OPT-OUT SHARED CARE GUIDELINE

It is assumed that shared care **will** be accepted unless the specialist is informed otherwise within 28 days of receipt of the request at the end of this document.

MEDICATION NAME: **METHOTREXATE ORAL 2.5mg tablets**

INDICATIONS COVERED: Rheumatoid Arthritis, Psoriatic Arthritis and other chronic inflammatory conditions in Adults

NHS Brighton and Hove CCG, Crawley CCG and Horsham and Mid-Sussex CCG
Traffic Light System Classification: Amber

NOTES to the general practitioner (GP) or primary care prescriber

For medicines which require specialist initiation and/or dose titration and specific ongoing monitoring. For initiation, dose stabilisation and prescribing (including monitoring) by a specialist until the patient is stabilised (usually for 3 months) after which the GP may be asked to work under shared care through the use of approved shared care guidelines.
The expectation is that these guidelines should provide sufficient information to enable GPs or primary care prescribers to be confident to take clinical and legal responsibility for prescribing these medicines.

The questions below will help you confirm this:

- Is the patient currently under your care (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge)?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care 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. It is assumed that shared care will be accepted unless the specialist is informed otherwise with 28 days of receipt of this request.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should inform the consultant or specialist within 28 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust or specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your CCG medicines management pharmacist will assist you in making decisions about shared care if you are unsure.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The GP or primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant or specialist.

Reason for update: New	**Prepared by:** Dr.U.Davies, D.Finney, Dr.S.Griffith, Dr.K.Jordan, Dr.R.Makadsi, Dr.G.Papasavvas, Dr.W.Shattles, SCT Medicines Management Team	**Updated by:** N/a
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Approved by (CCG Medicines Management Pharmacist): Stewart Glaspole, Specialist Interface Pharmacist		
Approved by NHS Brighton and Hove CCG on: 22.09.2015/02.12.2015		
Approved by Crawley CCG, Horsham and Mid-Sussex CCG on: 26.01.16		

Information

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SPC website**: http://www.medicines.org.uk/emc/

2. **Background to use for the indication(s), including licence status:**

Methotrexate 2.5mg tablets are used as an immunosuppressant either alone or in combination with other agents which influence the immune response.

Methotrexate has a marketing authorisation for rheumatoid arthritis. The maximum licensed dose in rheumatoid arthritis is 20 mg per week. Time to response: 6 weeks to 3 months.

ONLY prescribe the 2.5mg strength of tablets, the dose being multiples of the 2.5mg tablet strength once a week.

3. **Dose & administration:**

Oral methotrexate is usually administered once a week on the same day each week. It should be swallowed whole and not crushed or chewed.

Doses are initiated by the specialist for a once a week dose schedule and the dose may be titrated upwards or downwards by 2.5mg to 5mg dependent on response.

Folic acid may be prescribed as it reduces the toxic effects of methotrexate. It can be administered on any day except the day the patient takes the methotrexate. If taken once a week it is preferable the day after methotrexate.

4. **Cautions:**

- Patients with significant impaired renal function.
- Localised or systemic infection including hepatitis B or C or history of tuberculosis.
- Unexplained anaemia and/or cytopenia associated with bone marrow failure.
- Peptic ulceration, ulcerative colitis, diarrhoea and ulcerative stomatitis (withdraw if stomatis develops).
- Varicella Zoster Virus Infection – in patients with exposure to chickenpox or shingles contact the specialist. Passive immunization should be carried out using Varicella Zoster immunoglobulin.
- Risk of accumulation in pleural effusion or ascites—drain before treatment.
- Acute porphyria.
- Psychiatric disorders.
- Elderly patients, due to diminished hepatic and renal function and decreased folate stores, a reduction in dosage should be considered and these patients should be closely monitored for early signs of toxicity.
- Severe renal impairment requires a reduction in dose.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

5. **Contraindications:**

- Pregnancy – should not use methotrexate during pregnancy. Methotrexate is teratogenic and there is a theoretical risk of sperm mutation in males. Patients of either gender should use adequate contraception during treatment. In discussion with the specialist wait for at least three months but preferably six months (see SPC) after discontinuation of methotrexate before trying to conceive. Exclude existing pregnancy before initiating treatment.
- Patients with severe or significant hepatic impairment, including liver diseases such as fibrosis, cirrhosis, and recent or active hepatitis.
- Active infectious disease.
- Overt or laboratory evidence of immunodeficiency syndrome(s).
- Bone marrow failure with unexplained anaemia and cytopenia.
- Patients with known hypersensitivity to methotrexate or any of the excipients.
- Breastfeeding mothers. Methotrexate is excreted into breast milk in low concentrations (less than 10% of those in plasma.) It is not known whether these small amounts are potentially harmful to the developing child. In the absence of a clear evidence base, and because there is a danger of accumulation within foetal tissues, paediatric advice suggests avoidance of methotrexate during breast feeding.
- Presence of significant pleural effusion or ascites, because methotrexate can accumulate in these fluids, and its subsequent return to the circulation may cause myelosuppression.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption (depends on manufacturer).
- Alcoholism.
- Live vaccines (see drug interaction section).

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

6. Side effects:

Common: Nausea, anorexia, oral ulceration, minor hair thinning, abdominal discomfort, diarrhoea, headaches, ulcerative stomatitis, leukopenia, vasculitis, eye-irritation and loss of libido/impotence.

Uncommon: Rash, bone marrow suppression, causing thrombocytopenia, neutropenia, and rarely anaemia. Patients should be warned to report a sore throat and abnormal bleeding/bruising.

Hepatotoxicity. Rarely Methotrexate may cause liver fibrosis/cirrhosis. Where alcohol is avoided this has proven rare. Avoid if pre-existing liver disease.

Pulmonary toxicity. Acute pneumonitis or chronic pulmonary fibrosis may occur. This is not dose related. It presents with dry cough, dyspnoea and often fever.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

Table 1. Side effects and actions to take for abnormal results

SIDE EFFECT	ACTIONS
WBC $< 3.5 \times 10^9$/l, or Neutrophils $< 1.5 \times 10^9$/l, or Platelets $< 150 \times 10^9$/l	Withhold and discuss with specialist.
Liver Function AST/ALT > twice upper limit of reference range	Withhold and discuss with specialist.
Albumin-unexplained fall (in absence of active disease).	Withhold and discuss with specialist.
MCV>105 fl	Check serum B12, Folate and TFT and treat. If normal, continue treatment. Discuss with specialist if necessary.
Significant deterioration in renal function.	Withhold and discuss with specialist.
Rash, oral ulceration, nausea and vomiting, diarrhoea, stomatitis.	Withhold and discuss with specialist.
New or increasing dyspnoea or dry cough.	Assess chest and withhold treatment. Discuss urgently with specialist
Severe sore throat, abnormal bruising.	Withhold and check FBC urgently. Discuss with specialist.

Please note that in addition to absolute values, a rapid fall/rise or consistent downward/upward trend in haematological or biochemical index should prompt caution and extra vigilance.

7. Notable drug interactions:

- **Co-trimoxazole, trimethoprim: Antifolate effect of methotrexate is increased and greatly increases the risk of marrow aplasia. DO NOT prescribe folate antagonists to patients on methotrexate.**
- Acitretin, chloramphenicol, nitrous oxide, tetracyclines and any drugs with suspected or confirmed hepatotoxic or nephrotoxic effects.
- Phenytoin: Antifolate effect of methotrexate is increased.
- Probenecid, penicillin, non-steroidal anti-inflammatory drugs (NSAIDs): Methotrexate excretion is reduced. (Clinically significant interaction between NSAID and methotrexate is rare. There are no contra-indications to using standard doses of NSAIDs with doses of weekly methotrexate ≤ 30mg as long as the required methotrexate monitoring is undertaken as salicylates and some other NSAIDs delay the excretion of methotrexate. National guidance relating to cardio-vascular, gastro-intestinal and renal risk should be followed).
- **Inactivated vaccines** such as influenza vaccine are safe to use although they may elicit a lower response. **Live Vaccines - AVOID.** Severe or fatal infections may occur if a live vaccine is given concurrently. Therapy with a single, low-dose, non-biological oral immune modulating drug for treatment of rheumatoid arthritis and other conditions (e.g. methotrexate less than 0.4mg per kg per week) is **not** necessarily sufficiently immunosuppressive to contraindicate administration of zoster vaccine, so herpes zoster vaccine is not contraindicated in these patients (see http://tinyurl.com/nvdeqp2). The degree of immunosuppression should be assessed on a case by case basis. Primary care professionals with concerns about the degree of immunosuppression should contact the relevant specialist for advice.

This list is not exhaustive; refer to the Summary of Product Characteristics (SPC) or BNF for further guidance.

8. Criteria for use:

Chronic inflammatory conditions as determined by the appropriate specialist.
Specialist has initiated and dose stabilised (usually for a minimum 3 months).
GP or Primary Care Prescriber confident to take clinical and legal responsibility for prescribing this drug.

9. Any further information (e.g. supporting therapies):

See section 3 for folic acid supplementation.

10. References:

- Brighton and Hove CCG, *Effective Shared Care Agreement (ESCA): Methotrexate Tablets.* January 2013. Available at: http://www.gp.brightonandhoveccg.nhs.uk/files/sharedcareguidelines080715 (accessed 08.04.15).
- British Society for Rheumatology, Immunisation against shingles in people with inflammatory rheumatic disease. Available at http://www.rheumatology.org.uk/includes/documents/cm_docs/2013/i/immunisation_with_zostavax_for_people_with_inflammatory_rheumatic_disease.pdf (access 10.12.15).
- Chakravarty, K. et al, *BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists, British Society for Rheumatology*, Oxford University Press, 2008. Available at: http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/diseasemodifying_antirheumatic_drug_dmard_therapy.pdf (accessed 10/12/15).
- Crawley CCG, Horsham and Mid-Sussex CCG, *Effective Shared Care Agreement (ESCA): Methotrexate 2.5mg Tablets. August 2011*. Available at: http://www.horshamandmidsussexccg.nhs.uk/intranet/clinical/programmes/medicines-management/
- (accessed 09.04.15).
- Department of Health Immunisation against infectious diseases. Green Book. Chapter 28a, shingles (herpes zoster) updated 28/07/2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/448815/2904130_Green_Book_Chapter_28a_v1_0_0W_July2015.PDF (accessed: 28/07/2015).
- Joint Formulary Committee. *British National Formulary; Methotrexate,* March 2015, British Medical Association and Royal Pharmaceutical Society. London. Available at: https://www.medicinescomplete.com/mc/bnf/current/index.htm (accessed 09.04.15).
- Summary of Product Characteristics, *Maxtrex®25mg Tablets.* Pfizer Ltd. Last update 02.10.14. Available at: http://www.medicines.org.uk/emc/medicine/6003 (accessed 09.04.15).
- Summary of Product Characteristics, *Methotrexate 2.5mg Tablets.* Hospira UK Ltd. Last update 04.02.14. Available at: http://www.medicines.org.uk/emc/medicine/12033(accessed 09.04.15).
- Summary of Product Characteristics, Methotrexate 2.5mg Tablets. Amdipharm Mercury Company Ltd. Last update 17.09.14. Available at: http://www.medicines.org.uk/emc/medicine/22954 (accessed 09.04.15).
- UKMI. *Suggestions for Drug Monitoring in Adults in Primary Care.* February 2014. Available at http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug%20monitoring%20document%20Feb%202014.pdf (accessed 10.12.15).

RESPONSIBILITIES and ROLES

Consultant or Specialist responsibilities
1 Confirm diagnosis and indication for treatment with oral methotrexate, **2.5mg tablet strength**.
2 To discuss fully the aims, benefits, risks and side effects of treatment and a treatment plan with the patient and/or carer and for written information to be supplied to the patient and/or carer. Explain that the medication is usually taken once a week. Inform patients to report immediately any exposure to Varicella Zoster Virus.
3 Inform GP when initiating treatment so the GP is aware what is being prescribed and can add to GP clinical record.
4 Undertake baseline monitoring as required (FBC, U&E, LFT, plus see below) and chest X-Ray.
5 Prior to treatment ask GP whether patient has had pneumococcal vaccination and flu vaccination and, if not, immunise (unless contra-indicated). Inform patient not to start medication until after immunisation.
6 Record other medications and address potential drug interactions before starting therapy.
7 Exclude existing pregnancy in women with child bearing potential.
8 To discuss the potential implications of pregnancy and breastfeeding in women of child bearing potential and agree a risk minimisation strategy where appropriate.
9 To initiate treatment by prescribing and monitoring usually for a minimum of 3 months
10 Undertake monitoring if dose changed.
11 Monitor and prescribe according to guidelines until handover is appropriate (including when dose changes are made).
12 Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment.
13 Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to, or a copy of, the shared care guideline when requesting transfer of prescribing to GP or primary care prescribers.
14 Advise GP if treatment dose changes or treatment is discontinued.
15 Inform GP if patient does not attend planned follow-up.

GP or Primary Care Prescriber responsibilities
1 Continue prescribing of oral methotrexate, **2.5mg tablet strength,** at the dose recommended and undertake monitoring requirements.
2 Explain that the medication is usually taken once a week.
3 Undertake all relevant monitoring as outlined in the monitoring requirements section below, and take appropriate action as set out in this shared care guideline.
4 Prescribe any change in methotrexate dose as advised by the specialist team.
5 Monitor for adverse effects throughout treatment and check for drug interactions on initiating new treatments.
6 Add information about the medicine to patient record, initially as "hospital prescribed", and highlight the importance that this medicine is only to be prescribed under a shared care guideline in primary care.
7 Update the patient held record book, when possible.
8 Provide patient with pneumococcal vaccination and flu vaccination unless contra-indicated or already give pre-treatment.
9 Inform the consultant or specialist of any issues that may arise.
10 Inform patients to report immediately any exposure to Varicella Zoster Virus.
11 Refer patient back to the Consultant/Specialist if any concerns.
12 Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline (e.g. ensuring the patient record is correct in the event of a patient moving surgery).

Monitoring requirements and appropriate dose adjustments
1 **Pre-treatment**: FBC, U&Es, creatinine, LFTs ESR and / or CRP and usually CXR. Pulmonary function tests should be considered in selected patients e.g. abnormal shadowing on CXR. Consider NICE (PH guidance 43) recommendations regarding screening for hepatitis B and C in patients at increased risk of infection.
2 **Initiation:** FBC, U&E, creatinine, LFTs, ESR and / or CRP every 2 weeks until dose of methotrexate and monitoring stable for 6 weeks.
3 **Maintenance**: FBC, U&Es, creatinine, LFTs ESR and / or CRP every 2 to 3 months, with due consideration for risk factors.
4 **Increased dose change when on maintenance**: FBC, U&E, creatinine, LFTs, ESR and / or CRP every 2 weeks after a dose change until dose and monitoring stable for 6 weeks. Then revert to monitoring as per maintenance.
5 Monitor for adverse drug reactions throughout treatment.
6 Check for drug interactions on initiating new treatments.

Continued

Patient's or Carer's role
1 Make sure that you understand the treatment and ask for more information, if needed. 2 Share any concerns in relation to treatment with whoever is prescribing this medicine for you. 3 Tell the prescriber of this medication about any other medication being taken. Avoid over-the-counter medications including aspirin and ibuprofen without the knowledge of the specialist team. 4 Read the patient information leaflet included with your medication and report any side effects or concerns you have to whoever is prescribing this medicine for you. 5 Attend the follow up appointments with the consultant or specialist. 6 Attend any monitoring appointments (e.g. blood tests). 7 Bring hand-held monitoring booklet to appointments with GP, consultant, specialist and to the pharmacy when obtaining prescription supplies. 8 Check the dose and strength of the tablets with each prescription. 9 Report immediately the onset of any feature of blood disorders (e.g. sore throat, bruising, and mouth ulcers), liver toxicity (e.g. nausea, vomiting, abdominal discomfort, and dark urine), and respiratory effects (e.g. shortness of breath) or fever.

SHARED CARE GUIDELINE

MEDICATION NAME: Methotrexate 2.5mg tablets

INDICATION: Rheumatoid Arthritis, Psoriatic Arthritis and other chronic inflammatory conditions in Adults

DATE OF REQUEST:

Agreement to transfer prescribing to general practice or primary care prescriber:

Patient details:

Name:

Address:

DoB:

NHS No:

Hospital No:

Medication name, form and strength: Methotrexate **tablets (2.5mg strength only)**

The following tests and investigations have been carried out:

Date treatment initiated:

At the last patient review the drug appeared to be effectively controlling symptoms or providing benefit:
Yes/No

The patients has now been stabilised on a dose of:

The patient has been given written information about their medication:
Yes/No

The patient understands that this medication is being prescribed under a shared care agreement between their GP and specialist and that they have responsibilities under the agreement to ensure they attend their GP to be regularly monitored.
Yes/No

The patient has been informed that the GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient persistently does not attend for monitoring:
Yes/No

Date of next clinic appointment:

If the practice declines shared care, then the named consultant or specialist should be informed within 28 days of receipt of this request. Forms used to decline prescribing can be found here:

Brighton and Hove CCG: http://www.gp.brightonandhoveccg.nhs.uk/prescribing/joint-formulary-supporting-information

Crawley CCG, Horsham and Mid Sussex CCG:
http://www.horshamandmidsussexccg.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=415216

BACK-UP ADVICE AND SUPPORT

	Name and position	Telephone	Email
Specialist or Consultant			
Alternative specialist (e.g. departmental contact)			
Specialist pharmacist			
Out of hours (e.g. medical team on call)			

Link to full SCG: http:// http://www.sussexmskpartnershipcentral.co.uk/