What is a shared care document?

Suffolk D&T operates a traffic light system in an attempt to clarify prescribing responsibility and improve consistency across Suffolk:

Double Red – Prescribing within hospital or general practice would not be supported.
Red – Hospital only
Amber – Hospital initiated but suitable for GP prescribing if a suitable shared care document is in place.
Green – Hospital initiated; GP prescribing
Double Green – GP prescribing

The basic principles of a shared care arrangement are:
1) The shared care document will include a clear statement of the hospital specialist/GPs responsibilities
2) Shared care documents must provide sufficient information such that after patient stabilisation under hospital supervision, prescribing responsibility could safely be transferred to primary care
3) Both hospital specialist and general practitioner have a duty of care for the overall management of the patient
4) Patient convenience may be a major factor for GPs taking on prescribing responsibility and not the cost of the therapy
5) The onus is on the hospital specialist to liaise with the GP, and if the GP does not wish to undertake the clinical and legal responsibility for the drug he does not have to do so. Responsibility to prescribe will therefore remain with the hospital
6) Agreement to accept prescribing responsibility should be obtained from the GP before the patient is informed

For more details please refer to the traffic light document on the Suffolk Extranet website.

Document prepared on behalf of the rheumatology department at Ipswich Hospital – contact details later in document

Date received by Suffolk D&T and approved by the Local Medical Committee – March 2003

This document is available on the Suffolk Extranet website on the Traffic Lights

Prepared on behalf of Suffolk D&T by Adrian Barker, Interface Pharmacist

This is an NHS Suffolk document that has been adopted by the WSCCG.
Background to shared care document:
Leflunomide was made a red drug (hospital only) by Suffolk Health in November 1999. Local rheumatology units since then have gained significant experience with this drug and an audit of leflunomide use over the period November ‘99 to July ‘00 was undertaken at Ipswich hospital. The audit concluded that compared to other disease modifying anti-rheumatic drugs (DMARDs), leflunomide appeared to be reasonably effective (22 of 37 patients had continued past the six month mark) and there had been no unacceptable side effects.
Members of the Suffolk D&T agreed that given the experience now with this drug and in order to allow patients to allow patients from their GP rather than the hospital, leflunomide was suitable for re-classification as an amber (shared care) drug in Suffolk.

Important: Due to the additional risk of liver toxicity any patient prescribed a combination of leflunomide plus methotrexate should remain under the supervision of the rheumatology unit only.

The role of Leflunomide in the treatment of Rheumatoid Arthritis

Traditional disease-modifying antirheumatic drugs (DMARDs) such as sulphasalazine (SASP), methotrexate (MTX), gold and penicillamine have been shown to both lower the activity of rheumatoid arthritis (RA) and slow progression of radiographically assessed joint damage. If given early in disease and sometimes in combination, these agents may also prevent structural damage and preserve patients function. Unfortunately due to intolerance or lack of efficacy each one of the DMARDs may need to be considered for a patient during the course of their disease. Leflunomide, when it received its licence in 1999, was the first DMARD to be marketed for RA in more than 10 years. Clinical trials have shown it to be similar in efficacy to MTX or SASP (traditionally first choice DMARDs), and superior to placebo. Discontinuation rates are similar to other DMARDs and despite the need for regular monitoring of liver function (see later) leflunomide is thought to be a useful drug where MTX or SASP are ineffective or toxic. Leflunomide (in a similar way to other DMARDs) may take 4 to 6 weeks to show any response with maximum response taking up to 4 to 6 months. Guidance issued by NICE (March 02) on infliximab and etanercept for RA, may result in these agents being used more commonly in preference to leflunomide.
Patient Selection for leflunomide

- Suitability for leflunomide will be assessed by a hospital rheumatology consultant

Hospital Specialist Responsibilities

For the purposes of this document a hospital specialist may refer to either a rheumatology clinician or a rheumatology nurse specialist working under the supervision of a clinician

- Selection of patients suitable for leflunomide, including discussion with the patient of the monitoring requirements, side effect profile, fertility, faetal and breast feeding risks. Alcohol avoidance advice.
- The hospital specialist will also provide the patient with a drug information sheet (similar to that included in this document).
- Before initiating treatment with leflunomide the hospital specialist will check the patients blood pressure, serum ALT and full blood count including differential white cells and platelets.
- The hospital specialist will be responsible for writing prescriptions for leflunomide for the first six months of treatment.
- During this six month period full blood count including differential white cells and platelets will be measured by the hospital every two weeks, serum ALT every 4 weeks and blood pressure at every clinic visit (at least every 3 months).
- After six months of treatment, the hospital specialist may ask the GP to take over prescribing of leflunomide, however responsibility to prescribe remains with the hospital until the GP formally agrees (in writing) to the shared care arrangement.
- After handover to the GP the hospital specialist will be responsible for:
  - Review of the patient in clinic on a three to six monthly basis
  - Updating the GP with any recommended changes to therapy
  - Advising the GP on therapy changes after any suspected adverse effects to leflunomide therapy.
  - Seeing the patient urgently at the request of the GP.

GP responsibilities

- After a six month stabilisation period, any GP who is willing to accept the shared care agreement will notify the hospital specialist in writing, without undue delay, of their acceptance.
- The GP will continue to prescribe leflunomide at the dose recommended by the hospital specialist.
- The GP will arrange for the patients blood pressure, serum ALT, full blood count including differential white cells and platelets to be checked every two months.
- The GP will take appropriate action in response to suspected adverse events (summarised in the prescribing information section), notify the rheumatology unit and if necessary prescribe the washout medication as advised by the rheumatology specialist.

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• The GP will monitor for drug interactions as summarised in the prescribing information.

**Prescribing information for the Leflunomide**

Summary prescribing information for guidance only; please refer to the full SPC (available at [www.emc.vhn.net](http://www.emc.vhn.net) (registration required)), local specialist or medicines information centre. The information is correct at the time of writing – Jan 03 but maybe subject to change.

**Leflunomide (Arava®)**

**Pharmacology** – Immunomodulator with anti-inflammatory, analgesic & antipyretic activity.

**Preparations available** – 10, 20 and 100mg tablets

**Licensed indications** – Treatment of adult patients with active rheumatoid arthritis as a disease modifying anti-rheumatic agent (DMARD).

**Recommended dosage and administration** – Loading dose – 100mg daily for three days. Maintenance dose 10 to 20mg once daily (alternate day dosing may be useful for patients with diarrhoea). Therapeutic response takes 4 to 6 weeks with further improvement up to 4 to 6 months.

**Contra-indications** – liver function impairment, severe immunodeficiency states, significantly impaired bone marrow function or significant anaemia. Patients with severe infections, moderate to severe renal insufficiency, severe hypoproteinaemia. Pregnancy (excluded before treatment) or women of childbearing age who are not using reliable contraception. Breast feeding mothers. Male patients should be advised to also use reliable contraception whilst taking leflunomide. If planning to start a family, both men and women should undertake a washout and waiting period – see SPC. Leflunomide is not recommended in patients aged less than 18 years.

**Cautions** – Concomitant administration of hepatotoxic or haemotoxic DMARDs (e.g. methotrexate) is not advisable (but is occasionally chosen). The active metabolite of leflunomide has a half-life of between 1 & 4 weeks and if toxic reactions occur or when switching to another DMARD a washout procedure should be performed (seek specialist advice or consult the full SPC).

**Avoid alcohol consumption**

**Monitoring**

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1) Due to the possibility of severe liver impairment (most cases have occurred within the first six months), serum alanine aminotransferase (ALT) must be checked before treatment every four weeks for the first six months then every 8 weeks thereafter.

Action to be taken regarding elevated ALT:
ALT 2 to 3 times the upper limit of normal – consider dose reduction from 20mg to 10mg and monitor ALT weekly.
If ALT more than 2 fold upper limit for more than one reading or if single reading of more than 3 times upper limit – STOP leflunomide and perform washout. Contact rheumatology unit.

2) Full blood count including differential white blood cell and platelets before the start of leflunomide, every two weeks for the first six months then every 8 weeks thereafter.

3) Blood pressure before starting treatment and periodically afterwards (two monthly for the purposes of this document)

**Drug interactions** – There are no published studies at the point of writing which have assessed the safety of the combination of leflunomide with other DMARDs.
Caution is advised when leflunomide is given together with other drugs metabolised by CYP2C9 such as phenytoin, warfarin and tolbutamide.

Increased side-effects may occur with recent or concomitant use of hepatotoxic or haemotoxic drugs.

**Adverse effects**
Common (1-10%) – mild increase in BP, diarrhoea (alternate day dosing may be useful here), nausea & vomiting, anorexia, oral mucosal disorders, abdo pain, elevation of liver parameters, weight loss, headache, dizziness, asthenia, parasthesia, tenosinusitis, increased hair loss, eczema, dry skin, mild allergic reactions, rash, pruritus, leukopenia.

Uncommon (0.1-1%) – hypokalaemia, taste disturbance, anxiety, tendon rupture, urticaria, anaemia, mild thrombocytopenia.

Rare (0.01-0.1%) – hepatitis, jaundice, eosinophillic, leukopenia, pancytopenia.

Very rare (<0.01%) - severe liver injury, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, severe anaphylactic reactions, agranulocytosis.

**Washout procedure** – seek advice from rheumatology unit or see SPC
**Prescribing costs** – 28 days of leflunomide 10mg or 20mg tablets cost £43.40 (MIMS Feb 03)
## Rheumatology Department Contact Details

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Prepared on behalf of Suffolk D&T by Adrian Barker, Interface Pharmacist
**Leflunomide Patient Information Leaflet**

**Why am I being prescribed leflunomide?**
Leflunomide (trade name 'Arava') is used to treat rheumatoid arthritis and other types of arthritis where the body's immune system (defence system) attacks its own tissues. It is a 'disease-modifying' drug, which, by its action on the immune system, can reduce the inflammation that causes pain, swelling and stiffness in the joints.

**When do I take leflunomide?**
Leflunomide is taken in tablet form once a day. Leflunomide can be taken at any time of day, with or without food, and should be swallowed whole. It is best to take it at the same time every day.

**What dose do I take?**
Your doctor will advise you. Usually for the first three days of treatment you will take 100 mg a day, followed by either 10 mg or 20 mg a day after this.

Leflunomide is not a painkiller. So if you are on painkillers you may carry on taking these as well, unless your doctor advises otherwise.

**How long will leflunomide take to work?**
Leflunomide does not work immediately. It may be 4 to 6 weeks before you feel any benefit and may even be as long as 6 months before you feel the full effect of leflunomide.

**What are the possible side-effects?**
The most common side-effects of leflunomide are a feeling of sickness, diarrhoea, mouth ulcers, weight loss, abdominal (stomach) pain, headache, dizziness, weakness, skin dryness and hair loss. It may cause a slight rise in your blood pressure.

Leflunomide may cause mild allergic symptoms including rash and itching. Rarely, more severe allergic reactions and skin conditions can develop. If this happens, the leflunomide will have to be discontinued.

Taking leflunomide can also affect the blood count (one of the effects is that fewer blood cells are made) and it can make you more likely to develop infections. If you develop a sore throat or other infection, fever, unexplained bruising, bleeding or rash, or if you become breathless, or develop any other unexpected new symptoms after starting leflunomide, you should report to your doctor or rheumatology nurse specialist as soon as possible.

Leflunomide may affect the liver. This may cause problems ranging from abnormalities in the blood tests without causing ill health to severe liver damage which may be fatal. If you develop symptoms such as unusual tiredness, abdominal pain, or jaundice (eyes or skin turning yellow), inform your doctor at once.

**Do I need any special checks while on leflunomide?**
Your doctor will arrange for you to have regular blood tests and checks on your blood pressure. You may be asked to keep a record booklet with your
blood test and blood pressure records. Bring this with you when you visit your
general practitioner or the hospital. **You must not take leflunomide unless you are having regular checks.**

Can I take other medicines along with leflunomide?
Some other drugs interact with leflunomide and you should always tell any
doctor treating you that you are on leflunomide. You should not take 'over-the-counter' preparations without discussing this first with your doctor or pharmacist.

Can I have immunisation injections while on leflunomide?
You should avoid immunisations which involve any of the live vaccines such as polio, rubella (German Measles) and yellow fever. Flu vaccines and pneumovax are safe and recommended.

Does leflunomide affect fertility or pregnancy?
Leflunomide may harm an unborn baby. Therefore it should not be taken during pregnancy.

Whilst taking leflunomide both men and women must use reliable contraception. If you are planning a family, you should discuss this with your doctor. Women must wait two years between stopping leflunomide and becoming pregnant. The two-year 'waiting' period can be reduced to three months if you receive a special 'washout' treatment to help eliminate leflunomide from your body.

Men are advised to stop taking leflunomide, receive the 'washout' treatment, and wait three months before trying to father a child.

If you become pregnant while taking leflunomide, you should discuss this with your doctor as soon as possible.

You should not breast-feed if you are taking leflunomide.

May I drink alcohol while taking leflunomide?
Because leflunomide may affect the liver, you should avoid alcohol while taking this drug.

Where can I obtain further information?
If you would like further information about leflunomide, or if you have any concerns about your treatment, you should discuss this with your doctor.

Remember to keep all medicines out of reach of children.

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