Shared care guidelines

Drug: **LEFLUNOMIDE**

Specialty: *RHEUMATOLOGY*

Indication: RHEUMATOID ARTHRITIS OR PSORIATIC ARTHRITIS

Overview

Leflunomide is a disease-modifying anti-rheumatic drug, similar in efficacy to sulfasalazine and methotrexate. Adverse effects include myelosuppression, hepatotoxicity & rarely pneumonitis.

Hospital specialist's responsibilities

Initial screening: FBC, ESR/CRP, U&E, eGFR, creatinine, LFTs, BP & weight. Assessment for comorbidities such as lung disease and occult viral infection.

Initial regimen: 10 to 20 mg orally, once daily.

Clinical monitoring: For adverse effects and usual disease management.
Frequency: As required, typically every 3-6 months once stable.

Safety monitoring: FBC, ESR/CRP, U&E, eGFR, creatinine, LFTs, BP & weight
Frequency: Fortnightly for 6 weeks, then every month for 3 months, then every 3 months thereafter (or every month if co-prescribed with another immunosuppressant).
Monitor fortnightly for 6 weeks following any dose increase.

Prescribing arrangements: Initiated in hospital, transferred to GP after 3 months when stable

Documentation: Clinic letters and results to GP. Separate patient information and offer patient-held shared care diary.

GP's responsibilities

Maintenance prescription: 10 to 20 mg once daily as advised at transfer

Clinical monitoring: for adverse effects and usual disease management
Frequency: as required and determined by patient symptoms

Safety monitoring: FBC, ESR/CRP, U&E, creatinine, eGFR, LFTs, BP & weight 3 monthly (or monthly if co-prescribed with another immunosuppressant). Monitor fortnightly for 6 weeks following any dose increase

Duration of treatment: Long-term as recommended by specialist

Documentation: Practice records. Correspondence with specialist as required. Copies of blood results to specialist using shared care diary or available via webICE.

Adverse events

Adverse Event	Action required
WCC ↓<3.5 x10^9/L or Neutrophils ↓<1.6 x10^9/L Platelets ↓ <140 x10^9/L	Stop leflunomide, repeat FBC & discuss with specialist
>x2 rise in ALT/AST/ALP	Reduce dose to 10mg. Re-check weekly. If returning to normal continue 10mg, if not, stop & discuss with specialist
> x3 rise in ALT/AST/ALP	Re-check < 72 hrs. If not improved, stop & discuss with specialist
Renal: eGFR<30ml/min	Withhold drug, discuss with specialist. (Continue if eGFR 30-60 ml/min.)
Rash or itch	Check for other causes. If mild consider dose reduction & antihistamine. If severe, stop & discuss with specialist
Hair Loss / headache	Consider dose reduction. If severe, stop & discuss with specialist
Nausea / Diarrhoea	Consider anti-emetic / loperamide respectively. May respond to dose reduction. If severe, stop & discuss with specialist
Bruising / sore throat	Check FBC & withhold leflunomide until results available
Hypertension (confirmed BP > 140/90)	Treat; if BP remains uncontrolled, stop leflunomide & discuss with specialist
Weight loss (>10%)	If no other cause, reduce dose or stop & consider washout (see below)
Breathlessness / cough	If no other cause, stop leflunomide & discuss with specialist

Other information

See overleaf. Dose reduction will not result in a rapid diminution of adverse effects as the half-life is 2 weeks. If a rapid response is required then consider washout (see details below).

Contact details

Name	Sr Elaine Doyle	Sr Cath Hutton	Collette Stoddart	Stephanie Meadley
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Further Information

Leflunomide

As well as its licensed indications, Leflunomide is occasionally recommended in connective tissue disorders, seronegative spondyloarthritis and PMR. Clinical and haematological response may take 12 weeks or more, as loading dose is no longer recommended.

Intercurrent Infection
During an acute infection, Leflunomide should be temporarily discontinued until the patient has recovered from the infection.

Adverse Effects
Diarrhoea occurs in about 17% of patients and is usually self-limiting.

Increasing shortness of breath and/or persistent cough without other cause may rarely be due to pneumonitis (1 in 5000 risk).
Stop treatment and give either cholestyramine 8g tds for 11 days or activated charcoal 50g qds for 11 days.

Vaccinations
Live vaccines are not recommended, although the live shingles vaccine is appropriate in some patients (refer to Green Book for advice). We recommend annual flu vaccination and Pneumococcal vaccination in line with current guidance.(see JCVI Green Book).
If a patient is exposed to shingles or chickenpox, and lacks immunity to varicella-zoster virus, passive immunisation may be required (contact Rheumatology).

Fertility issues
Leflunomide is teratogenic and must not be given to pregnant women or women of childbearing age unless reliable contraception is used. Women planning to become pregnant must stop the drug 2 years beforehand or have a washout. Men should use effective contraception for 3 months after stopping the medication. Breast feeding must be avoided.

If you are thinking about discontinuing treatment please discuss with the Consultant or Rheumatology staff first. If the patient has any problems with their medication, adverse effects or an exacerbation of their disease requiring an earlier appointment in the Rheumatology Department, please contact the rheumatology specialist nurse practitioners using the contact details above.

Reference : BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology 2017 ; 56 : 865-8.

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