

GUIDELINE FOR THE PRESCRIPTION AND MONITORING OF LEFLUNOMIDE FOR THE RHEUMATIC DISEASES

Henry Aaverns

This shared care guideline sets out details for the sharing of care of patients with rheumatoid arthritis prescribed *leflunomide*. These guidelines provide additional limited information necessary to aid in the treatment of rheumatology patients. As with all shared care guidelines these highlight significant prescribing issues but should be used in conjunction with the summary of product characteristics (Data sheet) and **do not** replace the companies information .

INTRODUCTION/BACKGROUND INFORMATION

INDICATION FOR THE PURPOSES OF THIS GUIDELINE

Treatment of rheumatoid arthritis and psoriatic arthritis

DOSAGE

The dose is 10mg to 20mg once daily. Loading doses are not used so commonly any more

The tablet should be swallowed whole with a sufficient amount of fluid.

CONTRAINDICATIONS

- Significant renal or liver impairment
- Serious infection
- Severe immunodeficiency states
- Significantly impaired bone marrow function or blood disorders due to causes other than rheumatoid arthritis
- Severe hypoproteinaemia
- Under the age of 18 years
- Breastfeeding
- Pregnancy - it should not be given if there is a risk of pregnancy or if the patient (male or female) wishes to consider starting a family in the near future. Patients should be advised that a washout and blood tests to measure the levels of active metabolite might need to be carried out for up to 2 years before confirming drug elimination.

PRECAUTIONS:

- Note alcohol consumption. It is recommended that alcohol should be avoided during leflunomide therapy. However, pragmatic advice would be to suggest a maximum limit of 10 units per week.
- Increase vigilance when co-prescribing other hepatotoxic drugs (increased risk of liver problems)
- Combination with other DMARD drugs should not be considered without specialist advice

MONITORING

PRIOR TO STARTING THERAPY :

- CBC,
- liver and renal function,
- blood pressure.

ONGOING MONITORING -

- CBC,
- liver and renal function,
- blood pressure should be measured fortnightly for the first six months and monthly thereafter. N.B. A rise in blood pressure does not necessitate stopping treatment but should be treated with conventional antihypertensives.
- To monitor disease activity, a 3 monthly CRP would be helpful

Patients can have treatment discontinued abruptly. However, it is important to note that leflunomide has a long half-life. If necessary a ‘washout’ procedure can be carried out:

WASHOUT PROCEDURE

Cholestyramine 8g is administered three times daily for a period of 11 days

ALTERNATIVELY

- 50g of activated powdered charcoal is administered four times daily for a period of 11 days
- If the washout is being performed due to unexpected pregnancy or wish to start a family, two blood tests to measure the levels of the active metabolite of leflunomide, at least two weeks apart, should be carried out to confirm drug elimination. For those wishing to start a family, a further one and a half months waiting period is then recommended.
- Additional contraceptive precautions (barrier method) should be taken.

STOP AND REFER TO THE RHEUMATOLOGY TEAM IF:

- WCC falls on 3 successive occasions and/or WCC falls below 3.5×10^9
- Platelet count falls on 3 successive occasions

- Platelet count falls below 150×10^9
- Liver enzymes especially transaminase increased x 3 upper limit of normal. When LFTs returned to normal value, recommence treatment and repeat blood tests after one week.
- Consecutive fall in albumin – seek specialist opinion
- Hypertension resistant to treatment and dose reduction
- Renal impairment
- New evidence of dyspnoea or cough
- Severe, uncontrolled infection
- Severe nausea or diarrhoea
- Severe mouth or genital ulceration
- Severe skin reactions

SIDE EFFECTS

Patients must report mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count, liver function tests, urea and electrolytes.

Reports of dyspnoea or cough should be investigated for interstitial lung disease.

N.B. If dizziness impairs ability to concentrate and react, the patient should refrain from driving and using machines

(Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare)

Very common/Common:

- GI disturbances especially diarrhoea (usually settles)
- Bone marrow suppression
- Anorexia, weight loss (usually insignificant)
- Headache, dizziness, paraesthesia
- Hypertension
- Elevation of liver enzymes rarely hepatitis (transaminases, less often gamma-GT, alkaline phosphatase, bilirubin), Uric acid level decrease
- Increased hair loss, eczema, dry skin, pruritus
- Uncommon
- Anaemia, Hypokalaemia, Mild hypophosphataemia, Hyperlipidaemia
- Anxiety
- Taste disturbances
- Urticaria

Very Rare

- Interstitial lung disease.
- Severe infections
- Severe anaphylactic/anaphylactoid reactions, vasculitis
- Peripheral neuropathy
- Pancreatitis

- Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme
- Recent, concomitant or consecutive use of potentially myelotoxic agents may be associated with a higher risk of haematological effects.
- The risk of malignancy, particularly lymphoproliferative disorders, is increased with use of some immunosuppressive agents.

COMMON/SIGNIFICANT DRUG INTERACTIONS

- N.B. The long half-life of leflunomide means that serious adverse effects/interactions may occur after the treatment with leflunomide has been stopped
- Warfarin, Phenytoin and Tolbutamide (and other drugs metabolised by cytochrome CYP2C9) should be prescribed with caution and regular monitoring should occur.
- Vaccinations - no data available on efficacy and safety of vaccines under leflunomide treatment, live attenuated vaccines should be avoided. NB. Long half-life of Leflunomide should be considered when giving live vaccines after stopping treatment. For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients or <http://www.rheumatology.org.uk/guidelines/clinicalguidelines/vaccineguideline>.

Notes

Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

REFERENCES

Summary of Product Characteristics Avaraâ January 2006. <http://emc.medicines.org.uk/>
British Society of Rheumatologists Guidelines July 2000.

<http://www.rheumatology.org.uk>

BNF 50

Stockley Drug Interactions 7th ed.

Date of Issue **March 2008**; Review Date **Sept 2013**