SHARED CARE FRAMEWORK

The Pan Mersey Area Prescribing Committee recommends the prescribing of LEFLUNOMIDE for patients within adult services.

SHARED CARE

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 starts after 4 to 6 weeks and may further improve up to 4 to 6 months.

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].

2. Licensed Indications

- Rheumatoid arthritis (RA)
- 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

For Rheumatology patients managed by Wirral Trust, diagnosis and the provision of written instructions to GPs for the prescribing and escalation of treatment is to be completed by secondary care organisations.

Other Patients

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.

Dosing information

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 will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.

Supporting information

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.

Termination of treatment will be the responsibility of the specialist.

5. Rheumatology patients managed by Wirral Trust - Baseline investigations to be undertaken by specialist, initial monitoring and dose titration to be undertaken by GP.

Other Patients - Baseline investigations, initial monitoring, and dose titration to be undertaken by specialist.

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 for those <69 years but deemed clinically eligible for Zostavax by the Specialist Team. The pneumococcal vaccine should also be administered, if not already given. The GP should also be advised to add the patient to the influenza vaccine list.
- DMDs should be started 2-4 weeks AFTER administration of the shingles vaccine (Zostavax) as stated in the Green Book, therefore the Specialist Team should arrange this with the GP, in a timely manner so as not to delay commencement of DMDs.
- Patients should be assessed for comorbidities that may influence DMD choice, including evaluation of respiratory disease and screening for occult viral infection.
- Treatment should not be started for 4 weeks after live vaccines (eg oral typhoid, MMR, BCG, yellow fever)

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 and weight at each monitoring visit.

6. Ongoing monitoring requirements to be undertaken by primary care

Monitoring	Frequency
FBC, creatinine/eGFR, ALT and/or AST and albumin CRP and ESR (rheumatology patients only)	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 leflunomide is prescribed **with methotrexate**, monthly monitoring is recommended for the first 12 months.

7. Pharmaceutical aspects

Route of administration

Oral

Supporting information

Formulation

Leflunomide 10mg, 15mg, 20mg

Administration details

Tablets should be swallowed whole with sufficient liquid.

Other important information

The absorption of leflunomide is not affected by food.

8. Contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.

- Serious infections
- Patients with severe immunodeficiency states, e.g. AIDS,
- Impaired liver function due to any cause
- Severe unexplained hypoproteinaemia
- Renal impairment (chronic kidney disease (CKD) 4 and 5)
- Impairment of bone marrow function as indicated by anaemia and cytopenia due to causes other than RA and psoriatic arthritis
- Pregnancy and breastfeeding
- Hypersensitivity

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.

10.Adverse effects and management

Adverse effect	Management
Abnormal bruising or severe sore throat	Stop drug until FBC results available, contact Specialist Practitioner (SP)
Fall in WCC <3.5 x 10^9/l	Stop drug. Contact SP
Fall in neutrophils <1.6 x 10^9/l	
Fall in platelets <140 x 10^9/l	
Increased MCV >105fl	Check folate, B12 & TSH. Treat if abnormal, contact SP for advice and management if normal.
Unexplained reduction in albumin <30g/L	Stop drug. Contact SP
Abnormal LFTs – AST or ALT > 100 U/L	
Rash/itch	
Nausea, vomiting, diarrhoea	
Neuropathy symptoms	
Increase in serum creatinine >30% over period of 12 months or less OR decline in eGFR > 25%	Contact SP if there is new or unexplained renal impairment
Hair loss, headache, GI upset, unexplained weight loss> 10%	Contact SP
Hypertension	Consider anti-hypertensive agent. If hypertension persists, stop drug and contact SP
Ulcerative stomatitis	Stop drug. Contact SP
Localised or systemic infection	Discuss with SP

Supporting information

N.B. Leflunomide has a long half-life. Therefore, a washout procedure may be indicated, and the SP must be contacted if the drug is stopped.

11. Advice to patients and carers

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 and pregnancy prevention and planning information.

12. Pregnancy and breast feeding

Leflunomide is suspected to be teratogenic and must not be given to pregnant women or women of childbearing potential unless effective contraception is used during treatment and up to 2 years after treatment.

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 colestyramine washout procedure before switching to an alternative medication compatible with pregnancy.

If a woman becomes pregnant while taking leflunomide she should be referred immediately to the specialist.

Breastfeeding is contraindicated.

Based on very limited evidence, leflunomide may be compatible with paternal exposure but male patients should be made aware of the possible male-mediated foetal toxicity. Men should use effective contraception during treatment and for at least 3 months after stopping leflunomide.

BSR&BHPR guideline on prescribing in pregnancy and breastfeeding

13. Specialist contact information

See appendix 2

14. 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

1. Summary of Product Characteristics
2. BSR monitoring guidelines
3. The Green Book - Immunisation against infectious diseases

To be read in conjunction with the following documents.

1. Policy for Shared Care (see appendix 1).
2. Shared care agreement (see appendix 2).

When two or more DMDs are initiated, one shared care agreement form should be completed that includes all relevant drugs.

Supporting information

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

- For Rheumatology patients under Wirral Trust, Specialist to ensure baseline monitoring of full blood count and biochemical profile as described by the shared care framework.
- For all other patients, Specialists 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.
    - Is provided with 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 are 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.
- 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 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 Snomed code of "268529002 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.

Supporting information

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 / Prescribing member of Specialist Team (circle or underline as appropriate)

Date _____

Name of patient_____

Address _____

_____

Please add patient addressograph here

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

Dear Dr_____

I request that you prescribe (Include doses)

(1) _____

(2) _____

(3) _____

(4) _____

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

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.

Details of Specialist Clinicians

Name _____Date_____

Consultant / Prescribing member of Specialist Team (circle or underline as appropriate)

Signature _____

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

Supporting information

When the request for shared care is made by a prescriber who is not the specialist, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details:

Please add patient addressograph here

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.

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: