

Shared Care Fact Sheet - Leflunomide

Rheumatology Sub-Stream

This document is available under "Resources" at https://metronorth.health.qld.gov.au/specialist_service/refer-your-patient/rheumatology

Many patients with Rheumatoid Arthritis (RA) or Psoriatic Arthritis (PsA) are suitable for rheumatologist/GP **shared care** leflunomide (LEF) management. MNHHS rheumatologists are now advocating this where appropriate (including for this patient if this document is accompanying a clinic letter). Sharing care can improve specialist access and enhance patient compliance and satisfaction.

Please do the following for your patient:

- ☐ **Review vaccination status** – COVID, pneumococcal and yearly flu vaccinations recommended. Patients on LEF receiving a first flu vaccine should probably get 2 doses, 4 weeks apart. Biological & targeted synthetic DMARDs are a contraindication to live vaccines. [Vaccinations in Rheumatology](#)
- ☐ **Arrange a skin check** if not done within previous 6m and ensure repeated annually
- ☐ Monitor BP at each visit. LEF can cause hypertension
- ☐ **Discuss the critical importance of ongoing, effective contraception for up to 2 years post cessation in women** Consider offering long-acting reversible contraception. For paternal exposure the conditional recommendation is to continue but evidence is limited - *see links below*
- ☐ **Ensure pathology tests are done** and action results appropriately - *see Tab A: below*
- ☐ **Arrange clinical review** as appropriate and consider software reminders for regular tasks
- ☐ **Please contact the rheumatology team if you have any concerns (Registrar via switch)**

A: Pathology testing

- Regular **FBC, E/LFT, ESR/CRP** are required with **results to GP and rheumatologist**
- Please review the patient in the context of the clinical letter to assess symptoms, possible side effects and to action abnormal results. If the protocol outlined below recommends a change in treatment, please forward details to the rheumatology clinic
- Testing required at baseline, then 2–4 weekly for months 0-3, then 8–12 weekly for months 3-6
- When the dose of LEF is stable for 3 months and there are no other relevant changes (e.g. development of impaired renal function) the above tests should be performed at a **minimum of every 3 months**
- If **co-prescribed methotrexate (MTX)** the **minimum interval is 2 monthly** due to increased potential toxicity
- Regular cardiovascular risk review, including lipids, is advisable for all patients with autoimmune disease

If your patient has elected to use Queensland Health pathology, they have been provided with a form.
If your patient wishes to use a private pathology provider, their GP will need to issue pathology forms.
The rheumatologist may have given them a form for their first test. Ensure your details are in the cc field.

Managing abnormal tests:

- **Liver function**
 - If ALT/AST levels >2x upper limit of normal (ULN) but <3x ULN, LEF dose should be reduced by 50% and tests repeated in 1 month. Once ALT/AST improved to <2x ULN any further LEF increase must be monitored with monthly LFT until dose stable for 3 months
 - If ALT/AST >3x ULN, withhold LEF and discuss with rheumatology registrar
 - Consider screening for other causes of LFT derangement if ALT/AST >3x ULN 4 weeks after discontinuation
- **Haematology**
 - If Hb drops 20 g/L below baseline, WBC <2 x 10⁹/L, neutrophils <0.5 x 10⁹/L or platelets <50 x 10⁹/L withhold LEF and discuss with rheumatology registrar
 - If less severe abnormalities reduce LEF dose by 50% and repeat tests in 2 weeks
 - Myelosuppression is more common in initial months but can occur any time during treatment
 - Myelosuppression is increased in older patients and when combined with MTX

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B: Possible side effects

- Diarrhoea is commonest (up to 17% of patients). Taking LEF with food/in the evening may reduce this
- Hypertension is identified up to 10 % patients. LEF can aggravate existing hypertension or induce new-onset hypertension within 3 months of therapy
- Pruritis and various other skin conditions including: non-specific rash, mucosal ulcers, Stevens-Johnson syndrome, toxic epidermal necrolysis, lichenoid reaction, cutaneous vasculitis, erythema multiforme and subacute cutaneous lupus. These usually occur at initiation but can develop later
- Dose-dependent alopecia is a common transitory adverse effect of LEF (6–23%). Hair loss is diffuse and often mild to moderate. Aim to reassure patient of this and continue LEF at the same dose
- Peripheral neuropathy, (distal axonal, sensory, or sensorimotor) has been reported. Patients who stop LEF within 30 days of symptom onset may be more likely to have improvement/recovery
- Lipid dysfunction can occur
- Serious side effects of myelosuppression, hepatotoxicity and pneumonitis are much less common. LEF and MTX have synergistic toxicity so extra care is mandatory when prescribed in combination

Further Information

Dose titration will be directed by the rheumatologist:

- LEF tablets are available in 10mg or 20mg strengths
- Standard dose is 10-20mg as a single daily dose
- Please carefully consider the number of repeats you provide to ensure recommended monitoring is adhered to
- LEF is a very slow acting DMARD; response is assessed after 4-6 months on 20mg/day
- LEF is PBS-subsidised for RA and PsA if initiated by a specialist physician.

LEF and interactions:

- Caution is needed with drugs metabolised via cytochrome P450 2C9, such as warfarin and phenytoin
- LEF may reduce warfarin metabolism, increasing INR. Because of the active metabolite's long half-life, this effect may persist for 2–4 weeks after stopping
- No significant interactions between LEF and oral contraceptives have been found

LEF and infections:

- Patients can usually continue LEF while being treated with oral antibiotics

LEF can be taken with other medications including:

- Other DMARDs including MTX, biological and targeted synthetic DMARDs
- Steroids such as prednisolone
- NSAIDs / low dose aspirin / paracetamol

LEF and alcohol:

- LEF usage in heavy drinkers has been associated with liver cirrhosis
- It is not known precisely what level of drinking is safe when on LEF
- Maximum intake should remain within NHMRC alcohol consumption guidelines
- Drinking >4 std. drinks on one occasion, even infrequently, is strongly discouraged

Unplanned pregnancy / cholestyramine washout:

- In case of unplanned pregnancy: stop LEF, commence cholestyramine washout (8g tds for 11 days) and contact the treating rheumatologist promptly
- Washout may also be indicated when planning pregnancy or for other scenarios such as serious infections

Links

The [Australian Rheumatology Association \(ARA\)](#) website has more information including COVID advice and vaccine information:

Medications: [Rheumatology Medication Information](#)

Pregnancy: [Rheumatology Medications for Autoimmune Rheumatic Diseases in Pregnancy](#)

Vaccines: [Vaccinations in Rheumatology](#)

Brisbane North PHN and Metro North HHS HealthPathways is a GP decision-support tool including sections on all major rheumatology conditions. It aims to improve continuity of care between primary, community and hospital settings, **is free to join** and accessible for all health professionals: [HealthPathways Brisbane North \(communityhealthpathways.org\)](#)

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