Shared Care Guidance

Methotrexate in Adults

This shared care agreement outlines the way in which the responsibilities for managing the prescribing of methotrexate for the treatment of adult patients with rheumatoid arthritis, severe psoriasis and Crohn's disease can be shared between the Secondary Care Specialist and the General Practitioner. This guideline aims to ensure appropriate monitoring of methotrexate in adult patients to achieve optimal efficacy whilst monitoring the toxicity which is associated with this medication.

Indication and Licensed Status:

Methotrexate is a folic acid antagonist and its major site of action is the enzyme dihydrofolate reductase. Its main effect is inhibition of DNA synthesis but it also impairs RNA and protein synthesis.

Patients commenced on methotrexate are usually commenced on oral methotrexate. They may be switched to subcutaneous methotrexate injection if their response is suboptimal or they suffer from intractable nausea on oral methotrexate.

Methotrexate is licensed for the treatment of rheumatoid arthritis, other inflammatory arthritis conditions and severe psoriasis.

Methotrexate is also occasionally used off-license for the treatment of Crohn's disease.

Dose & Administration:

Methotrexate is administered as a once weekly dose regimen; given on the same day each week.

When given orally, only the 2.5mg strength of methotrexate tablets should be prescribed. Methotrexate can also be used as a subcutaneous injection which has the advantage of greater bioavailability and reduced gastrointestinal toxicity.

Methotrexate tablets must not be crushed or chewed and should be taken with food.

Methotrexate therapy is co-prescribed with 5mg folic acid tablets – usually given weekly, 48 hours after the day on which the methotrexate treatment is taken.

The first month's prescription will come from secondary care and is usually commenced at a dose of 7.5mg-10mg weekly, although it may be lower in elderly patients or patients with renal impairment.

Dose adjustments will be carried out within secondary care usually by increments of 2.5mg-5mg according to clinical need after review at 3-4 months.

The maximum dose of weekly methotrexate therapy is 25mg once a week, (maximum dose for RA is 20mg once a week)

Duration of Therapy:

Methotrexate is usually given for at least 3-4 months, but often is continued on long term; and the treatment can be continued if effective and if the patient can tolerate therapy.

Response to treatment cannot be expected before two or three months and may not occur until after six months of treatment.

Adverse Effects:

Common Adverse Effects: nausea, mouth ulcers, hair loss, leucopenia, gastro-intestinal disturbance, eye irritation, vasculitis and loss of libido/impotence

Uncommon Adverse Effects: headaches, anaphylaxis, bone marrow suppression, drowsiness, pneumonitis, hepatitis

Version: 1
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A dry, unproductive cough, shortness of breath and fever may indicate potentially severe lung disease and will warrant further investigation / chest X Ray.

Patients must be advised to report all signs and symptoms suggestive of infection – sore throat, etc.

Methotrexate has a rare but serious risk of acute pneumonitis and chronic pulmonary fibrosis.

Contraindications:

- Significantly impaired hepatic function
- Significantly impaired renal function
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, significant anaemia, leucopenia, or thrombocytopenia
- Alcoholism
- Severe acute or chronic infections and immunodeficiency syndrome
- Pregnancy and breast-feeding (see below).
- Hypersensitivity to methotrexate or any of the excipients
- During methotrexate therapy concurrent vaccination with live vaccines must not be carried out
- evidence of active infection

Pregnancy and Breast Feeding:

Methotrexate is teratogenic and pregnancy must be avoided whilst taking the medication. Appropriate contraception is advised throughout the treatment period duration and for at least 6 months following discontinuation of the drug. It is therefore strongly recommended that methotrexate should be stopped by both male and female users 6 months before any planned pregnancy.
It is also advised that breast feeding is avoided whilst taking methotrexate to ensure no transfer of the drug through breast milk

Chickenpox Caution:

Contact the patient's initiating consultant if the patient has been in close contact with chickenpox or shingles as they may require passive immunisation with Varicella Zoster Immunoglobulin.

Drug Interactions:

A complete list of methotrexate-associated interactions can be found within the most recent edition of the British National Formulary or the relevant Summary of Product Characteristics.

Methotrexate should not be co-prescribed with other folate antagonists such as Trimethoprim or Septrin (Co-trimoxazole). Patients should be made aware of this interaction.

Other concurrent medicines to be avoided include:

- Phenytoin
- Tolbutamide
- Probenecid
- Live vaccines (e.g. yellow fever/BCG/oral polio)

NSAIDs, aspirin and penicillins are known to reduce the excretion of methotrexate causing an increase in serum level but are not contra-indicated.

Annual influenza vaccination is recommended.

Monitoring Requirements:

Baseline checks:

- Full blood count
- Liver function tests, including serum albumin
- Renal function tests
- Chest X Ray

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Routine checks:

- Check Full Blood Count, Urea & Electrolytes, Liver Function Tests every 2 weeks until dose and monitoring stable (typically for 6 weeks) and monthly thereafter.
- The above blood tests should be performed 2 weekly for the first month after any increase in the dose of Methotrexate.
- ESR and CRP should also be performed at the prescriber's discretion to monitor disease activity.
- Once the disease has been stable for 12 months, consider reducing frequency to 2-3 monthly blood test monitoring.

Parameters for Intervention/Withholding Methotrexate Treatment:

Methotrexate therapy must be withheld and the initiating consultant consulted if any of the following are identified:

- Severe rash or bruising or ulceration of mucous membranes
- Any unexplained illness occurs including nausea or diarrhoea
- Any episode of infection
- WCC falls <3.5 x 109/l
- Neutrophils <2.0 x 109/l
- Eosinophils >0.5 x 109/l
- Platelet count falls below <150 x 109/l
- MCV > 105 f/l (if vitamin B12/folate checked and normal)
- Creatinine >30% of baseline
- LFTs (ALT or AST) increase > 2 fold rise above upper limit reference range
- Unexplained fall in serum albumin

Shared Care Responsibilities:

Secondary Care Specialist

1. Assess the suitability of the patient for methotrexate therapy, in accordance with the patient's condition.
2. Send a letter to the GP with Shared Care Guidelines requesting shared care for the patient.
3. Perform pre-treatment checks (CXR/FBC/LFTs/U&Es).
4. Provide first month's prescription of methotrexate, ensuring (and emphasising) that the methotrexate is a weekly treatment and not daily.
5. Provide written information (including the required Methotrexate Treatment Booklet) to the patient and explain the rationale for prescription and potential adverse effects.
6. To remind the patient that the Methotrexate Treatment Booklet must be brought with them every time they see a Healthcare Professional.
7. To advise the patient to report all signs and symptoms of infection.
8. Request blood tests for the first six months monitoring which will be copied to the GP.
9. Undertake regular review of the patient and communicate any dose adjustment to the GP.
10. Evaluate any concerns regarding adverse effects from the GP and provide advice when requested.
11. Make any required decision as to when to stop methotrexate therapy.

Primary Care Practitioner

1. Communicate with the relevant department at Colchester General Hospital their agreement to participate in this shared care guideline (by returning the signed copy attached to this document).
2. Continue prescribing the stated dose of methotrexate beyond the first month of treatment.
3. Ensure that only the 2.5mg tablet strength of methotrexate is prescribed.
4. Ensure that the patient fully understands that the methotrexate is a weekly treatment and not daily.
5. Continue to prescribe 5mg folic acid weekly (usually 48hrs after the weekly methotrexate dose; unless an alternative dose is specified).
6. Request subsequent blood tests for monitoring after a period of six months from the initial prescription. This should be monthly for the first year then two to three monthly thereafter as clinically indicated.
7. Check for potential drug interactions when co-prescribing other medication.
8. Liaise with the relevant department and report any concerns to the relevant Consultant accordingly.
9. To remind the patient that the Methotrexate Treatment Booklet must be brought with them every time they see a Healthcare Professional.
10. Perform urgent FBC if patients attend with multiple mouth ulcers, a sore throat or any other symptoms suggestive of infection.
11. Record all blood results in the patient's Methotrexate Treatment Booklet.

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Patient (and if appropriate, the carer):

1. Report to the Secondary Care Specialist or GP if he or she does not have a clear understanding of the prescribed treatment.
2. Share any concerns in relation to treatment with methotrexate.
3. Report any adverse effects to the Secondary Care Specialist or GP whilst taking methotrexate therapy.
4. Attend for blood test monitoring when advised to do so.
5. Carry an up-to-date Methotrexate Treatment Booklet.
6. Avoid excessive alcohol intake.
7. Ensure adequate contraception if relevant.

Contact Numbers for Advice and Support:

Colchester Hospital University NHS Foundation Trust	(01206) 747474 (Switchboard)
Colchester Hospital Rheumatology Department	(01206) 742165/742279
Colchester Hospital Gastroenterology Department	(01206) 742382/744233/742085/745210
Colchester Hospital Dermatology Department (via Concordia)	(01206) 588001
Consultant Rheumatologists:	
Dr Paul Byrne	paul.byrne@colchesterhospital.nhs.uk
Dr Tom Walton	tom.walton@colchesterhospital.nhs.uk
Dr Rachel Davies	rachel.davies@colchesterhospital.nhs.uk
Consultant Gastroenterologists:	
Dr Ian Gooding	ian.gooding@colchesterhospital.nhs.uk
Dr Donagh O'Riordan	donagh.o'riordan@colchesterhospital.nhs.uk
Dr Mary McStay	mary.mcstay@colchesterhospital.nhs.uk
Dr Achuth Shenoy	achuth.shenoy@colchesterhospital.nhs.uk
CHUFT Pharmacy Department	(01206) 742355
CHUFT Medicines Information Help Line:	(01206) 742161

References

(1) Methotrexate Summary of Product Characteristics (various generics) - http://www.medicines.org.uk/emc/

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Section A (to be completed by Secondary Care Specialist):

Hospital Number:	
NHS No:	
Date:	
GP Courier No:	
GP Name:	

Name of patient:	
Date of Birth:	
Address:	

Background:

Medications:

Dear GP,
See attached clinic letter. Please can you sign and return (using the above fax number) to indicate you are in agreement with the Shared Care Guidelines.

Yours sincerely,

Section B (to be completed by General Practitioner):

The above patient (with associated methotrexate treatment) has been accepted into our monitoring service.

Accepting GP Name:	
Accepting GP Signature:	
Date:	

Practice Stamp:

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