This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, Warrington, and West Lancashire CCGs

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PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
SHARED CARE FRAMEWORK
FIRST APC BOARD DATE: 27 SEP 2017
LAST APC BOARD DATE: 25 SEP 2019

NHS Pan Mersey Area Prescribing Committee

METHOTREXATE for patients within adult services

1. Background	Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. Methotrexate is used in the treatment of rheumatoid arthritis, psoriasis and Crohn's disease and other indications as outlined below. Indications, dose adjustments and monitoring requirements for disease modifying drugs (DMDs) (licensed and unlicensed indications) included in this Framework are in line with national guidance published by the British Society for Rheumatology 2017.
2. Licensed Indications	• Rheumatoid arthritis • Psoriasis
3. Locally agreed off-label use	• Inflammatory bowel disease • Steroid sparing agent • Other dermatology conditions • Myasthenia gravis, inflammatory myopathies and neuropathies, vasculitis and other immune-mediated central and peripheral nervous system diseases • Interstitial lung disease or cardiac involvement with sarcoidosis • Inflammatory arthropathies • JIA • Atypical neuroinflammatory disease • Off-label doses above the licensed dose for various indications
4. Initiation and ongoing dose regime	**Transfer of monitoring and prescribing to Primary care is normally after 3 months** **The duration of treatment will be determined by the specialist based on clinical response and tolerability.**
	Dose is variable (higher doses may be off-label), depending on the clinical indication and will be decided by the specialist initiating treatment. Time to response is variable. In psoriasis significant effect may not be seen before a month or more. In other indications a response may not be expected before 2 -3 months and in some cases may not occur until six months of treatment. Lower doses may be considered in renal or hepatic impairment or in the elderly. (CKD3: reduce dose by 50%). Contraindicated in CKD 4+5

<table>
<tr><td></td><td colspan="2">Usual starting dose 10-15mg and increased by 2.5-5mg per week as directed by specialist.
The maximum licensed oral dose in rheumatoid arthritis is 20mg.
Variable dose: usual range 2.5mg-30mg ONCE a WEEK on a fixed day</td></tr>
<tr><td></td><td colspan="2">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
Dose increases should be monitored by FBC creatinine/eGFR, ALT and/or AST and albumin every 2 weeks for 6 weeks after a dose increase, then revert back to previous schedule.</td></tr>
<tr><td></td><td colspan="2">Termination of treatment will be the responsibility of the specialist.</td></tr>
<tr><td>5. Baseline investigations, initial monitoring and dose titration to be undertaken by specialist</td><td colspan="2">Baseline:
Height, weight, BP, FBC, creatinine/eGFR, ALT and /or AST, albumin.
Vaccinations against pneumococcus and influenza are recommended.
Shingles vaccine (Zostavax) is recommended as per the JCVI for eligible patients; however it is contraindicated in doses greater than 0.4mg/kg/week
Specialist to highlight in the first clinic letter notifying the GP of the decision to initiate DMDs that the GP will need to give the shingles vaccine if the patient is older than 69 years and the pneumococcal vaccine if this has not already been given. The GP should also be advised to add the patient to the influenza vaccine list.
Patients should be assessed for comorbidities that may influence DMD choice, including evaluation of respiratory disease and screening for occult viral infection
Monitoring:
FBC, creatinine/eGFR, ALT and /or AST and albumin every 2 weeks until on stable dose for 6 weeks;
Once on stable dose, monthly FBC, creatinine/eGFR, ALT and /or AST and albumin for 3 months.
Thereafter, FBC, creatinine/eGFR, ALT and/or AST and albumin at least every 12 weeks.

Baseline chest X-ray according to indication. Spirometry in smokers, patients with known respiratory disease or older than 65 years.</td></tr>
<tr><td>6. Ongoing monitoring requirements to be undertaken by primary care.</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td></td><td>FBC, Creatinine/eGFR, ALT and/or AST, Albumin

CRP and ESR (rheumatology patients only)</td><td>After the initial monitoring period (see section 5), every 12 weeks, or more frequently in patients at higher risk of toxicity as advised by the specialist team. NB: Some of the initial monitoring (likely to be 1-2 months of monthly monitoring) may take place in primary care. The exact frequency of the monitoring to be communicated by the specialist in all cases.

When methotrexate is prescribed with leflunomide, monthly monitoring</td></tr>
</table>

		is recommended for the first 12 months.
	P3NP (psoriasis patients only) This test can be requested via the EMIS or Vision system and the normal range is 1.7-4.2 micrograms/L. Three P3NP levels >4.2mcg/L but <8.0mcg/L or two P3NP levels >8.0mcg/L over a 12-month period should be reported to the specialist.	Annually or every 12 weeks after a raised value (>4.2mcg/L) NB: There is a 4-week turnaround for this test.
7. Pharmaceutical aspects	Route of administration	Oral or subcutaneous injection
	Formulation	Oral – **only the 2.5mg strength tablet is to be prescribed**, irrespective of dose, to avoid overdose with the 10mg tablet. Solution for injection various strengths - pre-filled syringe. Methotrexate injection must be prescribed by the brand name and also the generic name (if this facility is available on the prescribing system).
	Administration details	The day of the week should be specified and consistent. Provision of cytotoxic waste disposal needs to be arranged according to locally commissioned service.
	Other important information	Patients should also receive Folic acid 5mg tablets daily, one to six times a week during treatment with methotrexate (but not on the same day as methotrexate) as advised by specialist. Folic acid to be prescribed by the specialist until the GP takes over the prescribing of methotrexate.
8. Contraindications **Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.**	• Significantly impaired hepatic function • Significantly impaired renal function (CKD 4 + 5) • Pre-existing blood dyscrasia • Severe acute or chronic infections and immunodeficiency syndrome • Methotrexate should not be used concomitantly with drugs with antifolate properties eg trimethoprim • **Pregnancy and breastfeeding** • Hypersensitivity to methotrexate or any of its excipients. • SPC cautions administration of live vaccines; however JCVI and BSR recommend that oral DMD therapy at standard doses is not a contraindication in most patients, clinician discretion is advised.	
9. Significant drug interactions	For a comprehensive list consult the BNF or Summary of Product Characteristics. SPC Seek advice from the initiating Specialist if there are any concerns about interactions.	

<table>
<tr><td></td><td colspan="2">Concomitant administration of folate antagonists such as trimethoprim, co-trimoxazole and nitrous oxide should be avoided.</td></tr>
<tr><td rowspan="8">10. Adverse Effects and managements</td><td>Result</td><td>Action</td></tr>
<tr><td>Abnormal bruising or severe sore throat</td><td>Stop drug until FBC results available, contact Specialist Nurse (SN)</td></tr>
<tr><td>New or increasing dyspnoea or dry cough</td><td>Stop drug and contact SN urgently.</td></tr>
<tr><td>Fall in WCC <3.5 x 10^9/l
Fall in neutrophils <1.6 x 10^9/l
Fall in platelets <140 x 10^9/l</td><td>Stop drug. Contact SN for advice and management.</td></tr>
<tr><td>Increased MCV >105f/l</td><td>Check folate, B12 & TSH, treat if abnormal, contact SN for advice and management if normal.</td></tr>
<tr><td>Unexplained reduction in albumin <30g/l (added from BSR)
Abnormal LFTs – AST or ALT > 100U/l
Rash
Mouth ulcers</td><td>Stop drug. Contact SN for advice and management.</td></tr>
<tr><td>Taste loss</td><td>Reassure, continue drug.</td></tr>
<tr><td>Nausea, vomiting, diarrhoea</td><td>Discuss with SN. N.B. nausea relating to methotrexate should be managed initially by prescribing anti-emetics.</td></tr>
<tr><td>Increase in serum creatinine >30% over period of 12 months or less OR decline in eGFR > 25%</td><td>Contact SN if new or unexplained renal impairment</td></tr>
<tr><td>11. Advice to patients and carers</td><td colspan="2">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 drugs.</td></tr>
<tr><td>12. Pregnancy (men and women) and breast feeding</td><td colspan="2">• Contraindicated in pregnancy and breast feeding. Manufacturer advises effective contraception[2] during and for at least 6 months after treatment in both men and women. Patients planning to become pregnant should be seen by a specialist.
• Present in breast milk in low concentration, breast feeding should be stopped prior to treatment.
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.</td></tr>
<tr><td>13. Specialist contact information</td><td colspan="2">See appendix 2</td></tr>
<tr><td>14. Additional information</td><td colspan="2">Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.</td></tr>
<tr><td>15. References</td><td colspan="2">1. BSR monitoring guidelines
2. Drug Safety Update: Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed? - GOV.UK</td></tr>
<tr><td>16. To be read in conjunction with the following documents.</td><td colspan="2">1. Policy for Shared care
2. Shared care agreement form</td></tr>
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	When two or more DMDs are initiated, one shared care agreement form should be completed for all relevant drugs.

Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey **Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary** document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.
- All information required by the shared care framework for the individual medicine has been provided to the patient's GP.
- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- To initiate the medicine, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
    - Is counselled with regard to the risks and benefits of the medicine.
    - Provide any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
    - Obtain and document informed consent from the patient when any medicines is prescribed for an off-label indication for any condition
- To be familiar with the shared care framework.
- To provide all information to the patient's GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- To assess the patient regularly as necessary for the duration of therapy.
- To review the patient promptly if required by the GP concerned.

- To meet any additional requirements as required by the individual medicine shared care framework.
- To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.
- **Addition of a second DMD**: Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must initiate, prescribe and monitor the new drug in accordance with the relevant shared care agreement including subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated for the new drug.

Primary Care Responsibilities in Shared Care

- To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked to:

- To provide prescribe or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
- To review the patient as required by the Shared Care Framework
- To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient`s clinical record. A READ code of “6652 Shared Care- Specialist/GP” can be used.
- To be familiar with the individual Shared Care Framework.
- To report any adverse effects of treatment to the specialist team.
- To inform the Specialist of any relevant change in the patient’s circumstances.
- To seek Specialist advice as appropriate.
- To meet any additional requirements as required by the individual Shared Care Framework.
- To respond to Specialist communication relating to any change or addition to the patient’s treatment covered by the Shared Care Agreement.

Where the GP wishes to withdraw prescribing, for example when the patient fails to attend for monitoring, they need to give the specialist team a minimum of 14 days’ notice of their need to resume responsibility for prescribing. The specialist is required to acknowledge this request within the 14-day time period.

Appendix 2: Shared Care Agreement

Disease modifying drugs (DMDs)

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1
To be signed by Consultant / Associate Specialist / Specialist registrar or Specialist Nurse (who must be a prescriber)

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

If using addressograph label please attach one to each copy

Dear Dr_____

I request that you prescribe

(1) _____

(2) _____

(3) _____

(4) _____

for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: ….. / ….. / ….. Next Supply Due: ….. / ….. / …..

Date of last blood test: ….. / ….. / ….. Date of next blood test: ….. / ….. / …..

Frequency of blood test: ……

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy. ☐

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received. ☐ N/A

Details of Specialist Clinicians

Name _____Date_____

Consultant / Associate Specialist / Specialist Registrar / Specialist Nurse ***circle or underline as appropriate***

Signature _____

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a Specialist Nurse, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details*:*

Telephone number: _____Ext:_____

Address for return of documentation _____

_____

_____

Part 2
To be completed by Primary Care Clinician

Patient name _____

I agree to prescribe _____for the above patient in accordance with the enclosed shared care framework.

GP signature _____Date _____

GP name _____Please print

GP: *Please sign and return a copy* ***within 21 calendar days*** *to the address above*

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: