

SHARED CARE GUIDELINES FOR LEFLUNOMIDE

Licensed indication

Leflunomide is licensed for the treatment of adult patients with active rheumatoid arthritis (RA) as a disease-modifying anti-rheumatic drug (DMARD) and for the treatment of active psoriatic arthritis (PsA).

Dosage and administration

The maintenance dose is 10-20mg/day for RA and 20mg/day for PsA.

Lower doses may be advisable in the elderly. A three-day loading dose (100mg/day for three days) referred to in product literature is optional but may increase the incidence of GI toxicity.

Recent treatment with hepatotoxic or haematotoxic DMARDs may result in increased side effects. A washout procedure should be performed when switching from Leflunomide to another DMARD or in the case of a desired pregnancy, due to its long half-life.

Clinical improvement usually starts after 4 to 6 weeks. Further improvement may be seen after 4 to 6 months.

Adverse Effects.

The most common adverse events seen with leflunomide treatment in clinical trials were gastrointestinal effects (diarrhoea, nausea, vomiting, anorexia, mouth ulceration, abdominal pain), weight loss, headache, dizziness, paraesthesia, tenosynovitis, alopecia, eczema and mild allergic reactions including rash and pruritis.

Adverse effects that require specific monitoring include:

- Elevation of liver enzymes and severe disturbance of liver function
- Increase in blood pressure (usually mild)
- Blood dyscrasias including leucopenia (common), anemia and thrombocytopenia.

The overall incidence of infections can increase including bronchitis and pneumonia.

See the SPC for more details on adverse events.

Pregnancy & Lactation

Leflunomide is teratogenic in animal studies & is contraindicated in women who are pregnant or not using reliable contraception. It is not recommended in men who may father a child. It is not recommended in breast-feeding women.

Interaction with other medications.

Increased side effects can occur when Leflunomide is given concomitantly with hepatotoxic or haematotoxic drug. Due to the potential for additive hepatotoxic effects it is recommended that alcohol be avoided during treatment with leflunomide.

Leflunomide can be given concomitantly with triphasic contraceptive pills, non-steroidal anti-inflammatory drugs and corticosteroids, but caution must be exercised when co-prescribing other drugs metabolized by Cyp2C9 such as phenytoin, warfarin & tolbutamide.

Vaccination with **live** vaccines is not recommended & the long half-life of Leflunomide must be considered before administering a live vaccine even after stopping treatment with Leflunomide.

Patients may receive cholestyramine or activated charcoal should a washout be required due to intolerance or prior to the commencement of an alternative DMARD. This rapidly decreases plasma levels of the active metabolite of Leflunomide.

Shared Care Responsibilities

Aspects of Care for which the Consultant is responsible.

- Assessing the need for leflunomide.
- Arranging for the patient to be given written patient information & an opportunity to discuss the potential benefits & risks of leflunomide.
- Providing pre-treatment blood pressure, biochemical and hematological checks.
- Providing the loading dose & first six months treatment of Leflunomide. Thereafter if patient stabilized on therapy, liaising with the GP for ongoing prescription.
- Monitoring for hepatic or hematological side effects or hypertension during first 6 months of therapy.
- Following the patient's response to treatment at the outpatient clinic.
- Advising on the indications for & use of a washout period with cholestyramine or activated charcoal if necessary.
- The Rheumatology department will review blood tests during first 6 months of therapy.
- Patients will be able to directly report potential adverse effects to the rheumatological clinical nurse specialist who will liaise with the relevant consultant if necessary.
- At any stage or treatment, advising GP of concerns re monitoring or potential adverse effects of treatment.

Aspects of care for which the General Practitioner is responsible.

- Prescribing Leflunomide under the guidance of hospital consultant once the patient's dose/treatment is stable (usually after six months therapy).
- Reporting any suspected adverse reactions to the hospital.
- Liaising with the hospital consultant regarding any complications of treatment.
- Monitoring the general health of the patient.
- Monitoring for hepatic or hematological side effects or hypertension after the patient stabilized on treatment.

Safety Monitoring

- **FBC, LFTs and ESR (or CRP):** every 2 weeks for 2 months, then every 4 weeks thereafter.
- **BP:** monthly for 6 months then every 8 weeks thereafter.

Withhold Leflunomide and contact Specialist if:

WCC < 4.0 X 10⁹/L

Neutrophils < 2.0 x 10⁹/L

Platelets < 150 x 10⁹/L

AST / ALT > 2 times the upper limit of normal

Rash, itch or oral ulceration.

Please note: A rapid fall or consistent downward trend in any haematological values should prompt caution and extra vigilance.

MTRAC's Verdict: RESTRICTED USE

"Leflunomide has been associated with potentially serious toxicity and the evidence base for psoriatic arthritis is currently limited. Leflunomide treatment should be initiated and stabilized in secondary care. It is then appropriate for GPs to prescribe leflunomide with the guidance of an ESCA. The summary of Product Characteristics states that it should be prescribed by specialists experienced in the treatment of rheumatoid and psoriatic arthritis; however, this does not preclude follow-up prescribing by GPs with appropriate experience".

Conclusions

Leflunomide was licensed for the treatment of rheumatoid arthritis in 1999 and for psoriatic arthritis in June 2004.

For more information, please refer to summary of produce characteristics or manufacturers data sheet.

To contact the Rheumatology Department, Cannock Chase Hospital, please ring:

01543 576453	Community Nurses Helpline
01543 576451	Dr Price's Secretary
01543 576456	Dr Sheeran's Secretary
01543 576457	Dr Mulherin's Secretary
01543 576468	Dr Chalam's Secretary

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