Northern Lincolnshire
Area Prescribing Committee

Prescribing Framework for Methotrexate for Immunosuppression in ADULTS

Patients Name: …… NHS Number: ……

Patients Address ..... (Use addressograph sticker)

GP's Name: ……..

Communication

We agree to treat this patient within this Prescribing Framework.

Consultant's / Specialist's
Signature:……..Date:……..

GP's Signature:…… Date:…….

If the General Practitioner is unable to accept prescribing responsibility for the above patient the consultant should be informed within two weeks of receipt of this framework and consultant's / nurse specialist's letter. In such cases the General Practitioner are requested to update the consultant, by letter, of any relevant changes in the patient's medication / medical condition.

Contact Details:

NLaG Contact:
Via the Pharmacy Office: 01724 290095

VirginCare Contact: 0300 2470051

Rheumatology Specialist Nurses: 03033 304849

APPROVAL PROCESS

Written by:	**Adapted from protocol written by Dr Tim Gillott**
Ratified by:	**Northern Lincolnshire and Goole Area Prescribing Committee**
Review Date:	**May 2024**

Methotrexate for patients within Rheumatology (NLaG) and Dermatology (VirginCare)

1. Background	Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. It may be used for the treatment of a wide variety of immune mediated disorders. Methotrexate is usually used orally, however a proportion of patients are unable to tolerate a potentially effective therapy due to gastrointestinal intolerance. This group of patients often benefit from subcutaneous methotrexate given on a weekly basis. Subcutaneous methotrexate remains a red drug in Northern Lincolnshire. These guidelines aim to provide a framework for the prescribing of oral methotrexate by GPs for patients requiring immunosuppression and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements. **For use in treatment of cancer – methotrexate remains Red**
2. Indications (Please state whether licensed or unlicensed)	Immune mediated disorders including moderate to severe rheumatoid arthritis, psoriasis and Crohn's disease. Specific information will be provided by the specialist on the indication for immunosuppression in individual patients.
3. Locally agreed off-label use	None
4. Initiation and ongoing dose regime Note - • Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results for at least 4 weeks • The duration of treatment will be determined by the specialist based on clinical response and tolerability. • All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician • Termination of treatment will be the responsibility of the specialist.	The usual starting dose is 7.5mg to 15mg **once a week** as a single dose. The dose may be adjusted on the basis on an individual status to a usual maximum of 25mg per week subject to regular full blood counts. NB: Test dose of 5mg and lower maintenance doses common in dermatology. Folic acid should also be prescribed at a dose recommended by specialist. Folic acid should not be taken within 24 hours of methotrexate. The use of folic acid helps reduce the incidence and severity of adverse effects. **Subcutaneous dose:** Subcutaneous administration is recommended in patients who have not tolerated oral dose or in those whom have had sub-optimal response to oral methotrexate, as advised by the specialist. Dose would typically remain the same as previous oral dose. Currently subcutaneous methotrexate prescription and supplies are coordinated by the hospital. The specialist remains responsible for doses and checking blood results in patients on subcutaneous methotrexate. Although subcutaneous methotrexate is now licenced, the prescribing and continuation responsibility lies within secondary care.
5. Baseline investigations, initial monitoring and dose titration to be undertaken by specialist	**Baseline:** • Chest X-ray • Full blood count (including platelets) • Differential white cell count • LFT • U&E

<table>
<tr><td></td><td colspan="2">Frequency:
Every 1-2 weeks for 2 months, then monthly for 4 months, followed by 3 monthly unless dose changes.</td></tr>
<tr><td rowspan="3">6. Ongoing monitoring requirements to be undertaken by primary care.</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>• Full blood count (including platelets)
• Differential white cell count
• LFT
• U&E</td><td>Once stable, monthly for 4 months, followed by 3 monthly unless dose changes. Frequency of monitoring may be reduced further following discussion with the specialist team, providing the dose and trend of results remain stable. If dose changes occur then monitoring should resume every 2 weeks as above.</td></tr>
<tr><td colspan="2">Patients should be monitored more frequently if there is a reason to suspect deteriorating renal function.

The blood tests should not be taken within 3 days of administration of methotrexate.</td></tr>
<tr><td>7. Responsibilities of clinicians involved</td><td colspan="2">
<table>
<tr><th>Stage of treatment</th><th>Specialist</th><th>GP</th></tr>
<tr><td>Initiation</td><td>• Access the patient following by GP
• Recommend appropriate treatment to the GP
• Carry out baseline full blood count, differential WCC, platelets, U&E and LFT
• Perform baseline chest X-ray (where not performed within the last 6 months)
• Ensure patient is competent to self-administer doses
• Supply a cytotoxic waste bin and advise patient on the safe disposal of waste products, where necessary
• Give patient NPSA Methotrexate booklet and complete where relevant</td><td>Prescribe on FP10 after first month of treatment</td></tr>
<tr><td>Maintenance</td><td>• Access clinical response to treatment
• Provide adequate advise and support for the GP
• Provide information to the GP on frequency of monitoring if doses are changed
• Complete NPSA Methotrexate where relevant</td><td>FBC (including platelets, differential white cell count), U&E, LFT (including AST or ALT) should be checked every 1-2 weeks until therapy stabilised, and provided it is stable monthly thereafter. (Frequency may reduce further on specialist advice).
Complete patients NPSA Methotrexate booklet, including any dose changes and results.
For Dermatology patients - Procollagen IIINP to be included as part of regular blood monitoring.</td></tr>
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</td></tr>
<tr><td rowspan="4">8. Pharmaceutical aspects</td><td>Route of administration :</td><td>Oral</td></tr>
<tr><td>Formulation :</td><td>2.5mg Tablet</td></tr>
<tr><td>Administration details :</td><td>Methotrexate tablets must only be supplied in 2.5mg strengths to avoid confusion.</td></tr>
<tr><td>Other important information:</td><td>Weekly dosing</td></tr>
<tr><td>9. Contraindications
Please note this does not</td><td colspan="2">• severe renal or hepatic impairment
• severe anaemia</td></tr>
</table>

replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	• leucopenia • thrombocytopenia • immunodeficiency syndromes • previous hepatitis B infection and active infection Methotrexate should be used with caution in patients with • pre-existing pulmonary fibrosis • diabetes • morbid obesity	
10. Significant medicine interactions For a comprehensive list consult the BNF or Summary of Product Characteristics (SPC)	• Increased risk of toxicity when methotrexate is given with other drugs which are haematotoxic, hepatotoxic, nephrotoxic or folate antagonists. • aspirin • NSAIDS - Methotrexate may be prescribed in combinations with NSAIDS under specialist advice. • tetracycline's • Concomitant administration of folate antagonists such as trimethoprim, cotrimoxazole and nitrous oxide should be avoided • Penicillins may potentiate levels of methotrexate (Patients should stop taking methotrexate if they have any infection/require antibiotics and restart once the antibiotic course is completed and the infection has resolved) • Acitretin - severe hepatitis reported when combined with MTX • Vitamin preparations containing folic acid • Avoid live vaccines (zoster safe if weekly MTX dose 20mg or less) Patients receiving methotrexate should be advised against immunization with live vaccines. (Influenza and Pneumococcal vaccines may be given in this group of patients). For a full list of interactions always check with BNF or Data Sheet (www.bnf.org or www.medicines.org.uk)	
11. Cautions	• Photosensitivity—psoriasis lesions aggravated by UV radiation (skin ulceration reported • Dehydration (increased risk of toxicity) • Extreme caution in blood disorders (avoid if severe) • Peptic ulceration (avoid in active disease) • Risk of accumulation in pleural effusion or ascites—drain before treatment • Ulcerative colitis • Ulcerative stomatitis	
12. Adverse Effects and management	Result	Action
	Oral use: anaemia; appetite decreased; diarrhoea; drowsiness; fatigue; gastrointestinal discomfort; headache; increased risk of infection; leucopenia; nausea; oral disorders; respiratory disorders; skin reactions; throat ulcer; thrombocytopenia; vomiting	withhold and discuss with specialist team
	Parenteral use: anaemia; appetite decreased; chest pain; cough; diarrhoea; drowsiness; dyspnoea; fatigue; fever; gastrointestinal discomfort; headache; leucopenia;	withhold until discussed with specialist team

	malaise; nausea; oral disorders; respiratory disorders; skin reactions; throat complaints; thrombocytopenia; vomiting	
	Other side effects include hair loss and cirrhosis of the liver. Rare effects include leucopenia, thrombocytopenia and acute or chronic interstitial pneumonitis.	

Monitoring parameter	Recommended response
WBC < 4.0 x 10 9/1	withhold **until discussed** with specialist team
Neutrophils <2.0 x 10 9/l	withhold **until discussed** with specialist team
Platelets <150 x 10 9/l	withhold **until discussed** with specialist team
>2 fold rise in AST, ALT (from upper limit reference range)	withhold **until discussed** with specialist team
MCV> 105 fl	Check **serum folate and B12 & TSH**. Withhold until results are available and **discuss** with specialist team
Albumin-unexplained fall (in absence of active disease)	withhold **until discussed** with specialist team
Renal function-significant deterioration (or Creatinine > 150 micromol/L)	withhold **until discussed** with specialist team
New or increasing dyspnoea or dry cough	withhold and **discuss urgently** with specialist team
Rash, oral ulceration, nausea & vomiting, diarrhoea	withhold **until discussed** with specialist team
Abnormal bruising or severe sore throat	withhold **until FBC results** available & discuss with the specialist team
Dermatology patients only: flare-up of skin condition	Discuss with specialist team
Procollagen IIINP (Dermatology patients only) 4.2-8.0 micrograms/L on 3 occasions within a 12 month period or two consecutive results >8.0 micrograms/L	withhold **until discussed** with specialist team

13. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	Explain current dose of ONCE WEEKLY methotrexate and dose of folic acid. Inform patient of expected response to treatment and possible side effects. Patients should be told to go to their GP immediately if they experience any fever, rash, bruising, bleeding, sore throat, oral ulceration, shortness of breath, dry cough, jaundice or infection. As per NPSA recommendations patients should be given a pre-treatment patient information leaflet and a patient held monitoring booklet.
14. Preconception care, Pregnancy and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	Methotrexate is teratogenic. It should not be administered to women who are pregnant or breast feeding. Effective contraception, in both male and female patients, should be established before commencing methotrexate and continued during treatment and continued for at least 3 months after treatment is completed.
15. Specialist contact information	Contact Dermatology consultant (VirginCare) via 01482 638571 Rheumatology Specialist Nurses: 03033 304849
16. Additional information	**Warnings/Caution:** Avoid in significant hepatic impairment. Not recommended in severe renal impairment (creatinine clearance <10ml/min) the dose should be reduced by 50% if the CrCl is between 10-20ml/min. Also consider dose reduction if CrCl 20-50ml/min. **Caution** when pre-existing haematological condition **Caution** - underlying chest disease/smoker Where history of excessive alcohol intake
17. References	https://bnf.nice.org.uk/drug/azathioprine.html#interactions
18. To be read in	https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-

conjunction with the following documents	prescribing-between-primary-secondary-care-v2.pdf