NHS
Telford and Wrekin
Clinical Commissioning Group

Leflunomide
Effective Shared Care Agreement
For use in Rheumatology

Section 1: Shared Care arrangements and responsibilities

Section 1.1 Agreement for transfer of prescribing to GP

Patient details

Name: _____

Address: _____

Date of Birth: _____

NHS number: _____

Specialist:
Address:

Email:

Contact number:

GP
Address:

Email:

Contact number:

Patient

Name:

Contact number:

Agreement to shared care, to be signed by GP and Specialist before prescribing is transferred to GP

Specialist Signature:

Date:

GP Signature:

Date:

Patient Signature:

Date:

Section 1.2: Shared Care responsibilities

This shared care agreement outlines suggested ways in which the prescribing responsibilities can be shared between the specialist and GP. GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient's health remains with the specialist. If a specialist asks the GP to prescribe, the GP should reply to this request as soon as practicable.
Sharing of care assumes communication between specialist, GP and patient.

If a specialist asks the GP to prescribe, the GP should reply to this request within 2 weeks

The prescriber of the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Responsibilities of the specialist initiating treatment

- Discuss with the patient options for treatment and the suitability of Leflunomide
- Discuss the potential benefits and side effects of treatment with the patient
- Undertake baseline tests: **FBC, LFT, U&Es, Creatinine, ESR & CRP, Blood pressure** (on 2 occasions 2 weeks apart-if >140/90 treat before starting leflunomide**, Body weight** (to allow assessment of weight loss that may be attributable to leflunomide)
- Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient. Consultant attaches copy of Shared Care Agreement (SCA) from the trust intranet to printed letter.
- Titrate leflunomide to an effective dose. If both GP and Consultant feel it is appropriate, shared care may be initiated before the patient is stabilised on the effective dose, as long as the dose is stable until the next Consultant appointment
- Or commence treatment with leflunomide and once patient is on a stable dose between visits, consider transfer of prescribing and monitoring to GP.
- Ensure agreed signed shared care form has been received back from GP to indicate that the GP is in agreement with prescribing and monitoring.
- Ensure this has been discussed with patient, and that patient has signed SCA form
- Once patient stabilised, transfer prescribing and monitoring to GP
- Regular follow-up of patient (at least annually)
- Communicate promptly with the GP when treatment is changed
- Advise GP on dosage adjustment and when and how to stop treatment
- Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition and ensure that clear backup arrangements exist for GPs to obtain advice and support
- Report adverse events to the MHRA (via Yellow Card)

Responsibilities of the General Practitioner

- Notify the specialist in writing within 2 weeks if they agree with this Shared Care Agreement.
- Prescribe Leflunomide at agreed dose.
- Arrange and record on-going monitoring as agreed with specialist, **FBC** every month for 6 months and if stable 2 monthly thereafter, **LFT** every month for 6 months and if stable 2 monthly thereafter, **ESR & CRP** every 2 weeks for 6 months then every 8 weeks thereafter, **Blood pressure & Weight** at each monitoring visit. **(Monthly blood tests should continue in the long term if co-prescribed with another immunosuppressant or potentially hepatotoxic agent.)**
- Ensure no drug interactions with other medicines.
- Check patient is using adequate contraception

- Continued prescribing is appropriate for patients attending regular review
- Report adverse events to the MHRA (via Yellow Card)
- Administer influenza vaccine annually unless otherwise advised by the initiating specialist
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia.) - see BNF or Green Book
- Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in nonimmune patients if exposed to chickenpox or shingles.
- Ask about oral ulceration/sore throat, unexplained rash or unusual bruising at every consultation.

Withhold leflunomide and contact the specialist if:

- WBC $<3.5 \times 10^9$/L
- Neutrophils $<2 \times 10^9$/L
- Platelets $<150 \times 10^9$/L
- Oral ulceration/sore throat
- Unusual bruising/unexplained rash
- Severe infections

Other actions to be taken:

- If AST/ALT between 2-3 x upper limit of reference range-reduce dose to 10mg if current dose >10mg daily and recheck weekly until normalised. If AST/ALT returning to normal leave on 10mg daily. If LFTs remain elevated withdraw drug and discuss with specialist team.

- If AST/ALT >3 times upper limit of reference range, recheck LFTs within 72 hours, if still more than 3X upper limit, stop drug and contact specialist.

- If rash or Itch consider reducing dose (with or without antihistamines). If severe, stop drug and contact specialist.

- Hair Loss, consider reducing dose, if severe, stop drug and contact specialist.

- BP>140/90 treat in line with NICE guidance, if BP uncontrolled, stop drug and contact specialist.

- Headache, consider dose reduction, if persists stop drug and contact specialist

- GI upset, give symptomatic treatment and consider dose reduction. If symptoms persist stop drug and contact specialist.

- Weight loss, monitor carefully and if >10% (with no other cause identified) reduce drug or stop drug and contact specialist.

- Breathlessness, if increasing shortness of breath, stop drug and contact specialist.

Responsibilities of the patient

- To take the prescribed medication regularly unless advised by GP or specialist
- To attend scheduled appointments with consultant and GP and for monitoring as detailed above
- Report any adverse effects to the consultant or GP.
- Share any concerns in relation to treatment.
- Report to the consultant or GP if they do not have a clear understanding of the treatment

Section 2: General Information on Leflunomide

Licensed Indication

- **Active rheumatoid arthritis**

- **Active psoriatic arthritis in adults**

Dosage and administration

A typical dose regimen may be:-

Rheumatoid arthritis
10-20mg once a day when monotherapy is used. In cases of combination therapy with another potentially hepatotoxic DMARD like methotrexate, 10mg once a day is recommended (therapeutic efficacy may be reduced with the reduced dosage).

Psoriatic arthritis
20mg once a day

Contraindications

- Hypersensitivity to the active substance (especially previous Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) or to any of the excipients.
- Patients with impairment of liver function.
- Patients with severe immunodeficiency states, e.g. AIDS.
- Patients with significantly impaired bone marrow function or significant anaemia, leucopenia, neutropenia or thrombocytopenia due to causes other than rheumatoid or psoriatic arthritis.
- Patients with serious infections
- Patients with moderate to severe renal insufficiency, because insufficient clinical experience is available in this patient group.
- Patients with 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 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.
- Breast-feeding women

Side effects

Nausea can occur at any time during therapy. The symptom may resolve with dose reduction from 20mg to 10mg and/or addition of anti-emetic

.

Diarrhoea: occurs in approximately 20% of patients and is sometimes self-limiting.
May respond to dose reduction or to loperamide/codeine phosphate.

Hypertension: mild increases in blood pressure are common. BP increases tend to affect those with pre-existing hypertension and may require additional antihypertensive therapy or cessation of treatment.

Decreased resistance to infection: especially respiratory/urinary tract or shingles/chickenpox. Temporarily withhold leflunomide if patient is systemically unwell with significant infection requiring anti-infective intervention (a washout procedure may be necessary if severe or persistent infection occurs). If in doubt, discuss with specialist.

Pulmonary Infiltration/ Reactions: Pulmonary infiltration as an acute allergic reaction has been described in a small number of patients, after starting leflunomide. Patients should be made aware of this rare complication (see Drug SPC).

Alopecia: diffuse hair loss may occur in up to 10% of patients. It is usually mild and is reversible on stopping medication. May respond to dose reduction.

Rash/skin itch: if mild, continue full dose and monitor. If moderate or severe, stop treatment and discuss with specialist (washout may be necessary).

Alcohol: patients are advised that alcohol consumption should be avoided or kept to a minimum, due to the increased potential for liver toxicity.

Pregnancy and breastfeeding- It is important that women of childbearing potential do not start leflunomide until pregnancy has been excluded and both men and women must use reliable contraception. If, during treatment, there is a delay in onset of menstruation or other reason to suspect pregnancy then the patient must notify their GP and specialist as soon as possible. It is possible that rapidly lowering the blood level of the active metabolite through the drug washout procedure the risk to the foetus may be reduced. Male and female patients should not procreate within two years of discontinuing leflunomide. Blood concentrations of its active metabolite should be measured two years after discontinuation before pregnancy occurs (this waiting time may be reduced by using the drug washout procedure).

Women must not breastfeed while they are taking leflunomide

Drug Interactions[1]

Caution is advised when leflunomide is given together with drugs (other than NSAIDs) metabolised by cytochrome P450 2C9 such as **phenytoin** and **warfarin**.

(Leflunomide has an extremely long elimination half-life and interactions with these drugs and other DMARDs may occur even after leflunomide has been discontinued)

Co-prescription of drugs with potential hepatotoxic or nephrotoxic effects is also inadvisable.

If combined with methotrexate there may be an increased risk of hepatotoxicity and more frequent monitoring may be necessary.

Alcohol should be avoided due to increased risk of hepatotoxicity.

Live Vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided.

Washout Procedure.

To aid drug elimination, in case of serious adverse effect, or before starting another DMARD, or before conception, stop treatment and give either colestyramine 8g 3 times daily for 11 days or activated charcoal 50g 4 times daily for 11 days: the concentration of the active metabolite after washout should be less than 20 micrograms/litre (measured on 2 occasions 14 days apart) in men or women before conception

[1] BNF 66 September 2013-March 2014