**Request to Share Care and Agreement Form**

**Leflunomide for patients within adult services**

**Shared Care Protocol: Guideline No 11; Version 1.2**

This request to share care provides key primary care information on responsibilities and monitoring. The aim is to support the GP to agree to share care arrangements. Refer to full shared care protocol for further information.

**GP to review and must respond to provider Trust request to share care within 2 weeks**. **This form is used to agree shared care between the specialist, patient and GP and a copy of the form to be retained in 1.Patients’ hospital records, 2. Given to patient, and 3. Retained in GP notes.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient Information or Addressograph label** | | **Drug information** | |
| Patient name: |  | Drug(s) and Dose at handover: |  |
| DOB: |  | Indication: |  |
| NHS number: |  | Estimated date for prescribing to be continued by the GP: |  |
| Patient weight (kg): |  | Date of first prescription by specialist |  |
| Next monitoring tests due and dates: | |  | |
| Specialist additional comments/advice: | |  | |

|  |  |  |
| --- | --- | --- |
| **Specialist and patient agreement**  **By signing below we accept:**   * The Herts and West Essex Area Prescribing Committee [shared care principles](https://www.hweclinicalguidance.nhs.uk/all-clinical-areas-documents/download?cid=1739&checksum=752d25a1f8dbfb2d656bac3094bfb81c) (HWE APC) and * The requirements and responsibilities defined in this drug specific shared care protocol | | |
| Specialist name: | Specialist signature: | |
| Designation: | Date: | |
| Direct telephone: | Patient signature or specialist confirmation of patient agreement to shared care arrangement: | |
| Provider trust: |
| Email/ Shared care email for use by GP: | Date: | |
| **GP response to shared care**  **Please return to specialist within two weeks of receipt of request to share care.**  ***This form is to be completed by the GP who is requested to share care.***  I agree to accept shared care for this patient as set out in this shared care protocol and APC [shared care](https://www.hweclinicalguidance.nhs.uk/all-clinical-areas-documents/download?cid=1739&checksum=752d25a1f8dbfb2d656bac3094bfb81c) principles  I do not accept shared care for this patient  My reason(s) for not prescribing are given below (refer to GP considerations for shared care at end of protocol): | | |
| GP name: | | Practice Address/Stamp: |
| Direct telephone number: | |
| Email: | |
| Date: | | GP Signature: |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Key Primary Care Information (refer to Full Shared Care Protocol for further information)**  **REFERRAL CRITERIA**   * These guidelines are for patients over 18 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.   **GP RESPONSIBILITIES**   * Consider request to shared care arrangements and prompt completion. Email return of signed response to the specialist using the Shared Care Agreement Form **within 14 days** of its receipt * If accepted, prescribe ongoing treatment as detailed in the specialist’s request and take into any account potential drug interactions. * Adjust the dose of leflunomide prescribed as advised by the specialist. * Arrange, record and share ongoing monitoring and take appropriate action as per protocol and advised by specialist (see monitoring table), ensuring GP practice systems are in place to recall patients for monitoring blood tests. * Re-iterating with the patient that non-attendance for blood testing may lead to withdrawal of the medication. Further help and advice can be sought from the hospital specialist team. * Ascertaining the reason for non-completion of routine blood testing, if one test is missed. * Conduct the required monitoring as outlined. Communicate any abnormal results to the specialist. * Manage adverse effects and discuss with specialist team when required. · Stop leflunomide and discuss urgently with the specialist if the patient develops signs of serious infection, liver or respiratory disease, unexplained bleeding or bruising, are exposed to chickenpox or shingles. * Discuss with the specialist if the patient plans to become pregnant. * Stop treatment as advised by the specialist. * Inform specialist of any change in the medical condition of patient which may have effect on disease/medications.  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **MONITORING AND ACTIONS TO BE TAKEN**  **Monitoring Table- see GP monitoring highlighted in grey**   |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | **Monitoring table** | | **Hospital specialist** | **Hospital specialist** | **Hospital specialist / GP** | | **GP** | **Hospital specialist** | | **Test** | **Indication** | Pre-treatment baseline | During TreatmentInitiation | Following Treatment  Initiation | | Ongoing | Annual review | | FBC | Baseline and ongoing assessment, including dose adjustment | ✔ | **Phase I monitoring\*** Every 2 weeks until stable dose for 6 weeks | **Phase II monitoring\***  Every 4 weeks for next 12 weeks  *Hospital specialist will undertake the first 4-week test*  *GP will undertake the second and third 4-week test)* | | **Phase III monitoring\***  Every 12 weeks | As part of annual review or as clinically indicated  \_\_\_\_\_\_\_\_\_\_\_  If clinically indicated | | LFTs, Albumin | | U&Es, eGFR | | BP and weight | ✔In addition to height | Every 4 weeks | | ESR/CRP (Rheumatology patients) | Disease activity scoring | ✔ | Every 12 weeks | Not routinely required | | Every 12 weeks on advice of specialist | | Hepatitis B, C & HIV | Baseline assessment, viral, respiratory and TB screening | If clinically indicated | Not routinely required | | | | | Chest X-ray | | TB screening if indicated | | Urinalysis | To assess for or monitor renal disease (proteinuria) or infection | ✔ | | Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding | | ✔ | At every consultation | | At every consultation | | At every consultation |   **\***If a further DMARD is added as combination therapy, or the dose is increased, the initial starting schedule should be reinstated. **For dose changes monitoring should start back with Phase I monitoring and be every 2 weeks until dose is stable for 6 weeks, then revert to previous schedule.** There may be clinical circumstances where the frequency of monitoring may vary and this should be specified by the initiating specialist.  **The exact frequency of monitoring to be communicated by the specialist in all cases.**  More frequent monitoring is appropriate in patients at higher risk of toxicity; e.g. concurrent use of more than one DMARD. This is particularly important for patients co-prescribed methotrexate and leflunomide. The combination is highly effective but potentially synergistically toxic to liver and bone marrow and increase monitoring frequency is strongly advised.  The specialist will retain the responsibility for monitoring the patient’s ongoing response to treatment and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually.  **Further baseline investigations by specialist:**   * Screening for viral infections as per local policy, e.g. HIV, hepatitis B and C, varicella zoster, Epstein Barr virus, cytomegalovirus * Screening for lung disease, including interstitial lung disease, should be undertaken at clinician discretion on a case-by-case basis. * Provide or request appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19) * Pregnancy should be excluded before starting treatment.   **Vaccinations in primary care**  **Patient Advice:**   * For susceptible immunosuppressed individuals with significant exposure to chickenpox (varicella) or shingles (zoster), follow latest national guidance on post exposure prophylaxis and use of anti-virals and varicella zoster immunoglobulin (VZIG) <https://www.gov.uk/government/publications/post-exposure-prophylaxis-for-chickenpox-and-shingles> * **Annual** influenza ([The Green Book, Chapter 19](https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19)) vaccinations are recommended. * COVID-19 vaccination is safe and recommended (see [The Green Book, Chapter 14a](https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a)). * Repeat pneumococcal vaccine may be indicated. See [Green Book Chapter 25](https://www.gov.uk/government/publications/pneumococcal-the-green-book-chapter-25) for advice. * Shingles vaccination (see green book [chapter 28a](https://assets.publishing.service.gov.uk/media/6603fedef9ab41001aeea371/Shingles_Green_Book_chapter_28a_20240315.pdf) for advice) * Other vaccinations as per national schedule.   **(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.**  **Action to be taken if Abnormal Result**  Normal reference range may vary slightly between labs. Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values; specialist will advise if required.  Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). For information on incidence of ADRs see relevant summaries of product characteristic   |  |  | | --- | --- | | **Abnormal Result** | **Action to be taken by GP** | | Full blood count:  · White blood cells <3.5x109/L  · Lymphocytes less than 0.5x109/L  · Neutrophils <1.6x109/L  · Platelets <140x109/L  Eosinophilia >0.5x109/L | Withhold and discuss with specialist team. | | Mean cell volume >105 fL | Consider interruption in treatment. Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal discuss with specialist team urgently | | Blood Pressure | Treat hypertension in line with NICE guidance. If BP remains uncontrolled, withhold leflunomide and discuss with specialist team | | Weight | If >10% weight loss with no cause identified, withhold leflunomide and discuss with specialist team | | Signs or symptoms of bone marrow suppression, e.g. unexplained bleeding or bruising with or without sore throat, mouth ulcers | Check FBC immediately and discuss with the specialist team. See haematological monitoring above. | | Acute infection | In patients with a serious infection (e.g. infection requiring intravenous antibiotics or hospitalisation), leflunomide should be discontinued temporarily until the patient has recovered from the infection.  It can be considered appropriate to continue these drugs in patients with minor infections (e.g. uncomplicated urinary tract infection treated with a short course of oral antibiotics). If a patient on leflunomide has an infection requiring oral antibiotics, an individual clinical decision is needed on the risks / benefits of continuation of immunosuppressants and GPs can contact the specialist team for advice and guidance if support is required with clinical decision making*.* | | Liver function tests:  ALT or AST >100 units/L, or any sudden  increases (e.g. double of baseline), OR  Unexplained fall in serum albumin <30g/L  Jaundice | Withhold and discuss with specialist team. Consider washout procedure. Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication. | | **Renal function:**  Creatinine increase of greater than 30% from  baseline in the last 12 months or GFR reduces  to less than 60mL/min | Withhold and discuss with specialist team. | | **Gastrointestinal disorders:**  Nausea  Diarrhoea | Review for reversible causes. Discuss with specialist team if persistent or severe. Washout, under specialist advice, may be required if severe.  Diarrhoea is common and usually settles. If persistent or severe, withhold and discuss with specialist team. | | Ulcerative stomatitis, haematemesis, black or  bloody stools, or suspected pancreatitis | Withhold and discuss with specialist team. Washout, under specialist advice, may be required if severe. | | Symptoms of interstitial lung disease e.g.  persistent cough, dyspnoea, fever | If leflunomide-induced lung disease is suspected, discuss with specialist team urgently. Consider washout procedure. Treat with corticosteroids as advised by specialist and do not restart leflunomide. | | Generalised rash | Discuss with specialist, washout may be required if severe. | | Pregnancy | Stop leflunomide immediately and discuss with specialist team urgently. Washout should be considered. | | |
|  |

* The expectation is that this information along with the full protocol provides sufficient information to enable GPs to be confident to take on the clinical & legal responsibility for prescribing and monitoring.
* Prescribing and monitoring responsibility will only be transferred under this shared care protocol when:
* Specialist has initiated treatment and prescribed/monitored treatment for initial stabilisation period.
* Specialist has provided pre-treatment counselling and discussed patient responsibilities, preferences and obtained consent to shared care arrangements.
* Specialist and patient have completed and signed the shared care agreement form (page 1).

**Full Shared Care Protocol**

**Leflunomide for patients within adult services**

**Shared Care Protocol: Guideline No 11; Version 1.2**

**This full protocol provides prescribing and monitoring guidance. It should be read in conjunction with HMMC shared care principles,** [**Summary of Product Characteristics (SPC)**](https://www.medicines.org.uk/emc) **and the** [**BNF**](http://www.bnf.org/bnf/index.htm)**.**

**BACKGROUND AND INDICATION(S) FOR USE**

Leflunomide is a conventional disease-modifying anti-rheumatic agent (DMARD). It exhibits anti-inflammatory and antiproliferative effects through the inhibition of pyrimidine synthesis via dihydroorotate dehydrogenase. It may be used as monotherapy or in combination with other DMARDs including methotrexate and sulfasalazine. The therapeutic effect usually begins after 4-6 weeks and benefit may accrue for up to 6 months. Leflunomide has a very long half-life of approximately 2 weeks, and in circumstances where rapid elimination is required a washout procedure may be given if advised by the specialist. This may be due to severe adverse effects, pregnancy, severe infection or if an alternative DMARD is indicated. Washout is typically given as colestyramine 8g taken three times daily or activated charcoal 50g four times daily, for up to 11 days.

**Licensed indications:**

Leflunomide is licensed for use in:

· Rheumatoid arthritis

· Psoriatic arthritis

**DOSAGE, ROUTE OF ADMINISTRATION AND TREATMENT REGIMEN**

**Adult dosage and administration**

**Initial stabilisation:**

An initial dose of 10-20mg once daily is normally given. Due to the long half-life, doses of 10mg

and 20mg may be given on alternate days. Short loading regimens may be used, however these may increase the risk of adverse effects and are considered optional.

**The loading period must be prescribed by the initiating specialist.**

**Maintenance dose (following initial stabilisation):**

10-20mg once daily. Due to the long half-life, doses of 10mg and 20mg may be given on

alternate days.

The initial maintenance dose must be prescribed by the initiating specialist.

**Preparations available:** Leflunomide 10mg, 15mg & 20mg tablets

Tablets should be swallowed whole with sufficient amounts of water. Administration with food does not affect absorption.

Swallowing difficulties

Please refer to the [‘specials’ alternative guidance](https://gbr01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.hweclinicalguidance.nhs.uk%2Fall-clinical-areas-documents%2Fdownload%3Fcid%3D2274%26checksum%3D95f8d9901ca8878e291552f001f67692&data=05%7C02%7Cheernamehta%40nhs.net%7Ccba67ac584344a90298108dcafcc3bcd%7C37c354b285b047f5b22207b48d774ee3%7C0%7C0%7C638578538908037976%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C0%7C%7C%7C&sdata=drWPIVzT4RkMn0VJJa96%2F2dIm19xPNtqcc0yghL%2FsEA%3D&reserved=0) for a list of commonly prescribed medicines and alternative methods of administration for patients with swallowing difficulties, feeding tubes or for patients prescribed unlicensed ‘specials’ medication. Each entry takes into account alternative medicines, formulations, cost and licensing. This list is not exhaustive. As not all medicines are listed, please contact the initiating specialist if required for individual patient advice if a patient has a swallowing difficulty.

Transfer of monitoring and prescribing to primary care is normally after the patient’s dose has been optimised, and with satisfactory investigation results for at least 4 weeks.

The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician. Termination of treatment will be the responsibility of the specialist.

|  |
| --- |
| **SPECIALIST RESPONSIBILITIES INCLUDING PRE-TREATMENT ASSESSMENT**   * Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol and communicated to primary care. * Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet. · * Assess for contraindications and cautions and interactions. * Conduct required baseline investigations and initial monitoring and provide results to GP. * Initiate and optimise treatment as recommended. Prescribe the maintenance treatment for at least 12 weeks and until optimised. * Once treatment is optimised, complete the shared care documentation, and send to patient’s GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information. * Prescribe the maintenance treatment until optimised, which will usually be after around 3 months. Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care. * Conduct scheduled reviews and monitoring and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring remains appropriate. * Provide advice to primary care on the management of adverse effects if required. * 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 possible. * 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 A SPECIALIST INTEREST IN RHEUMATOLOGY**   * 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. |

**GP RESPONSIBILITIES**

Refer to page 2 and GP Considerations for Shared Care page 13.

|  |
| --- |
| **PATIENT AND/OR CARER RESPONSIBILITIES IN COOPERATION WITH SPECIALIST AND GP**   * Take leflunomide as prescribed and avoid withdrawal unless advised by the primary care prescriber or specialist. * Attend regularly for monitoring and review appointments with primary care and specialist and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend. * Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms. * Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of leflunomide with their pharmacist before purchasing any OTC medicines. * Moderate their alcohol intake to no more than 4 units per week. * Not to drive or operate heavy machinery if leflunomide affects their ability to do so safely. * Patients of childbearing potential should use effective contraception during and for up to 2 years after treatment and take a pregnancy test if they think they could be pregnant and inform the specialist or GP immediately if they become pregnant or wish to become pregnant. |

**MONITORING AND ACTIONS TO BE TAKEN**

* Refer to page 2-5

**DISPENSING PHARMACIST RESPONSIBILITIES**

* Confirming that the patient has received verbal and written patient counselling / information and provide additional counselling should this be required.

|  |  |
| --- | --- |
| **SIGNIFICANT INTERACTIONS WITH OTHER MEDICATIONS**   * **Anticoagulants**: The anticoagulant effect of vitamin K anticoagulants may be increased by   leflunomide. Close INR monitoring and follow-up is recommended.   * **Live vaccines** (e.g. oral polio, oral typhoid, MMR, BCG) should generally be avoided. There   is evidence that doses at or below 20mg leflunomide, as either monotherapy or in  combination with 20mg prednisolone per day or less, can safely receive live shingles  vaccinations. Clinician discretion is advised, see section 9   * **JAK kinase inhibitors**, e.g. baricitinib, filgotinib: due to the increased risk of   immunosuppression.   * **Colestyramine and activated charcoal**: Co-administration leads to a rapid and significant   decrease in plasma levels of leflunomide metabolites by interrupting enterohepatic  recirculation   * **Repaglinide, paclitaxel, pioglitazone, ceflaclor, benzylpenicillin, ciprofloxacin,**   **indomethacin, ketoprofen, furosemide, cimetidine, zidovudine, venetoclax**:  Leflunomide may increase the exposure to these products.   * **Rosuvastatin** levels may be increased by leflunomide. A maximum rosuvastatin dose of   10mg is recommended. Caution is recommended with other statins and dose reduction may  be required.  **CONTRAINDICATIONS & CAUTIONS**  **Contraindications:**   * Hypersensitivity (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   * Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiencyor glucose-galactose malabsorption * Patients with significantly impaired bone marrow function or significant anaemia, leucopenia, neutropenia, * or thrombocytopenia due to causes other than rheumatoid or psoriatic arthritis * Serious infection * Liver impairment * Moderate to severe renal impairment * Severe hypoproteinaemia * Severe immunodeficiency * Pregnancy and breastfeeding, or patients who are not using effective contraception during   treatment. People of child-bearing potential should use effective contraception for up to 2  years after stopping treatment. Avoid where possible in people of child-bearing potential.  **Cautions:**   * Anaemia: avoid if significant and due to causes other than rheumatoid or psoriatic arthritis. * Localised or systemic infection which may be more severe * History of HIV, tuberculosis, hepatitis B or C * Impaired bone-marrow function, leucopenia, or thrombocytopenia: avoid if significant and due to causes other than rheumatoid or psoriatic arthritis. * Use of concurrent haematotoxic or hepatotoxic DMARDs e.g. methotrexate * There is a theoretical risk of male-mediated foetal toxicity so effective contraception should   be used throughout treatment. Those patients wishing to father a child should discuss with  the specialist who may want to follow the washout procedure before advising he attempt  conception   * Due to a potential for additive hepatotoxic effects, it is recommended that alcohol consumption be moderated during treatment with leflunomide. BSR guidelines recommend alcohol intake to be well within national limits of 4- 8 units per week. |  |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SIDE EFFECTS AND ACTIONS TO BE TAKEN (REFER TO** [**BNF**](http://www.bnf.org/bnf/index.htm) **AND** [**SPC**](http://www.medicines.org.uk/emc) **for full details)**   * GP to liaise with specialist if any side effects are a cause for concern * Patients should be instructed to report immediately any evidence of infection, unexpected bruising or bleeding or other manifestations of bone marrow depression - also refer to monitoring section.  |  |  | | --- | --- | | **SIDE EFFECTS** | **Action to be taken by GP** | | Full blood count:  · White blood cells <3.5x109/L  · Lymphocytes less than 0.5x109/L  · Neutrophils <1.6x109/L  · Platelets <140x109/L  Eosinophilia >0.5x109/L | Withhold and discuss with specialist team. | | Mean cell volume >105 fL | Consider interruption in treatment. Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal discuss with specialist team urgently. | | Blood Pressure | Treat hypertension in line with NICE guidance. If BP remains uncontrolled, withhold leflunomide and discuss with specialist team | | Weight | If >10% weight loss with no cause identified, withhold leflunomide and discuss with specialist team. | | Signs or symptoms of bone marrow  suppression, e.g. unexplained bleeding or bruising with or without sore throat, mouth ulcers | Check FBC immediately and discuss with the specialist team. See haematological monitoring above. | | Acute infection | In patients with a serious infection (e.g. infection requiring intravenous antibiotics or hospitalisation), leflunomide should be discontinued temporarily until the patient has recovered from the infection.  It can be considered appropriate to continue these drugs in patients with minor infections (e.g. uncomplicated urinary tract infection treated with a short course of oral antibiotics). If a patient on leflunomide has an infection requiring oral antibiotics, an individual clinical decision is needed on the risks / benefits of continuation of immunosuppressants and GPs can contact the specialist team for advice and guidance if support is required with clinical decision making*.* | | Liver function tests:  ALT or AST >100 units/L, or any sudden increases (e.g. double of baseline), OR  Unexplained fall in serum albumin <30g/L  Jaundice | Withhold and discuss with specialist team. Consider washout procedure. Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication. | | Renal function: Creatinine increase of greater than 30% from baseline in the last 12 months or GFR reduces to less than 60mL/min | Withhold and discuss with specialist team. | | **Gastrointestinal disorders:**  Nausea  Diarrhoea | Review for reversible causes. Discuss with specialist team if persistent or severe. Washout, under specialist advice, may be required if severe.  Diarrhoea is common and usually settles. If persistent or severe, withhold and discuss with specialist team. | | Ulcerative stomatitis, haematemesis, black or bloody stools, or suspected pancreatitis. | Withhold and discuss with specialist team. Washout, under specialist advice, may be required if severe. | | Symptoms of interstitial lung disease e.g. persistent cough, dyspnoea, fever | If leflunomide-induced lung disease is suspected, discuss with specialist team urgently. Consider washout procedure. Treat with corticosteroids as advised by specialist and do not restart leflunomide. | | Generalised Rash | Discuss with specialist, washout may be required if severe | | Pregnancy | Stop leflunomide immediately and discuss with specialist team urgently. Washout should be considered. | |
|  |

**PREGNANCY, PATERNAL EXPOSURE AND BREASTFEEDING**

It is the responsibility of the specialist to provide advice on the need for contraception to male

and female patients on initiation and at each review, but the ongoing responsibility for providing

this advice rests with both the primary care prescriber and the specialist.

**Pregnancy:**

Leflunomide is contraindicated in pregnancy. Patients of child-bearing potential should use

effective contraception during and for up to 2 years after treatment, unless a washout procedure

is followed (see below). See FSRH statement on contraception for women using known

teratogenic drugs for information on contraceptives considered highly effective.

The active metabolite of leflunomide is highly protein bound and because of extensive

enterohepatic recycling its half-life is prolonged. The manufacturer currently recommends a two-

year waiting period after discontinuation of the medicine before attempting to conceive. The

manufacturer also advises that the plasma levels of the active metabolite of leflunomide

(teriflunomide) should be below 0.02mg/L at the end of the two year period, confirmed by a

second test after an interval of at least 14 days. If both tests show plasma levels of teriflunomide

to be less than 0.02mg/L, then no teratogenic risk is expected. It is important to note that this

test may only be available to patients who are taking the branded Arava® leflunomide tablets.

If a waiting period of 2 years using effective contraception is considered unpractical, a washout

procedure may be advisable. Following this, the recommendations regarding

verification of teriflunomide levels remain. Two tests must be done no less than 14 days apart

and conception is not advised until one and a half months after the first plasma concentration

below 0.02mg/L. This test may only be available to patients who are taking the branded Arava®

leflunomide tablets.

If a woman becomes pregnant while taking leflunomide or within two years after discontinuation,

the manufacturer recommends an immediate 11-day washout procedure with colestyramine or

activated charcoal.

Information for healthcare professionals:

https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-LEFLUNOMIDE-IN-

PREGNANCY/

Information for patients and carers: <https://medicinesinpregnancy.org/Medicine--pregnancy/Leflunomide/>

**Breastfeeding**:

Leflunomide and its metabolites pass into breast milk in animal studies. Manufacturer states that leflunomide is contraindicated for breastfeeding patients. Information for healthcare professionals: <https://www.sps.nhs.uk/medicines/leflunomide/>

**Paternal exposure:**

Male patients should be aware of the possible male-mediated foetal toxicity. Effective contraception during treatment with leflunomide should also be guaranteed.

|  |
| --- |
| **ADVICE TO PATIENTS AND CARERS**  **The patient should be advised to report any of the following signs or symptoms to their**  **primary care prescriber without delay:**   * Symptoms of chickenpox or contact with a person with chickenpox or shingles. * Persistent cough, shortness of breath, or any other problems with breathing. * Sore throat, high temperature, skin rash, swollen glands, or any other signs or symptoms of   Infection   * Signs or symptoms of liver problems, such as yellow skin or eyes (jaundice), itching all over,   nausea or vomiting.   * Unexplained bleeding or bruising, black stools, or blood in the vomit or stools. * Suspected or confirmed pregnancy. * Any tingling, numbness or weakness in extremities that may indicate peripheral neuropathy.   **The patient should be advised:**   * Moderate their alcohol intake to no more than 4 units per week while taking leflunomide,   Taking alcohol and leflunomide together increases the risk of liver injury.   * Tell anyone who prescribes them a medicine that they are taking leflunomide. Always ask a   pharmacist before purchasing any medicines over the counter, including herbal remedies,  and ask if they are safe.   * To use effective contraception, and to take a pregnancy test if they think they could be   pregnant. Patients should inform the specialist or GP as soon as possible if they become  pregnant. All patients, both male and female, should inform their specialist well in advance if  they are planning a pregnancy so that changes can be made to their treatment regime.  **Patient information**:  Leflunomide in rheumatoid arthritis: [Leflunomide in rheumatoid arthritis (RA) | NRAS](https://nras.org.uk/resource/leflunomide/)  and: <https://www.versusarthritis.org/about-arthritis/treatments/drugs/leflunomide>  General Information: <https://patient.info/medicine/leflunomide-tablets-for-arthritis-arava> |

* **REFERENCES** British National Formulary (BNF) – accessed via <https://bnf.nice.org.uk/> on 18/01/23
* Electronic Medicines Compendium (EMC) –accessed via [https://www.medicines.org.uk/emc](https://www.medicines.org.uk/emc%20on%2024.08.23) on 18/01/23
* NICE CKS DMARDs: Last revised in December 2021; <https://cks.nice.org.uk/topics/dmards/>
* BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, Rheumatology 2017;56:865868 <https://academic.oup.com/rheumatology/article/56/6/865/3053478>
* NHS England shared care protocol – leflunomide for patients within adult services: Last updated July 2022; <https://www.england.nhs.uk/publication/shared-care-protocols/>

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CONTACT DETAILS for BACK-UP INFORMATION / ADVICE**  **East and North Hertfordshire NHS Trust**   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Department** | **Contact number** | **Specialist Team designated nhs.net email** | **Pharmacy Team shared care admin contact** | **Out of hours contact / switchboard** | | **Rheumatology** | 01438 285624 | [rheumsecretariesenh-tr@nhs.net](mailto:rheumsecretariesenh-tr@nhs.net) | [sharedcare.enh-tr@nhs.net](mailto:sharedcare.enh-tr@nhs.net)  01438 284032 | 01438 314333 |   **Princess Alexandra Hospital NHS trust**   |  |  |  |  | | --- | --- | --- | --- | | **Department** | **Contact number** | **Specialist Team designated nhs.net email** | **Out of hours contact / switchboard** | | **Rheumatology** | 01279827434 – DMARD helpline  01279827819- Nurse helpline | [tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net](mailto:tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net) | 01279 444455 |   **West Hertfordshire Hospitals NHS Trust**   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Department** | **Contact number** | **Specialist Team designated nhs.net email and direct dial for clinicians** | **Pharmacy Team shared care admin contact** | **Out of hours contact / switchboard** | | **Rheumatology** | **Rheumatology**  **Specialist Nurse Helpline (non urgent queries, may take up to 48 hours to respond)**  Watford General:  01923 217798  St Albans City:  01727 897912 | Watford General:  01923 217520  St Albans City:  01727 897859  Hemel Hempstead:  01442 287049  [wherts-tr.rheumatology@nhs.net](mailto:wherts-tr.rheumatology@nhs.net) | [wherts-tr.medinfowatford@nhs.net](mailto:wherts-tr.medinfowatford@nhs.net) | 01442 213141  Call medical on call team |   **Communication**  For any queries relating to a patient’s treatment with leflunomide, please contact the specialist as documented at the top of this document. Read in conjunction with HWE APC shared care principles document.  For advice if you have any concerns contact the specialist team. If unable to contact specialist team or out of hours, contact medical registrar on call. |

**GP Considerations for Shared Care**

This shared care agreement outlines suggested management for the prescribing of the specified drug(s) and indication(s) when the responsibility is shared between the specialist and general practitioner (GP). Sharing of care assumes communication between the specialist, GP and patient. It is important that patients are consulted about treatment and are in agreement with it. The intention to share care should be explained to the patient by the doctor initiating treatment and consent obtained.

Prescribing is to be initiated in secondary care by a provider Trust specialist and will usually be prescribed for 12 weeks unless otherwise stated within the agreed individual shared care protocol**. The expectation is that these shared care guidelines should provide sufficient information to enable GPs to be confident to take on the clinical and legal responsibility for the prescribing and the monitoring of this / these drug(s) in stable patients.** The questions below will help you confirm this:

* Is the patient’s condition predictable or stable?
* Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care document?
* Have you been provided with relevant clinical details including monitoring data?
* Have this document and BNF/SPC provided sufficient information for you to feel confident in accepting clinical and legal responsibility for prescribing?

**If you can answer YES to all of these questions (after reading this shared care guideline), then it is appropriate for you to accept the prescribing responsibility. GPs need to formally accept shared care by completing and returning the form provided within this protocol to the specialist within two weeks of receipt of request to share care.**

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should respond back to the consultant outlining your reasons for NOT prescribing on the agreement form within two weeks of receiving the request to share care. If you do not have the confidence to prescribe, you still have the right to decline. In such an event, the total clinical responsibility for prescribing the medication and any monitoring required remains with the specialist. Please note that medication cost is not an acceptable reason for refusal to take on shared care.

The prescribing doctor legally assumes clinical responsibility for the drug and the consequences of its useas well as responsibility of monitoring (securing and reviewing blood test results).

Prescribing and monitoring responsibility will only be transferred when the consultant and the GP agree that the patient’s condition is stable or predictable. This will usually be 12 weeks of treatment unless otherwise stated within the agreed individual shared care protocol.

**Approval Information**

|  |  |
| --- | --- |
| Version | Version 1.2 Updated in line with new shared care protocol template May 2025  Version 1.1: Updated weight and BP monitoring schedule, Updated wording on swallowing difficulties. September 2024  1.0 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include:   * Rebadging with HWE ICB * Review date removed and replaced with standard statement. |
| Developed by | Pharmacy and Medicines Optimisation Team, Hertfordshire and West Essex (HWE) ICB with relevant HWE ICS stakeholders. |
| Approved by | Hertfordshire & West Essex Area Prescribing Committee |
| Date approved/updated | May 2025 |
| Review date: | The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available. |
| Superseded version | Leflunomide shared care agreement – West Essex CCG, MOPB, Dec 2017  Leflunomide shared care agreement – Herts Valley CCG, July 2014 |