There is a new NEL-wide SCG for Azathioprine and Mercaptopurine for all indications which supersedes this document. Please refer to the new NEL-wide SCG for up to date information on use of Azathioprine, and continue to use this (existing) version for other listed medicines. Access the NEL-wide Azathioprine and Mercaptopurine here: https://primarycare.northeastlondon.icb.nhs.uk/home/meds/nel-wide-non-mental-health/

BHRCCGs and BHRuT NHS Trust Shared Care Guidelines

Disease Modifying Anti-Rheumatic Drugs (DMARDs): Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine

For the treatment of autoimmune rheumatic diseases in adults

The information in the shared care guideline has been developed in consultation with CCGs in Barking, Havering and Redbridge and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing DMARDs for the treatment of autoimmune rheumatic diseases.

The questions below will help you confirm this:

- Is the patient on stable medication?
- Do you have the relevant knowledge, skills and access to equipment to allow you 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 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 or attend hospital more frequently for prescriptions. 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**.

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 back to the requesting clinician.

GP DECISION FORM

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of **DMARDs: Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine for the treatment of autoimmune rheumatic diseases in Adults** 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 prescribing and monitoring of the DMARD for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe the drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE of Disease Modifying Anti-rheumatic Drugs (DMARDs):
Azathioprine and/or Hydroxychloroquine and/or Leflunomide and/or Methotrexate and/or Mycophenolate and/or Sulfasalazine
For the treatment of autoimmune rheumatic diseases in the following patient

Consultant / Specialist Name:	Patient Name:
Consultant / Specialist Signature:	Patient Hospital Number: Patient NHS Number:
Date completed:	Patient Agreement (delete as appropriate) Patient Agrees to shared care Patient does not agree to shared care
GP Name:	
This is to confirm that I agree / do not agree (delete as appropriate) to participate in shared care for DMARD(s): (tick as appropriate) Azathioprine ▫ Hydroxychloroquine ▫ Leflunomide ▫ Methotrexate ▫ Mycophenolate ▫ Sulfasalazine ▫ For the treatment of ……(please insert condition being treated) for this patient as outlined in this shared care document.	
GP Signature	Practice Stamp:
Date Signed:	

Hospital Specialist:
The request for shared care (together with full shared care guideline) should be emailed to the GP and the original filed in the patients notes.
On receipt of the GP signed decision – this should be uploaded to EPRO and filed in patient's notes.

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.

Email address: bhrut.rheumscg@nhs.net

If do not agree to participate in shared care, contact consultant or Rheumatology Nurse specialist and local Primary Care CCG Medicines Management Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patients, both the consultant and the local Primary Care CCG Medicines Management team should be informed.

AUTOIMMUNE RHEUMATIC CONDITIONS AND DMARD LICENSING

Note some patients may have overlap syndromes with clinical features of multiple diseases

O='off-label' but considered routine treatment option
X=unlicensed and not currently considered a routine option

	Azathioprine	Hydroxy-chloroquine	Leflunomide	Methotrexate	Mycophenolate	Sulfasalazine
Behcets	O	X	X	X	O	X
Churg-Strauss	O	X	X	O	X	X
Dermatomyositis	Licensed	O	X	O	O	X
Granulomatosis with Polyangitis (GPA)	O	X	O	O	O	X
Microscopic Polyangitis (MPA)	O	X	X	O	X	X
PolyarteritisNodosa (PAN)	Licensed	X	O	O	X	X
Polymyositis	Licensed	O	X	O	X	X
Psoriatic Arthritis (PsA)	X	X	Licensed	O	X	O
Relapsing Polychondritis	O	O	X	X	X	X
Rheumatoid Arthritis (RA)	Licensed	Licensed	Licensed	Licensed	X	Licensed
Scleroderma	O	O	X	O	O	X
Sjogrens	X	O	X	O	X	X
Systemic Lupus Erythematosis (SLE)	Licensed	Licensed	X	O	O	X
Takayasu's Arteritis	O	X	O	O	O	X

SHARED CARE

Sharing of care assumes communication between the specialist, GP and the patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy.

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

AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Ensure appropriate use of the DMARD(s) e.g. no contraindications, cautions, fits local or national agreement for use of the drug
- Undertake baseline investigations and initial monitoring
- Prescribe treatment until the patient is considered stable and shared care is agreed with GP
- Discuss adverse effects and any practical issues related to the use of the DMARD with the patient
- Notify the GP when DMARD therapy is initiated. The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
  - A clinical summary of the patient including information on prescribed medication, initial response and any adverse effects experienced
  - A request that the GP continue prescribing and monitoring
  - A copy of the shared care guidelines outlining required ongoing monitoring
  - Information on when the patient will next be reviewed by Consultant / Specialist team
- Evaluation of any reported adverse effects by GP or patient.
- Communicate (within 2 weeks) with the GP if treatment is changed or patient does not attend appointment.

General Practitioner responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the GP Decision Form (page 2)
- If do not agree to shared care discuss with requesting consultant or rheumatology nurse specialist within 2 weeks of receipt of shared care request
- Provide ongoing prescriptions and adjust dose as advised by the specialist.
- Undertake ongoing monitoring as outlined in the monitoring information
- Report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team
- Advise the specialist if non-compliance is suspected
- Refer back to specialist if the patient's condition deteriorates
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Report any suspected adverse effects to the MHRA via the Yellow Card scheme: http://www.yellowcard.gov.uk

CCG responsibilities

- To provide feedback to the Trust via Medicines Optimisation committee.
- To support GPs to make the decision whether or not to accept clinical responsibility for prescribing
- To support trusts in resolving issues that may arise as a result of shared care.

Patient's / Carer's responsibilities

- Read pre-treatment information leaflets and monitoring booklet
- Bring Oral Methotrexate Monitoring booklet to each appointment with GP / specialist and show the booklet to community pharmacist when having prescriptions dispensed.
- Contact the Specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- Agree to attend all hospital and GP appointments
- Inform GP and hospital of any changes in addresses or telephone contact numbers
- Report any adverse effects, new / worsening symptoms or if breastfeeding to GP or hospital specialist
- Inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.
- Inform the Specialist and GP if planning to get pregnant and notify when pregnancy is confirmed.
- Inform community pharmacists of all prescribed medication before purchasing medicines over-the-counter
- Take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others

CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for the respective DMARD 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).

AZATHIOPRINE					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral: Initially 1mg/kg/day (usually 50-75mg / day) increased at 4-6 weekly intervals to max 3mg/kg/day. **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein, thiopurine methyltransferase (TPMT) assay. Inform GP if patient is heterozygous for TPMT. If heterozygous, start on low dose and titrate slowly. **On Commencement of treatment, until GP takes over monitoring:** Full blood count, creatinine/calculated GFR and liver function tests 2 weekly until dose stable for 6weeks, then monthly for 3 months and at least 12 weekly thereafter. More frequent monitoring is appropriate in patients at higher risk of toxicity In patients heterozygous for TPMT, monitoring should continue at monthly intervals. Ask patient about any rashes, oral ulceration, bruising or bleeding at each visit.	Full blood count, creatinine/calculated eGFR and liver function tests 3 monthly, unless heterozygous for TPMT (continue monthly monitoring). Ask patient about any rashes, oral ulceration, bruising or bleeding at each medication review or if otherwise unwell. Monitor for signs and symptoms of infection.	Failure to respond to treatment or adverse effects necessitating withdrawal. In some patients pre-treatment results may be low and continued treatment may be appropriate following review of long term trend and discussion with Rheumatologist. **Withhold and discuss with Rheumatologist if any of the following occur:** WBC < 3.5 x 10^9/L, Neutrophils < 1.6 x 10^9/L, Platelets <140 x10^9/L, MCV > 105 fl, AST/ ALT > 100 U/L, unexplained reduction in albumin <30 g/L, unexplained eosinophilia >0.5 x 10^9/L Abnormal bruising or severe sore throat –Check FBC immediately. Rash or oral ulceration Renal Impairment (GFR <30 ml/min OR >30% increase in creatinine over 12 months from baseline).	Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.	**Specialist:** Subject to response to treatment: 3 monthly, 6 monthly or 12 monthly if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, TPMT status, most recent blood tests and frequency of visits. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Blood tests as outlined. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments.

AZATHIOPRINE (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **TPMT Deficiency -**Thiopurine methyl transferase (TPMT) deficiency (heterozygous state) may be associated with delayed (up to 6 months after starting azathioprine) haematological toxicity including bone marrow toxicity. Azathioprine can be fatal in homozygous TPMT states and is contraindicated.
2. **Abnormal laboratory parameters –** MCV >105 fl - check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with Rheumatologist.
3. **Adverse Effects -**Patients should be advised to use a sunscreen with a high protection factor and protective clothing to reduce sunlight exposure.
4. **Pregnancy and Breast Feeding -**Azathioprine can be prescribed to pregnant and breast feeding patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their consultant immediately and shared care will no longer apply for the duration of the pregnancy and while they continue to breast-feed.
5. **Vaccinations -**Patients must not receive immunisations with live vaccines such as oral Polio, MMR, BCG, yellow fever or varicella-zoster. Seasonal and pandemic influenza vaccination and Pneumovax are safe and recommended. Varicella vaccine should not be given to patients without discussing with the Consultant Rheumatologist to assess degree of immunosuppression. Patients may also be on biologic therapy, therefore, important to discuss with Consultant Rheumatologist. Patients exposed to Chicken Pox / shingles should receive passive immunisation with VZIG (varicella-zoster immunoglobulin), if they are varicella-zoster virus (VZV) susceptible (VZV IgG undetectable on blood testing).

Clinically Significant Drug Interactions (refer to BNF for full list):

- **Co-trimoxazole, trimethoprim, sulfamethoxazole**– avoid, increased risk of haematological toxicity
- **Allopurinol** – enhanced effects and increased toxicity of allopurinol – reduce azathioprine dose to 25% of the original dose. Discuss with rheumatologist if allopurinol to be initiated.
- **Febuxostat**- although interaction studies with febuxostat and azathioprine have not been performed, inhibition of xanthine oxidase (XO) is known to result in an increase in azathioprine levels. On the basis of the mechanism of action of febuxostat on XO inhibition, concomitant use is not recommended.
- **Coumarin anticoagulants** – reduced anticoagulant effect, monitor INR closely and increase maintenance dose if necessary
- **Ribavirin** – possible increased risk of myelosuppression

HYDROXYCHLOROQUINE					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral: 200-400mg/day (max 5mg/kg or 400mg daily – whichever is lowest). Use ideal body weight for calculating maximum dose. **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein. G6PD status should be considered in at risk ethnic groups. Ask about visual impairment that is not corrected by glasses. Advise patients to report any visual disturbance. The Royal College of Ophthalmologists (RCOphth) recommend that all patients planning to take hydroxycholoroquine long term (i.e. >5 years) should have a baseline ophthalmology review (ideally within 6 months, but definitely within 12 months of starting therapy), including colour retinal photograph and spectral domain optical coherence tomography (SD-OCT) scans of the macular. **Ongoing On Commencement of treatment, until GP takes over monitoring:** Nil	The Royal College of Ophthalmologists (RCOphth) recommend that patients should be referred for annual monitoring after 5 years of therapy. Individuals taking hydroxychloroquine who have additional risk factors for retinal toxicity (very high dose of drug therapy, concomitant Tamoxifen therapy or renal insufficiency) may require annual screening before 5 years of therapy. This may be decided by a consultant ophthalmologist following the baseline visit; but refer for earlier review if new risk factors develop.	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with Rheumatologist if any of the following occur:** Visual disturbances Renal impairment GFR < 50ml/min	Nil	**Specialist:** Subject to response to treatment: 3 monthly, 6 monthly or 12 monthly if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Check patient has arranged annual review by community optometrist. Refer back to ophthalmology for review if patient develops new visual symptoms or has new risk factors for retinal toxicity or after 5 years of therapy. Request patient seen earlier if disease flare or adverse effects experienced between appointments.

HYDROXYCHLOROQUINE (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **Adverse Effects -**GI disturbances, headache, rashes, pruritus, retinal damage.
2. **Eye Checks -** baseline ophthalmology review within 12 months of commencing therapy and annually after 5 years of therapy, or sooner if additional risk factors for retinal toxicity.
3. **Pregnancy and Breast Feeding -**Hydroxychloroquine can be prescribed to pregnant patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their consultant immediately and shared care will no longer apply for the duration of the pregnancy and while breastfeeding.

Clinically Significant Drug Interactions (refer to BNF for full list):

- **Tamoxifen** (annual ophthalmology review – increased risk of retinopathy)
- **Amiodarone**(avoid - increased risk of ventricular arrhythmias)
- **Moxifloxacin**(avoid - increased risk of ventricular arrhythmias)
- **Digoxin** (may increase digoxin levels - check for signs of toxicity and monitor levels if appropriate)
- **Ciclosporin** (increased ciclosporin levels - monitor levels and check for signs of toxicity)
- **Artemether with lumefantrine** (avoid - increased risk of convulsions)
- **Mefloquine** (avoid - increased risk of convulsions)
- **Droperidol** (avoid increased risk of ventricular arrhythmias)

LEFLUNOMIDE					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral: 10-20mg/day Usually 10mg/day if used in combination with other hepatotoxic drugs, e.g. Methotrexate. **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein, chest x-ray (unless done in last 6months). Hepatitis B, Hepatitis C and HIV screening as clinically appropriate. Blood pressure – if > 140/90 on two consecutive readings 2 weeks apart, treat as per NICE guidance before commencing Leflunomide. Weight – to allow assessment of weight loss. **Ongoing On Commencement of treatment, until GP takes over monitoring:** Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Check weight and BP at each visit. Ask patient about any rashes, oral ulceration, bruising or bleeding at each visit.	FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Increase monitoring frequency to monthly if co-prescribed Methotrexate. If in doubt discuss with rheumatologist. Check weight and blood pressure 3 monthly. If BP >140/90 treat in line with NICE guidelines. Ask patient about any rashes, oral ulceration, bruising or bleeding at each medication review or if otherwise unwell.	Failure to respond to treatment or adverse effects necessitating withdrawal. In some patients pre-treatment results may be low and continued treatment may be appropriate following review of long term trend and discussion with Rheumatologist. **Withhold and discuss with Rheumatologist if any of the following occur**: WBC < 3.5 x 10^9/L, Neutrophils < 1.6 x 10^9/L, Platelets <140 x10^9/L, MCV > 105 fl, AST/ ALT > 100 U/L, unexplained reduction in albumin <30 g/L, unexplained eosinophilia >0.5 x 10^9/L Abnormal bruising or severe sore throat –Check FBC immediately. Rash or oral ulceration Renal Impairment (GFR <30 ml/min OR >30% increase in creatinine over 12 months from baseline) Pregnancy / Breastfeeding	Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.	**Specialist:** Subject to response to treatment: 3 monthly, 6monthly or 12 monthly if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Blood tests as outlined. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments.

LEFLUNOMIDE (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **Abnormal laboratory parameters –** MCV >105 fl - check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with Rheumatologist.
2. **Adverse effects**
   Hypertension: Regular monitoring of blood pressure is necessary during treatment and any significant rise in blood pressure, should be treated as per NICE guidelines. In severe uncontrolled cases it may be necessary to consider stopping the drug after discussing with a rheumatologist.
   Respiratory: If patient develops new onset shortness of breath or cough, leflunomide should be stopped immediately and discuss with the rheumatologist
   Hepatotoxicity: leflunomide can cause hepatotoxicity and caution is advised when patients are prescribed other hepatotoxic drugs or if there is evidence of current or recent hepatitis B or C infection. Most cases of hepatotoxicity have occurred in the first 6 months of treatment and in the presence of multiple risk factors. Patients should limit alcohol intake within national limits of 4-8 units a week. Contact rheumatologist if there are any concerns over hepatotoxicity or co-prescribing with other drugs (see monitoring requirements above).
3. **Pregnancy, breastfeeding and contraception -**any patient considering family planning should be discussed with the rheumatologist. Leflunomide is contraindicated in pregnancy and breast feeding. Men and women taking Leflunomide must use reliable contraceptives. Women must wait 2 years between stopping the drug and becoming pregnant. This can be reduced to 3 months if patients are treated with a rapid washout under the supervision of a rheumatologist. Men should continue to use effective contraception for 3 months after stopping treatment.
4. **Vaccinations** - patients must not receive immunisations with live vaccines such as oral polio, MMR, BCG or yellow fever. Inactivated injectable polio vaccine is available but suboptimal response may be seen. Seasonal and pandemic influenza vaccination and Pneumovax are safe and recommended. Varicella vaccine should not be given to patients without discussing with the Consultant Rheumatologist to assess degree of immunosuppression. Patients may also be on biologic therapy, therefore important to discuss with Consultant Rheumatologist. Patients exposed to Chicken Pox / shingles should receive passive immunisation with VZIG (varicella-zoster immunoglobulin), if they are varicella-zoster virus (VZV) susceptible (VZV IgG undetectable on blood testing).

Clinically Significant Drug Interactions (refer to BNF for full list):

- Methotrexate – increased risk of hepatotoxicity
- Note: Leflunomide has a very long half-life (2 weeks) therefore the interactions can be potentially serious and a drug wash out procedure may be required. Discuss with consultant rheumatologist if necessary.

METHOTREXATE					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral or subcutaneous injection: 7.5 – 25mg once a week Only prescribe 2.5mg tablets or the appropriate strength of pre-filled pen/syringe. Concomitant folic acid 5mg once a week (usually 2 – 3 days prior to methotrexate – not to be taken on the day methotrexate is taken). **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein, chest x-ray (unless done in last 6 months) +/-lung function tests. Hepatitis B, Hepatitis C and HIV screening as clinically appropriate. **Ongoing On Commencement of treatment, until GP takes over monitoring:** Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Ask patient about any rashes, oral ulceration, bruising or bleeding at each visit.	FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Check weight and blood pressure 3 monthly. If BP >140/90 treat in line with NICE guidelines. Ask patient about any rashes, oral ulceration, bruising or bleeding at each medication review or if otherwise unwell.	Failure to respond to treatment or adverse effects necessitating withdrawal. In some patients pre-treatment results may be low and continued treatment may be appropriate following review of long term trend and discussion with Rheumatologist. **Withhold and discuss with Rheumatologist if any of the following occur:** WBC < 3.5 x 10^9/L, Neutrophils < 1.6 x 10^9/L, Platelets <140 x10^9/L, MCV > 105 fl, AST/ ALT > 100 U/L, unexplained reduction in albumin <30 g/L, unexplained eosinophilia >0.5 x 10^9/L Abnormal bruising or severe sore throat – Check FBC immediately. New or increasing dyspnoea or dry cough Unexplained acute widespread rash Oral ulceration, nausea, vomiting, diarrhoea, dark urine or abdominal cramps. Severe sore throat / abnormal bruising. Renal Impairment (GFR <30 ml/min OR >30% increase in creatinine over 12 months from baseline) Pregnancy / Breastfeeding	Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.	**Specialist:** Subject to response to treatment: 3 monthly, 6 monthly or 12 monthly if well controlled and stable. Remind patient of signs and symptoms of methotrexate toxicity and check understanding of once weekly administration and need for folic acid. Ask about any rashes or oral ulceration. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held medicines Oral Methotrexate Monitoring Booklet with most recent blood results. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Blood tests as outlined. Update patient held Oral Methotrexate Monitoring Booklet with most recent blood results. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments. Remind patient of signs and symptoms of methotrexate toxicity and check understanding of once weekly administration and need for folic acid. Ask about any rashes or oral ulceration.

METHOTREXATE (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **Abnormal laboratory parameters** - MCV > 105 fl- if B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with rheumatologist.
2. **Adverse Effects** - nausea/dizziness/headache–if tolerable continue. Severe symptoms may require dose reduction or cessation of treatment. Consider increasing folic acid (max 6 times weekly avoiding the day methotrexate is taken) or using an anti-emetic if nausea is severe. Discuss ongoing nausea with rheumatologist.
   Abnormal bruising or severe sore throat – Check FBC immediately and withhold until results available. Discuss with rheumatologist.
   New onset shortness of breath or dry cough – stop methotrexate immediately and discuss with rheumatologist. Pneumonitis is more likely to occur in first year of treatment but can occur at any time.
   Unexplained acute widespread rash – withhold and discuss with rheumatologist.
   Severe oral ulceration – withhold and discuss with rheumatologist.
3. **Pregnancy, breastfeeding and contraception** - methotrexate is contraindicated in pregnancy and breastfeeding. Whilst taking methotrexate and for at least 3* months after stopping, both men and women must use reliable contraception. For patients considering family planning, discuss with rheumatologist. Women must wait at least 3 full menstrual cycles (or 3* months) after stopping methotrexate before conceiving. Men should continue to use contraceptives for 3* months after stopping methotrexate.***NOTE: Some manufacturers recommend using reliable contraception for 6 months after cessation of methotrexate therapy. Always consult the Summary of Product Characteristics for the product being prescribed (www.medicines.org.uk).** Methotrexate may be excreted in breast milk so breast feeding must be avoided.
4. **Vaccinations -**patients must not receive immunisations with live vaccines such as oral polio, MMR, BCG or yellow fever. Inactivated injectable polio vaccine is available but suboptimal response may be seen. Seasonal and pandemic influenza vaccination and Pneumovax are safe and recommended. Varicella vaccine to prevent chickenpox should not be given to patients without discussing with the Consultant Rheumatologist to assess degree of immunosuppression. Zostavax to prevent Shingles is NOT contraindicated for patients on doses of Methotrexate <0.4mg/kg/week (this equates to 25mg / week for a 62.5kg individual). Patients should be assessed on an individual basis as the degree of immunosuppression can vary. Patients on combination therapy should be discussed with the Consultant Rheumatologist. Beware patients may also be on biologic therapy which is a contraindication to Zostavax.. Patients exposed to Chicken Pox / shingles should receive passive immunisation with VZIG (varicella-zoster immunoglobulin), if they are varicella-zoster virus (VZV) susceptible (VZV IgG undetectable on blood testing).
5. **Risk factors for hepatotoxicity** - obesity, diabetes and alcohol excess increase the likelihood of methotrexate induced liver damage. Alcohol consumption should be well within national guidelines and should be in the region of 4-6 units a week.
6. **Methotrexate injection** - follow local Trust procedures to ensure patient or carer is appropriately trained and can demonstrate competence on injection technique and disposal of cytotoxic sharps. Barking, Havering & Redbridge University Hospitals NHS Trust has a protocol available on intranet and copies available from medicines information or specialist nurses.

Clinically Significant Drug Interactions (refer to BNF for full list):

- **Co-trimoxazole, trimethoprim, sulphonamides** (avoid - may increase anti folate effect and lead to increased risk of marrow aplasia)
- **NSAIDs** (monitor for signs / symptoms of toxicity – excretion of methotrexate probably reduced by NSAIDs). Patients should be advised to avoid self-medication with over-the-counter **aspirin, ibuprofen** and **naproxen**. Discuss with rheumatologist before commencing patients on newly prescribed NSAIDs.
- **Neomycin** (monitor efficacy – possible reduced absorption of methotrexate)
- **Ciprofloxacin** (monitor for signs/symptoms of toxicity – excretion of methotrexate possibly reduced)
- **Doxycycline/tetracycline** (increased risk of toxicity)
- **Penicillins** (increased risk of toxicity)
- **Clozapine** (avoid methotrexate as increased risk of agranulocytosis)
- **Ciclosporin** (increased risk of toxicity)
- **Leflunomide** (increased risk of toxicity)
- **Nitrous oxide** (increased risk of toxicity avoid concomitant use)
- **Probenecid** (increased risk of toxicity)
- **Acitretin** (increased risk of toxicity avoid concomitant use)
- **Pyrimethamine** (increased risk of toxicity)
- **Cisplatin** (increased pulmonary toxicity)

MYCOPHENOLATE MOFETIL					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral: Initially 500mg daily in divided doses, increased weekly by 500mg to optimal / maximum tolerated dose. Usual maximum dose 3 grams daily in divided doses. **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein, chest X-ray (unless done in the last 6 months). Hepatitis B, Hepatitis C or HIV screening as considered clinically appropriate. **Ongoing On Commencement of treatment, until GP takes over monitoring:** Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Ask patient about any rashes, oral ulceration, bruising or bleeding at each visit.	FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Ask patient about any rashes, oral ulceration, bruising or bleeding at each medication review or if otherwise unwell.	Failure to respond to treatment or adverse effects necessitating withdrawal. In some patients pre-treatment results may be low and continued treatment may be appropriate following review of long term trend and discussion with Rheumatologist. **Withhold and discuss with Rheumatologist if any of the following occur:** WBC < 3.5 x 10^9/L, Neutrophils < 1.6 x 10^9/L, Platelets <140 x10^9/L, MCV > 105 fl, AST/ ALT > 100 U/L, unexplained reduction in albumin <30g/L, unexplained eosinophilia >0.5 x 10^9/L Unexplained fall in serum albumin (in absence of active disease). Severe sore throat / abnormal bruising / bleeding – check FBC immediately Unexplained anaemia Suspected malignancy Localised or systemic infections Pregnancy/Breastfeeding	Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule	**Specialist:** Subject to individual patient response: 3 monthly, 6 monthly or 12 monthly if well controlled and disease activity stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Blood tests as outlined. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments.

MYCOPHENOLATE MOFETIL (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **Abnormal laboratory parameters** - MCV > 105 fl- if B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with Rheumatologist
2. **Adverse Effects -** Diarrhoea, nausea, vomiting, abdominal cramps and dyspepsia. If intolerable discuss with rheumatologist. Patients should avoid exposure to sunlight by wearing protective clothing and a sunscreen with a high protection factor.
3. **Pregnancy, breastfeeding and contraception –** mycophenolate is contraindicated in pregnancy. Pregnancy should be excluded prior to treatment. Effective contraception should be used before commencing and whilst on mycophenolate and for 3 months after discontinuation of treatment. Any patients planning pregnancy should be referred back to the consultant. Breast feeding must be avoided.
4. **Vaccinations -**Patients must not receive immunisations with live vaccines such as oral Polio, MMR, BCG or yellow fever. Seasonal and pandemic influenza vaccination and Pneumovax are safe and recommended. Varicella vaccine should not be given to patients without discussing with the Consultant Rheumatologist to assess degree of immunosuppression. Patients may also be on biologic therapy, therefore, important to discuss with Consultant Rheumatologist. Patients exposed to Chicken Pox / shingles should receive passive immunisation with VZIG (varicella-zoster immunoglobulin), if they are varicella-zoster virus (VZV) susceptible (VZV IgG undetectable on blood testing).
5. **Renal Impairment –** it is not uncommon in diseases treated with mycophenolate mofetil. Poor renal function can indicate disease worsening and need to increase the dose rather than stop. Discuss with Rheumatologist.

Clinically Significant Drug Interactions (refer to BNF for full list):

- **Metronidazole** and **norfloxacin** - bioavailability of mycophenolatemofetil possibly reduced
- **Rifampicin –** plasma concentration of active metabolite of mycophenolatemofetil reduced
- **Co-amoxiclav –** plasma concentration of mycophenolate possibly reduced

SULFASALAZINE EC					
Route, Dose, Duration	**Monitoring Undertaken by Specialist before requesting shared care**	**Ongoing monitoring to be undertaken by GP once shared care agreed**	**Stopping Criteria**	**Monitoring following dose changes**	**Follow Up**
Oral: 500mg/day increasing by 500mg weekly to 2–3g /day in 2-4 divided doses. **Duration of Treatment:** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline:** Full blood count, electrolytes, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein. **Ongoing On Commencement of treatment, until GP takes over monitoring:** Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity Ask patient about any rashes, oral ulceration, bruising or bleeding at each visit.	FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity. Ask patient about any rashes, oral ulceration, bruising or bleeding at each medication review or if otherwise unwell. After discussion with Consultant Rheumatologist, the frequency of monitoring may be reduced to 6 monthly after the first year providing the dose and blood results are stable.	Failure to respond to treatment or adverse effects necessitating withdrawal. In some patients pre-treatment results may be low and continued treatment may be appropriate following review of long term trend and discussion with Rheumatologist **Withhold and discuss with Rheumatologist if any of the following occur:** WBC < 3.5 x 10^9/L, Neutrophils < 1.6 x 10^9/L, Platelets <140 x10^9/L, MCV > 105 fl, AST/ ALT > 100 U/L, unexplained reduction in albumin <30 g/L, unexplained eosinophilia >0.5 x 10^9/L Severe sore throat / abnormal bruising / bleeding – check FBC immediately Renal Impairment: GFR 10-20 ml/min –use with caution and ensure high fluid intake. GFR <10 ml/min avoid	Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule	**Specialist:** Subject to individual patient response: 3 monthly, 6 monthly or 12 monthly if well controlled and disease activity stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP:** Blood tests as outlined. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments.

SULFASALAZINE EC (CONTINUED)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to BNF for full list)**:**

1. **Abnormal laboratory parameters** – MCV > 105 fl - check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with rheumatologist.
2. **Adverse effects** – nausea/dizziness/headache – if possible continue. Severe symptoms may require dose reduction or cessation of treatment. Discuss with rheumatologist.
   Abnormal bruising or severe sore throat – check FBC immediately and withhold until results available. Discuss with rheumatologist.
   Unexplained acute widespread rash or oral ulceration – withhold and discuss with rheumatologist.
3. **Infertility** – oligospermia and infertility may occur in men. Discontinuation appears to reverse these effects within 2 to 3 months. Discuss with rheumatologist
4. **Pregnancy and breastfeeding** – patients considering family planning should be referred to their rheumatologist. An assessment of risk / benefit should be discussed with the Consultant Rheumatologist and patient. Avoid breastfeeding in very preterm jaundiced neonates – discuss with Obstetrician and Neonatologist
5. **Prescription Selection** – due to risk of drug selection error ensure prescription reads sulfasalazine NOT SulfaDIAZINE. For more information: https://www.gov.uk/drug-safety-update/recent-drug-name-confusion

Clinically Significant Drug Interactions (refer to BNF for full list):

- No clinically significant drug interactions

COMMUNICATION AND SUPPORT

Hospital Switchboard: 01708 435 000

Consultant / Specialist team	
Rheumatology Consultants: • Dr Daniels • Dr Doherty • Dr Habibi • Dr Lynn • Dr Perera • Dr Roussou • Dr Stapleton • Dr Wickramaratne Associate Specialist: • Dr Williams	Telephone Secretary: King George Hospital: 020 8970 8160 Queen's Hospital: 01708 435 000 Ext 2721 or 2723
Rheumatology Specialist Registrar	via hospital switchboard Bleep 8238
Rheumatology Specialist Nurse helpline Clinical Nurse Specialists and Rheumatology Nurses are: • Ratidzo Maboreke • Diana Simeon • Janice Leahy • Patricia Lewis • Janette Viterbo • Karen Bowmer • Victoria Katsande • Helen Burke • Sariyu Mogaji	Telephone: King George Hospital: 020 8970 8408 Queen's Hospital: 01708 435 000 Ext 4821
Clinical Pharmacist, Rheumatology Lead – Sajid Master	Telephone: 01708 435 000 Ext 8979
Department Email (Shared Care Guidelines only)	**bhrut.rheumscg@nhs.net**

Medication – Prescribing Advice, interaction, availability of medicines	
Pharmacy Medicines Information Department BHR Medicines Management Team	01708 435 418 0203 182 3133

REFERENCES

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2. The Royal College of Ophthalmologists Clinical Guidelines. Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on Monitoring. January 2020.
3. K. Chakravarty et al. on behalf of the British Society for Rheumatology, British Health Professionals in Rheumatology Standards, Guidelines and Audit Working Group in consultation with the British Association of Dermatologists
4. South East London Shared Care Prescribing Guideline for DMARDs - Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine for the treatment of autoimmune rheumatic diseases in Adults Date approved: January 2016 Document review date: January 2019
5. British national Formulary 70
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7. NICE National Clinical Guideline 79: Rheumatoid Arthritis, February 2009
8. NICE CKS for DMARDs July 2015: http://cks.nice.org.uk/dmards