SHARED CARE AGREEMENT

Name of medicine	Leflunomide
Indication	For the treatment of inflammatory rheumatic diseases

Version: **2.2** Approval date: **September 2024** Review date: **September 2027**

The Shared Care Agreement (SCA) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. It does not contain all of the relevant product information, which should be sought using the current British National Formulary and manufacturer's Summary of Product Characteristics. The SCA must be used in conjunction with the NHS Lothian Procedure for the Shared Care of Medicines, available here.

Roles and responsibilities

Listed below are specific responsibilities that are additional to those included in the NHS Lothian Policy and Procedures for Shared Care. Please refer to the policy for core roles and responsibilities that apply to all Shared Care Agreements.

Consultant

- Assessing the need for leflunomide therapy.
- Undertaking and assessing the relevant baseline investigations.
- Arranging for the patient to receive verbal and written information on leflunomide.
- Counselling patients on the risk of leflunomide in pregnancy and the need for contraception for male and female patients as appropriate.
- Treatment will be initiated by the consultant and the supply made by secondary care for the first 8 weeks. During this time rheumatology will provide comprehensive patient support including monitoring for adverse effects, addressing any treatment-related issues and responding to patient queries via the patient helpline.
- Making arrangements for the results of blood tests to be reviewed during the first 6 weeks of treatment.
- Making arrangements for the patient to be reviewed 3-4 months after initiation of treatment to assess response.
- Providing advice to the GP regarding monitoring, adverse effects and dose modifications when required.
- Specialist service to refer patients for vaccinations which are out with routine vaccination schedules or recall programmes via the clinician referral form (NHS Lothian HSCP Vaccination Service (scot.nhs.uk). Please note that Patient Specific Directions (PSD) are required for bespoke vaccination schedules where there is no PGD in place. The referral forms should be sent to the partnership that is responsible for administering vaccinations to their residents.
- Making arrangements for the patient to be kept under long term review.

General Practitioners and Primary Care Non-medical Prescribers

- Prescribing leflunomide in consultation with the specialist after the first 8 weeks.
- Bloods are taken in primary care and reported to the specialist service during the first six weeks of treatment. The GP is to arrange for blood tests to be taken at appropriate intervals thereafter as detailed in `Monitoring`.
- Advising on a suitable form of contraception where relevant.
- Monitoring blood tests and for specific side effects as detailed in 'Monitoring' section after the first 8 weeks.

Patient, Relatives, Carers

- As listed in NHS Lothian Policy and Procedures for the Shared Care of Medicines.
- Ensuring adherence to phlebotomy requirements throughout treatment
- Patients can access advice via the rheumatology patient helpline by calling 0131 537 1405.

Support and Advice for the GP and primary care non-medical prescribers

SPR or Rheumatology Consultant on call 13.00-17.00 on weekdays and 09.00-12.00 on Saturdays and public holidays via the switchboard (0131 537 1000). Urgent queries outwith these times will be dealt with by the on-call medical team.

GPs can access advice from the rheumatology specialist service using the rheumatology on call e-mail which aims to give advice with a 24 hour response time: loth.rheumatologyoncall@nhs.scot. Advice will be communicated back to the GP by e-mail. The GP should copy in the practice's clinical e-mail address and ask that the reply is sent to all, so that the reply is picked up even if the sender is not available.

Key Information on the Medicine

Please refer to the current edition of the British National Formulary (BNF), available at www.bnf.org, and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

Helpful information on DMARDs can be found in the 2017 British Society for Rheumatology *Guideline for the prescription and monitoring of non-biologic Disease-Modifying Anti-Rheumatic Drugs*.
Link: https://www.rheumatology.org.uk/Knowledge/Excellence/Guidelines

Background to disease and use of drug for the given indication

Leflunomide may be used as monotherapy or in combination with other DMARDs and biologic drugs in the management of a number of inflammatory rheumatic conditions.

Dosage and Administration

Treatment is commenced as 10mg once daily. In some cases, the dose may be increased to 20mg once daily if the response is inadequate. A loading dose is no longer used.

Monitoring

On initiation of treatment, patients are provided with pre-labelled forms for blood tests. Bloods are taken in primary care and reported to rheumatology during the first 6 weeks of treatment.

Note that abnormal trends in blood monitoring should prompt extra vigilance and may be a sign of toxicity even if absolute levels are normal.

<table>
<tr><th>Test</th><th>Frequency</th><th>Abnormal Result</th><th>Action if Abnormal Result</th></tr>
<tr><td rowspan="3">FBC</td><td rowspan="5">Every 2 weeks until on a stable dose for 6 weeks

Then monthly for 3 months.

Thereafter every 3 months.

Revert to initial schedule in the event of a dose increase or when a new DMARD is added.

When leflunomide is used in combination with methotrexate, monitoring should be carried out monthly.</td><td>Platelets 100-140
WCC 2.0-3.5
Neutrophils 1.0-1.6</td><td>Stop therapy for 2 weeks and recheck.
If normal recommence at lower dose i.e. reduce leflunomide dose by 10mg/day.</td></tr>
<tr><td>Platelets < 100
WCC < 2.0
Neutrophils <1.0
Lymphocytes <0.5</td><td>Stop treatment and contact rheumatology.</td></tr>
<tr><td>MCV >105</td><td>Check B12, folate, TFTs and consider discussing with specialist service</td></tr>
<tr><td rowspan="2">LFTs</td><td>ALT >100</td><td>Stop therapy for 2 weeks, and recheck.
If ALT <100, recommence at lower dose i.e. reduce leflunomide dose by 10mg/day.</td></tr>
<tr><td>ALT 50-100</td><td>Continue treatment and recheck.
If ALT stable, continue treatment.
If ALT rising, contact rheumatology.</td></tr>
<tr><td>Creatinine</td><td>Creatinine: note trend</td><td>If rising, reduce dose by 50%, and contact rheumatology.</td></tr>
<tr><td>BP</td><td>At each visit</td><td>As per NHS Lothian Hypertension Guidelines.</td><td>Treat BP as per local guidelines; if BP cannot be controlled stop leflunomide and for further advice contact loth.rheumatologyoncall@nhs.scot</td></tr>
<tr><td colspan="4">Advice on avoiding conception /contraception as appropriate if patient circumstances change</td></tr>
</table>

- Please inform rheumatologist of any discontinuation, adverse effect or for advice on washout.
- Trends in ESR are useful in decision-making and can be undertaken during periods of increased disease activity. Routine ESR monitoring is not required.

Contraindications - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

Cautions - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- Temporarily withdraw leflunomide if the patient reports sore throat, unexplained bleeding or bruising, mouth ulcers or other signs of blood dyscrasia or evidence of infection. Perform repeat blood monitoring.
- Temporarily discontinue leflunomide during serious infection.

Adverse effects - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- In the event of an unexplained acute widespread rash, headache, GI upset, or hair loss - reduce dose of leflunomide. If severe, stop leflunomide and provide washout*****
- For rashes: seek urgent specialist (preferably dermatological) advice.
- If increasing shortness of breath occurs, stop leflunomide and provide washout*****

***** Washout, when required, is with cholestyramine or charcoal – refer to rheumatology specialist for advice.

Drug interactions - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

Increased side-effects may occur in the case of recent or concomitant use of hepatotoxic medicines.

Pregnancy & Fertility - For full detail, refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

- Patients who are planning a pregnancy should be referred to the rheumatology specialist.
- Leflunomide is contraindicated in pregnancy as its active metabolite is suspected to cause serious birth defects. Women of childbearing potential should wait for a period of 2 years after treatment discontinuation before they may become pregnant. If a waiting period of up to approximately 2 years under reliable contraception is considered impractical, a washout procedure may be advisable.
- The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify the physician immediately for pregnancy testing, and if positive, the physician and patient must discuss the risk to the pregnancy.
- Patients should avoid breastfeeding if taking leflunomide.

Vaccinations

- Individuals who on immunosuppressant therapy should be given inactivated vaccines in accordance with national recommendations.
- It is recommended that patients with autoimmune inflammatory diseases on immunosuppressant therapy should be offered pneumococcal, COVID19 and influenza vaccination.
- Immunosuppressed patients who are 50 years and over should be offered the varicella-zoster vaccine, Shingrix, to help protect them against shingles. Shingrix is a non-live alternative to the live shingles vaccine, Zostavax.
- When considering suitability for live vaccines concurrent DMARD therapy should also be taken into account.

For further information see: Immunisation against infectious disease - GOV.UK (www.gov.uk)

The presence of this SCA does not compel a primary care prescriber to prescribe if they feel that it is out with the scope of their competencies (as per GMC guidance on safe prescribing) or resources, as ultimate responsibility lies with the prescribing, not the recommending, clinician.

For office use only:

Approved by the General Practice Prescribing Committee (GPPC) on 10th September 2024