**SHARED CARE GUIDELINE**

**Mycophenolate in Rheumatology**

**Implementation Date: 1st December 2019 Review Date: 1st December 2022**

***This guidance has been prepared and approved for use within Sunderland and South Tyneside in consultation within the CCGs, and Secondary Care Trust.***

***The guideline sets out the details of the transfer of prescribing and respective responsibilities of GPs and specialist services within shared care prescribing arrangements. It is intended to provide sufficient information to allow GPs to prescribe this treatment within a shared care setting***

**Approved by:**

|  |  |
| --- | --- |
| **Committee** | **Date** |
|  |  |
|  |  |

**Instructions for completion:**

## Consultant to counsel patient on medication and ensure patient has been provided with information leaflet

## Consultant to ensure all clinical details completed on this document

## Consultant to ensure patient understands proposed monitoring and prescribing arrangements if a shared care agreement is entered into

## GP to complete final section of form and return to specialist prescriber within 28 days

## GP to retain copy of document on patient record within surgery

 **Clinical details:**

|  |
| --- |
| SHARED CARE GUIDELINE |
| Non-proprietary name | Mycophenolate mofetil | Brand name | Cellcept | LicensedY/N? | N |
| Dosage form and strength | Oral tablets (500mg)Oral capsules (250mg)  | BNF class | 8.2.1 |

|  |  |
| --- | --- |
| Indication | Moderate to severe inflammatory arthritis vasculitis, SLE, connective tissue disease (other) (unlicensed indications) |
| Dosage and Administration | Initial dose to be determined by consultant rheumatologist, then adjusted according to response. **Typical dose:** 0.5-3g/dayDose and frequency should be stated clearly on the prescription |
| Eligibility criteria for shared care | Patients must be under the care of a consultant rheumatologist Must have a diagnosis of inflammatory arthritisPatients who have been stabilised and have been treated by specialist for at least three months.Patients who are not stable should not be transferred to primary care for monitoring. |
| Excluded patients | Not for patients under the age of 16 years.Patients in whom mycophenolate is contraindicated or not tolerated  |
| Initiation | Shared care to be initiated once patient has been stable on maintenance dose for three months |
| Monitoring | **Baseline assessment will be completed by specialist prior to initiation****Monitoring**Ongoing blood test monitoring of high risk or low risk patients according to monitoring schedules below and review of laboratory abnormalities prior to transfer. Monitoring of high risk patients * The patient is ‘high risk’ if any of the following apply:
* Extremes of weight: BMI <18 or >30kg/m2
* Renal impairment: CKD stage III or above
* Pre-existing liver disease (including NAFLD)
* Significant other co-morbidity (e.g. malignancy)
* Age >80 years
* Previous DMARD toxicity.

**Routine Bloods:** FBC, U&E, ALT and/ or AST, Albumin, creatinine/eGFR **Frequency:** Every two weeks until stable on a dose for 6 weeks. * Once on a stable dose: monthly blood tests.
* Following a dose increase, bloods should be checked every two weeks for 6 weeks, then revert back to previous schedule

For patients who are NOT high risk:**Routine Bloods:** FBC, U&E, ALT and/ or AST, Albumin, creatinine/eGFR**Frequency:** Every 2 weeks until stable on a dose for 6 weeks* Once on a stable dose: monthly blood tests for 3 months
* Then: at least every 12 weeks for the duration of treatment
* Following a dose increase bloods should be checked 2 weekly for 6 weeks, then revert back to previous schedule

**Laboratory abnormalities requiring action**The abnormalities in table below should trigger action/review. **If any abnormal blood test results are obtained, withhold the medication and discuss with the patient’s consultant rheumatologist. Do** not forget to consider the possibility that the abnormal blood result may be unrelated to the immunosuppressant medication.

|  |  |
| --- | --- |
| **Test** | **Result** |
| White cell count | <3.5 \* 109/l (or downward trend over 2 consecutive tests) |
| Neutrophils | <1.6 \* 109/l |
| Unexplained eosinophilia | >0.5 \* 109/l |
|  |  |
| Platelet count | <140 \* 109/l |
| MCV | > 105 f/l |
| Creatinine/eGFR | Creatinine increase >30% over 12 months and/or GFR <60ml/min/1.73m2 |
| ALT (and/or AST) | >100 U/L  |
| Albumin | Unexplained reduction in albumin to <30g/l |

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| Infections | **Infections**Patients treated with immunosuppressant agents (IAs) are at increased risk for opportunistic infections (bacterial, fungal, viral and protozoal). During serious infections, the IA should be temporarily discontinued, until the patient has recovered from the infection. It is usually appropriate to continue them in minor infections (e.g. a treated, uncomplicated UTI or URTI). Patient should be seen by GP/clinician within 12 hours of onset of infective symptoms. If the patient develops recurrent infections or respiratory symptoms this should be investigated as mycophenolate has been associated with hypogammaglobulinaemia, bronchiectasis and pulmonary fibrosis (MHRA alert January 2015). If recurrent infections or respiratory symptoms are present, please contact consultant rheumatologist to discuss.If Herpes Zoster occurs stop mycophenolate and prescribe aciclovir. If patient is in contact with chicken pox, contact specialist (may need Zoster Immunoglobulin). |
| Vaccinations | Live vaccinations are not recommended. Vaccinations against influenza and pneumococcus should be recommended. Shingles vaccination (Zostavax®) contains live, attenuated virus. The Green Book advises that specialist advice should be sought as to the suitability for shingles vaccination: <https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>  |
| Pregnancy and breastfeeding | Contact specialist. It is generally advised to ensure that the patients are NOT pregnant before the drug is commenced and advised to use contraception for at least 6 weeks after discontinuation of treatment. It is not recommended for mothers who are breast feeding (manufacturer’s advice). Reproductive issues: * MMF is teratogenic and it should not be taken during pregnancy nor while breast-feeding
* Women of child-bearing age should use appropriate contraception whilst taking the drug. Hormonal methods of contraception should be supplemented with a barrier method
* Women should not attempt to get pregnant until at least 6-12 weeks after stopping MMF

The European Medicines Agency updated its advice for men and mycophenolate (15 December 2017); it is advised that : * Either the male patient or his female partner must use reliable contraception during mycophenolate treatment and for at least 90 days after stopping treatment.

The manufacturers of MMF have produce risk materials for healthcare professionals and patients to reflect the above advice<https://www.medicines.org.uk/emc/product/1102/rmms>  |
| Perioperative use | Steroid exposure should be minimised prior to surgical procedures and increases in steroid doses to prevent adrenal insufficiency are not routinely requiredDMARD therapy should not routinely be stopped in the perioperative period, although individualised decisions should be made for high-risk procedures. |
| Specialist Responsibilities | * The decision to initiate immunosuppressive therapy must be made in conjunction with the patient/carer and be supervised by an expert in the condition in question
* Patients must be provided with education about their treatment
* Patient will be provided with a mycophenolate patient information leaflet
* Patients must be assessed for contra-indications and co-morbidities
* Where appropriate, patients should be advised about the impact of the immunosuppressive agent (IA) on fertility, pregnancy and breastfeeding
* Vaccinations against pneumococcus and influenza are recommended
* Interactions between the proposed IA and current medication should be identified and actioned
* Direct the patient to report any sign of infection or side effect to their GP or hospital clinic
* Conduct baseline monitoring
* Prescribe medication until responsibility agreed to be transferred to patients GP
* Supply general immunosuppressant background information to GP as per this guidance
* Request GP participate in shared care in writing no sooner than 3 months after initiation and patient is stable
* At least 4 weeks of medication supplied at point of transfer
* The secondary care specialist will communicate with the patient and GP when treatment is changed and/or needs to be changed by GP on future prescriptions, and/or when any changes to the monitoring are required, usually within 24 hrs
* Conduct routine monitoring as per schedule while prescribing responsibility with specialist – this could be during initiation or at any point in time where the responsibility has been transferred back to the specialist
* Observe advice relating to vaccination, perioperative use, infections etc. contained in this document
* Specialist responsible for ongoing disease monitoring– clinical response to therapy will be assessed by the hospital physician in all cases and communicated to the GP
* Specialist responsible for assessing if a patient is defined as ‘high risk’ and communicating this to the GP
 |
| GP Responsibilities | * The GP should reply to the request for shared care as soon as possible, but always within 14 days, either accepting shared care or informing the specialist why shared care is not felt appropriate in this case.
* If GP declines shared care responsibilities it is still the GPs responsibility to record on the primary care record that the drug is being prescribed by secondary care
* Shared care to be initiated once patient is stable and at least 3 months after initiation
* Prescribe medication as per document
* Observe advice relating to vaccination, perioperative use, infections etc. contained in this document
* **Conduct routine monitoring as per schedule while responsible for prescribing**
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| Adverse Effects, Precautions and Contraindications | **Contra-indications**Known hypersensitivity to the productSuspected local or systemic infectionPregnancy and breast feeding Bone marrow failure, with unexplained anaemia and cytopeniaPre-existing blood dyscrasiasSevere acute or chronic infectionsHereditary deficiency of the enzyme hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan or Kelley-Seegmiller syndrome**Precautions**Very frail and elderly patientsActive serious gastro-intestinal disease. Hereditary deficiency of hypoxanthine-guanine (presents with early onset gout)Localised or systemic infection.**Chronic kidney disease (CKD)**In renal disease, IAs that are renally excreted accumulate, and some IAs are nephrotoxic. Mycophenolate is not felt to be nephrotoxic but does accumulate in renal failure. Patients with CKD should be graded as per NICE definition of CKD (table 1) and have IA dose reductions as per recommendations by the British Society of Rheumatology (BSR) (table 2). GPs should contact specialist for advice in the case of CKD or abnormal CrCl/eGFR results. Table **1: NICE Definitions of CKD**

|  |  |
| --- | --- |
| **Degree of Impairment** | **Calculated GFR ml/min/1.73m2** |
| Normal, Stage I | >90 (other evidence of kidney damage) |
| Mild, Stage II | 60-89 (other evidence of kidney damage) |
| Moderate, Stage III | 30-59 |
| Severe, Stage IV | 15-29 |
| Established renal failure, Stage V  | <15 |

**Table 2: Recommended dose adjustment in CKD by the BSR**

|  |  |
| --- | --- |
|  | Recommended adjustment(% of standard dose) |
| Drug | Accumulates in renal failure | Nephrotoxic | CKD III | CKD IV | CKD V |
| Azathioprine | No | No | Normal dose | 75-100 | 50-100 |
| Methotrexate | Yes | Yes | 50% | Contraindicated |
| Mycophenolate | Yes | No | Normal dose | 1g BD maximum |

**Haematological*** Suppression of haematopoiesis/myelosuppression
* Neutropenia and cases of pure red cell aplasia reported Abnormal bruising with or without sore throat may indicate bone marrow failure. Severe neutropenia occurs in 0.5% patients receiving MMF in the full dose.
* STOP the drug. Check FBC immediately also discuss with specialist team. Temporary suspension of MMF for 10–14 days will usually result in recovery of the cell count. Once the cell count recovers, the drug can be re-administered in half the previous dose and gradually increased until a stable dose is attained without any toxic effect.
* It is often difficult to assess the exact cause of leucopenia or neutropenia because many causes may lead to the development of these disorders such as additional immunosuppressive regimens, concomitant medications and viral infections or combination of all the above. It is most commonly seen within the first 6 months.
* Cases of pure red cell aplasia (PRCA) have been reported in patients treated with MMF in combination with other immunosuppressants. PRCA may resolve with dose reduction or cessation of MMF (Roche communication May 2009).

**Adverse Effects**Nausea, diarrhoea GI inflammation, ulceration and bleeding, abdominal cramps and dyspepsia. (STOP drug if evidence of GI bleeding),cough, dyspnoea, hyperglycaemia, tremor, dizziness, headache, flu-like syndrome hepatitis, jaundice, pancreatitis, hypertension, hypotension, tachycardia, insomnia, blood disorders (including leucopenia, anaemia, thrombocytopenia, pancytopenia and red cell aplasia), disturbances of electrolytes and lipids, malignancy (particularly of the skin), renal impairment, progressive multifocal leukoencephalopathy, interstitial lung disease, pulmonary fibrosis, alopecia, rash, uro-genital (sterile haematuria, urinary tract infection, renal tubular necrosis).Clinician should review severity of side effect and contact specialist for advice if needed. For a full list of contraindications/precautions/side effects please consult either the current BNF or SPC**For a full list of contraindications/precautions/side effects please consult either the current BNF or SPC:** [**https://bnf.nice.org.uk/**](https://bnf.nice.org.uk/)[**https://www.medicines.org.uk/emc**](https://www.medicines.org.uk/emc) |
| Common Drug Interactions | **Interactions:*** Antacids: Containing aluminium and magnesium hydroxide cause a decrease in the absorption of MMF by 33% and bioavailability by 17%. Antacids/PPIs impair mycophenolate absorption and should be taken 1hr prior or 2hrs after.

**For a full list of interactions please consult either the current BNF or SPC:** [**https://bnf.nice.org.uk/**](https://bnf.nice.org.uk/)[**https://www.medicines.org.uk/emc**](https://www.medicines.org.uk/emc) |
| Communication/ Contact Details | * For acute advice:
	+ Monday to Friday, 9.00 am to 5.00 pm, phone the on-call monitoring nurse, rheumatology registrar or rheumatology consultant on call via the switchboard on **(0191) 565 6256**. Please use the bleep number **53546** in order to contact the rheumatology monitoring nurse for routine queries.
	+ Out of hours, phone the on-call medical registrar on **(0191) 565 6256**.
* For non-acute advice, send a letter to the consultant in charge of the patient’s care.
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***This information is not inclusive of all prescribing information and potential adverse effects. Please refer to full prescribing data in the SPC or the BNF.***

## Shared Care Request/Confirmation Private and Confidential

**Patient information:
*To be completed by specialist prescriber:***

|  |  |  |
| --- | --- | --- |
|  |  | **Patient details (use hospital label if preferred)** |
| **Consultant** | …………………………………… | **Name** | …………………………………………… |
| **Department** | …………………………………… | **Address** | …………………………………………… |
| **Hospital** | …………………………………… |  | …………………………………………… |
|  |  | **Postcode** | ................................. | **Sex** | ………... |
|  |  | **NHS or Hosp. Reg. No.** | ………………… | **DoB** | ………... |

 **Treatment Requested for Prescribing in Accordance with Shared Care Arrangement:**

***To be completed by specialist prescriber:***

|  |  |
| --- | --- |
| **Drug name** |  |
| **Dose** |  |
| **Frequency** |  |
| **Indication** |  |
| **Other information** |  |

Name (print)……………………….… Signature (of specialist prescriber)…………………..……….. Date……..

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**Acceptance/rejection of treatment under Shared Care Agreement:
*To be completed by GP:***

|  |  |
| --- | --- |
|  | Please tick one box |
| ***I ACCEPT the proposed shared care arrangement for this patient***  | **❑** |
| or |  |  |
| ***I ACCEPT the proposed shared care arrangement with the caveats below*** | **❑** |
| or |  |  |
| ***I DO NOT ACCEPT the proposed shared care arrangement for this patient*** | **❑** |
| My caveats / reason(s) for not accepting include: …………………………………………………………………………………… ………………………………………………………………………………………………………………………………………Name (print)…………………………..… Signature (of GP)………………………………..………….... Date……… | . |

**N.B. Participation in this shared care arrangement implies that prescribing responsibility is shared between the specialist prescriber and the patient’s GP**