BNSSG Joint Formulary DMARD Monitoring Advice Guidance

LEFLUNOMIDE for use in rheumatic diseases

Background
This sheet provides guidance on monitoring of leflunomide in primary care. These recommendations have been primarily taken from current BSR guidance on DMARD monitoring. Some rheumatology departments may have slight variations in their monitoring practices. For the full shared care protocol and responsibilities for primary care refer to www.bnssgformulary.nhs.uk/Shared-Care-Protocols

Treatment schedule
Leflunomide is given once daily be mouth at a dose of 10 or 20mg. When used in combination with other potentially hepatotoxic DMARDs such as methotrexate, a dose of 10mg is recommended. Treatment should be continued as long as clinically indicated unless there is a serious side effect or the drug becomes ineffective.

Cautions and special recommendations
Cautions

- Localised or systemic infection including hepatitis B or C and history of TB
- Drug potentiation: caution should be used if co-prescribed with methotrexate

Contra-indications

- Pregnancy and breast feeding. Effective contraception must be used whilst taking leflunomide and for two years after stopping the drug in women and three months after treatment for men (or consider the wash out procedure to reduce this).
- Severe immunodeficiency
- Serious infection
- Impaired liver function due to any cause or severe unexplained hypoproteinaemia
- Moderate to severe renal impairment (if eGFR <20 use with caution. Protein binding is variable in CKD)
- Impairment of bone marrow function

Washout procedure
Leflunomide elimination can be achieved by a washout regimen of cholestyramine 8gm, 3 times daily for 11 days or activated charcoal 50 gm, 4 times daily for 11 days.

Side-effects
The most common side effects are rash, diarrhoea, reversible alopecia, weight loss, nausea and mouth ulceration. Diarrhoea usually settles with continuing therapy but may require loperamide or dose reduction.

Elevation of liver enzymes and cases of severe liver injury have been reported. For ALT elevations between 2-3x the upper limit of normal, the dose may be reduced from 20mg to 10mg and monitoring should be performed weekly (discuss with specialist team). If the ALT is elevated more than 3x the upper limit of normal, leflunomide may be discontinued and wash out procedures considered (discuss with specialist team).

Low white cell count and thrombocytopaenia may occur, although serious myelosuppression is rare. Mild hypertension is reported in up to 10% of patients and should be treated if necessary. In severe uncontrolled cases it is necessary to consider stopping the drug.

Pulmonary infiltration/pneumonitis is a rare, acute, allergic reaction that has been described in a small number of patients after starting leflunomide. If the patient becomes short of breath leflunomide should be stopped at once and urgent medical advice should be sought.

Drug interactions
Lefunomide may enhance the effects of phenytoin and tolbutamide although significant interactions are unlikely. Leflunomide also interacts with warfarin and the INR should be closely monitored in patients on warfarin who are given leflunomide, including for several weeks after leflunomide is discontinued. If the patient is already receiving nonsteroidal anti-inflammatory drugs (NSAIDs) and/or corticosteroids, these may be continued after starting leflunomide.

Monitoring

Pre-treatment assessment:	FBC, renal function and LFT's will be checked pre-treatment. BP will also be checked. If >140/90 on 2 consecutive readings at least 2 weeks apart then treat hypertension before commencing leflunomide.
Monitoring:	FBC and LFT's should be checked monthly for 6 months and, if stable, 2 monthly thereafter. BP and weight should also be checked at every visit.

Actions to be taken: Leflunomide should be WITHHELD if any of the following occur. Please repeat monitoring bloods in 1 week and if still low/high then discuss with the rheumatology team. Falling trends may also prompt discussion.

- Neutrophils <1.5 $x10^9$/L
- Platelets <100 $x10^9$/L
- ALT >twice upper limit of reference range
- Rash or oral ulceration
- Severe sore throat, abnormal bruising: immediate FBC and withhold until the result of FBC is available.
- Hypertension (BP>140/90) if not controlled with standard anti-hypertensives
- Breathlessness
- Unexplained weight loss >10%

Rheumatology Departments' contact details

Trust / Hospital	Contact	Telephone / Fax	On call service	Availability
University Hospitals Bristol Foundation Trust, Bristol Royal Infirmary	Rheumatology Telephone Advice Line	T: 0117 3424881 F: 0117 3423841	Registrar pager: 07623972925	**Mon – Thu 9am to 5pm** **Fri 9am to 1pm**
North Bristol Trust, Southmead Hospital	Consultant secretary as per clinic letter OR Rheumatology Telephone Advice Line	T: 0117 4140600 F: 0117 4140570 For clinicians only T: 07894800989	T: 07894800989 Sat/Sun 9am-noon (GP service for existing NBT rheum patients only)	**Mon – Fri 9am to 5pm**
Weston Area Health Trust, Weston General Hospital	Rheumatology Telephone Advice Line	T:01934 881075 F: 01934 647025	01934 636363 Bleep 279	**Mon – Fri 9am to 5pm**