Attach Patient Banda Label here

Coventry & Warwickshire Area Prescribing Committee

Shared Care Agreement

Leflunomide: *for treatment of rheumatoid arthritis and psoriatic arthritis*

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement (SCA) outlines suggested ways in which the responsibilities for managing the prescribing of **Leflunomide** can be shared between the specialist and general practitioner (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 for the diagnosed condition remains with the specialist.
If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

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

Specialist Responsibilities

1. Discuss with the patient options for treatment and the suitability of Leflunomide.
2. Discuss the potential benefits and side effects of treatment with the patient.
3. Explain the intention to share care with the patient/ carer
4. Following agreement with the patient, initiate Leflunomide seek to initiate shared care.
5. Ask the GP whether he or she is willing to participate in shared care by emailing the shared care request letter, (continue to prescribe until GP has agreed to take over prescribing).
6. Perform monitoring of FBC, U&Es, LFTs, albumin, CRP, eGFR, VZV specifying frequency of blood monitoring and communicate the results with the GP.
7. Initiate and stabilise treatment. Supply 3 months (in instalments as appropriate).
8. Communicate to the GP the established regimen and when to refer back to specialist care.
9. Inform GP and patient of dosing adjustments.
10. Have a mechanism in place to receive rapid referral of a patient from the GP in event of abnormal blood results or deteriorating clinical condition.
11. Ensure clear backup arrangements exist for GPs to obtain advice and support and be available for review if requested.

Report adverse events to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard, and to the GP and appropriate Medicines Optimisation team.

General Practitioner Responsibilities

1. Reply to the request for shared care as soon as practicable, preferably within 2 weeks, by emailing back the shared care letter. If declining the request please indicate the reason for declining.
2. Adjust the dose as advised by the specialist.
3. Check for possible drug interactions when prescribing new medication and avoid prescribing interacting drugs.
4. To ensure blood forms issued by secondary care are used for routine blood test monitoring and if necessary patient to attend surgery for blood tests as specified on pre-printed blood form. Record BP on booklet issued by rheumatology.
5. Ensure that blood pressure and weight monitoring is arranged every 12 weeks or at dose increases for the duration of the treatment i.e. request patient to phone in or arrange consultation.
6. Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
7. Refer the patient to the specialist if his/ her condition deteriorates.
8. Stop treatment on the advice of the specialist.

Report adverse events to the MHRA on a Yellow Card (www.mhra.gov.uk/yellowcard), the specialist, and the appropriate Medicines Optimisation team.

Patient/carer's Rrole

1. Attend follow up and other appointments.
2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Agree to routine blood monitoring, blood pressure and weight monitoring every 12 weeks or at dose increase for the duration of treatment. Ensure that you make appointments for blood testing and BP/weight monitoring. Agree with your GP on the best approach to ensuring that this is done.
4. Inform specialist if you feel you are having problems taking your medication or have stopped taking it.
5. Inform specialist or GP of any other medication being taken, including over-the-counter products.
6. Report any adverse effects or warning symptoms to the specialist or GP.

The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card , available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours).
The form can also be downloaded from www.mhra.gov.uk/yellowcard

This SCA should be read in conjunction with the Summary of Product Characteristics (SPC) and the current edition of the British National Formulary

Back-up Advice and Support: See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care.

SUPPORTING INFORMATION:

Licensed indications: Leflunomide is licensed for the treatment of adult patients with active rheumatoid arthritis (RA) as a disease-modifying anti-rheumatic drug (DMARD) and for the treatment of active psoriatic arthritis (PsA).

Dosage and administration: Leflunomide therapy is initiated with an oral loading dose of 100 mg/day for 3 days. The maintenance dose is 10 to 20 mg/day for RA and 20 mg/day for PsA.

A washout period should be followed when switching to another hepato- or haematotoxic drug (e.g. methotrexate), or in cases of acute leflunomide toxicity (see the [SPC] for more details). A therapeutic effect usually starts at 4-6 weeks and may further improve up to 4 - 6 months.

Monitoring: Pre-treatment Assessment: Height, weight, blood pressure, FBC, U&Es, LFTs, albumin, eGFR, CRP, VZV checked and results must be back before treatment commences.

After commencing treatment: Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity.

Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Monitor BP and weight every 12 weeks or at dose increase.

Monitoring of combination DMARD therapy (e.g. methotrexate and leflunomide) is monthly for 12 months then patients who have been stable can be considered for reduced frequency monitoring on an individual patient basis.

Interruption of Treatment: Contact rheumatology team urgently and withhold treatment if any of the following develop: white cell count <3.5 x 10^9/l; mean cell volume >105 Fl and if B12 or folate low start supplementation; neutrophils <1.6 X 10^9/l; creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min; unexplained eosinophilia >0.5 X10^9/l; ALT and/or AST >100 U/l; If ALT elevations of more than 2-fold the upper limit persist, or more than 3-fold the upper limit of normal are present, leflunomide treatment must be discontinued and wash-out procedures initiated.

The SPC recommends that monitoring of liver enzymes be continued after discontinuation of treatment until liver enzyme levels have normalised.
platelet count <140 X10^9/l; unexplained reduction in albumin <30 g/l

During a serious infection, Leflunomide should be temporarily discontinued until the patient has recovered from the infection.

Dose reduction: If WBC <3.5 x 10^9/l, Neutrophils <2.0 x 10^9/l: Halve dose
Reduce dose if patient suffering from nausea, rash or recurrent infections.
If ALT (SGPT) elevations of 2- to 3-fold the upper limit of normal occur then the dose can be reduced from 20 mg to 10 mg and monitoring must be performed weekly.

Contra-indications: Leflunomide must not be used in patients with Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiforme. Leflunomide is also contraindicated in patients with impaired immune, liver or bone marrow function; serious infections, or severe hypoproteinaemia. See the SPC for further details.

Pregnancy: Contraindicated (the active metabolite is suspected of causing serious birth defects). Not to be used in women of child bearing age who are not using contraception.

Side effects: The most common adverse events with leflunomide treatment in clinical trials were gastrointestinal effects, pruritus, rash, hypertension, alopecia and liver enzyme elevations. Post-marketing, there have been rare reports of serious hepatic reactions and pancytopenia. See the SPC for more details on adverse events.

Leflunomide does not have black triangle (▼) status. All serious suspected adverse reactions (even well recognised or causal link uncertain) should be reported to the MHRA.

Drug interactions: Recent treatment with hepatotoxic or haematotoxic (eg.methotrexate) drugs may result in increased side effects; care should be taken when initiating leflunomide therapy. Switching to another DMARD after leflunomide treatment may raise the possibility of additive risks because of its long half-life. A washout period is required.

Patients treated with leflunomide should not receive concomitant treatment with cholestyramine or activated powdered charcoal, because this leads to rapid and significant decreases in plasma leflunomide concentration.

Cost: At current prices one year's treatment of 10 mg to 20 mg daily will cost £85.04 to £91.49 (Prescription Pricing Division (PPD). NHS Business Services Authority. Drug Tariff March 2018. Accessed 6.3.18 via www.nhsbsa.nhs.uk)

References:

1. Summary of Product Characteristics. Leflunomide. Last updated 26.8.16. Available via www.medicines.org.uk accessed 14/8/172.
2. Ledingham J, Gullick N, Irving N et al. on behalf of the BSR and BHPR Standards, Guidelines and Audit Working Group; BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, Rheumatology, Volume 56, Issue 6, 1 June 2017, Pages 865–868. Available at https://academic.oup.com/rheumatology/article/56/6/865/3053478/BSR-and-BHPR-guideline-for-the-prescription-and