NHS Cumbria Clinical Commissioning Group | North Cumbria University Hospitals NHS Trust | University Hospitals of Morecambe Bay NHS Foundation Trust

SHARED CARE GUIDELINE

Drug: LEFLUNOMIDE

Contact Details	Patient ID Label
Name: _____	**Surname:** _____
Tel ☎: _____	**Forename/s:** _____
Location: _____	**NHS Number:** _____
Date: _____	**Date of Birth:** _____

Introduction	**Indication**: Treatment of active rheumatoid arthritis and psoriatic arthritis. **Background:** Leflunomide is a disease modifying anti-rheumatic drug (DMARD). It inhibits the enzyme dihydroorotate dehydrogenase and thus inhibits pyrimidine biosynthesis. It has immunomodulating/immunosuppressive characteristics, acts as an antiproliferative agent and displays anti-inflammatory properties. Response to treatment cannot be expected before two or three months and may further improve up to four to six months.
Dose & Administration	• 10 – 20mg once daily when used as monotherapy. • 10mg once daily when used in combination with another potentially hepatotoxic DMARD. NB. The loading dose described in the SPC is not given due to a high incidence of GI side-effects.
Secondary Care Responsibilities	1. Discuss the benefits and side effects of treatment with the patient. Ensure that the patient understands which warning signs and symptoms to report. 2. Perform pre-treatment screening (FBC, LFTs, U&Es, blood pressure and body weight). 3. Provide the patient with a monitoring and dosage record booklet and ensure that the patient knows when and where to attend for monitoring. Encourage the patient to take responsibility for ensuring that results of tests are entered in the monitoring booklet. 4. Arrange shared care with the patient's GP once stable. 5. Review the patient regularly to monitor the patient's response to therapy. 6. Request copies of test results for the patient's GP by completing the "copy to" section on the pathology form. 7. Advise the GP on dose adjustments and when to stop treatment. 8. Ensure that clear backup arrangements exist for GPs to obtain advice.
Primary Care Responsibilities	1. Provide the patient with prescriptions for leflunomide. 2. Ensure that the patient understands which warning signs and symptoms to report. 3. Arrange on-going monitoring at the recommended frequencies (see MONITORING below) ensure that test results are recorded in the monitoring booklet. Request copies of test results for the patient's consultant by completing the "copy to" section on the pathology form.

	4. Report any adverse events to the consultant or specialist nurse and stop treatment on their advice or immediately if an urgent need arises (see MONITORING below). 5. Report any worsening of control of the condition to the consultant or the specialist nurse. 6. Refer immediately if a patient discovers she is pregnant whilst taking leflunomide or within 2 years of discontinuation if drug washout has not been performed.
Monitoring Required in Primary Care	• FBC, LFTs, ESR and blood pressure monthly for the first 6 months then, if stable, 2 monthly thereafter. • If Leflunomide is co-prescribed with another immunosuppressant or potentially hepatotoxic drug monitoring should be continued long-term at least once a month. **Laboratory adverse event** **STOP leflunomide and seek advice if:** **WBC** **< 3.5 x 10^9/L** **Neutrophils** **< 2.0 x 10^9/L** **Platelets** **< 150 x 10^9/L** **AST, ALT** **> 2 times the upper limit of reference range**
Washout Procedure	The active metabolite of leflunomide has a long half-life (1 - 4 weeks). To aid drug elimination in cases of serious adverse events, before conception or before switching to another potentially hepatotoxic or haematotoxic DMARD, give colestyramine 8 grams three times daily or activated charcoal 50 grams four times daily for 11 days.
Adverse Effects	• Nausea/diarrhoea: Give symptomatic treatment and consider dose reduction. If symptoms are severe or persistent **STOP** leflunomide and consider washout (see WASHOUT PROCEDURE above). • Weight loss: If >10% weight loss with no other cause identified, reduce dose or stop leflunomide and consider washout. • Decreased resistance to infection: **STOP** leflunomide and consider washout if patient is systemically unwell with significant infection. • **Severe** sore throat or abnormal bruising: Perform FBC and withhold leflunomide until results are available. • Cough or dyspnoea: **STOP** leflunomide and seek advice. Pulmonary infiltration as an acute allergic reaction has been described in a small number of patients taking leflunomide. Patients should be made aware of this rare complication and any patient presenting with an unexplained dry cough or dyspnoea must be referred immediately to the consultant. • Rash or itch: If mild consider dose reduction and/or an antihistamine. If severe **STOP** leflunomide and consider washout. • Hair loss: If mild consider dose reduction. If severe **STOP** leflunomide and consider washout. • Hypertension: Consider dose reduction and/or treatment with anti-hypertensive therapy. If BP remains uncontrolled **STOP** leflunomide and consider washout. • Headache: If severe or persistent **STOP** leflunomide and consider washout.
Common Drug Interactions	• Increased risk of toxicity with other hepatotoxic or haematotoxic drugs. Patients should be advised to limit their alcohol intake well within national limits; BSR guidance suggests 4 - 8 units a week. • The active metabolite of leflunomide inhibits cytochrome P4502C9. Caution is

	advised when leflunomide is given together with drugs metabolised by CYP2C9 such as phenytoin, tolbutamide and warfarin.
Contra-indications	• Severe immunodeficiency • Serious infections • Impaired liver function due to any cause • Severe unexplained hypoproteinaemia • Moderate to severe renal impairment • Impairment of bone marrow function as indicated by significant anaemia and cytopenias due to causes other than RA or PsA • Pregnancy and breastfeeding: Strictly contra-indicated - a pregnancy test is advised in women of child bearing potential prior to starting the drug. Reliable contraception should be used by both men and women whilst on leflunomide and for at least 2 years after stopping leflunomide unless the washout procedure is used (see above and the SPC for further details). • LIVE vaccines should be avoided. • Annual flu vaccine should be given.
This guidance does not replace the SPC's, which should be read in conjunction with this guidance.	