Heatherwood and Wexham Park Hospitals NHS
NHS Foundation Trust

Department of Rheumatology

Leflunomide

Oxford and Berkshire Regional Rheumatology Guidelines

To be read in conjunction with the shared care agreement between Oxfordshire and Berkshire Primary Care Trusts and the Rheumatology Department.

Leflunomide is a disease modifying anti rheumatic drug of proven benefit in the treatment of rheumatoid arthritis and other inflammatory arthritides. The therapeutic effects start after 8-12 weeks and may further improve after several months. Leflunomide should only be initiated on the recommendation of a rheumatologist.

Dosage.
Typical dosage 10- 20mg daily. 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.

Pre-treatment assessment
FBC, LFT, U&E's, ESR, CRP and blood pressure. If BP is > 140/90 on 2 consecutive readings 2 weeks apart; treat hypertension before commencement. Baseline measurement of weight.
Pregnancy must be excluded before starting treatment with Leflunomide.

Monitoring
FBC, U&Es, ESR, CRP, LFTs, BP and weight every 2 weeks for 6 months and if stable 2 monthly thereafter.
Monitoring must be monthly when used in combination with another immunosuppressant or potentially hepatotoxic agent such as Methotrexate.

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance

Side effects	**Actions**
WBC < 3.5 X 10^9/l Neutrophils <2 X 0^9/l	Stop leflunomide and repeat WBC. If repeat count is normal continue, if abnormal discuss with specialist team.
Platelets <150 X 10^9/l	Stop leflunomide and repeat WBC. If repeat count is normal continue, if abnormal discuss with specialist team.
Liver function > 2 fold rise in AST/ALT (from upper limit of	Strict monitoring of LFT's is essential due to hepatotoxicity. Caution is necessary when used

reference range)	concomitantly with other hepatotoxic medication eg MTX or if evidence current or recent hepatitis B or C infection. If on 20mg/day reduce dose to 10mg/day. Recheck weekly until normalised and maintain at 10mg/day. If ALT/AST remain elevated withhold until discussed with specialist rheumatology team. If persistent consider washout
AST/ALT > 3 fold rise from upper limit of reference range	Stop drug, Re-check LFTs within 72 hours. If persistent consider washout.
Renal Impairment. i.e eGFR <30 mls minute	Reduce dose by 50% Increase frequency of monitoring
Hypertension	If B/P > 140/90 Treat according to NICE guidance. If B/P remains uncontrolled, discontinue drug. Discuss with specialist team any patient not responding to treatment.
Rash or severe mouth ulcers	Consider dose reduction with or without antihistamines. If severe stop and consider washout procedure,
Severe sore throat, abnormal bruising	Immediate FBC and withhold until result of FBC available
GI upset/nausea, diarrhoea	Is not uncommon, usually settles, but if severe may require reduction in dose/discontinuation of the drug with or without washout procedure.
Weight loss	If greater than 10% with no identified cause, reduce or discontinue with or without washout.
Headache	If severe consider dosage reduction
Alopecia	Most cases are mild/ moderate and resolve during treatment. If severe consider dosage reduction
Tenosynovitis and rarely tendon rupture.	Discuss with specialist team. .

Notes:

- Pneumovax and annual flu vaccinations are recommended.
- NSAID's may be continued

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.
Pregnancy and breast feeding	Leflunomide is teratogenic and must not be given to women of child bearing 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. Men should also receive the washout and use effective contraception for 3 months after stopping leflunomide prior to planning to conceive. Notify pharmaceutical company in the event of pregnancy. Breast feeding is contra-indicted
Chicken pox /Shingles	Patients suffering from chickenpox or active skin lesions in shingles withhold leflunomide and inform specialist team. Exposure to chickenpox or shingles passive immunization should be carried out using VZIG
Alcohol	Limit alcohol intake to 4-8 units per week
Infection	Vigilance required in detection and treatment
Pulmonary infiltration /reactions	Acute allergic reactions can occur. Added risk when used in combination with methotrexate. Patients should be made aware of this rare complication.

Washout procedure

We advise referral back to rheumatology. After stopping Leflunomide

- Cholestyramine 8G is administered 3 times daily for a period of 11 days
- Alternatively 50 g of activated charcoal is administered 4 times daily for a period of 11 days.

Before conception 2 blood tests are required for men and women, 14 days apart to check plasma levels, which must drop below 0.02mg/l. This is a free service through Aventis Pharma.Ltd. To request a lab form call 01732 584493.

Notable Drug Interactions (refer to BNF and SPC)

- Phenytoin, /tolbutamide: leflunomide may enhance the effects.
- **Warfarin**; monitor INR closely
- NSAID's may be used

Leflunomide has an extremely long elimination half-life and interactions with these drugs may continue for at least 8 weeks after leflunomide has been discontinued.

Contact telephone Numbers

Heatherwood and Wexham Park Hospital	**01753 633000** **Bleep Rheumatology registrar**
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