Sussex MSK Partnership

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NHS
Brighton and Hove Clinical Commissioning Group
Crawley Clinical Commissioning Group
Horsham and Mid Sussex Clinical Commissioning Group
High Weald Lewes Havens Clinical Commissioning Group

OPT-OUT SHARED CARE GUIDELINE

It is assumed that shared care **will** be accepted unless the specialist is informed otherwise within 28 days of receipt of the request at the end of this document.

MEDICATION NAME: **Methotrexate 2.5mg tablets**

INDICATIONS COVERED: **Rheumatoid Arthritis, Psoriatic Arthritis and other chronic inflammatory conditions in Adults**

NHS Brighton and Hove CCG, Crawley CCG and Horsham and Mid-Sussex CCG
Traffic Light System Classification: Amber

NOTES to the general practitioner (GP) or primary care prescriber

For medicines which require specialist initiation and/or dose titration and specific ongoing monitoring. For initiation, dose stabilisation and prescribing (including monitoring) by a specialist until the patient is stabilised (usually for 3 months) after which the GP may be asked to work under shared care through the use of approved shared care guidelines.
The expectation is that these guidelines should provide sufficient information to enable GPs or primary care prescribers to be confident to take clinical and legal responsibility for prescribing these medicines.

The questions below will help you confirm this:

- Is the patient currently under your care (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge)?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. It is assumed that shared care will be accepted unless the specialist is informed otherwise within 28 days of receipt of this request.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should inform the consultant or specialist within 28 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust or specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your CCG medicines management pharmacist will assist you in making decisions about shared care if you are unsure.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The GP or primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant or specialist.

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Approved by (Specialist or Consultant): Dr Kelsey Jordan on behalf of SMSKP		
Approved by (Chief Trust Pharmacist): Iben Altman Chief Pharmacist SCFT		
Approved by (CCG Medicines Management Pharmacist): Via APC`		
Approved by Brighton and Hove and HWLH CCG on: 27/2/2018		
Approved by Crawley CCG, Horsham and Mid-Sussex CCG on: 27/3/2018		

Information

This information sheet does not replace the Summary of Product Characteristics (SmPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SmPC website**: http://www.medicines.org.uk/emc/ .

2. **Background to use for the indication(s), including licence status:**

Methotrexate 2.5mg tablets are used as an immunosuppressant either alone or in combination with other agents which influence the immune response. Methotrexate has a marketing authorisation for rheumatoid arthritis. The maximum licensed dose in rheumatoid arthritis is 20 mg per week, however rheumatology specialists frequently use doses of 25 or even 30mg weekly, this is common practice nationally. Time to response: May take up to six months for improvement to be noticed.

3. **Dose & administration:**

- Methotrexate is usually given in tablet form ONCE weekly on the same day each week. The tablets should be swallowed whole and not crushed or chewed.
- Doses of 5mg – 15mg weekly are initiated and the doses may be titrated upwards or downwards in 2.5 – 5mg doses dependant on response.
- Folic acid should, if appropriate, be prescribed as it reduces the toxic effects of methotrexate .
    - It can be given any day except the day the patient takes their methotrexate. The folic acid regime will be made clear to the GP on shared care handover.

ONLY prescribe the 2.5mg strength of tablets, the dose being multiples of the 2.5mg tablet strength <u>once</u> a week.

4. **Cautions:**

This list is not exhaustive; refer to the Summary of Product Characteristics (SmPC) or BNF for further guidance.

- Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, and psychiatric disorders.
- Peptic ulceration, ulcerative colitis, diarrhoea and ulcerative stomatitis (withdraw if stomatitis develops).
- Elderly patients, due to diminished hepatic and renal function and decreased folate stores, a reduction in dosage should be considered and these patients should be closely monitored for early signs of toxicity.
- Patients of either gender should use adequate contraception during treatment and wait for at least 3 months after discontinuation of methotrexate before trying to conceive.

5. **Contraindications:**

This list is not exhaustive; refer to the Summary of Product Characteristics (SmPC) or BNF for further guidance.

- Patients with a known allergic hypersensitivity to methotrexate should not receive methotrexate.
- Methotrexate is contra-indicated in the presence of severe***/***significant renal or significant hepatic impairment.
- Liver disease including fibrosis, cirrhosis, recent or active hepatitis;
- Active infectious disease; and overt or laboratory evidence of immunodeficiency syndrome(s).
- Serious cases of anaemia, leucopenia or thrombocytopenia.
- Concomitant use with drugs with antifolate properties (e.g. co-trimoxazole).
- Pregnancy – should not use methotrexate during pregnancy. Methotrexate is teratogenic and there is a theoretical risk of sperm mutation in males. Patients of either gender should use

adequate contraception during treatment. In discussion with the specialist wait for at least three months but preferably six months (see SmPC) after discontinuation of methotrexate before trying to conceive. Exclude existing pregnancy before initiating treatment.

6. Side effects:

Side effects include:

- Common – nausea, anorexia, oral ulceration, minor hair thinning, abdominal discomfort, diarrhoea, headaches
- Uncommon – rash, bone marrow suppression, causing thrombocytopenia, neutropenia, and rarely anaemia. Patients should be warned to report sore throat and abnormal bleeding/bruising
- Hepatotoxicity. Rarely Methotrexate may cause liver fibrosis/cirrhosis. Where alcohol is avoided this has proven rare. Avoid if pre-existing liver disease.
- Pulmonary toxicity. Acute pneumonitis or chronic pulmonary fibrosis may occur. This is not dose related. It presents with a dry cough, dyspnoea and often fever.

This list is not exhaustive; refer to the Summary of Product Characteristics (SmPC) or BNF for further guidance.

7. Notable Drug Interactions

Prescribers are advised to check the BNF or ask a pharmacist for advice where required. This is not a comprehensive list

DO NOT prescribe folate antagonists such as trimethoprim or co-trimoxazole to patients on Methotrexate

Other drugs which should be used with caution include:
Acitretin, sulphonamides (although sulfasalazine is occasionally co-prescribed by rheumatology specialists with appropriate monitoring), tetracyclines, thiazide diuretics, probenecid, sulfinpyrazone, oral hypoglycaemics and any drugs with suspected or confirmed hepatotoxic or nephrotoxic effects.
NB.
There are no contra-indications to using standard doses of NSAIDs with doses of weekly methotrexate ≤ 30mg as long as the required methotrexate monitoring is undertaken. National guidance relating to cardio-vascular, gastrointestinal and renal risk should be followed.

Vaccines

- Live vaccines are not generally recommended in patients on immunosuppression. This is relevant for patients seeking vaccination for foreign travel (e.g. yellow fever vaccination) if considering the shingles vaccine discuss with specialist.[2,3]
- Inactivated vaccines such as influenza vaccine are safe to use although they may elicit a lower response.

8. Criteria for use:

Chronic inflammatory conditions as determined by the appropriate specialist.

Specialist has initiated and dose stabilised (usually for a minimum 3 months).

GP or Primary Care Prescriber confident to take clinical and legal responsibility for prescribing this drug

9. Any further information (e.g. supporting therapies):

See above for advice on folic acid supplementation.

10. References:

1. Guidelines for the management of inflammatory bowel disease in adults. Mowat C, et al. Gut (2011).

2. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. 2017 Jo Ledingham et al. http://www.rheumatology.org.uk/includes/documents/cm_docs/2017/f/full_guideline_dmards.pdf (accessed 9/10/17)

3. Immunisation of individuals with underlying medical conditions https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/566853/Green_Book_Chapter7.pdf (accessed 09/10/2017)

4. Handbook of systemic drug treatment in dermatology 2nd edition (2015) S Wakelin et al British Society for Rheumatology, Immunisation against shingles in people with inflammatory rheumatic disease. Available at http://www.rheumatology.org.uk/includes/documents/cm_docs/2013/i/immunisation_with_zostavax_for_people_with_inflammatory_rheumatic_disease.pdf (accessed 13/11/17).

5. Summary of Product Characteristics, Available at: http://www.medicines.org.uk/emc/

6. UKMI. *Suggestions for Drug Monitoring in Adults in Primary Care.* February 2014. Available at http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug%20monitoring%20document%20Feb%202014.pdf (accessed 13/11/17)

RESPONSIBILITIES and ROLES

Consultant or specialist responsibilities
• Confirm diagnosis and indication for treatment with methotrexate. • To discuss fully the aims, benefits, risks and side effects of treatment and a treatment plan with the patient and/or carer and written information to be supplied to the patient and/or carer. • Prior to treatment ask GP whether patient has had pneumococcal vaccination and flu vaccination and, if not, immunise (unless contra-indicated). • Inform GP when initiating treatment so the GP is aware what is being prescribed and can add to GP clinical record. • Undertake baseline monitoring as required (specific to the medication). • Record other medications and address potential medicine interactions before starting therapy. • Discuss the potential implications of pregnancy and breastfeeding in women of child bearing potential and agree a strategy. • To initiate treatment by prescribing and monitoring usually for a minimum of 3 months. • Undertake monitoring if dose changed. • Monitor and prescribe according to guidelines until handover is appropriate (including when dose changes are made). • Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment. • Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to, or a copy of, the shared care guideline when requesting transfer of prescribing to GP or primary care prescribers. • Advise GP if treatment dose changes or treatment is discontinued. • Inform GP if patient does not attend planned follow-up.

GP or primary care prescriber responsibilities
• Continue prescribing at the dose recommended and undertake monitoring requirements. • Undertake all relevant monitoring as outlined in the monitoring requirements section below, and take appropriate action as set out in this shared care guideline. • Monitor for adverse effects throughout treatment and check for medicine interactions on initiating new treatments. • Add information about the medicine to the patient record, initially as "hospital prescribed", and highlight the importance that this medicine is only to be prescribed under a shared care guideline in primary care. • Report any adverse events to the MHRA and specialist team. • Refer patient back to the Consultant/Specialist if any concerns. • Provide patient with pneumococcal polysaccharide vaccine and flu vaccination unless contra-indicated. • Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline (e.g. ensuring the patient record is correct in the event of a patient moving surgery).

Patient and/or carer role
• Make sure that you understand the treatment and ask for more information, if needed. • Share any concerns in relation to treatment with whoever is prescribing this medicine for you. • Tell the prescriber of this medication about any other medication being taken, including over-the-counter products. • Read the patient information leaflet included with your medication and report any side effects or concerns you have to whoever is prescribing this medicine for you. • Report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding. • Attend any follow up appointments with the consultant or specialist.

Monitoring Requirements

Monitoring schedule[2]

Test	Frequency	Duration
FBC	Every 2 weeks	For first six weeks and until on stable dose for 6 weeks
Creatinine/ calculated GFR	Monthly	For three months
ALT and / or AST Albumin	3 monthly	To continue.

- Continued more frequent monitoring (monthly) is appropriate in patients at higher risk of toxicity.
- When MTX is co-prescribed with leflunomide enhanced monitoring is recommended, after initial period monthly for first 12 months and then if stable may drop to 3 monthly.

Contact specialist team urgently and consider interruption in treatment if any of the following develop:

White Cell Count <3.5x10^9/l	Mean cell volume >105 f/l
Neutrophils <1.6 x10^9/l	Creatinine increase >30% over 12 months and/or calculated GFR <60ml/min/1.73m^2
Unexplained eosinophilia >0.5 x 10^9/l	ALT and/or AST >100 U/l
Platelet count <140 x10^9/l	Unexplained reduction in albumin <30 g/l

Whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance.

This list is not exhaustive; refer to the Summary of Product Characteristics (SMPC) or BNF for further guidance.

Other Warning Signs

- Rash, itch, oral ulceration, nausea & vomiting or diarrhoea : Withhold treatment and discuss with specialist service
- New/increasing dyspnoea or cough: Withhold treatment and discuss with specialist service
- Abnormal bruising or severe sore throat: Check FBC and withhold treatment until results available.

This list is not exhaustive; refer to the Summary of Product Characteristics (SMPC) or BNF for further guidance.

SHARED CARE GUIDELINE

MEDICATION NAME: Methotrexate 2.5mg tablets

INDICATION:

DATE OF REQUEST:

Agreement to transfer prescribing to general practice or primary care prescriber:

Patient details:

Name:

Address:

DoB:

NHS No:

Hospital No:

Medication name, form and strength:

The following tests and investigations have been carried out:

Date treatment initiated:

At the last patient review the medication appeared to be effectively controlling symptoms or providing benefit:
Yes/No

The patients has now been stabilised on a dose of:

The patient has been given written information about their medication:
Yes/No

The patient understands that this medication is being prescribed under a shared care agreement between their GP and specialist and that they have responsibilities under the agreement to ensure they attend their GP to be regularly monitored.
Yes/No

The patient has been informed that the GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient persistently does not attend for monitoring:
Yes/No

Date of next clinic appointment:

If the practice declines shared care, then the named consultant or specialist should be informed within 28 days of receipt of this request. Forms used to decline prescribing can be found here:

Brighton and Hove CCG:
http://www.gp.brightonandhoveccg.nhs.uk/prescribing/joint-formulary-supporting-information
Crawley CCG, Horsham and Mid Sussex CCG:
http://www.horshamandmidsussexccg.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=415216

BACK-UP ADVICE AND SUPPORT

	Name and position	Telephone	Email
Specialist or Consultant			
Alternative specialist (e.g. departmental contact)			
Specialist pharmacist			

Out of hours (e.g. medical team on call)			

Link to full SCG: http://