# Shared Care Guideline:

## *Methotrexate* for the treatment of *rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, sarcoidosis, psoriasis, eczema, vasculitis, bullous disease, alopecia areata, connective tissue disease, lichen sclerosus et atrophicus*

NHS
County Durham and Darlington Area Prescribing Committee

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| **Drug** | Methotrexate |
| **Indication** | Licensed<br>• Rheumatoid arthritis<br>• Psoriasis<br><br>Unlicensed<br>• Psoriatic arthritis<br>• Ulcerative colitis<br>• Crohn`s disease<br>• Sarcoidosis<br>• Eczema<br>• Vasculitis<br>• Bullous disease<br>• Alopecia areata<br>• Connective tissue disorders<br>• Lichen sclerosus et atrophicus |
| **Overview** | Methotrexate is an immunosuppressant drug |
| **Specialist's Responsibilities** | **Initial investigations:**<br><br>FBC, U&Es, LFTs, ESR/CRP, chest x-ray (unless chest x-ray done within last 6 months).<br><br>Pulmonary function tests should be considered in selected patients.<br><br>Check Varicella status if there is an uncertain history and recent exposure to the virus.<br><br>**Initial regimen:**<br><br>Initial dose of 5-15mg as a single dose once weekly, increasing by 2.5mg - 5mg every 2-6 weeks until stabilised.<br><br>Maximum licensed dose is 25mg/week.<br><br>**Folic acid** is co-prescribed with methotrexate to reduce toxicity.<br><br>Patients should be prescribed folic acid 5mg, usually once weekly, to be taken preferably the day after methotrexate.<br><br>In some cases the dose may be increased to daily, except the day methotrexate is taken. Folic acid should not be taken on the same day as methotrexate<br><br>**Clinical monitoring:**<br><br>FBC, U&Es, and LFTs every 2 weeks until monitoring **and** dose have been stable for 6 weeks, then monthly thereafter. ESR/CRP should be done monthly. |

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| | Monitor every 2 weeks for 6 weeks following dose increase.<br><br>**Safety monitoring:**<br><br>• Monitoring for response and adverse drug reactions (ADRs) during the initiation period.<br>• Evaluating ADRs raised by the GP and evaluating any concerns arising from physical checks and reviews undertaken by GP<br><br>**Prescribing details:**<br><br>Prescribe as 2.5mg tablets **(do not prescribe as 10mg tablets).**<br><br>Also available as subcutaneous injections via Homecare provider.<br><br>Once stable initiate shared care<br><br>**Documentation:**<br><br>• The patient will be provided with the methotrexate information leaflet produced by Arthritis Research UK (www.arthritisresearchuk.org), Crohn's Colitis UK (www.nacc.org.uk), or British Association of Dermatologists and the content discussed<br>• Obtaining agreement of GP to participate in shared-care arrangement for methotrexate therapy (by sending a copy of this document) with an accompanying letter.<br>• Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment.<br>• Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required. |
| **GP's Responsibilities** | **Maintenance prescription:**<br><br>Prescribe methotrexate 2.5mg tablets in accordance with the specialist's recommendations.<br><br>**Clinical monitoring:**<br><br>**Rheumatology, Gastroenterology, Respiratory**<br><br>Monthly - FBC, ESR/CRP, U&Es and LFTs. For certain patients it can be reduced to every 2 months.<br><br>Once dose and disease has been stable for a year, frequency of monitoring may be reduced to 3 monthly, considering risk factors e.g. age, co-morbidity, renal impairment - where monthly monitoring should continue.<br><br>Monitor every 2 weeks for 6 weeks following dose increase<br><br>**Dermatology**<br><br>FBC, U&Es, LFTs, ESR every 3 months.<br><br>Monitor every 2 weeks for 6 weeks following dose increase<br><br>**Safety monitoring:** |

**Inform Specialist Team in the event of:**

- Failure to attend for review or undertake blood tests
- Intolerance of drugs
- Communications failure

| Factor | Result | Action to be taken |
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| WBC | 2.5-3.5 x $10^9$/L | If neutrophils within normal range, continue and recheck in 1 week, otherwise withhold and discuss |
| | < 2.5 x $10^9$/L | Withhold and discuss with specialist team |
| Neutrophils | < 1.5 x $10^9$/L | Withhold and discuss with specialist team |
| | 1.5 - 1.7 x $10^9$/L | Continue, and recheck in 1 week |
| Platelets | < 120 x $10^9$/L | Withhold and discuss with specialist team |
| ALT | x 2 rise in AST / ALT from upper limit of normal | Withhold and discuss with specialist team |
| Albumin | Unexplained fall | In absence of active disease, withhold and discuss with specialist team |
| Respiratory | New or increasing dyspnoea or cough | Discuss with specialist team |
| MCV | > 105 | Check $B_{12}$, folate, TFTs and discuss with specialist team |
| Renal impairment | >50% change from serum creatinine values over previous 12 months | Withhold and discuss with specialist team |
| Other | Rash, oral ulceration, diarrhoea, nausea, vomiting, abnormal bruising, sore throat | Withhold and discuss with specialist team |

**Please note: Any rapid fall or consistent downward trend for blood counts or rapid rise or consistent upward trend for liver enzymes should prompt caution. Action may be required even if values are within normal range. If in doubt please contact specialist team**

**Documentation:**

- Reply to request for shared-care as soon as practical (within 28 days)
- Blood results to specialist via use of patient-held record.

## Adverse Events

| Adverse events | Action |
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| See below | Report / discuss with specialist |

Incidence and severity of side effects are generally dose related and include:

- Nausea, vomiting, diarrhoea
- Anorexia, weight loss
- Stomatitis, mouth ulcers
- Rash, urticaria
- Alopecia
- Liver toxicity
- Bone marrow depression
- Pulmonary fibrosis

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| | • Leucopenia, thrombocytopenia, megaloblastic anaemia, pancytopenia<br>• Transient oligospermia |
| **Contra-indications Cautions Drug Interactions** | **Contraindications**<br>• Known hypersensitivity to methotrexate.<br>• Pregnancy and breast feeding.<br>• Current serious infection<br>• Bone marrow failure with unexplained anaemia and cytopenia.<br>• Concurrent treatment with anti-folate drugs e.g. co-trimoxazole.<br><br>**Cautions**<br>• Significant renal impairment<br><br>**Drug Interactions**<br><br>Methotrexate interacts with numerous drugs.<br><br>• Most Non-Steroidal Anti-Inflammatory drugs (NSAIDs) can be continued as long as monitoring is regular and caution exercised regarding liver and renal function particularly in the elderly..<br>• Avoid concomitant use of folate antagonists e.g. trimethoprim and co-trimoxazole. This can potentially be fatal.<br>• Severe hepatitis has been reported following concomitant use of methotrexate and acitretin (a treatment for psoriasis).<br>• Vitamin preparations containing folic acid or its derivatives may alter response to methotrexate.<br>• Hepatic and nephrotoxic drugs should be avoided.<br>• Concurrent administration of methotrexate with acidic drugs (e.g. salicylates, sulphonamides, tetracyclines, thiazide diuretics, oral hypoglycaemic drugs) increases methotrexate toxicity. |
| **Other Information** | **Vaccinations**<br>• Live vaccines are not recommended.<br>• Annual influenza vaccination recommended.<br>• Pneumococcal vaccination recommended as per Department of Health guidelines.<br><br>**Fertility**<br>• Methotrexate is teratogenic and is contraindicated in pregnancy. Effective contraception should be used by men and women whilst they are taking methotrexate and for 6 months after stopping. |
| **Contact Details** | Thank you for sharing the care of this patient. If you have any concerns or queries, please contact the Consultant or secretary.<br><br>UHND Rheumatology Helpline: 0191 3332763<br>DMH Rheumatology Helpline: 01325 743881<br><br>UHND Gastroenterology Helpline: 0191 3332333<br>DMH Gastroenterology Helpline: 01325 743434<br><br>Dermatology/Respiratory – Contact Consultant's Secretary via UHND or DMH Switchboard |