Effective Shared Care Agreement (ESCA)

MYCOPHENOLATE

For Connective Tissue Disease (Off label use)

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of mycophenolate for Connective Tissue Disease can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are not obliged to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with Connective Tissue Disease are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of connective tissue disease.
2. Discuss with the patient options for treatment and the suitability of mycophenolate.
3. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient.
4. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made
5. Initiate treatment and stabilise patient on maintenance dose of mycophenolate in the following patients (all criteria must be met): 1) Patients who have been on treatment for more than 9 months, AND 2) Patients on ≤2g/day mycophenolate AND 3) Patients are taking no more than 10mg prednisolone AND 4) Disease activity has been well controlled with no escalation of treatment required in the last 6 months.
6. Review the patient's condition and monitor response to treatment regularly.
7. Communicate promptly with the GP when treatment is changed.
8. Advise GP on dosage adjustment and when and how to stop treatment.
9. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
10. Report serious adverse events to the MHRA www.yellowcard.gov.uk
11. Ensure clear backup arrangements exist for GPs, for advice and support.

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days.						
2. Prescribe mycophenolate at the dose recommended.						
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement.						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments as advised by the specialist.						
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment						
6. Monitor as outlined below. If results fall outside normal ranges, use clinical judgement before referral and consider any other factors that may be contributing to the abnormality. If uncertainty and concerns remain seek specialist advice.						
7. Report serious adverse events to specialist and MHRA www.yellowcard.gov.uk						
8. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with mycophenolate with the specialist, clinical nurse specialist or GP.
3. Report any adverse effects to the specialist or GP whilst taking mycophenolate.
4. Attend regular outpatient appointments with the specialist.

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

SUPPORTING INFORMATION

Indication	Mycophenolate inhibits B and T cell proliferation and has other immunomodulatory effects. Mycophenolate has been used for systemic lupus erythematosus (SLE), vasculitis and dermatomyositis. Time to response is between 6 weeks to 3 months.
Dosage and Administration	Dose and titration (based on how well tolerated by the patient and the current blood picture) Starting dose: 500 mg daily for the 1st week, 500 mg twice daily for the 2nd week and increase it gradually by 500 mg each week until the optimal or maximum tolerated dose is reached. Typical dose 1–2 g/day. Maximum dose: Up to 3 g/day. Mycophenolate is available as oral tablets/capsules (250 mg or 500mg) and suspension.
Contra-indications / Cautions	**Contra-indications** (1) Pregnancy and breast feeding. Mycophenolate mofetil and its active metabolite mycophenolic acid are associated with a high rate of serious birth defects and increased risk of spontaneous abortion. Male and female patients should be reminded when they are prescribed the drug that it is important they use effective contraception while on treatment and for three months after stopping treatment. (2) Localised or systemic infections. **Important updated safety advice (December 2015**): • Physicians should ensure that women and men taking mycophenolate mofetil and mycophenolic acid understand: the risk of harm to a baby; the need for effective contraception; the need to plan for pregnancy and change treatment as necessary; and the need to immediately consult a physician if there is a possibility of pregnancy. • Mycophenolate mofetil or mycophenolic acid treatment should only be initiated in women of child bearing potential when there is a negative pregnancy test result to rule out unintended use in pregnancy. • Mycophenolate mofetil or mycophenolic acid should only be given to women of childbearing potential who are using highly effective contraception. • Women should use 2 forms of effective contraception during treatment and for 6 weeks after stopping treatment. • Men (including those who have had a vasectomy) should use condoms during treatment and for at least 90 days after stopping treatment. This advice is a precautionary measure due to the genotoxicity of these products. • Female partners of male patients treated with mycophenolate mofetil or mycophenolic acid should use highly effective contraception during treatment and for 90 days after the last dose. **Cautions** (1) Patients with suspected lymphoproliferative disorder or unexplained anaemia, leucopenia and thrombocytopenia. (2) Localised or systemic infection. (3) Patients with active serious digestive system disease. (4) Very frail and elderly.
Side Effects	Commonest adverse reactions are as follows: (1) Gastrointestinal: diarrhoea, nausea, vomiting, abdominal cramps and dyspepsia. (2) Uro-genital: sterile haematuria, urinary tract infection, renal tubular necrosis. (3) Haematological: abnormal bruising with or without sore throat may indicate bone marrow failure. Severe neutropenia occurs in 0.5% patients receiving mycophenolate in the full dose. STOP the drug. Check FBC immediately and also discuss with specialist team. (4) Malignancy: lymphomas caused by oncogenic viruses (e.g. EBV) and skin tumours. Excessive sun exposure should be avoided.

Important notes	• Live vaccines should **not** be administered. • Influenza and Pneumovax vaccines are recommended • Patients without immunity who are exposed to chickenpox or shingles should be administered Varicella Zoster Immunoglobulin – seek specialist advice. • Effective contraception should be recommended during therapy. • Patient should be counselled to observe for signs of bone marrow suppression i.e. inexplicable bruising, bleeding or infection.

Monitoring

Treatment should not be initiated unless patients can be adequately monitored for toxic effects throughout the duration of therapy.

Pre- treatment Assessment	Full Blood Count (FBC), Urea and Electrolytes (U&Es), Liver Function Tests (LFTs), Renal, C-reactive protein (CRP). Chest X-ray.
After commencing treatment	FBC weekly for 1 month. Then fortnightly for 2 months. Then monthly for 9 months. Monitoring requirements can be more relaxed after 12 months of therapy, e.g. every two months for the second year of treatment, then every three months from the third year of treatment onwards, providing there is no history of monitoring abnormalities and unless advised differently by the supporting secondary care team.
Disease monitoring	ESR/CRP helps assessment (auto-antibodies for connective tissue disease)
Withhold treatment and seek advice from specialist	▪ Platelets < 120 x 10^9/L ▪ WBC < 3 .5 x 10^9/L ▪ Neutrophils < 2.0 x 10^9/L ▪ LFTs > 2x upper limit of reference range ▪ MCV > 105 fl **(unless documented by the rheumatologist to be a feature of the disease process in which case alternative patient-specific thresholds will be defined)**
Dose reduction	Side effects:- GI upset, mouth ulcers, rash, recurrent infection

Notable Drug Interactions (please refer to SmPC for full list of interactions)	Interacting Medication (1) **Antacids** and oral **magnesium** supplement: reduce the absorption of mycophenolate and if required should be separated from mycophenolate by 2–3 hours. (2) **Cholestyramine**: may decrease the absorption of mycophenolate and bio-availability by 40%. (3) **Probenecid**: prevents renal tubular secretion and causes an increase in plasma concentration of mycophenolate. (4) **Aciclovir**: causes increase in the concentration of both mycophenolate and aciclovir. However, the increase is significant only in renal impairment. (5) **Rifampicin**: plasma concentration of active metabolite of mycophenolate reduced by rifampicin. (6) **Ciclosporin A** reduces the absorption of mycophenolate but no effect of mycophenolate on CicA. If Cic A stopped expect an increase in mycophenolate absorption (7) Antibacterials: plasma concentration of nmycophenolate possibly reduced by **co-amoxiclav**; bioavailability of mycophenolate possibly reduced by **metronidazole** and **norfloxacin.** (8) **Azathioprine:** do not use in combination with mycophenolate because such concomitant administration has not been studied.

References

British Society for Rheumatology (BSR) guidelines
SmPC Mycophenolate Tablets (accessed July 2015)
MHRA Drug Safety Update (December 2015)

This ESCA should be read in conjunction with the Summary of Products Characteristics (SmPC) & used in line with recommendations made in the BSSE APC Formulary.

Based on MTRAC Template

I agree to participate in this shared care agreement for the treatment connective tissue disease with mycophenolate in the below named patient.

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at:
