South West Yorkshire
Area Prescribing Committee

METHOTREXATE (Oral Low dose) - Shared Care Guideline

Introduction	
General Statements	• The patient will receive supplies of the drug from the hospital until the transfer of shared care is agreed between the Consultant and GP. • The GP must reply in writing to the request for shared care as soon as practicable if **unwilling** to participate. • Responsibility for prescribing and monitoring must be clearly documented in the patient's hospital and GP notes. • The agreement to consider the use of a shared care guideline should only be considered when the patient's clinical condition is stable or predictable.
Indication	**Licensed indications** – Rheumatoid arthritis, Psoriatic arthritis **Unlicensed indication** - Other inflammatory arthritides, connective tissue disease

Individual's Responsibilities	
Hospital Specialist's Responsibilities	➢ Record patient consent to unlicensed use in medical notes (if applicable) ➢ Baseline monitoring and initial prescribing until the patient is established on treatment (minimum of 8 weeks). ➢ Monitoring disease progression and response to treatment ➢ 3-monthly P3NP monitoring - psoriasis patients only ➢ Supporting and advising GPs ➢ Give patient information leaflet and monitoring booklet & complete as appropriate (including dose changes, test dates & results, when available) ➢ Ensure that the patient has an adequate supply of medication until GP supply can be arranged. ➢ Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP. ➢ Provide patient with rheumatology nurse helpline contact number.
General Practitioner's Responsibilities	➢ Ensure hospital is notified if **unwilling** to undertake prescribing and monitoring when requested ➢ Prescribing following written request from specialist. Patients should only be prescribed/dispensed one strength of tablets. ➢ The prescription must specify the tablet strength, dose, once weekly frequency (unless split dose – see below)) and duration/quantity (not to exceed 3 months) and the day of administration. **2.5mg strength** tablets must always be prescribed unless a specific discussion has taken place between GP, Hospital Specialist and patient and a documented decision to prescribe 10mg strength tablets made ➢ Ensure monitoring is undertaken according to shared care guideline and only continue prescription if compliance with monitoring and results satisfactory. ➢ Follow guidance in the event of reaction or abnormality, record it and

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	report back to the specialist ➢ Update patient's monitoring booklet with dose changes, test dates & monitoring results, when available. ➢ Encourage influenza and pneumococcal vaccination as per Green Book ➢ Ensure no drug interactions with concomitant medicines ➢ To inform Rheumatology Team if patient repeatedly does not attend routine blood monitoring.
Monitoring Required	**Baseline** - CXR, lung function if indicated, HRCT may be advisable if TLCO <70% or clinical concern, FBC, U&Es, ALT, consider pregnancy test The Hospital Specialist must confirm to the GP which stages of the maintenance monitoring have already been completed at the point when prescribing and monitoring are transferred to the GP **Maintenance** FBC, LFTs every 2 weeks for 2 months, then monthly for 4 months then 3 monthly at consultants discretion. Serum creatinine 3 to 6 monthly If dose increased after a period of stable monitoring has been achieved a further period of 8 weeks more intensive monitoring is required. This will be advised by the hospital specialist **Psoriasis patients** – also require a liver biopsy after every 1.5g or if P3NP blood levels are elevated (above 4.2) on 3 occasions. This will be arranged by the hospital specialist.
When and How to Discontinue Treatment	Please see overleaf for detailed guidance as regards stopping treatment
Information given to the patient	**Patient information and monitoring booklet (ideally NPSA approved). This is used to record dose and monitoring results and must be kept up to date by the responsible prescriber.** Patients should be warned to report any immediately the onset of any feature of blood disorder (eg. sore throat, bruising & mouth ulcers), liver toxicity (eg. nausea, vomiting, abdominal discomfort, dark urine) and respiratory effects (eg. shortness of breath).
Contact Details	Documented in letter from specialist care to GP

Product Information	
The information in this Shared Care Guideline should be used in conjunction with the latest edition of the BNF and Summary of Product Characteristics	
Dosage	➢ Starting dose in range 10-20mg taken **once weekly** increasing to (usual) maximum of 25mg weekly. Oral doses above 20mg are unlicensed but endorsed by national and regional guidelines. ➢ Total weekly dose may be split on the day of treatment or taken as a split dose twice weekly if tolerance problems occur**.** This will be decided by the hospital specialist ➢ Folic acid supplements (usually 5mg daily except day of methotrexate) should be prescribed

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Adverse Effects	**Haematological** – neutropenia, thrombocytopenia, macrocytosis, rarely aplastic anaemia. **Mucocutaneous** – mouth ulcers, alopecia, rash **GI** – nausea, diarrhoea **Hepatic fibrosis** – risk factors include alcohol intake above recommended safe limits (21 units women, 28 units men per week), psoriasis, obesity and previous liver disease **Pulmonary** – rare acute severe pneumonitis, pulmonary fibrosis Suppression of ovarian and testicular function (thought to be reversible) **Infections** – opportunistic infections may occur. Infections can require early and vigorous treatment. Patients advised to stop methotrexate until infection resolved. Headaches, depression, irritability Refer to the BNF online and www.medicines.org.uk/emc/ for complete and up to date information
Precautions and Contra-indications	**Contraindications** – significant hepatic, renal or haematological impairment, pregnancy (discontinue at least 3 months pre-conception in both men and women), breastfeeding, alcohol consumption above recommended limits **Precautions** – Mild renal impairment (methotrexate is renally excreted). Significant pre-existing lung disease other than asthma **Avoid live vaccines** – examples could include oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster – for full details check the latest SPC before administration
Clinically relevant Drug Interactions and their management	**Methotrexate interacts with a significant number of other medicines. It is essential to check for interactions using appropriate reference sources (see below) when prescribing any new medication**. **NSAIDS** may reduce methotrexate excretion but this is rarely of clinical significance. **Antibacterials** -cotrimoxazole and trimethoprim must be avoided due to antifolate effects leading to risk of subsequent myelotoxicity and death. Penicillins reduce methotrexate excretion and should be used with caution. Other antibacterials may interact with methotrexate, including neomycin, ciprofloxacin, doxycycline and tetracycline Probenecid is contraindicated due reduction in excretion Avoid live vaccines – examples could include oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster – for full details check the latest SPC before administration. Please note that current advice in the Green Book suggests low doses of methotrexate do not contra-indicate the use of zoster vaccine. Further details here (page 9): https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/448815/2904130_Green_Book_Chapter_28a_v1_0_0W_July2015.PDF Refer to the current BNF and www.medicines.org.uk/emc/ for complete and up to date information

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Recommended action for abnormal results

Investigation	Action
WBC <3.5 x10^9/L Neutrophils < 2 x10^9/L Platelets < 150 x10^9/L	Stop and contact hospital specialist
Hb fall >1g in 4 weeks or below 10g	Check for increased disease activity Ask about NSAID use and symptoms of GI blood loss or dyspepsia and stop NSAIDS if implicated. Check MCV and iron studies Consider endoscopy
ALT above normal range but below 3x upper limit ALT > 3x upper limit	Repeat bloods every 2 weeks Ask patient about viral/bacterial infections Check that it is not due to another drug or NSAID particularly diclofenac and stop this first Stop and contact hospital specialist
Creatinine rising above normal range	Monitor closely and contact hospital specialist for advice

Recommended action for adverse effects

Adverse effect	Action
Bruising, bleeding	Check FBC, clotting screen
Itching	Reduce dose* and review
Rash	Check for other causes e.g. Complications of disease, vasculitis, steroid effects. Mild – reduce dose* Severe – stop and contact hospital specialist
Alopecia	Reduce dose*, stop if severe and contact hospital specialist
Oral ulcers, stomatitis	Check WBC Check for candida & treat accordingly. Mild- advise mouthwash and increased dental hygiene Severe – stop and contact specialist department
Nausea, anorexia, vomiting, taste disturbance	Advise to take at night Consider anti-emetic, split dose Severe – stop and contact hospital specialist
Diarrhoea	Check for other cause Mild -treat symptomatically reduce dose* if persistent. Stop if severe and contact hospital specialist.
New or increasing dyspnoea or persistent cough	Exclude infection and cardiac failure Stop and contact hospital specialist
Headache	Check for other causes Mild – try analgesia and reduce dose* Severe – stop and contact hospital specialist

* Specific dosage reduction advice is not always possible, and will vary according to the patient's individual circumstances. As most adverse effects are likely to occur during or shortly after dose titration, it is suggested that if adverse effects do occur, the dose is reduced to the previously tolerated dose and the patient assessed accordingly. If this is ineffective, consider discontinuation and seek advice from the hospital specialist