

Shared Care Guideline

Methotrexate 2.5mg tablets for rheumatoid arthritis and other rheumatological diseases (Adults)

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.

Indications:

Rheumatoid arthritis and other rheumatological diseases.

Dosage and administration:

Initiation 7.5mg – 15mg **ONCE WEEKLY** titrating according to clinical response in increments of no greater than 10mg to a maximum of 30mg once weekly. **Weekly doses over 20mg are considered unlicensed.**

Patients should be on a regimen of folic acid supplementation to help prevent toxicity. For rheumatology patients, a regimen of 5mg once a week on a different day to methotrexate or more may reduce side effects.

Additional information:

- Excess alcohol must be avoided. For rheumatology patients, safe limits are viewed as the national guidelines i.e. no greater than 21units per week for men and 14 units per week for women.
- All patients, male and female, should be advised against conception and pregnancy during treatment with methotrexate as it is an abortifacient as well as a teratogenic drug. Patients should be advised to continue contraception for at least 3 months after stopping methotrexate.
- Patients should be advised to report all symptoms and signs suggestive of infection, especially sore throat.

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

Before treatment:

- Full blood count (FBC), urea and electrolytes (U&Es), creatinine and liver function tests (LFTs)
- Chest X Ray (unless done within previous 6 months)

During treatment:

- FBC, LFTs, U/Es and creatinine weekly for the first month, then monthly for 3 months, then every 2 months thereafter if stable.
- If dose is increased, repeat FBC, LFTs, U&Es & creatinine weekly for one month then return every 2 months.

- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)
- ESR monthly for disease monitoring purposes

Responsibility for monitoring rests with the GP.

Action to be taken if abnormal results/adverse effects:

- | | |
|-------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| • WBC <3.5 x 10 ⁹ /L | Check neutrophil count. |
| • Neutrophils < 2.0 x 10 ⁹ /L
(2 consecutive weeks) | Contact Rheumatology Helpline |
| • Platelets < 150 x 10 ⁹ /L | Monitor weekly. If falls below 100, contact Rheumatology Helpline |
| • MCV > 100fl | Check B ₁₂ , folate and TSH and if low, start appropriate supplements. |
| • 3 fold increase in ALT/AST | Monitor weekly. If ALT continues to rise, contact Rheumatology Helpline. |
| • Rash/alopecia: | Assess severity and ensure taking folic acid.
If mild, consider reducing dose of methotrexate.
If severe, contact Rheumatology Helpline. |
| • Abnormal bruising | Repeat FBC and act on results as above |
| • Sore throat | Repeat FBC and act on results as above |
| • Oral ulceration | Repeat FBC and act on results as above
Mild: salt water mouth wash
Moderate: Hydrocortisone (Corlan) pellets (1 applied to affected area qds)
Severe: Hydrocortisone (Corlan) pellets and contact helpline |
| • Acute shortness of breath and or dry cough | Contact Rheumatology Helpline. If severe, refer to Acute Medical Assessment Unit |
| • Gastrointestinal symptoms: | Consider a bedtime regimen. Consider co-prescribing an anti-emetic.
Consider increasing the frequency of the folic acid regimen. |
| • Deteriorating renal function may increase the risk of toxicity. | Contact rheumatology helpline |

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:

- Pregnancy (see additional information)
- Breastfeeding
- Pre-existing blood dyscrasias, such as significant marrow hypoplasia, leucopenia, thrombocytopenia or anaemia
- Active Infections
- Live vaccines are contra-indicated in patients with impaired immune response
- Immunodeficiency syndromes

Drug interactions: (For full information see appendix 1 of the current edition of the British National Formulary (BNF))

- Avoid concomitant administration of **co-trimoxazole or trimethoprim** with methotrexate – can cause severe bone marrow suppression.

- Probenecid and penicillins reduce methotrexate excretion (increased risk of toxicity) - for patients in whom it is unavoidable to co-prescribe penicillins and methotrexate closer monitoring is recommended.
- Non-steroidal anti-inflammatory drugs (NSAIDs) also reduce excretion of methotrexate but are NOT contraindicated in combination with methotrexate

Cautions:

- 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
- Acute porphyria

Adverse Effects

Myelosuppression, mucositis, pneumonitis, liver cirrhosis, gastrointestinal ulceration and bleeding, diarrhoea, toxic megacolon, hypotension, pleuritic pain, pulmonary fibrosis, Stevens-Johnson syndrome, changes in nail and skin pigmentation, menstrual disturbances, neurotoxicity, arthralgia and myalgia.

Specialist responsibilities:

- Obtain baseline blood results for FBC, LFTs, U&Es, Cr and chest x-ray unless done in previous 6 months
- Discuss with the patient, the benefits and side effects of treatment.
- If the patient is a woman of child bearing potential or male – ensure that they are aware of the importance of 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 methotrexate toxicity or intolerance
- Ensure that the patient understands and accepts their responsibilities (see section below)
- Seek consent for treatment and document in the patient's notes.
- Explain the weekly dosage regimen and number of 2.5mg tablets required for dose.
- Explain the need for 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 activity, the efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
- Discontinue 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 via a clinic letter any changes in treatment, 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 had been made – specifically highlighting the new dose in comparison with the preceding one.
- Report serious adverse events (e.g. those requiring hospitalisation) at <https://yellowcard.mhra.gov.uk/>
- Provide clear arrangements for back-up, advice and support.

GP responsibilities:

- Initial referral to Consultant Rheumatologist raising the possibility of rheumatological disease
- Monitor the FBC, LFTs and U&Es as per recommended schedule and document in the patient's monitoring booklet.
- 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. The patient should allow at least 48 hours for the GP to generate a prescription.
- Ensure patient's NPSA booklet and practice computer systems 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 Rheumatology Helpline.
- If patient fails to attend more than 2 monitoring visits it is not safe to continue treatment – contact the Rheumatology Helpline for advice.
- Report serious adverse events to the specialist and at <https://yellowcard.mhra.gov.uk/>
- Administer Pneumococcal Vaccine/ Pneumovax® II and annual influenza vaccines.
- Consider passive immunisation with Varicella zoster immunoglobulin in non-immune patients exposed to chicken pox or shingles.

Patient responsibilities:

- Read the written patient information provided about the drug 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.
- Report any adverse effects to their 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: During initiation: 4 – 6 weekly until controlled

Once disease controlled: Annual review by consultant

Availability:

Methotrexate 2.5mg tablets - £2.29 for 28 tablets

Prices from Online Drug Tariff February 2016

Back up advice and support:

Rheumatology Helpline

Telephone

0151 604 7505

Written by

Rachael Pugh, Prescribing Adviser,
Abigail Cowan, Prescribing Adviser
Paul Wallace Practice
Pharmacist,
Wirral Medicines Management
MLCSU

Dr Geraldine M^cCaffrey, Lead Pharmacist,
Division of Medical Specialties and Acute Care,
Wirral University Teaching Hospital NHS Trust
(WUTH)
Dr Yee Ho Chiu, Consultant Rheumatologist,
WUTH
Dr Mano George, Consultant Rheumatologist,
WUTH