SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR ORAL LEFLUNOMIDE (ADULTS ONLY, NON-RENAL PATIENTS)

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 AND BRAND 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

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
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:
  - Full Blood Count (FBC); liver function tests.
  - LFTs; urea, U&Es; lipids, urinalysis & 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 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 for further details).
- Initiation of therapy and recommendations for dose increments. This should remain under the control of the specialist service.
- Decision on final dose required for patient.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given; patients should be referred to receive these vaccines in accordance with local protocol.

RESPONSIBILITY OF PRIMARY CARE

A Practice agreeing to prescribe Leflunomide should:

- Prescribe medication (by brand name) under the guidance of the Consultant from the relevant specialist service.
- The General Practitioner (GP) has primary responsibility for monitoring according to the Monitoring Schedule for DMARDs.
- 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
  - Be aware of potential drug interactions
- Patients should be asked about the presence of sore throat, abnormal bruising or bleeding at each visit.
- Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
- Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and abnormal results are acted upon promptly.
- Only continue to prescribe medication if it is being satisfactorily monitored.
- 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.
- 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 annual vaccinations in order to ensure patients receiving DMARDs are called yearly by the HSCP teams for required vaccinations.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

- Prescribe medication) under guidance of the relevant specialist service.
- Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- Report any adverse events to consultant and the MHRA using the Yellow Card System.
- If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient's medication.
- If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
- A single dose of pneumococcal polysaccharide vaccine and annual influenza vaccine should be given; patients should be referred to receive these vaccines in accordance with local protocol.

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.

Note: If something unexpected occurs contact on call registrar or Consultant for the appropriate specialty. Notify the consultant if the 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.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

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.
- 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.
- The patient should ensure all blood tests are undertaken at the correct intervals.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

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.
- Serious infections.
- 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 should not be used during pregnancy unless there is no suitable alternative treatment. Discuss with relevant specialist service.

BREAST-FEEDING

Further discussion is required with the relevant specialist service.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

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)

For a full list of the numerous drug interactions with leflunomide, please refer to the current Summary of Product Characteristics (SmPC) available on www.medicines.org.uk

- Live vaccines should be avoided in patients taking leflunomide. Some important interactions to consider include the following:
  - Combination of leflunomide with other hepatotoxic or haematotoxic medicines increases the risk of toxicity.
  - The long half-life of leflunomide means that serious adverse effects and interactions can occur after treatment has been stopped. Additional monitoring is required after treatment is continued.
  - 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) and warfarin (increases the INR).
  - Concomitant use with other DMARDs is usually not advised. The combinations may be recommended by the relevant specialist service only.
- 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.
- 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.

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.

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