

# Leflunomide

ESCA: For the treatment of rheumatoid arthritis or psoriatic arthritis

## AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of leflunomide for rheumatoid arthritis or psoriatic arthritis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with Rheumatoid Arthritis or Psoriatic Arthritis are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

**The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

### RESPONSIBILITIES and ROLES

Specialist responsibilities	
1. Confirm the diagnosis of rheumatoid arthritis or psoriatic arthritis	
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient	
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made	
4. Do baseline monitoring prior to initiation of leflunomide	
5. Initiate treatment and stabilise dose of leflunomide	
6. Review the patient's condition and monitor response to treatment regularly	
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay	
8. Report serious adverse events to the MHRA	
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below)	

General Practitioner responsibilities					
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days					
2. Prescribe leflunomide at the dose recommended					
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement					
GP Prescribing System	Read Code	Description	GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing	SystemOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist					
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment					
6. Refer back to specialist if condition deteriorates					
7. Report serious adverse events to specialist and MHRA					
8. Stop treatment on advice of specialist					

Patient's role	
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment	
2. Share any concerns in relation to treatment with leflunomide with the specialist, clinical nurse specialist or GP	
3. Report any adverse effects to the specialist or GP whilst taking leflunomide	
4. Attend regular outpatient appointments with the specialist	

### BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

**SUPPORTING INFORMATION**

<b>Indication</b>	<p>Leflunomide is indicated for the treatment of adult patients with:</p> <ul style="list-style-type: none"> <li>• active rheumatoid arthritis as a "disease-modifying antirheumatic drug" (DMARD),</li> <li>• active psoriatic arthritis.</li> </ul>	
<b>Dosage and Administration</b> <b>BSR Recommendations</b>	<p>Typical dose is:</p> <p>RA: 10–20 mg once a day when monotherapy is used. In cases of combination therapy with another potentially hepatotoxic DMARD like methotrexate, 10 mg once a day is recommended (therapeutic efficacy may be reduced with the reduced dosage).</p> <p>PsA: 20 mg once a day. But dose may be reduced if there is poor tolerance or adverse effects</p> <p>Loading dose: 100 mg once daily for 3 days may be used to speed up the onset of effect. Unacceptable gastrointestinal (GI) side effects such as diarrhoea may occur when a loading dose is given and this is often omitted in routine practice. A loading dose is not recommended when used as part of combination therapy.</p>	
<b>Renal Impairment</b>	<p>No dose adjustment recommended in patients with mild renal insufficiency.</p>	
<b>Hepatic impairment</b>	<p>Contraindicated</p>	
<b>Contra-indications / Special precautions</b>	<p><b>Contraindications</b></p> <ul style="list-style-type: none"> <li>• Severe immunodeficiency.</li> <li>• Serious infections.</li> <li>• Impaired liver function due to any cause.</li> <li>• Severe unexplained hypoproteinaemia.</li> <li>• Renal impairment (moderate to severe).</li> <li>• Impairment of bone marrow function as indicated by anaemia and cytopenias due to causes other than RA and PsA.</li> <li>• Pregnant women, or women of childbearing potential who are not using reliable contraception during treatment with leflunomide and thereafter as long as the plasma levels of the active metabolite are above 0.02 mg/l. Pregnancy must be excluded before start of treatment with leflunomide.</li> </ul> <p><b>Cautions</b></p> <ul style="list-style-type: none"> <li>• Localised or systemic infection including hepatitis B or C and history of tuberculosis.</li> <li>• Drug potentiation: haematotoxic or hepatotoxic drugs such as methotrexate. Leflunomide SPC states caution if used together with methotrexate it may result in increased risk of hepatotoxicity; therefore, the initiation of leflunomide treatment has to carefully be considered regarding these benefit/risk aspects and closer monitoring is recommended in the initial phase after switching.</li> <li>• The use of leflunomide with antimalarials used in rheumatic diseases (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine and other immunosuppressive agents (with the exception of methotrexate) has not been studied up to now. The risk associated with combination therapy, in particular in long-term treatment, is unknown. Since such therapy can lead to additive or even synergistic toxicity (e.g. hepato- or haematotoxicity), combination with another DMARD (e.g. methotrexate) is not advisable.</li> </ul>	
<b>Side Effects</b>	<b>Common</b>	<p>Leucopenia (leucocytes &gt;2 G/l), mild allergic reactions, CPK increased, paraesthesia, headache, dizziness, peripheral neuropathy, mild increase in blood pressure, diarrhoea, nausea, vomiting, oral mucosal disorders (e.g., aphthous stomatitis, mouth ulceration), abdominal pain, elevation of liver parameters (transaminases [especially ALT], less often gamma-GT, alkaline phosphatase, bilirubin), increased hair loss, eczema, rash (including maculopapular rash), pruritus, dry skin, tenosynovitis, anorexia, weight loss (usually insignificant), asthenia</p>

<b>Monitoring</b>	Pre-treatment Assessment	<ul style="list-style-type: none"> <li>FBC, renal and LFTs</li> <li>Blood pressure               <ul style="list-style-type: none"> <li>If &gt;140/90 mmHg on two consecutive readings 2 weeks apart treat hypertension before commencing the drug</li> </ul> </li> <li>Weight: to allow assessment of weight loss: this may be attributable to leflunomide.</li> </ul>
	After commencing treatment	FBC, LFTs every month for 6 months and, if stable, 2 monthly thereafter. Blood checks should be continued long-term, at least once a month, if co-prescribed with another immunosuppressant or potentially hepatotoxic agent. Blood pressure and weight should be checked at each monitoring visit.
	Disease monitoring	Occasional ESR/CRP helps assessment
	Cessation of treatment (seek advice)	<ul style="list-style-type: none"> <li>Platelets &lt;120,000</li> <li>WBC &lt;3.5</li> <li>N &lt;2.0</li> <li>LFTs 2x upper normal limit</li> <li>Uncontrolled hypertension may rarely be due to leflunomide therapy</li> </ul>
	Dose reduction	<ul style="list-style-type: none"> <li>For side effects, e.g. mouth ulcers, headache, GI upset, rash, recurrent infection</li> <li>For raised blood pressure as above</li> </ul>
<b>Action to be taken: BSR Recommendations</b>	WBC <3.5 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team.
	Neutrophils <2.0 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team.
	Platelets <150 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team.
	AST, ALT between two and three times the upper limit of reference range	If the current dose is more than 10 mg daily reduce the dose to 10 mg daily and recheck weekly until normalised. If the AST & ALT is returning to normal, leave on 10mg a day. If LFTs remain elevated withdraw the drug and discuss with the specialist team.
	AST, ALT more than three times the upper limit of reference range	Recheck LFTs within 72 h, if still more than three times the reference range, stop drug and consider washout
	Rash or itch	Consider dosage reduction with or without antihistamines; if severe, stop and consider washout
	Hair loss	Consider dosage reduction with or without antihistamines; if severe, stop and consider washout
	Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results are available
	Hypertension	If BP >140/90 mmHg treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide and consider washout
	Headache	If severe, consider dosage reduction. If headaches persist, stop and consider washout
	GI upset (nausea, diarrhoea)	If loading dose has been used, give symptomatic treatment. If steady state has been reached, give symptomatic treatment and consider dosage reduction. If symptoms are severe or persistent, stop and consider washout
	Weight loss	Monitor carefully. If >10% weight loss with no other cause identified, reduce dosage or stop and consider washout
	Breathlessness	If increasing shortness of breath occurs, stop leflunomide and consider washout
<b>Washout procedure:</b>	To aid drug elimination in cases of serious adverse effect or before conception, stop treatment and give either cholestyramine 8 g three times daily for 11 days or activated charcoal 50 g four times daily for 11 days; the concentration of active metabolite after washout should be less than 20 µg/l (measured on two occasions 14 days apart) in men and women before conception (consult product literature).	
<b>Important notes</b>	<ul style="list-style-type: none"> <li>Live vaccines should not be administered</li> <li>Influenza and pneumovax vaccines are recommended</li> <li>Leflunomide is contraindicated in pregnancy and would not be continued</li> <li>Patients without immunity who are exposed to chickenpox or shingles should be administered varicella zoster immunoglobulin</li> </ul>	

**Drug Interactions**

**Leflunomide** has the following interaction information:

**Note:** Increased risk of toxicity with other haematotoxic and hepatotoxic drugs

Colestyramine	the effect of leflunomide is significantly decreased by colestyramine (enhanced elimination)—avoid unless drug elimination desired <b>Note:</b> Other drugs should be taken at least 1 hour before or 4–6 hours after colestyramine to reduce possible interference with absorption
Fosphenytoin	leflunomide possibly increases plasma concentration of fosphenytoin
Methotrexate	risk of toxicity when leflunomide given with methotrexate
Phenytoin	leflunomide possibly increases plasma concentration of phenytoin
Rifampicin	plasma concentration of active metabolite of leflunomide possibly increased by rifampicin
Tolbutamide	leflunomide possibly enhances hypoglycaemic effect of tolbutamide
Vaccines	risk of generalised infections when leflunomide given with live vaccines —avoid concomitant use
Warfarin	leflunomide possibly enhances anticoagulant effect of warfarin

**References**

- British Society for Rheumatology (BSR) guidelines
- Arava tablets SmPC
- Leflunomide BNF

I agree to participate in this shared care agreement for the treatment of the below named patient with leflunomide for rheumatoid arthritis and psoriatic arthritis

*General Practitioner*

Name (please print) \_\_\_\_\_ Signature \_\_\_\_\_ Date \_\_\_\_\_

*Hospital Specialist/Consultant*

Name (please print) \_\_\_\_\_ Signature \_\_\_\_\_ Date \_\_\_\_\_

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: