LINCOLNSHIRE CLINICAL COMMISSIONING GROUPS in association with UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE:Leflunomide treatment of active rheumatoid arthritis (RA) and active psoriatic arthritis (PsA)

General Principles

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF* 74, September 2017 – March 2018 , pg.5)
Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.
(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.
(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.
(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further Copies

Further copies of any guidelines in this series are available from members of the Optum Medicines Management and Optimisation Team.

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Principles of shared care

NHS England published Guidance - Responsibility for Prescribing between primary, secondary and tertiary care – January 2018.
Key recommendations from guidance:

1.0 Introduction

1.1 Shared Care Prescribing guidelines are local policies to enable General Practitioners to accept responsibility for the prescribing and monitoring of medicines/ treatments in primary care in agreement with the initiating service.
1.4 Where possible shared acre should be disease specific rather than medicine specific and link into complement local integrated care pathways and shared acre policies. Medicines and conditions suitable for shared care will be identified by local medicines committees and will be classified as AMBER (AMBER 1 for Lincolnshire) through the traffic light system. … However it should be remembered that the provision of shared care prescribing guidelines does not necessarily mean that the GP has to agree to accept clinical and legal responsibility for prescribing; that they should only do so if they feel clinically confident in managing that condition.

2.3 reasonable predictable clinical situation

2.3.1 Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stale or predictable.

2.4 Agreement of shared care between consultant and GP

2.4.1 Referral to the GP should only take place once the GP has agreed in each individual case and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that the supply arrangements have been finalised. The secondary/ tertiary provider must supply an adequate amount of the medication to cover the transition period. The patiet should then be informed to obtain further prescriptions from the GP.

2.7 Clear definition of responsibility

2.7.1 The areas of care for which each clinician has responsibility should be clearly defined.

2.8 Clinical responsibility

2.8.1 Clinical responsibility for prescribing is held by the person signing the prescription who must also ensure adequate monitoring.

2.9 Communication network & emergency support

2.9.1.Telephone details and (if appropriate) secure email addresses of both parties should be exchanged and recorded. This will enable the practice to access timely advice, guidance and information if problems arise, and will also enable secondary care clinicians to easily contact the GP if necessary. This should include out of hours contact numbers, how to access the on-call duty doctor. Patients and their carers should also be provided with contact details for support and help if required both in and out of hours.
2.9.2 People who are being treated on the advice of a secondary acre team, but are no longer being seen in that setting , may still need a review should problems arise. The appropriate level of care or advice should be available from the secondary care team in a timely manner without necessarily requiring a new referral.

6.0 Monitoring

6.0.1 All appropriate monitoring arrangements must be fulfilled. The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered.

Drug Details
Approved Name: Leflunomide
Brand Name: generic tablets or leflunomide
Form and Strength: 10mg, 20mg film coated tablets - generic.
Due to the price difference between the branded and generic products clinicians are advised to prescribe leflunomide generically.

Specialist Responsibilities
The specialist secondary/tertiary care service will:

1. Send a letter to the GP requesting that the GP participates in shared care. As part of the communication the GP should be signposted to where they can find a copy of the shared care protocol e.g. the PACEF website http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef.
2. Exclude TB, severe immunodeficiency status e.g. AIDS and severe infections. Check for absence of pregnancy in women of child bearing age and ensure the patient understands the importance of contraception. Reliable contraception should be used by both men and women whilst on leflunomide and for at least 2 years after stopping leflunomide unless the washout procedure is used. Discuss the benefits and side effects of treatment with the patient. Ensure the patient understands which warning signs and symptoms to report.
3. Undertake baseline monitoring Full Blood Count (FBC) which should include differential white blood cell count and a platelet count, U&Es, creatinine, Liver Function Tests (LFTs) and body weight. Blood pressure measurement should be taken, if BP is >140/90 on two consecutive readings 2 weeks apart ensure hypertension is treated before commencing the drug.
4. Initiate leflunomide according to dosage regimen and undertake monitoring of clinical response and side effects.
5. Ensure that the patient receives supplies of leflunomide from the hospital or prescribed on FP10 HP until the GP formally agrees to share care.
6. Continue the monitoring and prescribing of leflunomide until the patient is stabilised and shown both to clinically respond to and tolerate the treatment.
7. Undertake fortnightly monitoring for the first six weeks. Then monthly monitoring of FBCs and LFTs for 3 months and then every 3 months if stable then two monthly thereafter. Blood pressure and weight should be checked at each blood test visit. FBCs & LFTs should continue to be monitored at least once a month and continued long term if another immunosuppressant drug or potent hepatotoxic agent is co-prescribed. **It is the specialist responsibility to ensure the GP is informed of the required frequency of monitoring, and to continue to undertake the required monitoring until they have received written confirmation that the GP has agreed to do so.**
8. Counsel patients both male and female to take contraceptive precautions during treatment. Men should continue to use effective contraception for three months after stopping treatment with lefluomide but women should wait two years before trying to conceive. Record in GP referral letter that contraceptive advice has been given. For women of child bearing potential, pregnancy must be excluded before commencing treatment with leflunomide.
9. Periodically review the patient's clinical condition.
10. Communicate promptly any changes in biochemistry monitoring and modification of leflunomide dose to the GP if applicable.

11. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
12. Follow up any adverse drug reactions reported by the GP and report back to the GP.
13. Immediately review any patients in the event of an unplanned pregnancy.
14. **Be responsible for and undertake the washout procedure for rapid elimination of leflunomide in the event of a severe adverse effect, before commencing treatment with another DMARD or as recommended by the manufacturer for patients planning a pregnancy after discontinuing treatment with leflunomide**.
15. Advise the GP on continuing or stopping leflunomide therapy following medical review of the patient and associated drug therapies.

GP Responsibilities

The GP will:

1. Notify the consultant in writing, within two weeks, if they agree to share care.
2. Prescribe leflunomide for the patient once the dose has been stabilised.
3. Undertake the ongoing monitoring as detailed on page 6 of this protocol and report immediately to the specialist if the biochemical values either lie outside the "normal range" or if there is a rapid fall or downward trend in recorded values.
4. Check the patient's weight and blood pressure every time they attend for a monitoring visit.
5. Monitor the patient's health and general wellbeing.
6. If patient has suspected or confirmed infection and/or receiving treatment with antibiotics advise to stop taking leflunomide and recommence once all signs of infection gone and antibiotic course completed.
7. Check with specialist before prescribing and administering any vaccines. Avoid immunisation with live vaccines (see page 6)
8. Monitor the patient for adverse drug reactions following the advice in the monitoring section.
9. Contact the specialist immediately if patient reports an unplanned pregnancy.
10. Carry out any investigations that are communicated and deemed appropriate.
11. Provide repeat prescriptions according to recommendations on dosage by specialist service.

Referral Criteria

1. Patients will have been stabilized on leflunomide, normally having received at least 12 weeks treatment.
2. The specialist will have carried out an assessment of efficacy and tolerability.

Licensed Indications

Treatment of adult patients with active rheumatoid arthritis (RA) as a disease modifying antirheumatic drug (DMARD) and active psoriatic arthritis (PsA)
The treatment should be initiated and supervised by specialists experienced in the treatment of rheumatoid arthritis and psoriatic arthritis.

Recommended Dosage and Administration

RA – adults over 18 years of age 10-20mg, once a day as monotherapy. When used in combination with another potentially hepatotoxic DMARD such as methotrexate the recommended daily dose is 10mg.
PsA - adults over 18 years of age 20mg once a day.
The therapeutic effect usually starts after 4 to 6 weeks and may further improve up to 4 to 6 months.
ULHT Rheumatologists have advised use of loading dose (100mg once daily for 3 days) is no longer recommended.

Background Pharmacology

Leflunomide inhibits the enzyme dihydroorotate dehydrogenase and this inhibits pyrimidine biosynthesis. It has immunomodulating/immunosuppressive characteristics, acts as an antiproliferative agent and displays anti-inflammatory properties.

Adverse Effects

For further information on adverse effects please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk
Rare cases of severe liver injury, including cases with fatal outcome, have been reported during treatment with leflunomide. Most of the cases occurred within the first 6 months of treatment. Co-treatment with other hepatotoxic medicinal products was frequently present. It is considered essential that monitoring recommendations are strictly adhered to.
Discontinue treatment (and institute washout procedure – consult product literature) or reduce dose according to liver function abnormality. If liver function abnormality persists after dose reduction, discontinue treatment and institute wash out procedure.

Common adverse effects

Abdominal pain, appetite decreased, diarrhoea, gastro intestinal disorders, nausea, vomiting, oral mucosal disorders, headache, dizziness, asthenia, paraesthia, peripheral neuropathy, leucopenia, tenosynovitis, alopecia, skin reactions - rash, dry skin, pruritus.

Uncommon adverse effects

Anaemia, anxiety, electrolyte inbalance, hyperlipdaemia, taste altered, thrombocytopenia.

Rare or very rare

Agranulocytosis, eosinophillia, hepatic disorders (hepatitis, jaundice),infection, pancreatitis, pancytopenia, respiratory disorders, sepsis, severe cutaneous adverse reactions (SCARs), interstitial lung disease, vasculitis.

Frequency not known

Cutaneous lupus erythematosus, hypouricaemia, pulmonary hypertension,renal failure.

Increased blood pressure commonly occurs and regular monitoring of blood pressure should be done throughout treatment with leflunomide. A significant increase in blood

pressure should be treated however in severe cases it may be necessary to consider discontinuing leflunomide.
As leflunomide is an immunosuppressant there is an increase risk of the patient developing an infection.. All types of infections can occur.
Agranulocytosis,
Rare side effects: hepatitis, jaundice (see warnings on hepatotoxicity, above), interstitial lung disease, severe infection, eosinophilia and pancytopenia.
Pulmonary infiltration/pneumonitis is an acute allergic reaction and may occur in a small number of patients. If patient experiences shortness of breath they should be advised to stop the medication immediately and seek medical advice. (See monitoring section for further details)
Simple dose reduction is unlikely to produce a rapid diminution of adverse effects as the half life of leflunomide is approximately two weeks. If severe adverse effects occur discontinue treatment and institute a washout procedure.
For further advice on managing adverse effects please refer to monitoring section on page 6 & 7 and for details on the washout procedure – please refer to precautions and cautions pages 6.

Drug Interactions

For detailed information on drug interactions, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk
Leflunomide can interact with many drugs in particular there is an increased risk of toxicity with other haematotoxic and hepatotoxic drugs.
Due to long half life of active metabolite, drug interactions may occur after leflunomide has been stopped.
Concomitant administration of hepatotoxic or haematotoxic DMARDs (e.g. methotrexate) is not advisable.
Below is a summary of some of the key interactions.

Live vaccines
Avoid immunisation with live vaccines. BCG vaccine, influenza (live), MMR (live), rotavirus, typhoid (oral), varicella –zoster, yellow fever (live) increases risk of generalised, potentially life threatening infection.

Charcoal (Activated)
Avoid. Significantly reduces the effect of leflunomide.

Cholestyramine
Avoid. Significantly reduces the effect of lefluomide.

Phenytoin
Caution. Possible enhanced effect of phenytoin.

Rifampicin
Caution. Possible increase of leflunomide active metabolite.

Tolbutamide
Caution. Possible enhanced effect of tolbutamide.

Warfarin
Caution. Possible enhanced effect of warfarin, monitor INR closely during concurrent treatment and for several weeks following discontinuation of leflunomide.

Precautions and Contraindications

For further information on contraindications and cautions in use, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk

Contraindications

Serious infections

Hypersensitivity to leflunomide or to any of the excipients, especially previous Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) to the active substance, to the principal active metabolite teriflunomide or to any of the excipients

Liver impairment. Avoid as active metabolite may accumulate.

Rare cases of severe liver injury, including cases with fatal outcome, have been reported during treatment with leflunomide. Most of the cases occurred within the first 6 months of treatment. Co-treatment with other hepatotoxic medicinal products was frequently present. It is considered essential that monitoring recommendations are strictly adhered to.

Impaired bone marrow function including anaemia, leucopenia or thrombocytopenia (avoid if significant and due to causes other than rheumatoid or psoriatic arthritis.

Severe immunodeficiency e.g. AIDS.

Moderate to severe renal impairment, because insufficient clinical experience is available in this patient group.

Patients with severe hypoproteinaemia e.g. in nephrotic syndrome.

Patients with galactose intolerance, congenital lactose deficiency, glucose-galactose malabsorption as contains lactose.

Breast feeding.

Pregnancy

Pregnancy must be excluded before the start of treatment with leflunomide.

Leflunomide is tetratogenic and must not be given to pregnant women or women of childbearing potential unless reliable contraception is used during and up to two years after treatment.

Women planning to have children should either discontinue treatment two years prior to conception or have a rapid removal of its active metabolite by following the wash out procedure.

The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify the physician immediately for pregnancy testing, and if positive, the physician and patient must discuss the risk to the pregnancy.

Blood concentrations of the active metabolite should be checked prior to a planned pregnancy. A771726 plasma levels can be expected to be above 0.02 mg/l for a prolonged period. The concentration may be expected to decrease below 0.02 mg/l about 2 years after stopping the treatment with leflunomide. After 2 years the A771726 plasma levels should be measured for the first time. Thereafter the A771726 plasma level should be determined again after an interval of at least 14 days. If both plasma levels are below 0.02mg/l no teratogenic risk is to be expected.

Men should use effective contraception for 3 months after stopping leflunomide. The manufacturer states there is no specific data on the risk of male mediated fetal toxicity but recommend that to minimise any potential risk men wishing to start a family should also undergo a wash out procedure if the time period from discontinuation of treatment is less than two years.

Any pregnancy within two years of discontinuation of leflunomide should be discussed with a rheumatologist if drug wash-out has not been performed. The drug company needs to be notified in the event of a pregnancy whilst the patient is still receiving treatment with leflunomide.

Cautions

Leflunomide is a potentially hepatoxic drug and caution is advised when using leflunomide concomitantly with another hepatotoxic or myelotoxic disease modifying antirheumatic drugs e.g methotrexate Washout procedures are recommended for serious adverse effects or before being switched to other disease modifying antirhematic drugs. (**See product literature and BNF for further advice).**
if there is evidence of current or recent hepatitis with hepatitis B or C virus. It is highly recommended that LFTs should be monitored closely (at least once a month) if leflunomide is co-prescribed with a potentially hepatotoxic dug.
Patients should limit alcohol intake within national limits 4-8 units a week.
Patients exposed to chicken pox or shingles passive immunisation is required using Varicella-Zoster immunoglobulin (VZIG).
Not recommended for use in patients below 18 years since efficacy and safety in juvenile rheumatoid arthritis (JRA) have not been established

Washout procedure

To aid drug elimination in case of serious adverse effect or before starting another DMARD or before conception stop treatment and give either colestyramine 8g three times daily for eleven days or activated charcoal 50g four times daily. Duration of washout period is usually eleven days. The duration may be modified depending on clinical trial or laboratory variables.
The concentration of the active metabolite should be less than 20mcg/l measured on 2 occasions 14 days apart in men & women before conception.
Procedure may be repeated as necessary.

Monitoring

Baseline:

Baseline monitoring FBC including a differential white blood cell count and a platelet count, U&E's, LFTs – Alanine Aminotransferase (ALT) & Serum Glutamopyruvate Transferase (SGT), creatinine, body weight and blood pressure.

Full Blood Count (FBC's), Liver function tests (LFTs) and Urea and Electrolytes (U&E)

Following initiation of treatment monitor every two weeks for first six weeks, and then monthly thereafter for 3 months. Then every 3 months. FBCs, U & E's & LFTs should continue to be monitored if another immunosuppressant drug or potent hepatotoxic agent is co-prescribed.

If co-prescribed with methotrexate continue monthly monitoring until informed otherwise by specialist dependent on patient's results.

Blood pressure

Check blood pressure at each visit. If BP>140/90 treat in line with local & NICE guidance.

Weight

Check weight at each visit.

In summary

Treatment status	FBC & U&E	LFT	weight	ESR or CRP	BP

Initial monitoring for first 6 weeks	Every 2 weeks	Every 2 weeks	Every 2 weeks	Every 3 months (for RA only)	Every 2 weeks
Monthly after first 6 weeks for 3 months. **If used with methotrexate continue monthly monitoring until informed otherwise by specialist**	Every month	Every month	Every month	Every 3 months until patient's condition stable then frequency of testing at discretion of the responsible consultant.(for RA only)	Every month
Every 3 months thereafter	Every 3 months	Every 3 months	Every 3 months	Every 3 months	Every 3 months

N.B if leflunomide is co-prescribed with another immunosuppressant or potentially hepatotoxic drug <u>all</u> monitoring should be continued long-term at least once a month.

<u>Risk of pregnancy</u>
The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify the physician immediately for pregnancy testing, and if positive, the physician and patient must discuss the risk to the pregnancy.

Treatment should be stopped and advice from the supervising specialist Sought if:
<u>Laboratory results</u>
WBC < 3.5x 10^9 /L
Neutrophils <2.0 x 10^9 /L
Platelets <150 x 10^9 /L
LFTs > if AST, ALT are 2 to 3 times the upper normal limit.
If ALT (SGPT) elevations of more than 2-fold the upper limit of normal persist or if ALT elevations of more than 3-fold the upper limit of normal are present, leflunomide must be discontinued and wash-out procedures initiated.
It is recommended that monitoring of liver enzymes be maintained after discontinuation of leflunomide treatment, until liver enzyme levels have normalised.
In additional to haematological values a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance.
Health professionals and patients who are receiving leflunomide need to be aware of the risk of developing liver injury upon starting therapy, especially if other medication associated with disturbance of liver function such as methotrexate is also being taken.
If symptoms such as unusual tiredness, abdominal pain or jaundice develop the frequency of monitoring should be increased and the dose of leflunomide reduced or stopped as necessary.

Treatment should be reviewed and advice from the supervising specialist sought if:

Clinical condition

Signs of active infection, with or without current antibiotic therapy – suspend treatment and seek specialist advice

Rash or itch– Consider dosage reduction, consider co-prescribing antihistamines. If severe stop until discussed with rheumatologist

Ulcerative stomatis – Discontinue treatment and seek specialist advice.

Very rare cases of Stevens Johnson syndrome or toxic epidermal necrolysis have been reported in patients treated with leflunomide. As soon as skin and/or mucosal reactions are observed which raise the suspicion of such severe reactions, discontinued treatment, and seek urgent specialist advice, a leflunomide washout procedure may need to be initiated.

Hair loss – Consider dosage reduction; if severe, stop drug until discussed with rheumatologist**.**

Abnormal bruising or severe sore throat - Check FBC immediately and withhold treatment until results are available and discussed with rheumatologist.

Hypertension. If BP >140/90. – Treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide until discussed with rheumatologist**.**

Severe headache - Consider dose reduction. If headaches persist stop until discussed with rheumatologist

Weight loss - no other cause identified reduce dose or stop treatment until discussed with monitor carefully. If >10% weight loss with rheumatologist.

Breathlessness - if increasing shortness of breath occurs, stop leflunomide until discussed with rheumatologist.

Severe infection - in the event that a severe uncontrolled infection occurs, it may be necessary to interrupt leflunomide treatment and administer a washout procedure.

Indication of Likely Cost of Therapy in Primary Care

leflunomide	10mg	£6.02 for 30 tabs
leflunomide	20mg	£6.17 for 30 tabs

Information Given to the Patient

Information leaflet produced by Arthritis Research Campaign (ARC)

Contact Details

ULHT Rheumatology Team:

First contact the nurse's helpline
Rheumatology Nurses Lincoln (01522) 573828 (Helpline)
Rheumatology Nurses Pilgrim (01205) 445730

Dr Joshi's secretary (01522) 573036
Dr Obaid's secretary (01522) 573413
Dr Chikura's secretary (01522) 573413
Dr Palkonyai's secretary (01522) 573036

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Approved at meeting of Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) November 16th 2018.

Appendix 1
Example of patient information leaflet provided from ULHT.
Original copies can be obtained from ULHT Rheumatology services or from the Arthritis Research Campaign.

Leflunomide

A DRUG Information Sheet

Why am I being prescribed leflunomide?

Leflunomide (brand name Arava) is used to treat rheumatoid arthritis and other types of arthritis where the immune system (the body's own 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 and how 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 you will take either 10 mg or 20 mg a day. For the first 3 days of treatment you may be prescribed a higher dose of 100 mg a day.

How long will leflunomide take to work?

Leflunomide does not work immediately. It may be 4–6 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 risks or 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, a fever, unexplained bruising, bleeding or rash, or if you become breathless, or develop any other unexpected new symptoms after starting leflunomide, you should tell your doctor or rheumatology nurse

specialist straight away. If any of these symptoms are severe, you should stop leflunomide and see your doctor immediately.

If you have not had chickenpox but come into contact with someone who has chickenpox or shingles, or if you develop chickenpox or shingles, you should stop leflunomide and see your doctor immediately as you may need special treatment. This is because chickenpox and shingles can be severe in people on treatment such as leflunomide which has effects on the immune system. Therefore you may require antiviral treatment.

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), you should tell your doctor or rheumatology nurse straight away.

If any of these symptoms are severe, you should stop leflunomide and see your doctor immediately.

What other treatments could be used instead of leflunomide?

A number of other drugs are used in the treatment of rheumatoid arthritis and related conditions (see **arc** leaflet 'Drugs and Arthritis'). Your doctor will discuss these other options with you.

Do I need any special checks while on leflunomide?

Your doctor will arrange for you to have a blood test and blood pressure measurement before you start treatment and then regular checks while on leflunomide. 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 GP or the hospital. **You must not take leflunomide unless you are having regular checks.**

May I take other medicines along with leflunomide?

Leflunomide may be prescribed along with other drugs in treating your condition. Some drugs interact with leflunomide (e.g. warfarin, which thins the blood), so you should discuss any new medications with your doctor before starting them, and you should always tell any other doctor treating you that you are taking leflunomide.

Leflunomide is not a painkiller. If you are already on a non-steroidal anti-inflammatory drug (NSAID) or painkillers you may carry on taking these as well as leflunomide, unless your doctor advises otherwise.

Do not take over-the-counter preparations or herbal remedies without discussing this first with your doctor, rheumatology nurse or pharmacist.

Can I have immunisations while on leflunomide?

It is recommended that you should not be immunised with 'live' vaccines such as yellow fever. However, in certain situations a live vaccine may be necessary (for example rubella immunisation in women of child-bearing age) in which case your doctor will discuss the possible risks and benefits of the immunisation with you.

Pneumovax and yearly flu vaccines are safe and recommended.

May I drink alcohol while taking leflunomide?

Leflunomide and alcohol may interact and damage the liver, so if you drink alcohol you should only drink it in small amounts. Discuss this with your doctor.

Does leflunomide affect fertility or pregnancy?

Leflunomide may harm an unborn baby. Therefore it should not be taken during pregnancy.

While 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 2 years between stopping leflunomide and becoming pregnant. The 2-year 'waiting' period can be reduced to 3 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 3 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.

What about breastfeeding?

You should not breastfeed if you are taking leflunomide.

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, rheumatology nurse or pharmacist.

Remember to keep all medicines out of reach of children.

PLEASE NOTE: We have made every effort to ensure that the content of this information sheet is correct at time of going to press, but remember that information about drugs may change. This sheet does not list ***all*** the uses and side-effects associated with this drug. For full details please see the drug information leaflet which comes with your medicine. Your doctor will assess your medical circumstances and

draw your attention to any information or side-effects which may be relevant in your particular case.

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A team of people contributed to this publication. The original text was written by an expert in the subject. It was assessed at draft stage by doctors, allied health professionals, an education specialist and people with arthritis. A non-medical editor rewrote the text to make it easy to understand and an **arc** medical editor is responsible for the content overall.

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