SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR ORAL LEFLUNOMIDE (ADULTS)

This SCA is applicable for ALL conditions/specialities.

If leflunomide is being used as combination therapy with methotrexate both SCAs must be referred to. The correct Monitoring Schedule for DMARDS, i.e. single agent or combination therapy should be followed.

Note: This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC NAME (formulations and strength)

Name: Leflunomide

Formulation: Tablet

Strength: 10mg, 15mg and 20mg

STATUS OF MEDICINE

Licence status: Licensed

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: YES. See RMM Directory - (emc) as there are RMM for multiple leflunomide preparations.

CONDITION(S) TO BE TREATED UNDER THIS SCA

Treatment of active rheumatoid arthritis and active psoriatic arthritis.

TYPICAL DOSAGE REGIME	
Licensed dose	See Specialist service/SmPC for advice – variable according to condition being treated
Route of administration	Oral
Recommended starting dose	See Specialist service for advice – variable according to condition being treated

TYPICAL DOSAGE REGIME	
Titration dose/increment	See Specialist service for advice
Maximum dose	See Specialist service for advice
Situations requiring dose adjustment	See Specialist service for advice and Monitoring Schedule for DMARDs
Duration of treatment	See Specialist service for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Baseline as per Monitoring Schedule for DMARDs:
  - Full Blood Count (FBC), Liver Function Tests (LFTs), and Urea and Electrolytes (U&Es)
  - Blood pressure (BP)
- Copy of baseline results to be shared with primary care.
- Exclude pregnancy before starting therapy:
  - Advise patient to contact their physician immediately should pregnancy occur
  - Ensure the patient understands the importance of reliable contraception
  - Reliable contraception should be used by both men and women whilst on leflunomide and for at least 2 years (3 months for men) after stopping leflunomide unless the washout procedure is used (see the SmPC/RRM for further details)
- Request for initiation of therapy and recommendations for dose increments to Primary Care.
- Monitoring clinical response to treatment and advising on final dose required for the patient. Clinical decision regarding final dose required for patient.
- Pneumococcal polysaccharide vaccine (PPV), COVID-19 vaccine and annual influenza vaccine should be given as per Joint Committee of Vaccination and Immunisation (JCVI)/The Green Book recommendations. Shingles vaccine should be given to those individuals who are severely immunocompromised, or anticipating immunosuppressive therapy, and eligible in line with JCVI/The Green Book recommendations and Scottish Government vaccination programme. Patients should be referred by specialist services to receive these vaccines in accordance with local protocol.

RESPONSIBILITY OF PRIMARY CARE/PRESCRIBING CLINICIAN

A Practice agreeing to prescribe leflunomide should:

- Prescribe medication under the guidance of the Consultant from the relevant specialist service.
- Checking before prescribing each instalment of medication that the monitoring is up to date and that results are within a satisfactory range.
- Note: for individuals referred for vaccinations by the specialist service it is ideal to wait for vaccinations before starting immunosuppressive treatments. However this risks not controlling the autoimmune condition quickly which can negatively affect long term prognosis. Therefore specialties do not insist on a delay in starting immunosuppressive treatment to allow for vaccinations and recommend vaccinations happen as soon as possible after starting immunosuppressive treatment.

- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
- The General Practitioner (GP) has primary responsibility for monitoring according to the Monitoring Schedule for DMARDs and review of results.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- Ensure the GP is aware that the drug can cause:
    - Nephrotoxicity
    - Increase in blood pressure
    - Infection and increased risk of malignancy – benign, malignant neoplasms and skin malignancies
    - Gastrointestinal upset
- Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.
- Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and abnormal results are acted upon promptly. If an intercurrent illness occurs, when completing laboratory request always include details of the patient's medication.
- If bloods are taken due to intercurrent illness, ensure they are monitored and contact specialist consultant to advise if results are out with range.
- Infection - During a serious infection leflunomide should be temporarily discontinued until the patient has recovered from the infection and is off antibiotics for 2 weeks with no recurrence of infection. (This excludes any transplant patients who should be discussed with specialist service).
  It can be considered appropriate to continue these drugs in patients with minor or uncomplicated viral infections or, if deemed clinically appropriate by the Specialist, in patients requiring long term antibiotic prophylaxis e.g. for prevention of recurrent UTIs.
- Contact the relevant specialist service in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
- Be alert for any of the known adverse reactions.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- The patient should be encouraged to ensure blood tests are undertaken at the correct intervals.
- It is responsibility of primary care to ensure that the medication is recorded on the patient's clinical medication record. This will facilitate central searches for vaccinations in order to ensure patients receiving immunosuppressants are called by the HSCP teams for required vaccinations, e.g. influenza and covid programmes.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- Post exposure prophylaxis (PEP) should be considered in non-immune individuals if exposed to shingles or chickenpox as per The Green Book.
- If something unexpected occurs contact Consultant for the appropriate speciality.
- Notify consultant/specialist service if drug is stopped.

MONITORING

Refer to the NHSG Guidelines For The Monitoring of Disease Modifying Anti-Rheumatic Drugs (DMARDs) For Healthcare Professionals. Results should be reviewed and action taken as per monitoring guidance.

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Primary Care are responsible to ensure results are reviewed and action taken as per monitoring guidance.

Note: In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- The patient should ensure all blood tests are taken at the correct intervals.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimise the risk of skin cancer, exposure to sunlight and Ultra Violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor (minimum SPF 30).

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children BNF (British National Formulary) | NICE

CONTRAINDICATIONS

For full detail please refer to the current Summary Product Characteristic (SmPC) available at www.medicines.org.uk

- Hypersensitivity (especially previous Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) to the active substance, to the principal active metabolite teriflunomide, peanut or soya or to any of the excipients.
- Impaired liver function.
- Severe immunodeficiency states, e.g. AIDS.
- Severely impaired bone marrow function or significant anaemia, leucopenia, neutropenia or thrombocytopenia due to causes other than rheumatoid arthritis.
- Severe infections - during a serious infection leflunomide should be temporarily discontinued until the patient has recovered from the infection and is off antibiotics for 2 weeks with no recurrence of infection. (This excludes any transplant patients who should be discussed with specialist service).
- Moderate to severe renal insufficiency, because insufficient clinical experience is available in this patient group.
- Severe hypoproteinaemia, e.g. in nephrotic syndrome.
- Pregnant women, or women of childbearing potential who are not using reliable contraception during treatment with leflunomide and thereafter. **Note:** Pregnancy must be excluded before start of treatment with leflunomide.

PREGNANCY

Leflunomide is contra-indicated in pregnancy. British Society for Rheumatology Guideline on prescribing drugs in pregnancy and breastfeeding: Immunomodulatory anti-rheumatic drugs and corticosteroids from April 2023 states that leflunomide is not considered compatible with pregnancy.

Women on leflunomide should be advised to seek specialist advice prior to conception as they should undergo a cholestyramine washout procedure and switch to another pregnancy compatible drug prior to conception.

Men should be advised to have a 3 month period after discontinuation prior to conception. Contact Specialist Service immediately should pregnancy occur.

BREAST-FEEDING

Leflunomide is not recommended while breast-feeding.

COMMON SIDE EFFECTS

Blood and lymphatic system disorders	Leucopenia
Metabolism and nutrition disorders	Increased creatine phosphokinase (CPK)
Musculoskeletal and connective tissue disorders	Tenosynovitis
Gastrointestinal disorders	Diarrhoea, nausea, vomiting, oral mucosal disorders (e.g. aphthous stomatitis, mouth ulceration), abdominal pain, colitis including microscopic colitis such as lymphocytic colitis, collagenous colitis.
Skin and subcutaneous tissue disorders	Increased hair loss, eczema, rash (including maculopapular rash), pruritus, dry skin.
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Benign neoplasm and neoplasm.
Nervous system disorders	Paraesthesia, headache, dizziness, peripheral neuropathy.
Hepatobiliary disorders	Elevation of liver parameters (transaminases [especially ALT], less often gamma-GT, alkaline phosphatase, bilirubin).
Other very common or common side effects	Mild increase in blood pressure, anorexia, weight loss (usually insignificant) and asthenia.

Action abnormal monitoring results are per NHSG Disease Modifying Anti-Rheumatic Drugs (DMARDs) Monitoring Guidance.

The specialist service should be contacted if there are any patient specific issues or concerns regarding side effects or abnormal results.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

Advice should be obtained from the specialist service if required.

Some important interactions to consider include the following:

- The long half-life of leflunomide means that serious adverse effects and interactions can occur after treatment has been stopped. Additional monitoring is required even after treatment is continued.
- Combination of leflunomide with other hepatotoxic or haematotoxic medicines increases the risk of toxicity.
- Caution is advised when leflunomide is given together with drugs (other than NSAIDs) metabolised by cytochrome P450 such as:
  - phenytoin (enhances the effects)
  - tolbutamide (enhances the effects)
  - warfarin (increases the INR)
- DMARDS - concomitant use with other DMARDs/immunosuppressants is usually not advised. The combinations may be recommended by the relevant specialist service only.
- Alcohol - patients should be advised that alcohol consumption should be avoided or kept well within recommended safe national guidelines, due to the increased potential for liver toxicity.
- Live Vaccines - the use of live attenuated vaccines should be avoided.
- To minimise the risk of skin cancer, exposure to sunlight and ultra violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.

This information is not intended to be a complete list of interactions. For further information consider appropriate reference sources such as SmPC/Vision system.

ADVERSE DRUG REPORTING

If an adverse reaction should occur, inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

- Leflunomide 10 mg Film-coated Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of a concern being raised, the primary care practitioner should contact the referring consultant for the appropriate specialist service via the hospital switchboard, via their secretary, by email or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Registrar for the speciality may be contacted via the switchboard.

Publish: Public	**Applies to:** NHS Grampian	**Version:** 5	
Prepared by: Medicines Management Team and Rheumatology	**Authorised for issue by:** Medicine Guidelines and Policies Group	**Document no:** MGPG/SCA_Leflunomide/ DMARD/1689	
		Effective Date: August 2025 **Review Date:** July 2028	
Signature: Dr Lindsay Robertson **Date:** August 2025	**Signature:** Lesley Coyle **Date:** August 2025	**Supersedes:** MGPG1323, Version 4	
Review/Consultation Group: This document has been reviewed by rheumatology Consultants at ARI and approved by NHSG Medicines Guidelines and Policies Group			