NORTH AND EAST DEVON HEALTHCARE COMMUNITY SHARED CARE PRESCRIBING GUIDELINE

http://www.devonpct.nhs.uk/Treatments/NE_Devon_Shared_Care_Guidelines.aspx#M
https://nww.devonpctinfo.nhs.uk/Prescribing/SCG/

DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS)

ORAL & SUBCUTANEOUS METHOTREXATE FOR JUVENILE ARTHRITIS

This shared care guideline sets out details for the sharing of care of **children and young people** with inflammatory joint disease and autoimmune disease prescribed ***methotrexate orally or by the subcutaneous route***. These guidelines provide additional limited information necessary to aid in the treatment of rheumatology patients. **As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the ABPI summary of product characteristics (SPC/Data sheet) and *do not* replace them**. Further information regarding the unlicensed subcutaneous methotrexate can be obtained by contacting the PCT prescribing department.

INTRODUCTION/BACKGROUND INFORMATION

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent.

The National Patient Safety Authority (NPSA) has highlighted the risks when prescribing methotrexate including failings from poor monitoring of therapy, which have led to fatalities. This Shared Care Guideline has been updated to reflect their recommendations.

INDICATIONS FOR THE PURPOSES OF THIS GUIDELINE

Treatment of children and young people with inflammatory joint disease and autoimmune disease.

Transition of the patient to adult services is expected between 16 and 18 year old.

Methotrexate requires careful monitoring to avoid toxicity. It is recommended that oral methotrexate be initiated in primary care after consultant recommendation and under consultant supervision.

The prescription and supply of subcutaneous (sc) methotrexate will be organised by the consultant paediatrician with responsibility for rheumatology but monitoring may still be required by the GP. This administration route is used if:

(1) There has been a good response to oral methotrexate but patients suffer severe GI side effects
(2) Poor response to oral preparation due to suspected reduced absorption.

DOSAGE

For both oral and sc methotrexate, the usual dose range is 2.5mg – 20mg once weekly.

Oral - Oral methotrexate should be prescribed as multiples of 2.5mg tablets.

Subcutaneous - The consultant paediatrician with responsibility for rheumatology prescribes sc methotrexate with the dose individualised for each patient. Pre-filled sc methotrexate syringes are currently an unlicensed treatment.

To limit the side effects of methotrexate, all patients should receive folic acid 5mg orally daily (2.5mg daily may be used for children <2years old) ***except*** on the day they take methotrexate.

CONTRAINDICATIONS

- Severe/significant renal or hepatic impairment
- Active acute infectious disease, evidence of immunodeficiency syndrome.
- Serious cases of anaemia, leucopenia, thrombocytopenia
- Receiving drugs with antifolate properties e.g. co-trimoxazole, trimethoprim, sulphonamides.
- Pregnancy - Methotrexate can affect fertility of men and is a known teratogen and abortifacient during pregnancy and is therefore contra-indicated prior to conception and for at least six months after treatment. Both men and women of childbearing age should use a reliable method of contraception to avoid the risk of an unplanned pregnancy during treatment. When planning a pregnancy it is important that both men and women on this drug discuss medication with the Paediatrician (at least six months before conception).

PRECAUTIONS

- Bone Marrow Disease.
- Renal impairment (reduce dose).
- Alcohol consumption – increases risk of hepatic complications.

MONITORING

PRIOR TO STARTING THERAPY – CONS PAEDIATRICIAN:

- Assessment of renal and liver function.
- FBC.
- Varicella zoster IG antibody test.

ONGOING MONITORING - GENERAL PRACTICE:

It is recommended that all blood counts are monitored and recorded in the patient record and patient booklet to comply with NPSA and GMS.

- FBC, renal function and LFTs fortnightly for 3 months and monthly thereafter (unless specifically directed otherwise). If there is evidence of renal impairment check that renal function has not deteriorated after 4 weeks.
- FBC should be measured fortnightly for 1 month after any increase in dose, before returning to monthly testing.
- In order to monitor disease activity a 3 monthly CRP would be helpful.

Always look at the mean corpuscular volume (MCV). A rising value may precede marrow dysplasia…**BUT** check for underlying causes before stopping treatment (B_{12}, TFT, folate and alcohol consumption).

STOP AND REFER TO THE CONS PAEDIATRICIAN IF:

- WCC falls on 3 successive occasions and/or WCC falls below 3.5 x 10^9.
- Platelet count falls on 3 successive occasions
- Platelet count falls below 150 x 10^9
- Liver enzymes especially transaminase increased x 3 upper limit of normal.
- Consecutive significant fall in albumin – seek specialist opinion.
- ***Severe*** nausea or diarrhoea.
- ***Severe*** mouth or genital ulceration.

NB: Do not stop treatment prior to surgery

SIDE EFFECTS

NB. The risk of side effects indicated are relative to all the licensed uses of methotrexate and are expected to be less common when taken at low dose on a weekly basis.

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

Very common/Common:

- Mouth ulcers.
- Nausea and diarrhoea.
- Hair loss.

Uncommon:

- Headaches
- Bone marrow suppression.
- Lung and liver inflammation.
- Renal impairment.

Very rare:

- Drowsiness.
- Anaphylactic reaction.

COMMON/SIGNIFICANT DRUG INTERACTIONS

- Folate antagonists should be avoided – nitrous oxide, co-trimoxazole, **trimethoprim**, sulphonamides, phenytoin and some antimalarials e.g. pyrimethamine.
- NSAIDs (including aspirin) – will increase levels of methotrexate. **This is not considered to be a problem in patients with Rheumatoid arthritis as the doses used take this interaction into account**.
- Ciclosporin.
- Retinoids e.g. Acitretin and Etretinate.
- Clozapine.
- Drugs affecting renal tubular transport
- Caution when co-prescribing hepatic or nephrotoxic drugs.
- Vaccinations - Live attenuated vaccines (e.g. BCG and MMR) should be avoided. For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients http://www.rheumatology.org.uk/guidelines/clinicalguidelines/vaccineguideline

Patients must report mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

The Consultant Paediatrician must be contacted if the patient has contact with chickenpox that has been diagnosed by a health professional.

If pulmonary symptoms are reported, these should be investigated urgently with a chest x-ray to exclude pneumonitis.

NOTES

- Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.
- Flu vaccination is indicated and Pneumococcal vaccines may be given if required.
- Live vaccines include: measles, mumps and rubella; BCG; poliomyelitis - oral Sabin vaccine; yellow fever; typhoid – oral.
- Methotrexate can cause dizziness, fatigue, blurred vision and eye-irritation.

PRODUCT INFORMATION

- Methotrexate 2.5mg tablets.
- Methotrexate pre-filled syringes – individualised dosages.

REFERENCES

1. Summary of Product Characteristics Maxtrex (Wyeth) / Methotrexate (Mayne Pharma) January 2006.
2. Immunisation of the Immunocompromised Child - Royal College of Paediatricians February 2002. http://www.rcpch.ac.uk/publications/recent_publications/Immunocomp.pdf
3. British Society of Rheumatologists Guidelines August 2000.
4. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. Z Ortiz, D Moher, BJ Shea, ME Suarez-Almazor, P Tugwell, G Wells Year: 1999. Reported at Cochrane Library
5. NPSA Towards safer use of Methotrexate http://www.npsa.nhs.uk/site/media/documents/716_towards_safer_use_oral _methotrexate.pdf

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AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

These are suggested ways in which the responsibilities for the management of patients with rheumatoid arthritis who are prescribed oral or **subcutaneous methotrexate** can be shared between the specialist and the general practitioners. GPs are **invited** to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event the total clinical responsibility for the patient for the diagnosed condition remains with the specialist**. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Specialist:

- ❑ Decision to prescribe methotrexate. In the case of **subcutaneous methotrexate** to generate the prescriptions and inform the GP that monitoring will be required.
- ❑ Discussion with the patient regarding the benefits and side effects of treatment. Refer patient to specialist nurse service where appropriate (e.g. new patient) for advice on taking the drug, its cautions, side effects associated with treatment, monitoring requirements and the timing of re-assessment and by whom.
- ❑ A patient information leaflet and booklet for recording test results must be issued.
- ❑ Ask the GP whether they are willing to participate in shared care.
- ❑ Prompt communication with GP (and responsible nurse in the case of patients unable to self administer) of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- ❑ Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- ❑ Advice to GPs on when to stop treatment.
- ❑ Ensure clear arrangements for back-up advice and support.
- ❑ Reporting adverse events to the CSM.

General Practitioner:

- ❑ Reply to request for shared care as soon as practical.
- ❑ Prescribing of oral methotrexate after communication with specialists regarding the need for treatment.
- ❑ Monitoring of oral or sc methotrexate as outlined in the shared care guideline.
- ❑ Recording of the results of monitoring in GP system and in the patient held record (and communication to the responsible nurse in the case of patients unable to self administer).
- ❑ Ensure that the GP computer system has an alert flag in accordance with NPSA guidance.
- ❑ Prompt referral to a specialist if there is a change in the patient's status.
- ❑ Annual flu vaccination in guidance with DoH recommendations.
- ❑ Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- ❑ Reporting adverse events to specialist and CSM.
- ❑ Stopping treatment in the case of a severe adverse event or as per shared care guideline.

Patient / Carer:

- ❑ Report any adverse effects to their GP and/or specialist whilst being treated with oral or **sc methotrexate**.
- ❑ Ensure that they have a clear understanding of their treatment and have read the information leaflet.
- ❑ Confirm that any hospital prescription for methotrexate is accurate if attending as an inpatient.
- ❑ Be aware that taking OTC NSAIDS in addition to methotrexate may interfere with treatment.
- ❑ Ensure they attend for monitoring requirements as per shared care guideline.
- ❑ Ensure they record the results of any monitoring in their booklet.
- ❑ Aware that treatment will be stopped if patient does not attend for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No:	Bleep	Fax:	E-mail address
Dr Nigel Osborne:	01392 405261	Radiopage via 01392 411611	01392 405312	nigel.osborne@rdeft.nhs.uk

Shared Care Agreement Letter - Consultant Request

To: Dr.....

Practice Address: .....

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Patient Name:
Hospital number:
Date of birth:
Address:

DIAGNOSED CONDITION:

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I recommend treatment with the following drug:

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I am requesting your agreement to sharing the care of this patient according to the Devon Primary Care Trust North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

Signed:	
Consultant name:	
Department:	
Contact telephone number:	
Date:	

GP RESPONSE

I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: ..... Date: .....

GP name: ..... *Delete as appropriate