Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

CUH
Ospidéal Ollscoile Chorcaí
Cork University Hospital

Department of Rheumatology

Leflunomide (Arava)
GP Information Sheet

Leflunomide
Leflunomide is an immunomodulatory agent which arrests activated lymphocytes thought to be involved in inflammatory arthritis pathogenesis. The active metabolite has a long half-life usually 1-4 weeks.

Pre Treatment Assessment
FBC, LFT, U&E and blood pressure

Administration:
Oral - the tablets being swallowed whole with plenty of water. Absorption not affected by food.

A typical dose regime is:
10mg or 20mg daily depending on disease severity and patient toleration.

Precautions and Contraindications
Leflunomide may inhibit the metabolism of **warfarin** and **phenytoin.** It has an extremely long elimination half-life and interaction with these drugs and with other DMARDs may occur even after Leflunomide has been discontinued. **Therefore patients on warfarin and Leflunomide will require careful monitoring of INR levels**.

If a severe and undesirable side-effect occurs a washout procedure is available that will rapidly remove its active metabolite. This involves administration of cholestyramine 8g three times a day or activated charcoal 50g five times a day.

Male and female patients should not procreate within two years of discontinuing Leflunomide. Effective contraception is essential in women during treatment and 2 years post treatment. Contraception is essential in men for 3 months after treatment (after washout period). Blood concentrations of its active metabolite should be measured 2 years after discontinuation before pregnancy occurs.

Leflunomide is contraindicated in patients with liver impairment or moderate to severe renal failure, severe immunodeficiency states, for example AIDS and severe hypoproteinemia, for example nephrotic syndrome.

Time to Response
Begins after 4-6 weeks, but improvements may continue for 4-6 months.

Monitoring
FBC, LFT's and BP check monthly for 3 months then every 3 months thereafter

Actions to be taken

Neutrophils <2.0* 10^9/1	Hold drug and repeat in 2 weeks
Platelets <150* 10^9/1	

>2 but <3 fold rise in ALT or AST (from upper limit of reference range)	Reduce dose and monitor
>3 fold rise	Hold Leflunomide and repeat LFT within 2-4 weeks

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

Eczema, dry skin, itching, uticaria, oral ulceration and alopecia, (Diffuse hair loss may occur in about 10% of patients, usually reversible on dose reduction or discontinuation*)*

NB In case of ulceration stomatitis, stop treatment. If Stevens-Johnson syndrome or toxic epidermal necrolysis occur treatment should be stopped. A complete washout is essential in such cases.

Haematological: Leucopenia, anaemia mild thrombocytopenia, eosinophilia and rarely agranulocytosis.

Gastrointestinal: Nausea, vomiting, anorexia, abdominal pain, taste disturbance and diarrhoea (usually self-limiting)

Hepatic: Hepatotoxicity, pancreatitis, severe liver dysfunction rare but small LFT elevation more common. **Patients should be advised that alcohol consumption should be avoided, or kept to a minimum.**

Nervous System: Headaches, dizziness, asthenia, parasthesia, insomnia, migrane, vertigo and anxiety**.**

Musculo-Skeletal System: Tenosynovitis, tendon rupture**.**

Cardiovascular: Hypertension may occur in about 10% of patients. Pre-existing hypertension predisposes**.**

Allergic Reactions: Mild allergic reactions may occur (rash, pruritis urticaria). Anaphylaxis rare.

Infection: Severe infection may necessitate stopping the drug and administering a washout. Patients with previous TB need careful monitoring as there is increased risk of reactivation.

Vaccinations: No clinical data is available on the efficacy and safety of vaccinations and Leflunomide treatment.

Vaccination with live vaccine is therefore not recommended. The prolonged half-life of Leflunomide should be considered when contemplating live vaccine after stopping the drug.

Please consult up to date relevant literature (data sheets) or BNF when prescribing this agent. Please contact the Rheumatology team if you have any other queries regarding the prescribed medication.

Contact Details

Dr. S. Harney, Consultant Rheumatologist *(secretary):* (021) 4922422
Dr. J. Ryan, Consultant Rheumatologist *(secretary):* (021) 4922468
Dr. G. Murphy, Consultant Rheumatologist *(secretary):* (021) 4922468
Louise Murphy, Candidate ANP in Rheumatology: (021) 4920266
Joan Swan, Clinical Nurse Specialist in Rheumatology: (021) 4922645
Davida Hehir, Clinical Nurse Specialist in Rheumatology: (021) 4234511