NHS
St Helens
Clinical Commissioning Group

SHARED CARE FRAMEWORK
APC BOARD DATE: 28 SEP 2017

LEFLUNOMIDE

1. Background	Leflunomide is a disease-modifying drug (DMD) and is used either as a single agent or in combination with other DMDs. The response time for leflunomide is 8-12 weeks. 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 • Psoriatic arthritis
3. Locally agreed off-label use	• Systemic lupus erythematosus and other rheumatology conditions • Axial spondyloarthropathy • Dermatology conditions • Interstitial lung disease • Vasculitis
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.**
	Usual dose is 10-20mg daily. The therapeutic effect usually starts after 4 to 6 weeks and may further improve up to 4 to 6 months Please note for rheumatology conditions a patient may be initiated on more than one DMD
	All dose adjustments (increase/decreases) 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 the dose increase, then revert back to previous schedule.

<table>
<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 and albumin.
Vaccinations against pneumococcus and influenza are recommended.
Shingles vaccine (Zostavax) is recommended as per the JCVI for eligible patients.
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.
Initiation:
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
BP & weight at each monitoring visit</td></tr>
<tr><td rowspan="2">6. Ongoing monitoring requirements to be undertaken by primary care.</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>FBC, creatinine/ eGFR, ALT and/or AST and albumin, BP and weight

CRP and ESR (rheumatology patients only)</td><td>Every 12 weeks or more frequently in patients at higher risk of toxicity as advised by the specialist team. The exact frequency of the monitoring to be communicated by the specialist in all cases.</td></tr>
<tr><td>N.B. For <u>Rheumatology patients only - under the care of St Helens and Knowsley Hospitals</u>: GP to choose whether they are monitored under Option 1 or Option 2</td><td colspan="2">Option 1: GP to prescribe DMARD while monitoring undertaken via computerised Rheumatology Monitoring System (RMS).
For patients with GPs who have access to Whiston pathology ICE system – results will be available via ICE
For patients with GPs who do not have access to Whiston ICE, patients will be provided with blue record card of results which they will be advised to be made available to GP when writing prescription.
N.B. Option 1 will be implemented by the Rheumatology Team if the patient’s GP has not responded to the request for shared care after 21 days
Option 2: GP to prescribe DMARD and monitoring to be undertaken via GP surgery.</td></tr>
<tr><td rowspan="4">7. Pharmaceutical aspects</td><td>Route of administration</td><td>Oral</td></tr>
<tr><td>Formulation</td><td>Leflunomide 10mg, 20mg</td></tr>
<tr><td>Administration details</td><td>Tablets should be swallowed whole with sufficient liquid.</td></tr>
<tr><td>Other important information</td><td>The absorption of leflunomide is not affected by food.</td></tr>
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<tr><td>8. Contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.</td><td colspan="2">• Severe immunodeficiency
• Serious infections
• Patients with severe immunodeficiency states, e.g. AIDS,
• Impaired liver function due to any cause
• Severe unexplained hypoproteinaemia
• Renal impairment (CKD 4 and 5)
• Impairment of bone marrow function as indicated by anaemia and cytopaenias due to causes other than RA and psoriatic arthritis
• Hypersensitivity</td></tr>
<tr><td>9. Significant drug interactions</td><td colspan="2">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.</td></tr>
<tr><td rowspan="12">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>Fall in WCC <3.5 x 10^9/l</td><td rowspan="3">Stop drug. Contact SN for advice and management.</td></tr>
<tr><td>Fall in neutrophils <1.6 x 10^9/l</td></tr>
<tr><td>Fall in platelets <140 x 10^9/l</td></tr>
<tr><td>Increased MCV >105fl</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</td><td rowspan="5">Stop drug. Contact SN for advice and management.</td></tr>
<tr><td>Abnormal LFTs – AST or ALT > 100 U/L</td></tr>
<tr><td>Rash/itch</td></tr>
<tr><td>Nausea, vomiting, diarrhoea</td></tr>
<tr><td>Neuropathy symptoms</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 there is new or unexplained renal impairment</td></tr>
<tr><td>Hair loss, headache, GI upset, unexplained weight loss> 10%</td><td>Contact SN</td></tr>
<tr><td>Hypertension</td><td>Consider anti-hypertensive agent. If hypertension persists, stop drug and contact SN</td></tr>
<tr><td></td><td colspan="2">N.B. Leflunomide has a long half-life. Therefore a washout procedure may be indicated and the SN must be contacted if the drug is stopped</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>
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12. Pregnancy and breast feeding	Leflunomide is teratogenic and must not be given to pregnant women or women of child bearing potential unless reliable contraception is used. Women planning to have children should either discontinue the drug 2 years prior to conception or have a rapid removal of its active metabolite by following the washout procedure. Breastfeeding is not recommended. Based on very limited evidence, leflunomide may be compatible with paternal exposure. Men should use effective contraception for 3 months after stopping leflunomide. (BSR&BHPR guideline on prescribing in pregnancy and breastfeeding)
13. Specialist contact information	See appendix 2
24. Additional information	**Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.**
15. References	BSR monitoring guidelines
16. To be read in conjunction with the following documents.	1. Policy for shared care 2. Shared care agreement form 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.

- ***For <u>Rheumatology patients only - under the care of St Helens and Knowsley Hospitals</u>: where GP chooses Option 1*** *– Blood test monitoring will remain the responsibility of Rheumatology department via Rheumatology Monitoring System. Rheumatology department takes responsibility for actioning abnormal blood test results. Blood test results will be available to GP via Whiston Pathology ICE (or for GP practices that do not have access to this, via patient hand held blue results card)*

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.
- ***For <u>Rheumatology patients only - under the care of St Helens and Knowsley Hospitals</u>: where GP chooses Option 1*** *– GP to prescribe medication and ensure patient has been attending for blood tests via rheumatology monitoring system and that blood test results are available (via Whiston Pathology ICE system or patient held blue result card blood test monitoring).*
- 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 patients treatment covered by the Shared Care Agreement.

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

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

For Rheumatology patients only under the care of St Helens and Knowsley Hospitals
I would like monitoring to be undertaken

Option 1 - via Rheumatology Monitoring System **Yes / No**
N.B. Option 1 will be implemented by the Rheumatology Team if the patient's GP has not responded to the request for shared care after 21 days.
Option 2 - at GP surgery **Yes / No**

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:

St Helens Rheumatology Monitoring System (RMS)

St Helens Rheumatology Department has developed an in-house computerised blood monitoring system for patients on DMARD therapies which has now been running for over 15 years. It was upgraded to a web-based programme in 2009.

Overleaf is a flow chart of this system.

It has a number of advantages over tradition shared care monitoring (where blood tests are taken, checked and transcribed in to patient held monitoring booklet by hand).
These include:

1) It minimises the number of health professionals involved in the process, reducing the risk of miscommunication
2) It ensures prompt action on any abnormality being taken by an experienced rheumatology nurse specialist
3) It is an efficient use of human resources – using the computer to do the detection of the abnormality
4) It reduces risk of human error – an abnormal result being overlooked, or inaccurate transcription of blood test result to patient held monitoring booklet.
5) It has a robust mechanism for detecting DNAs and enabling the appropriate action to be taken.

However its major disadvantage is that the results of the tests are sent to the patient on a blue card but the prescribing GP is then reliant on either the patient remembering to bring the blue card record of all their blood tests to the surgery when requesting a repeat prescription or the GP checking the results on the Whiston pathology system assuming they have access to this or the GP trusting in our monitoring system (and I appreciate that they may not feel able to do so).

RHEUMATOLOGY MONITORING SYSTEM (RMS) PATHWAY (2018)