

## LEFLUNOMIDE

For up to date version of Shared Care Agreement contact specialist team or latest version on website  
<https://westessexccg.nhs.uk/your-health/medicines-optimisation-and-pharmacy/shared-care-medicines>

### Referral Criteria

- These guidelines are for patients over 16 years of age.
- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patients' GP
- Safe prescribing must be accompanied by effective monitoring
- When transfer is agreed, the patient will be given a supply of leflunomide sufficient for 4 week maintenance therapy
- **The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.**

From April 2019 West Essex patients under the care of Princess Alexandra Hospital Rheumatology Consultant will be assessed and those patients with stable disease markers and DAS<3.2 after 6 months of consultant led care will be transferred for ongoing case management to a West Essex General Practitioner with Specialist Interest (GPSI) in Rheumatology. Thereafter shared care for the management of DMARD will be between the Consultant/GPSI (further referred to as Specialist) and the GP.

### SHARED CARE RESPONSIBILITIES

#### Consultant

Undertake the necessary testing to confirm a diagnosis for which leflunomide treatment is recommended.

Ensure the patient's concurrent drug therapy is stabilised and there are no contra-indications to treatment with leflunomide

Ensure that patient is aware of risks and benefits of medication and has read appropriate information leaflet.

Ensure the patient understands the shared care agreement and has signed the Patient Agreement Letter (page 7-8)

Perform baseline tests (see Monitoring section) and provide results to GP

Initiate treatment and prescribe until the patient has been on a stable dose for minimum of SIX weeks.

Send a letter to the GP requesting shared care for this patient.

Review the patient in outpatients as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the specialist.

Inform GP, by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.

Evaluate any reported adverse effects by GP or patient.

Inform GP of patients who do not attend clinic appointments, admin to contact patient to rearrange

Ensure that backup advice is available at all times. (see Contacts section) and respond to any GP queries as soon as practicable

Report any adverse effects to the GP and CHM

<http://www.mhra.gov.uk/Safetyinformation/Howwemonitorthesafetyofproducts/Medicines/TheYellowCardScheme/Informationforhealthcareprofessionals/index.htm>

For patients under the care of Princess Alexandra Hospital Rheumatology Consultant refer patients with stable disease markers and DAS<3.2 for ongoing case management after 6 months of consultant led care to General Practitioner with Specialist Interest in Rheumatology; inform the GP.

#### General Practitioner with Specialist Interest in Rheumatology (for West Essex patients under the care of Princess Alexandra Hospital)

Accept patients with stable disease markers and DAS<3.2 for ongoing case management after 6 months of consultant led care.

Provide ongoing patient education

Annual review of all patients as per NICE guidance

Review the patient annually or as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the Specialist.

Inform GP, by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.

Evaluate any reported adverse effects by GP or patient.

Inform GP of patients who do not attend clinic appointments and contact patient to rearrange.

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### General Practitioner

Monitor patient's overall health and well-being.

Consider request to prescribe under shared care arrangements and reply only if you do not agree to share care, in a timely manner within 14 days as outlined on page 6 with clinical reasons and return to Consultant and Pharmacy department.

Ensure compatibility with other concomitant medication.

Prescribe at the dose recommended

Monitor U&E, creatinine, FBC and LFTs at recommended frequencies (see Monitoring section) and refer if abnormal.

Adjust the dose as advised by the specialist.

Stop treatment on advice of specialist or immediately if any urgent need to stop treatment arises (see monitoring section).

Report any adverse events to the specialist and CHM.

<http://www.mhra.gov.uk/Safetyinformation/Howwemonitorthesafetyofproducts/Medicines/TheYellowCardScheme/Informationforhealthcareprofessionals/index.htm>

Inform specialist of any change in the medical condition of patient which may have effect on disease / medications.

Ensure patient is offered an annual flu vaccination and a one off pneumococcal vaccination

### Patient

Report to specialist or GP if there is not a clear understanding of their treatment and discuss any concerns in relation to treatment

Report any adverse effects to their GP and/or specialist whilst taking Leflunomide, especially unexplained bruising/bleeding, fever, infections or mouth ulcers which should be reported immediately.

Report any changes in disease symptoms to specialist whilst taking Leflunomide.

Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy whilst taking Leflunomide.

Inform GP or specialist of any other medicines being taken including over-the-counter products.

Attend for regular reviews and blood monitoring tests.

### CONTACT NUMBERS FOR ADVICE AND SUPPORT

**Advice and guidance:** Access Advice & Guidance tool via e-RS referral system selecting the relevant speciality for non-urgent queries

#### Princess Alexandra Hospital NHS Trust - Rheumatology

Consultant	<b>For GPs only:</b> contact Rheumatologist via switchboard if urgent <a href="mailto:tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net">tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net</a> for non-urgent queries.
Rheumatology Specialist Nurse for DMARDs	01279827434 helpline (voice mail only) for non-urgent queries only, Lily Robinson
Rheumatology Specialist Nurse / Pharmacist for Biologic queries	01279827819 helpline (voice mail only) for non-urgent queries only, Mona Kamal Zou / Sachini Amarasekera
	<b>Patients can email</b> <a href="mailto:tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net">tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net</a> for non-urgent queries.

#### Princess Alexandra Hospital NHS Trust - Pharmacy

Medicines Information (for medicines related queries)	01279 827054
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### CLINICAL INFORMATION

#### Prescribed Indications

Licensed indications

Rheumatoid arthritis  
Psoriatic arthritis

#### Therapeutic Summary

## LEFLUNOMIDE

Leflunomide is a disease-modifying anti-rheumatic drug (DMARD) for the treatment of adult patients with active rheumatoid arthritis. Leflunomide is similar in efficacy to sulfasalazine and methotrexate but these remain the agents of choice in the majority of patients.

Leflunomide has a long half-life of 1-4 weeks. This means that occasionally a washout procedure using cholestyramine or activated charcoal will be necessary to enhance the elimination of leflunomide if the patient is experiencing a serious adverse reaction.

### Dose and Route of Administration

#### Rheumatoid Arthritis

Starting dose of 10mg and can be increased to 20mg daily depending on treatment response. The recommended dose for rheumatoid arthritis is leflunomide 10 mg to 20 mg once daily for monotherapy. In cases of combination therapy with another potentially hepatotoxic DMARD (eg methotrexate) 10mg once daily is recommended.

#### Psoriatic Arthritis

Recommended daily dose is 20mg once daily.

The therapeutic effect usually starts after 4 to 6 weeks and may further improve up to 4 to 6 months.

There is no dose adjustment recommended in patients with mild renal insufficiency but it is contraindicated in moderate /severe renal failure.

No dosage adjustment is required in patients above 65 years of age.

Leflunomide tablets should be swallowed whole with sufficient amounts of liquid. The extent of leflunomide absorption is not affected if it is taken with food.

See SPC for more details <http://www.medicines.org.uk/emc/medicine/26343>

### Adverse Effects and Management

Main side effects are rash, hair loss, GI upset, headache, weight loss and breathlessness

#### IMMUNOSUPPRESSION

For patients who have not had chicken pox and are in contact with anyone with the virus follow guidance from Public Health England June 2019 <https://www.gov.uk/government/publications/varicella-zoster-immunoglobulin>

### Cautions

Localised or systemic infection including Hepatitis B or C or history of TB

Concomitant administration of hepatotoxic or haematotoxic drugs (e.g. methotrexate) is not advisable according to manufacturer, although combination therapy has been used (BSR guidelines).

The active metabolite of leflunomide, A771726, has a long half-life, usually 1 to 4 weeks. Serious undesirable effects might occur even if the treatment with leflunomide has been stopped. (See washout procedure)

Due to a potential for additive hepatotoxic effects, it is recommended that alcohol consumption be avoided during treatment with leflunomide, if possible. BSR guidelines recommend alcohol intake to be well within national limits of 4-8 units per week.

### Contraindications

Hypersensitivity to leflunomide, or to any of the excipients.

Severe immunodeficiency

Serious infections

Impaired liver function due to any cause

Severe unexplained hypoproteinaemia

Renal impairment

Patients with significantly impaired bone marrow function or significant anaemia, leucopenia, neutropenia or thrombocytopenia due to causes other than rheumatoid or psoriatic arthritis.

Patients should avoid 'live' vaccines such as oral polio, MMR, BCG and yellow fever. An inactivated form of polio is readily available.

Written by: Clare Macpherson, Senior Pharmacist

Approved Dec 2017 Review date Dec 2019 The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics and British National Formulary.

## LEFLUNOMIDE

### Pregnancy and Lactation

Leflunomide is teratogenic and must not be given to pregnant women or women of child bearing potential unless reliable contraception is used. Women planning to have children should either discontinue the drug 2 yrs prior to conception or have a rapid removal of its active metabolite by following the washout procedure.

Men should use effective contraception for 3 months after stopping leflunomide.

Blood concentrations should be checked prior to planned pregnancy especially if within 2 years of stopping leflunomide or following wash out. Any pregnancy within 2 yrs of discontinuation of leflunomide should be discussed with rheumatologist if drug washout has not been performed. Notify pharmaceutical company in the event of pregnancy while on leflunomide.

Breast feeding is contra-indicated.

### Washout procedure

To aid drug elimination in cases of serious adverse effect or before conception, stop treatment and give either:

Cholestyramine 8g three times day for 11 days **OR**

Activated charcoal 50g four times a day for 11 days

However, also following either of the washout procedures, verification by 2 separate tests at an interval of at least 14 days and a waiting period of one-and-a-half months between the first occurrence of a plasma concentration below 0.02 mg/L and fertilisation is required. (See SPC for full information).

### Interactions with other medications

Tolbutamide

Phenytoin

Warfarin

Please note that as leflunomide has an extremely long half life, interactions can potentially be serious and more actions may be required beside just discontinuation of the drug e.g. washout. This may also be of practical importance when switching from leflunomide to another DMARD.

### MONITORING STANDARDS FOR LEFLUNOMIDE AT PRINCESS ALEXANDRA HOSPITAL NHS TRUST

The following standards have been agreed for the monitoring of leflunomide in all patients at Princess Alexandra Hospital NHS Trust.

<b>Pre-treatment by Specialist</b>	Height, weight, blood pressure, FBC, U&Es, LFTs, TPMT phenotype, creatinine, varicella status, hepatitis B&C status Blood pressure: if > 140/90 on two consecutive readings 2 weeks apart, treat hypertension prior to commencing therapy.	
<b>Initial monitoring by Specialist</b>	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Every 2 weeks until on stable dose for 6 weeks.
<b>Ongoing monitoring by GP</b>	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Then once on stable dose monitor monthly for 3 months.
	FBC Creatinine / calculated GFR ALT +/- AST Albumin	At least every 12 weeks
<b>BP and weight at each monitoring visit</b>		

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<b>Dose increase</b>	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Every 2 weeks until on stable dose for 6 weeks, then revert to previous schedule
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### Action and Advice

If a GP has taken blood tests for the general medical management of a patient and blood test results fall into the categories below or the patient reports one of the adverse events below, these are recommendations for considering the withdrawal of Leflunomide therapy:

<b>Blood Test Results</b>	
WBC < 3.5 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team
Neutrophils < 2.0 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team
Platelets < 150 x 10 <sup>9</sup> /l	Withhold until discussed with specialist team
> 2-fold rise in AST, ALT (from upper limit of reference range)	Withhold until discussed with specialist team
<b>Symptoms</b>	
Rash or itch	Withhold until discussed with specialist team
Abnormal bruising or bleeding	Withhold until FBC results available & discuss with specialist team
Severe sore throat	Withhold until FBC results available & discuss with specialist team
Hypertension	If BP >140/90 treat as per NICE guidance. If remains uncontrolled, withhold until discussed with rheumatologist.
Hair loss	Seek advice from rheumatologist
Weight loss	If >10% with no cause identified, withhold until discussed with rheumatology team.
Breathlessness	If increasing shortness of breath, withhold until discussed with rheumatology team.
GI Upset	Give symptomatic treatment and discuss with rheumatology team.

### Further Information

This document does not replace the SPC and BNF and should be read in conjunction with it.

BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs  
<https://academic.oup.com/rheumatology/article/56/6/865/3053478>

### Useful information

West Essex CCG webpage for Shared Cared Guidelines –

[Shared Care Letter - West Essex CCG](#)

Arthritis Research UK Patient Information Leaflet

<http://www.arthritisresearchuk.org/arthritis-information/drugs/methotrexate.aspx>

CKS DMARD

<http://cks.nice.org.uk/dmards#!scenario:7>

Arthritis Research UK Patient Information Letter

<http://www.arthritisresearchuk.org/arthritis-information/drugs/leflunomide.aspx>

GMC Prescribing Guidance: Shared Care

[https://www.gmc-uk.org/guidance/ethical\\_guidance/14321.asp](https://www.gmc-uk.org/guidance/ethical_guidance/14321.asp)

**LEFLUNOMIDE**

**GP response to Shared Care Agreement**

(only complete & send if NOT participating in shared care)

**This shared care agreement has been approved by the Medicines Management Optimisation Programme Board**

Patient Name:	NHS No:
Consultant:	Medicine requested for shared care: <b>leflunomide</b>

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care agreement. My clinical reasons for declining shared care for this patient are listed in the box below:

Yours sincerely

{GP name}

{Surgery}

**Please send a copy of this response to:**

1. The Specialist/consultant requesting shared care
2. **ANONYMISED COPY OF THIS FORM ONLY** to the E-MAIL: [tpa-tr.ClinicalPharmacy@nhs.net](mailto:tpa-tr.ClinicalPharmacy@nhs.net)

(sending a copy of this form to the PAH pharmacy will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG Medicines Optimisation Team of the reasons shared care is not being undertaken by GPs allowing for changes to be made in future updates to improve patient safety)

Information for patients:

## SHARED CARE:

### Agreement information and confirmation

<p><b>Patient name:</b></p> <p>.....</p> <p><b>Medicine:</b></p> <p>.....</p>
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**We would be grateful if you would take time to read this information as it will help us work with you to manage your condition and ensure safe prescribing of the specific medicine listed above.**

### What is a Shared Care Agreement (SCA)?

A Shared Care Agreement (SCA) enables the care you have for a specific condition to be shared between the hospital and your GP.

The agreement means that the medicine the hospital has started, can be continued by your GP, so you won't have to visit the hospital to collect your medicine.

The SCA gives information on your medicine, guidance on the prescribing and monitoring responsibilities for your consultant (in the hospital), your GP and you. For an SCA, to work everyone involved must understand it and communicate effectively.

Your consultant and your GP will need to sign the agreement and if you agree to this approach, we would ask you to sign this letter, to indicate your agreement to have your care managed in this way.

### How does shared care work?

#### Your consultant and GP share responsibility for your care.

The consultant is a specialist in your condition and will start prescribing your medicine, making sure it is suitable for you. There will come a point in your treatment when you may not need to be monitored by the consultant as often and this monitoring can be done by your GP.

Once your GP has agreed to the SCA, they will be able to prescribe the same medicine for you at the dose recommended by the consultant.

The organisation which regulates GPs, the General Medical Council, says that 'when a GP prescribes a medicine, the GP needs to satisfy themselves that the prescription is needed, appropriate for the patient and within the limits of their competence'.

So, your GP can only issue a prescription if the consultant and you keep to the responsibilities you have agreed (see below). If responsibilities are not kept or if the GP no longer feels it is safe to prescribe the medicine, he/she will explain the reasons to you and your consultant, then prescribing responsibilities will be transferred back to the hospital.

### What do I need to do to ensure the SCA can continue?

#### ▶ Attend hospital outpatients

You must still attend the hospital for regular reviews as directed by your consultant (these may be less frequent than before and you may be seen by a specialist pharmacist or a specialist nurse). If you do not attend your hospital appointments, your GP will not be able to continue issuing prescriptions for this medication.

#### ▶ Attend GP appointments

You must attend any appointments you have with your GP in relation to this medicine, so they can look after you effectively

▶ **Have blood tests as you have been**

**advised to:** Your consultant should have informed you if and how often you need to have blood monitoring tests. You can usually have your blood taken at an appropriate clinic and not need to go to the hospital.

- ▶ If you do not have the blood monitoring tests as advised by your consultant, your GP will no longer be able to issue you with prescriptions as it would not be safe to do so.

## What do I do if I am having side-effects to the medicine?

Your consultant should have informed you of the common side-effects to expect and what to do if you experience them. If you think you may be having side-effects from a medicine report these directly to your consultant. Your GP may need to seek advice from your consultant before issuing you with another prescription; this is to ensure it is safe for you to continue on the medication.

## What if my disease symptoms change or get worse?

Report any changes in disease symptoms or circumstances that could affect management of your disease to your consultant.

## What about the other medicines I take?

Inform your GP and the consultant of all other medicines you are taking, including those you may have bought yourself. Do not take new medicines (including those you could buy) until you have discussed this with your pharmacist, GP or consultant.

If you would like to go ahead with a shared care agreement for the specific medication identified on page 1, please sign below to confirm that you:

- ▶ Understand the shared care agreement.
- ▶ Are happy to have your care for this aspect of your health managed by a shared care agreement.
- ▶ You agree to attend regular review appointments as requested.
- ▶ You agree to have blood tests as required.

## What happens if I change GP Practice?

If you register at a new GP Practice a new agreement needs to be put in place between your new GP and the specialist team.

The specialist team can start this process if you provide them with information before you move to make sure there is a smooth handover.

Patient's signature .....

Date .....

Print name .....

If at any point in time you would like this shared care agreement to stop, please talk to your GP.

