**Shared Care Guideline**

# Methotrexate subcutaneous injection for rheumatoid arthritis and other inflammatory 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:** | **Dosage and administration:** |
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| Rheumatoid arthritis and other rheumatological diseases in those patients that cannot tolerate oral methotrexate despite all measures to reduce gastric side effects; and when the next step would be to commence a biological agent. | Dose range 7.5mg to 25mg **ONCE WEEKLY** titrating according to clinical response. Doses exceeding 20 mg/week are associated with significant increase in toxicity, especially bone marrow suppression**.**<br>Weekly doses over 25mg are unlicensed.<br>Dosage in renal impairment:<br>Creatinine clearance 20-50 ml/minute : 50% dose<br>Creatinine clearance < 20 ml/minute : do not use methotrexate<br>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
- All patients, male and female, should be advised against conception and pregnancy during treatment with methotrexate as it is an abortificient 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 electrolyes (U&Es), creatinine and liver function tests (LFTs)

- Chest X Ray if newly commenced on methotrexate OR if reinstating therapy after a rest period (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 to two monthly.
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)
- ESR every month for disease monitoring purposes

**Responsibility for monitoring rests with the GP.**

**Action to be taken if abnormal results/adverse effects:**

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| • WBC <3.5 x $10^9$/L | Check neutrophil count. |
| • Neutrophils < 2.0 x $10^9$/L | Contact Rheumatology Helpline |
| • (2 consecutive weeks) | |
| • 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.<br>If mild, consider reducing dose of methotrexate.<br>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<br>Mild: salt water mouth wash<br>Moderate: Hydrocortisone (Corlan) pellets (1 applied to affected area qds)<br>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 antiemetic.<br>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
- Severe renal or hepatic impairment
- Alcohol abuse
- Pre-existing blood dyscrasias, such as significant marrow hypoplasia, leukopenia,

thrombocytopenia or anaemia
- Active Infections
- Live vaccines are contra-indicated in patients with impaired immune response
- Immunodeficiency syndromes

**Drug interactions:** (For full information see 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

**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. 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.
- Arrange training by a specialist rheumatology nurse for self administration of subcutaneous injection
- Explain the need for folic acid regimen and explain the difference in regimen and presentation to methotrexate,
- Prescribe methotrexate for a one month trial period.
- Discontinue methotrexate if no response, or if significant adverse event occurs.
- 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.
- Advise GPs when to stop treatment.
- Report serious adverse events (e.g. those requiring hospitalisation) to the MHRA via 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.
- Once the specialist has recommended continuation following the trial period provide the patient with monthly repeat prescriptions of methotrexate, stating the total once weekly subcutaneous dose. 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 MHRA via 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 subcutaneous 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 (as disodium) 50mg/ml soln for inj in pre-filled pen:
7.5mg/0.15ml x 1 = £14.85; 10mg/0.2ml x 1 = £15.29; 12.5mg/0.25ml x 1 = £16.50; 15mg/0.3ml x 1 = £16.57; 17.5mg/0.35ml x 1 = £17.50; 20mg/0.4ml x 1 = £17.84; 22.5mg/0.45ml x 1 = £18.45; 25mg/0.5ml x 1 = £18.48; 27.5mg/0.55ml x 1 = £18.89; 30mg/0.6ml x 1 = £18.95. *Prices correct at time of writing, online MIMS March 2016*
**Disposal** - Sharp safe 1 litre cytotoxic sharps bins can be used to dispose of 4 Metoject PENs including caps = 1 month. These can be prescribed on FP10.

| **Back up advice and support:** Rheumatology Helpline | | **Telephone** 0151 604 7505 |
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