to continue participation in shared care.

GP DECISION FORM

This agreement outlines suggested ways in which the responsibilities for ***continuing*** to manage prescribing of mycophenolate mofetil for the prevention of organ rejection in adult liver transplant recipients can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is 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 a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE
Mycophenolate Mofetil for the prevention of organ rejection in adult liver transplant recipients already being prescribed this drug in primary care (i.e. existing patients only)

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient Agreement:**
Hospital requesting shared care:	Patient agrees to shared care ☐ Patient does not agree to shared care ☐
GP Name:	
This is to confirm that I agree to continue to participate in shared care for mycophenolate mofetil for the prevention of organ rejection in adult liver transplant recipients for this patient as outlined in this shared care document	
GP Signature:	
Date signed:	

ACTION

1. HOSPITAL CONSULTANT **Tick to confirm**

- Explain shared care to patient and obtain agreement Date agreement obtained:_____ ☐
- Indicate requesting hospital ☐
- Complete and sign agreement ☐
- Email or fax (email preferred) full shared care guideline (including signed agreement to GP) ☐
- Place original in patient's notes ☐

2. GP PRACTICE

- If **in agreement** to participate in shared care, sign and email this sheet back **within 2 weeks** of receipt **of request from specialist** to the lead transplant co-ordinator at wendy.littlejohn@nhs.net.

- If **you do not agree** to participate in shared care, contact consultant and local CCG Medicines Management Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local CCG Medicines Management team should be informed.
- Once decision reached file a copy in the Patient's medical notes.

Mycophenolate Mofetil tablets for the prevention of organ rejection in adult liver transplant recipients already being prescribed this drug in primary care (i.e. existing patients only)

Mycophenolate mofetil is added in to augment immunosuppression in those with rejection or for those experiencing nephrotoxicity with tacrolimus (Prograf or Advagraf). Mycophenolate mofetil should **never** be used as a single agent. It is usually given in combination with tacrolimus (Prograf or Advagraf) or prednisolone.

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- Shared care will only be requested for **existing** patients who are already being prescribed this drug in primary care by their GP practice. Having a shared care agreement in place will help support safer prescribing in primary care and clarify responsibilities of clinicians and patients.
- The hospital will have provided the patient with a supply of therapy for at least the first 3 months post discharge.

2. AREAS OF RESPONSIBILITY

Consultant / Specialist Team responsibilities

Before agreement to shared care

- Ensuring patient fits criteria for use of this drug (e.g. no contraindications, cautions, fits local agreement for use of the drug)
- Baseline monitoring
  - Liver function tests including aspartate transaminase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin and albumin
  - Urea and electrolytes including magnesium
  - Full Blood Count
  - Clotting – INR
  - Mycophenolate level
- Discuss treatment with patient and ensure they have a clear understanding of it. Where appropriate obtain signed consent.

  Information provided
  - Detailed patient education program including self-medication program on ward prior to discharge
  - Post-transplant patient education booklet which includes diet and lifestyle advice.

- Email or fax (email preferred) a signed shared care guideline with patient details completed to GP for consideration of shared care request.
- Acceptance of shared care should NOT be assumed. Confirmation to participate is required from GP.
- It is the responsibility of the initiating hospital clinic to contact GP.
- Initiate treatment and provide a supply of therapy for at least the first 3 months post discharge.
- Prescribe and monitor treatment according to local guideline or formulary until patient's condition is stable or predictable

After agreement to shared care

- Inform GP when patient's condition is stable or predictable and > 3 months post-transplant.
- Inform GP of abnormal monitoring results and any changes in therapy.
- Evaluate adverse events reported by GP or patient.
- Carry out ongoing monitoring and follow up in line with page 5 and 6 of this shared care guideline, including continued need for therapy.
- To review patient at the request of GP should any problems arise (side-effects / lack of efficacy) within 2 weeks.
- To communicate promptly with the GP if immunosuppression treatment is changed within 3 working days.
- To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk.

General Practitioner responsibilities

Before agreement to shared care

- Consider shared care proposal within 2 weeks of receipt. **Note:** this agreement covers existing patients already being prescribed this drug by the practice in primary care. It does not cover transfer of new patients to primary care.
- If in agreement to continue shared care prescribing responsibility, confirmation to the requesting consultant is required within 2 weeks of receipt of this shared care request by completing and emailing the agreement on page 2.
- If do not agree to shared care discuss with requesting consultant or local CCG medicines management team within 2 weeks of receipt of shared care request.

After agreement to shared care

- Prescribe dose as recommended once the patient's condition is stable or predictable and > 3months post-transplant. To adjust dose as advised by the specialist.
- Monitor general health of patient and check adverse effects as appropriate.
- Inform Transplant Specialist of suspected adverse effects and also report to the MHRA via yellow card scheme via http://www.yellowcard.gov.uk if necessary.
- Stop treatment on advice of specialist.
- Check compatibility interactions when prescribing new or stopping existing medication. If advice is needed from the specialist team, please see communication information on page 8.
- Carry out monitoring and follow up according to page 6 of this shared care guideline.
- Discuss any abnormal results with specialist consultant and agree any action required.
- Refer to Transplant Specialist urgently if patient non-compliance with immunosuppression is suspected.
- Only ask specialist to take back prescribing if unmanageable problems arise, for example erratic blood levels or nonadherence.
- To refer back to specialist if the patient's condition deteriorates.

Patient's / Carer's responsibilities

- To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.
- To inform community pharmacists that they are using mycophenolate mofetil before purchasing medication over-the-counter
- To attend all hospital and GP appointments
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others
- To read the patient information leaflet included with the medication.
- To report any adverse effects or warning symptoms to GP or hospital specialist
- To inform GP and hospital of any changes in addresses or telephone contact numbers.

3. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for mycophenolate mofetil prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Indication(s)

Prevention of organ rejection following liver transplantation in adults.

Place in Therapy

In combination with other immunosuppressants. Mycophenolate mofetil should never be used as a single agent post liver transplant. Mycophenolate mofetil is usually given in combination with tacrolimus (Prograf or Advagraf) and /or steroids. Mycophenolate mofetil may be added in to augment immunosuppression in those with graft rejection or at increased risk of graft rejection, or for those with nephrotoxicity with tacrolimus (Prograf or Advagraf). **Mycophenolate mofetil should never be prescribed with azathioprine.**

Dose & route of administration

Mycophenolate mofetil is available as a capsule (250mg), a tablet (500mg) and as an oral suspension (1g/5ml).

Post-transplant dose in Adults:

- 250 - 500mg BD, increased as tolerated to a maximum dose of 1500mg BD.
- Mycophenolate mofetil dose is adjusted according to blood levels (max 12 hour post dose trough level 3mg/L), liver function and tolerability. Any dose adjustment will be advised by the Specialist Transplant Physician at King's College Hospital.

Duration of treatment

Life-long.

Criteria for stopping treatment

Only after discussion with Transplant Consultant.

Monitoring Requirements including frequency

Transplant Consultant:

Each review appointment will include the following;

- Clinical assessment including examination of suspicious skin lesions.
- Bloods tests are taken at each clinic appointment for trough mycophenolate mofetil levels, FBC, INR, urea and creatinine, eGFR and LFT's. Additional test may be required for individual patients.
- Post transplant clinic appointments will be weekly initially immediately post transplant. The interval between appointments will be gradually increased based on individual patient needs. All post transplant will be reviewed annually as a minimum for life.

GP:

- Monitor patients overall health and wellbeing.
- Monitor for any signs or symptoms of bone marrow suppression e.g. infection or unexplained bruising or bleeding. Any suspicion of bone marrow suppression should necessitate immediate liaison with the Transplant Centre.
- Skin care – Skin cancers account for the commonest malignancies after liver transplantation. Suggested preventative measures include:
    - Regular dermatological screening for early detection and ablation of premalignant lesions. All patients should undergo a full dermatological examination on at least an annual basis. Any suspicious lesions should prompt specialist referral. In addition, patients should be instructed in self-examination and reporting of new lesions.
    - Patients should avoid direct sun exposure, use appropriate clothing for outdoor activities and apply sunscreens with high sun protection factor. Guidelines for patients can now be found on the web (http://www.scopnetwork.org, http://www.itscc.org).
- Liver function – any deterioration in liver function (including deterioration in aspartate transaminase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin and albumin, INR) should necessitate immediate liaison with the Transplant Centre.
- Mycophenolate mofetil trough levels should be checked if there is clinical suspicion of toxicity (signs and symptoms include nausea and diarrhoea, bone marrow suppression, patients are advised to report any inexplicable bruising or bleeding), non-adherence, and interacting medication is commenced or any other cause for concern. Blood samples (3ml of blood in an EDTA tube) should be sent to Philip Morgan, Institute of Liver Studies, King's College Hospital, Denmark Hill, SE5 9RS, for assay. There is no charge for mycophenolate mofetil assays.
- Pneumococcal vaccine is recommended for all adults who are immuno-compromised. Revaccination is not recommended. Confirm patient's vaccine status.
- Flu vaccine: is recommended annually for all patients who are immunocompromised.
- Report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk.

Follow up arrangements

Transplant Consultant:

- Frequency of outpatient appointments is dependent on individual patient progress. Each patient will be reviewed annually at a minimum. Following each outpatient clinic or inpatient stay, any medication changes will be communicated to the patient and the GP by letter within 3 working days. The patient will be informed by telephone of any changes in drug doses that need to be made on a more urgent basis.
- Assess need for further investigations.

Follow up arrangements cont'd

GP:

- Monitor patients overall health and wellbeing.
- Carry out monitoring requirements as detailed above annually or at more frequent intervals dependent on individual patient needs.

Practical issues including other relevant advice/information

Reminder: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for mycophenolate mofetil prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk).

Adverse effects

N.B. These are common adverse reactions but this list exhaustive. Refer to BNF for list of all potential adverse effects.
Nausea and diarrhoea can occur initially and is usually managed by introducing a low dose and titrating up as tolerated. Refer to specialist if persistent or severe.
Bone marrow suppression. Patient should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or unexplained bruising or bleeding. Contact specialist for immediate clinical advice.

Important Drug Interactions

N.B These are the common drug interactions but this list is not exclusive. Refer to BNF for list of all potential drug interactions with mycophenolate mofetil. The Liver Team at King's would appreciate the opportunity to discuss the introduction of any new drug which may interfere with the metabolism of mycophenolate mofetil before it is initiated. The Liver Pharmacy Team can be contacted for advice on 0203 299 9000 extension 5714 or 0203 299 9000 and ask for aircall number KH1121.

Interacting medication;

- Colestyramine and antacids containing aluminium or magnesium impair absorption of mycophenolate mofetil and should not be taken at the same time of day.
- Aciclovir may increase mycophenolate mofetil plasma levels, however this is not considered clinically significant.
- Live vaccines should not be given to patients with an impaired immune response. The antibody response to other vaccines may be diminished.

Vaccines

Live vaccines are contra-indicated and should be avoided. Examples of live vaccines that are contra-indicated include BCG, typhoid (oral) and yellow fever. For further information on vaccines see BNF, chapter 14. Please contact the Liver Transplant Pharmacist for further advice on vaccines.

Contraception

Please contact the Liver Team at King's regarding contraception advice.

Pregnancy

Patients planning to become pregnant or in whom pregnancy has occurred should contact the Transplant Consultant for review on their immunosuppression regimen. In general, immunosuppression should be continued during pregnancy. However it is likely that mycophenolate mofetil will be switched to an alternative immunosuppressant in patients planning to become pregnant and/or in pregnant patients. All patients who wish to become or who are pregnant should be reviewed by a Transplant Consultant for consideration of immunosuppressive regimen choice and/or dose adjustment. It is essential to maintain adequate immunosuppression levels during pregnancy and pregnancy can dramatically affect immunosuppressant drug handling.

Breastfeeding

Breastfeeding should be avoided if taking mycophenolate mofetil.

Information provided to the patient

- Detailed patient education program including self-medication program on ward prior to discharge
- Post-transplant patient education booklet including information about brand prescribing and how to obtain further supplies.

Evidence Base for treatment and key references
1. British National Formulary 70. September 2015-March 2016 2. Summary of Product Characteristics. Mycophenolate Mofetil 500mg film coated tablets. Accessed via www.medicines.org.uk. Last updated 08/02/2016 3. Immunisation against infectious disease: The Green Book. Accessed via www.doh.gov.uk. Updated December 2013.

4. COMMUNICATION AND SUPPORT

NOTE: King's College Hospital NHS Foundation Trust is the only Trust in SEL that manages this patient group.

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
Consultant/specialist team - Liver Transplantation Prof. Michael Heneghan Prof. John O' Grady Dr. Kosh Agarwal Dr. Varuna Aluvihare Dr. Abid Suddle Dr Deepak Joshi	Consultant Hepatology Transplant Secretary Tel: 0203 299 4952 Fax: 0203 299 3899
Consultant Surgical Team – Liver Transplantation Prof. Nigel Heaton Mr. Andreas Prachalias Mr. Parthi Srinivasan Mr. Hector Vilca-Melendez Mr Krishna Menon Mr Wayel Jassem	Consultant Surgical Transplant Secretary Tel: 0203 299 3762
Immediate medical advice, and out of hours Transplant Registrar	 Tel: 0203 299 9000 Bleep 142 or out-of-hours via switchboard (0203 299 9000)
Immediate general advice, and out of hours Transplant Co-Ordinators Post-transplant Co-Ordinator: Wendy Littlejohn	 Tel: 0203 299 4024 or out of hours via switchboard (0203 299 9000), Aircall 842688 via switchboard (0203 299 9000)
Medication – Prescribing advice, interactions, availability of medicines Transplant Pharmacist: Alison Orr	 Pharmacy Department Secretary; 0203 299 3347 Aircall KH1121 via switchboard (0203 299 9000) Direct extension: 0203 299 5714 Email: kch-tr.liverpharmacy@nhs.net
Transplant ward Todd ward	0203 299 3310
Immunosuppressant Drug Monitoring Phillip Morgan	020 3299 3147