Whittington Health NHS

Rheumatology Department
Magdala Avenue
London N19 5NF

Consultants:
Prof. J. Dacre
Dr. I. Wamuo
Dr L. Congi
Dr A. Nuttall
Dr E. Nikiphorou

Switchboard 020 7272 3070
Main Appts: 020 7288 5511
Secretaries: 020 7288 5259/5740

Rheumatology Nurse 02072885257

Rheumatology Clinic 3D: Ext: 5708

British Society of Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR); (Feb, 2017) recommends harmonisation of monitoring schedules, for all DMARDs that require laboratory monitoring. These should follow the same frequency of testing.

PROTOCOL FOR THE ADMINISTRATION OF LEFLUNOMIDE – INFORMATION FOR GENERAL PRACTITIONERS

BACKGROUND FOR USE

Leflunomide is a disease modifying anti rheumatic drug of proven benefit in the treatment of Rheumatoid Arthritis and other inflammatory arthritis. The therapeutic effects start around 6-8 weeks and may further improve after several months. Leflunomide should only be initiated on the recommendation of a Rheumatologist.

DOSAGE REGIME

Typical dose is 10 -20 mg daily. A loading dose is NOT required. There is no dose adjustment required in patients over 65yrs or those with mild renal insufficiency. If used in combination therapy 10mg daily is recommended. This drug has a long elimination half-life of several weeks, so specific 'wash out' measures may be necessary in cases of significant adverse reaction.

For details, contact Rheumatology Dept.

PRETREATMENT ASSESSMENT BY RHEUMATOLOGIST

• FBC, LFT, U&Es, ESR and CRP and blood pressure.

If BP>140/90 on 2 occasions 2 weeks apart, treat hypertension before commencing leflunomide.

• Weight (to allow assessment of weight loss)

• Pregnancy must be excluded before starting treatment with leflunomide.

MONITORING

- • FBC, Creatinine, Calculated GFR, ALT, AST ; two weekly for six weeks then, once on stable dose, monthly for three months.
- Thereafter, FBC, Creatinine, Calculated GFR, ALT, AST and Albumin, at least every 12 weeks.
- More frequent monitoring is appropriate in patients at higher risk of toxicity
- Combination therapy of Methotrexate and Leflunomide require monitoring to be extended for a longer term. **– (extend monthly monitoring beyond 6 months)**

• Blood pressure and weight should also be recorded at each blood test.

Please note that in addition to absolute values for haematological and biochemical indices a rapid fall/rise or a consistent downward/upward trend in any value should prompt caution and extra vigilance. See below for specific actions.

• NSAIDs may be continued

NOTABLE DRUG INTERACTIONS (refer to British National Formulary and Summary of Product Characteristics)

• Leflunomide has a long elimination half-life and interactions with some drugs may continue for at least 8 weeks after leflunomide has been discontinued.

• May increase plasma concentrations of warfarin, phenytoin and tolbutamide.

• Monitor INR closely in warfarin treated patients

• Rifampicin increases leflunomide levels

Side effects	Actions
WBC < 3.5 X 10^9/l Neutrophils <2.0 X 0^9/l Platelets <150 X 10^9/l	Stop leflunomide and repeat WBC. If repeat count abnormal discuss with rheumatologist
Liver function > 2 fold rise in AST/ALT (from upper limit of reference range) but < 3-fold	If on 20mg/day reduce dose to 10mg/day. Recheck AST/ALT weekly until normalised and maintain at 10mg/day. If ALT/AST remains elevated withhold until

AST/ALT > 3 fold rise from upper limit of reference range	discussed with rheumatologist. STOP drug. Recheck LFTs after 1 week. Discuss with Rheumatologist If persistent consider washout*.
Hypertension	If B/P > 140/90 Treat as per NICE guidance. If B/P remains uncontrolled, consider drug discontinuation. Discuss with rheumatologist any patient not responding to treatment.
Rash or severe mouth ulcers	Do urgent FBC. Consider dose reduction. Consider antihistamine. If severe stop drug, discuss with rheumatologist to consider washout*.
Severe sore throat, abnormal Bruising	Severe sore throat, abnormal bruising do immediate FBC and withhold until result of FBC available.
GI upset/nausea, diarrhoea	In 1 in 200 patients. Usually settles, but if severe may require reduction in dose/discontinuation of the drug with or without washout procedure*.
Weight loss	If severe consider dosage reduction
Alopecia	Most cases are mild/ moderate and resolve during treatment. If severe consider dosage reduction
Increasing breathlessness or persistent dry cough	Pneumonitis reported but rare. Stop and discuss with Rheumatologist. Consider washout**.***

CONTRAINDICATIONS AND PRECAUTIONS

Vaccination with LIVE vaccines	Patients receiving leflunomide must NOT receive immunization with LIVE vaccines. Inactivated polio is available although sub-optimal response may be seen.
Chicken pox /Shingles	Patients suffering from chickenpox or active skin lesions in shingles withhold leflunomide and inform rheumatologist Exposure to chickenpox or shingles passive immunization should be carried out using VZIG
Pregnancy and breast feeding	Leflunomide is teratogenic and must not be given to women of childbearing potential unless reliable contraception is used. Women planning to have children should either discontinue the drug for 2 years prior to conception or have rapid removal of its active metabolite by following the washout procedure. Blood concentrations should be checked prior to planned pregnancy. Breast feeding should be avoided. Men should use effective contraception for 3 months after stopping leflunomide.

Alcohol	Avoid if co-prescribed with hepatotoxic drug
Pulmonary infiltration /reactions	Acute allergic reactions rarely occur. Added risk when used in combination with methotrexate. Stop leflunomide and discuss with Rheumatologist.

- **FLU AND PNEUMOCOCOCCAL VACCINES ARE RECOMMENDED FOR PATIENTS ON IMMUNOSUPRESSIVE THERAPY**

***Washout Procedure:**

Cholestyramine 8g is administered 3 times daily. Alternatively, 50g of activated powdered charcoal is administered 4 times daily. Duration of a complete washout is usually 11 days. The duration may be modified depending on clinical or laboratory variables.

REFERENCE:

https://academic.oup.com/rheumatology/article/3053478/BSR-and-BHPR-guideline-for-the-prescription-and

http://www.rheumatology.org.uk/about_bsr/press_releases/bsr_publishes_updated_guideline_nonbiologic_dmards.aspx