ADULT SHARED CARE GUIDELINES

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).
This guideline reinforces the basic premise that:

- When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the 'sharing of information with the individual GP and their mutual agreement to the transfer of care".
- These are not rigid guidelines. In all cases, Consultants and GPs should discuss the appropriate management of individual patients personally. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Drug Name:

METHOTREXATE 2.5mg TABLETS – Asthma and sarcoidosis (unlicensed indications)

Indications:	**Dosage and administration:**
Sarcoidosis Asthma	For both sarcoidosis and asthma, the recommended starting dose is 7.5mg **ONCE WEEKLY** For sarcoidosis the maximum dose is 10mg **ONCE WEEKLY** For severe asthma (which does not respond to other treatments) the maximum dose is 15mg **ONCE WEEKLY** Patients should be prescribed folic acid supplementation at a dose of 5mg WEEKLY (taken 3 days after the methotrexate dose) to help prevent toxicity.

Monitoring requirements must be recorded in the National Patient Safety Agency "patient-held blood monitoring and dosage record booklet":

Before treatment

Baseline U&Es, FBC, creatinine, LFTs and chest x-ray

During treatment

FBC, U&Es and LFTs (including transaminases) checked weekly for the first month, then monthly for 3 months, then every 2 months thereafter if stable.

If dose is increased – repeat FBC, U&Es and LFTs weekly until stabilised, then every 2 months thereafter.

Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)

Patients should be reminded to report any incidence of rash, oral ulceration, sore throat, or unexplained dyspnoea/cough to their GP and should be specifically asked about any of these symptoms at each visit

Responsibility for monitoring lies with the GP.

Action to be taken if abnormal results/adverse effects:

Adverse effect	Action required
WBC < 3.5 x 10^9/L	Withhold treatment and check neutrophil count
Neutrophils < 2.0 x 10^9/L for two consecutive weeks	Withhold treatment and contact respiratory consultant
Platelets < 150 x 10^9/L	Monitor weekly. If falls below 100, withhold treatment and contact respiratory consultant
MCV > 105fl	Check B_{12} and folate. If low, start appropriate supplementation
≥3-fold increase in ALT/AST	Withhold treatment and monitor weekly. If ALT continues to rise, contact respiratory consultant.
Rash/alopecia	Assess severity and ensure taking folic acid If mild, consider reducing dose of methotrexate. If severe, contact respiratory consultant.
Oral ulceration, sore throat, abnormal bruising	Withhold treatment and check full blood count Mild: salt water mouth wash Moderate: Hydrocortisone (Corlan) pellets (1 to affected area qds) Severe: Hydrocortisone (Corlan) pellets and contact helpline
Acute shortness of breath +/- dry cough	Withhold treatment and contact Respiratory Consultant. If severe, refer to Acute Medical Assessment Unit
Gastrointestinal symptoms	Consider a bedtime regimen, co-prescribing an anti-emetic, increasing the frequency of folic acid or reducing the dose of methotrexate

In addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Contraindications:

Methotrexate is contra-indicated in patients who:

- Are pregnant or likely to become pregnant. Both male and female patients receiving methotrexate should use effective contraception throughout the treatment period and for at least 3 months after cessation of therapy
- Are breastfeeding
- Have severe renal, hepatic (e.g. fibrosis, cirrhosis, ascites, recent or active hepatitis) or haematological (e.g. severe anaemia, leucopoenia or thrombocytopenia) impairment
- Have active infectious disease and overt or laboratory evidence of immunodeficiency syndrome(s).
- Have a known hypersensitivity to methotrexate

Cautions:

- Haematological disorders
- Peptic ulceration
- Ulcerative colitis
- Ulcerative stomatitis
- Risk of accumulation in ascites or pleural effusion – drain before treatment
- Acute porphyria
- Significantly impaired renal function
- Significantly impaired hepatic function
- Diarrhoea

Adverse Effects:

Common	Uncommon	Rare	Very rare
Myelosuppression	Pneumonitis	Liver cirrhosis	Pleuritis
Mucositis	Interstitial fibrosis	Gastrointestinal ulceration and bleeding	
Diarrhoea	Stevens-Johnson syndrome	Hypotension	
Vomiting		Depigmentation of nails and skin	
		Menstrual disturbances	
		Arthralgia & myalgia	

The current summary of product characteristics (SPC) for methotrexate can be accessed via www.medicines.org.uk for a comprehensive, up-to-date list of adverse effects associated with methotrexate treatment.

Drug interactions: (A comprehensive, up-to-date list may be found in the current edition of the British National Formulary (BNF))

- **Co-trimoxazole or trimethoprim** – can cause severe bone marrow suppression.
- **Probenecid and Penicillins** – reduce methotrexate excretion: closer monitoring is recommended if concomitant use is necessary.
- **Live vaccines** (e.g. oral polio, measles, mumps, Rubella, BCG, oral typhoid, yellow fever) should not be administered to patients receiving methotrexate
- **Aspirin** at analgesic doses; however low-dose aspirin (75-300mg OD) is ok
- **Non-steroidal anti-inflammatory drugs (NSAIDs)** – closer monitoring is recommended if concomitant use is unavoidable. Patients should be advised to avoid purchasing over-the-counter (OTC) NSAIDs
- **Nephrotoxic and hepatotoxic medicines** should be avoided in patients taking methotrexate
- **Acitretin** – methotrexate levels may be increased by etritinate (a metabolite of acitretin) and severe hepatotoxicity may result if the two are used concomitantly.

Specialist responsibilities:

- Obtain chest x-ray and baseline blood results for FBC, U&Es and LFTs.
- Discuss the benefits and side effects of methotrexate treatment.
- If the patient is a woman of child bearing potential or a male – ensure that they are aware of the importance of using effective contraception and the need to discuss with their consultant if they wish to become pregnant both during treatment and for 3 months after treatment is complete.
- Issue and explain the NPSA methotrexate patient information and patient-held blood monitoring and dosage record booklet.
- Discuss how the patient /carer can be aware of possible signs of possible methotrexate toxicity or intolerance.
- Ensure the patient understands and accepts their responsibilities (see section below), in particular the importance of attending for blood tests at the required intervals, to ensure continuation of therapy.
- Seek consent for treatment and document in the patient's notes.
- Explain the once weekly dosage regimen and the number of 2.5mg tablets required for the dose.
- Explain the need for a folic acid regimen and explain the difference in regimen and presentation to methotrexate.
- Provide written instruction to the GP for initiation and escalation of methotrexate.
- Review the patient at the intervals specified below to monitor the patient's disease progression, efficacy of treatment, patient's ability to tolerate treatment and concordance.
- Consider whether continuation of treatment is appropriate.
- Discontinue treatment if no response or patient has a significant adverse effect.
- Update the patient's NPSA booklet with any dose changes.
- Promptly communicate with the GP any changes in treatment, including dosage adjustments, results of monitoring undertaken, and assessment of adverse events. The clinic letter should clearly state if the dose has remained the same or if a dose adjustment has been made, specifying the new dose in comparison with the previous one.
- Decide if a liver biopsy is necessary (eg. when total accumulative dose of methotrexate reaches 1.5 - 2g.) Advise GPs when to stop treatment.
- Report serious adverse events (eg. those requiring hospitalisation) to the Commission on Human Medicines (part of the MHRA) using the Yellow Card scheme.
- Provide clear arrangements for back-up, advice and support.

GP responsibilities:

- Initial referral to respiratory consultant for suspected sarcoidosis or asthma management.
- Monitor FBC, LFT's and U&E's as per recommended schedule and document in the patient's monitoring booklet.
- Initiate methotrexate on the written advice of the respiratory consultant.
- Provide the patient with monthly repeat prescriptions of methotrexate, prescribing oral methotrexate 2.5mg strength tablets, stating the total once weekly dose following written instructions for initiation and escalation by the specialist.
- Ensure patient's NPSA booklet and practice computer system are updated with any dose changes.
- Refer promptly to the specialist if there is a change in the patient's status or concerns regarding compliance. In most cases, do not stop treatment without discussion with the respiratory consultant.
- Report serious adverse events to the specialist and the MHRA (via the Yellow card reporting system).
- Administer Pneumococcal Vaccine/Pneumovax and annual influenza vaccines.
- Passive immunisation with Varicella zoster immunoglobulin should be carried out in non-immune patients exposed to chicken pox or shingles.

Patient responsibilities:

- Read the written patient information provided and have a clear understanding of the risks / benefits of oral methotrexate treatment.
- Attend for blood tests.
- Limit intake of alcohol to the national safe weekly limits (males & females: 2units per day, with 1-2 alcohol free days per week).
- Report any adverse effects to GP and/or specialist whilst treated with methotrexate.
- Take monitoring booklet every time the patient sees the GP, has a hospital appointment or visits the pharmacist.

Secondary care review:

Asthma patients: every 2 months by consultant or specialist respiratory nurse until stable.
Sarcoidosis patients: every 3 months by consultant until stable.

Thereafter patients should be reviewed every 6 months by consultant or specialist respiratory nurse.

Adverse Drug Reaction reporting:

It is the responsibility of all healthcare professionals involved in patient care to report adverse drug reactions where appropriate.

Visit https://yellowcard.mhra.gov.uk/ for the online reporting form and advice.

Back up advice and support:	**Telephone**	**Email:**
Dr N Stevenson - Respiratory Physician	Sec: 0151 604 7768	n.stevenson@nhs.net
Dr J Corless - Respiratory Physician	Sec: 0151 604 7046	John.Corless@nhs.net
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