BNSSG Shared Care Guidance

Section 1: Heading

Drug	Methotrexate
Amber ***one month***	
Indication	Autoimmune rheumatologic conditions including inflammatory arthritis, connective tissue diseases and vasculitis Ocular inflammation Sarcoidosis
Speciality / Department	Rheumatology Ophthalmology Respiratory
Trust(s)	University Hospital Bristol & Weston NHS Foundation Trust
	North Bristol Trust

Section 2: Treatment Schedule

Usual dose and frequency of administration	Methotrexate is usually started at a dose between 7.5mg-15mg ONCE weekly orally. The starting dose will vary depending on the severity of the condition, age, renal function and other co-morbid conditions. Doses may go up to 25mg/week. The decision to increase the dose will be taken by the specialist team. It is also available in an injectable form. Patients may require switching to a subcutaneous preparation if they do not tolerate the oral form or to increase bioavailability and efficacy. The decision to switch to a subcutaneous preparation will be taken by the specialist team. All patients should be co-prescribed folic acid supplementation at a minimal dose of 5 mg once weekly. Folic acid frequency can be increased up to a maximum of 5mg six days a week (not on day of Methotrexate) to reduce adverse effects of Methotrexate.
Route and formulation	Oral tablets. Subcutaneous injection.
Duration of treatment	Long term. As long as clinically indicated- unless a serious side effect occurs or the drug becomes ineffective.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate

Pre-treatment assessment: This will be performed by the rheumatology/ophthalmology/respiratory department.

Height, weight, blood pressure, FBC, renal function/GFR, LFT's, and screening for viral infection (HIV, Hep B, Hep C) will be done prior to commencing methotrexate.

In patients with a clinical suspicion of parenchymal lung disease, formal lung function testing and appropriate imaging (chest radiograph with or without high-resolution CT imaging) should be performed and referral to a respiratory specialist be considered. Some specialist departments may arrange baseline chest X-Ray routinely for all patients. Any patient currently smoking should be offered access to smoking cessation services.

Subsequent tests - where appropriate

Monitoring: This will be performed primarily by the patient's GP, with support from the specialist team in the event of abnormal results (see below).

Check FBC, creatinine/calculated GFR, ALT and/ or AST and albumin every 2 weeks until on stable dose for 6 weeks.
Once on stable dose, **monthly** FBC, creatinine/calculated GFR, ALT and/ or AST and albumin for 3 months. Then 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.

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 back to previous schedule.

If Leflunomide is used in combination with methotrexate then monthly monitoring should be extended longer term (Individual patients who have been stable for 12 months can be considered for reduced frequency of monitoring).

Note that a rise in alkaline phosphatase may reflect disease activity rather than drug toxicity. Similarly a low WCC may be a feature of the underlying disease. If in doubt please contact the patient's specialist.

Chicken pox/shingles infection - stop and commence aciclovir.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	**Common side-effects** include nausea, diarrhoea and dyspepsia (consider increasing folic acid frequency e.g. 5mg 3-6 days per week). Serious but rare side-effects include neutropaenia and pneumonitis **Side effects with unknown frequency**: acne, alopecia, anaphylactic reactions, arthralgia, confusion, conjunctivitis, drowsiness, mood changes, mucositis, rash, reduced libido, visual disturbance, vomiting. Treatment with folinic acid may be required in acute toxicity.

Referral back to specialist	**Actions to be taken by patient's GP**: Methotrexate should be WITHELD if any of the following occur: Abnormal bruising or sore throat - Stop drug and check FBC WCC <3.5 x10^9/L Neutrophils <1.6 x10^9/L Platelets <100 x10^9/L Unexplained eosinophilia >0.5 x 10^9/L Mean cell volume >105 f/L ALT and or AST >twice upper limit of reference range Unexplained reduction in albumin Renal impairment: Creatinine increase >30% over 12 months and/or unexplained reduction in calculated GFR: stop drug if acute change. If gradual may need dose reduction. Rash or oral ulceration **Please repeat monitoring bloods in 1 week and if still low/high then discuss with the specialist team. Falling/rising trends may also prompt discussion.**

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	DO NOT prescribe trimethoprim or co-trimoxazole as severe bone marrow suppression may occur with concurrent use of methotrexate. It is safe to co-prescribe prophylactic co-trimoxazole (960mg three times a week) with Methotrexate as maintenance therapy for patients with ANCA-associated vasculitis. DO NOT prescribe etretinate (acitretin metabolite) or acitretin. Theoretical interactions may occur with salicylates, hypoglycaemics, diuretics, phenytoin, tetracyclines, chloramphenicol, penicillin, probenecid, tolbutamide, NSAIDs and omeprazole but at the doses used in rheumatic diseases this is rarely a problem. Interactions are also described with aminophylline, antibacterials, antimalarials, antipsychotics, and digoxin.
Reminder to ask patient about specific problems	Nil

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

Cautions:

The patient should be warned to report immediately sore throat and bruising (which may indicate blood disorders) and shortness of breath.

Based on limited data Methotrexate at a dose of <20mg a week is compatible with paternal exposure (the

BNF advises effective contraception should be used during and for at least 3 months after treatment in men and women)
Significantly impaired renal function (eGFR <50 reduces clearance. If eGFR 20-50: use 50-100% of normal dose; if eGFR 10-20: use 50% of normal dose; if eGFR<10: contra-indicated).
Significantly impaired hepatic function
Localised or systemic infection (including hepatitis B or C and TB)
Unexplained anaemia / cytopaenia associated with marrow failure
Pre-existing lung disease (In patients with a clinical suspicion of parenchymal lung disease, formal lung function testing and appropriate imaging (chest radiograph with or without high-resolution CT imaging) should be performed and referral to a respiratory specialist be considered. Any patient currently smoking should be offered access to smoking cessation services).
Excessive alcohol consumption. Patients should be advised to limit their alcohol intake to well within national recommendations
Avoid live vaccines (e.g. yellow fever vaccination); shingles vaccine (Zostavax) is live and therefore relatively contraindicated in individuals who are immunosuppressed.
Acute porphyria Photosensitivity

Patients should avoid contact with people who have active chickenpox or shingles and report any contact to their GP and hospital specialist. If immunosuppressed patients are exposed to chickenpox or shingles, they will need to be assessed for susceptibility and the need for aciclovir post exposure prophylaxis, see: UKHSA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles and the Green Book Chapter 34.

Contraindications:
Active infection, immunodeficiency Severe renal impairment (see above)
Ascites and significant pleural effusion (risk of accumulation, drain before treatment)

Methotrexate is contraindicated in pregnancy and breast feeding. It is strongly recommended that methotrexate should be stopped by female users 3 months before any planned pregnancy. If methotrexate is stopped, effective contraception will need to continue for a further 3 months.

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. Discuss potential benefits and side-effects of treatment with the Specialist and/or GP.
2. Share any concerns they have in relation to their treatment.
3. To report any side-effects to the Specialist and/or GP (see individual drug fact sheet for specific information).
4. To ensure that the patient held record is presented at every consultation (in primary or secondary care).
5. To agree to and attend for the monitoring of therapy (including having blood tests carried out at agreed intervals) and assessment of outcomes, to assist health professionals to provide safe, appropriate treatment.
6. To avoid excessive alcohol intake and stay well within national recommendations.
7. Female users must use adequate contraception, report any suspected pregnancy to the GP and/or Specialist and inform specialist in a timely manner any plans to conceive.
8. To inform GP/Specialist/pharmacist of all medicines (including OTC preparations) that they are currently taking.

Section 8: Responsibilities for Secondary Care Core responsibilities

1. Confirm diagnosis and indication for drug treatment.
2. Discuss potential benefits and side-effects of treatment with patient.
3. Carry out baseline monitoring requirements and initiate therapy. The GP will receive copies of the baseline blood test results.
4. The specialist will advise the GP of any dose adjustments required. The GP will then take over prescribing and blood test monitoring responsibilities.
5. An initial prescription will be provided by the specialist for 1 month.
6. Secondary care will advise on the appropriate monitoring blood tests as well as frequency.
7. Monitor the patient's response to therapy.
8. Decide when to stop therapy on safety grounds and inform the GP.
9. Secondary care will direct the GP to a copy of the concise drug information sheet and the shared care guidelines via the BNSSG Joint Formulary website.
10. Secondary care will supply the patient with a 'patient held record' and explain its role.
11. The dosage regimen should be clearly explained to the patient.
12. The patient should be asked to report side-effects (see individual drug fact sheet for specific information) and the GP should be informed if any side effects are reported to secondary care. Serious side-effects should be reported to the MHRA via the yellow card scheme.

Section 9: Responsibilities for Primary Care Core responsibilities

1. Take on shared care proposal from the specialist after the first month of treatment (including prescription and blood monitoring).
2. If shared care is declined, an arrangement should be made with the rheumatology/ophthalmology department to ensure patients are adequately supported. The GP practice and rheumatology/ophthalmology department should also inform the interface pharmacists at the CCG, see contact details section below.
3. To ensure that all relevant staff and patients are aware of the shared care arrangements. Blood test results, dosage adjustments, should be recorded in the patient held record and GP medical record. Any dosage adjustments should also be recorded in computer-based prescribing systems.
4. The dosage regimen should be clearly explained to the patient.
5. Contact the specialist to discuss any significant changes in the blood test results or patient's condition e.g.; the medication becomes less effective.
6. Respond to dosage changes advised and prescribe appropriately. Receive copies of any blood test results carried out in secondary care for information and record in patient's record appropriately.
7. Monitor the patient for any side-effects to therapy and refer back to the Specialist should any serious side-effect occur. Side-effects / discontinuation of medication should be documented in the patient held record.

Section 10: Contact Details

Organisation	Contact	Contact details	Availability
University Hospitals Bristol and Weston	UHBW – Bristol Rheumatology Telephone Advice Line	Tel: 0117 3424881 Registrar bleep: 7021	Mon - Thu 9am to 5pm Fri 9am to 1pm
	UHBW – Weston Rheumatology Telephone Advice Line	Tel:01934 881075 Fax: 01934 647025 On Call registrar bleep: 279	Mon - Fri 9am to 5pm
	UHBW – Bristol Eye Hospital Ocular inflammation specialist nurses	Nurse Tel: 0117 342 1421 Secretary Tel: 0117 342 1400 0117 342 1401	Mon- Fri 9am to 5pm
	UHBW – Interstitial lung disease (ILD) team Specialist nurse	Nurse Tel: 0117 342 4101	Mon- Fri 9am to 5pm
North Bristol Trust, Southmead Hospital	Consultant secretary as per clinic letter OR Rheumatology Telephone Advice Line	Tel: 0117 4140600 Fax: 0117 4140570 Tel: 07894800989 On Call Tel: 07894800989 Sat/Sun 9am-noon (GP service for existing NBT rheum patients only)	Mon - Fri 9am to 5pm
	Interstitial lung disease team – Telephone advice line	Tel: 0117 414 7762	Mon- Fri 9am to 5pm
BNSSG CCG	Interface Pharmacists	Bnssg.formulary@nhs.net	**Mon-Fri 9am to 5pm**

Section 11: Document Details

Date prepared	August 2017 (updated to include ocular inflammation 26/10/2021; ILD update NBT ILD team 11/11/21)
Prepared by	Collated and updated from previous guidelines by Dr Randa Alshakh on behalf of Bristol and Weston Rheumatology consultants (updated to include ocular inflammation 26/10/2021 completed by BNSSG Formulary Team). ILD update NBT ILD team 11/11/21 Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.
Date approved by JFG	November 2021
Date of review	October 2019
Document Identification: Version	V3.3

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

This document has been sent to rheumatology consultants across Bristol and Weston for comment and approval.

Interstitial lung disease updates agreed with consultants and nursing staff from UHBW and NBT.

Section 13: References

Please list references

BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, February 2017

BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids, January 2016

BNF 73 (March -September 2017)