**SHARED CARE GUIDELINE**

**Leflunomide for use in Rheumatology**

**Implementation Date: 1st December 2019 Review Date: 1st December 2022**

***This guidance has been prepared and approved for use within Sunderland and South Tyneside in consultation within the CCGs, and Secondary Care Trust.***

***The guideline sets out the details of the transfer of prescribing and respective responsibilities of GPs and specialist services within shared care prescribing arrangements. It is intended to provide sufficient information to allow GPs to prescribe this treatment within a shared care setting***

**Approved by:**

|  |  |
| --- | --- |
| **Committee** | **Date** |
|  |  |
|  |  |

**Instructions for completion:**

## Consultant to counsel patient on medication and ensure patient has been provided with information leaflet

## Consultant to ensure all clinical details completed on this document

## Consultant to ensure patient understands proposed monitoring and prescribing arrangements if a shared care agreement is entered into

## GP to complete final section of form and return to specialist prescriber within 28 days

## GP to retain copy of document on patient record within surgery

**Clinical details:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| SHARED CARE GUIDELINE | | | | | |
| Non-proprietary name | Leflunomide | Licensed  Y/N? | Y | | |
| Dosage form and strength | 10mg and 20mg tablets | | | BNF class | 10.1.3 |

|  |  |
| --- | --- |
| Indication | Moderate to severe inflammatory arthritis |
| Dosage and Administration | 10-20mg daily |
| Eligibility criteria for shared care | Patients must be under the care of a consultant rheumatologist  Must have a diagnosis of inflammatory arthritis  Patients who have been stabilised and have been treated by specialist for at least three months.  Patients who are not stable should not be transferred to primary care for monitoring. |
| Excluded patients | Any patient in whom lefunomide is contraindicated or not tolerated.  Not for patients under the age of 16 years |
| Initiation | Shared care to be initiated once patient has been stable on maintenance dose for three months |
| Monitoring | **Baseline assessment will be completed by specialist prior to initiation**  **Monitoring**  Ongoing blood test monitoring of high risk or low risk patients according to monitoring schedules below and review of laboratory abnormalities prior to transfer.  Blood pressure and weight should be checked at each monitoring interval.  Monitoring of high risk patients  The patient is ‘high risk’ if any of the following apply:   * Extremes of weight: BMI <18 or >30kg/m2 * Renal impairment: CKD stage III or above * Pre-existing liver disease (including NAFLD) * Significant other co-morbidity (e.g. malignancy) * Age >80 years * Previous DMARD toxicity.   **Routine Bloods:** FBC, U&E, ALT and/or AST, Albumin, creatinine/eGFR  **Frequency:** Every two weeks until stable on a dose for 6 weeks.   * Once on a stable dose: monthly blood tests. * Following a dose increase bloods should be checked every two weeks for 6 weeks, then revert back to previous schedule   **BP**: High BP can be treated in line with usual protocols in primary care. Contact consultant rheumatologist for advice if there are any concerns e.g. persistent high blood pressure despite treatment.  For patients who are NOT high risk:  **Routine Bloods:** FBC, U&E, ALT and/or AST, Albumin, creatinine/eGFR  **Frequency:** Every 2 weeks until stable on a dose for 6 weeks   * Once on a stable dose: monthly blood tests for 3 months * Then: at least every 12 weeks for the duration of treatment * Following a dose increase bloods should be checked 2 weekly for 6 weeks, then revert back to previous schedule   **BP**: High BP can be treated in line with usual protocols in primary care. Contact consultant rheumatologist for advice if there are any concerns e.g. persistent high blood pressure despite treatment.  **Laboratory abnormalities requiring action**  The abnormalities in table below should trigger action/review. **If any abnormal blood test results are obtained, withhold the medication and discuss with the patient’s consultant rheumatologist.** Do not forget to consider the possibility that the abnormal blood result may be unrelated to the immunosuppressant medication.   |  |  | | --- | --- | | **Test** | **Result** | | White cell count | <3.5 \* 109/l (or sequential falls in WBC on 3 occasions) | | Neutrophils | <1.6 \* 109/l (or sequential falls neutrophils >10% on 3 occasions) | | Unexplained eosinophilia | >0.5 \* 109/l | | Platelet count | <140 \* 109/l or sequential falls | | MCV | > 105 f/l | | Creatinine/ eGFR | Creatinine increase >30% over 12 months and/or GFR <60ml/min/1.73m2 | | ALT (and/or AST) | >100 U/L | | Albumin | Unexplained reduction in albumin to <30g/l |   If the patient develops oral ulceration, abnormal bruising, sore throat or an unexplained rash then reduce dose or withhold leflumomide if severe until FBC available and discuss with specialist |
| Infection | During serious infections, the immunosuppressant agent (IA) should be temporarily discontinued until the patient has recovered from the infection. If infection develops requiring antibiotics, **stop leflunomide for duration of antibiotics**. Patient should be seen by GP/Clinician within 12 hours of onset of infective symptoms.  It is usually appropriate to continue IAs in minor infections (e.g. a treated, uncomplicated UTI). The IA would usually be restarted after antimicrobial treatment is complete and the patient has started to make a significant clinical improvement. When the IA is restarted, the same monitoring schedule should be followed.  Patients treated with immunosuppressants are at increased risk for opportunistic infections (bacterial, fungal, viral and protozoal).  If Herpes Zoster occurs stop leflunomide and prescribe aciclovir. If patient is in contact with chicken pox, contact specialist (may need Zoster Immunoglobulin). |
| Vaccination | Live vaccinations are not recommended. Vaccinations against influenza and pneumococcus should be recommended.  Shingles vaccination (Zostavax®) contains live, attenuated virus. The Green Book advises that specialist advice should be sought as to the suitability for shingles vaccination: <https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book> |
| Pregnancy and breastfeeding | Leflunomide is contraindicated in pregnancy; the active metabolite is teratogenic.  Leflunomide is also contraindicated in breastfeeding.  Effective contraception is essential during treatment and for at least 2 years after treatment in women and at least 3 months after treatment in men.  Plasma concentration monitoring is required; please contact the specialist for advice if patients wish to become pregnant or father a child.  If the patient becomes pregnant, contact the specialist immediately. A washout procedure may be required. |
| Perioperative use | Steroid exposure should be minimised prior to surgical procedures and increases in steroid doses to prevent adrenal insufficiency are not routinely required |
| Nausea and vomiting | IAs may cause nausea, vomiting or diarrhoea on their introduction or on an escalation of the dose. In this situation, contact the specialist. Once the patient has been established on a stable dose of an IA it would be unusual for this to cause significant GI symptoms. |
| Specialist Responsibilities | * The decision to initiate immunosuppressive therapy must be made in conjunction with the patient/carer and be supervised by an expert in the condition in question * Patients must be provided with education about their treatment * Patient will be provided with a leflunomide patient information leaflet * Patients must be assessed for contra-indications and co-morbidities * Where appropriate, patients should be advised about the impact of the immunosuppressive agent (IA) on fertility, pregnancy and breastfeeding * Vaccinations against pneumococcus and influenza are recommended * Interactions between the proposed IA and current medication should be identified and actioned * Direct the patient to report any sign of infection or side effect to their GP or hospital clinic * Conduct baseline monitoring * Prescribe medication until responsibility agreed to be transferred to patients GP * Supply general immunosuppressant background information to GP as per this guidance * Request GP participate in shared care in writing no sooner than **3 months after initiation** and patient **is stable** * At least 4 weeks of medication supplied at point of transfer * The secondary care specialist will communicate with the patient and GP when treatment is changed and/or needs to be changed by GP on future prescriptions, and/or when any changes to the monitoring are required, usually within 24 hrs * Conduct routine monitoring as per schedule while prescribing responsibility with specialist – this could be during initiation or at any point in time where the responsibility has been transferred back to the specialist * Observe advice relating to vaccination, perioperative use, infections etc. contained in this document * Specialist responsible for ongoing **disease** monitoring – clinical response to therapy will be assessed by the hospital physician in all cases and communicated to the GP * Specialist responsible for assessing if a patient is defined as ‘high risk’ and communicating this to the GP | |
| GP Responsibilities | * The GP should reply to the request for shared care as soon as possible, but always within 14 days, either accepting shared care or informing the specialist why shared care is not felt appropriate in this case. * If GP declines shared care responsibilities it is still the GPs responsibility to record on the primary care record that the drug is being prescribed by secondary care * Shared care to be initiated once patient is stable and at least 3 months after initiation * Prescribe medication as per document * **Conduct routine monitoring as per schedule while responsible for prescribing** * Observe advice relating to vaccination, perioperative use, infections etc. contained in this document | |
| Contraindications,  Precautions and Adverse Effects | **Contra-indications**  Known hypersensitivity to the product  Suspected local or systemic infection  Pregnancy and breast feeding  Bone marrow failure, with unexplained anaemia and cytopenia  Alcohol abuse  Significant liver impairment/disease  Severe immunodeficiency states e.g. AIDS  Severe hypoproteinaemia e.g. in nephrotic syndrome  **Precautions**  *Chronic kidney disease (CKD)*  In renal disease, IAs that are renally excreted accumulate, and some IAs are nephrotoxic. Patients with CKD should be graded as per NICE definition of CKD (table 1) and have IA dose reductions as per recommendations by the British Society of Rheumatology (BSR) (table 2).  **Table 1: NICE Definitions of CKD**   |  |  | | --- | --- | | **Degree of Impairment** | **Calculated GFR ml/min/1.73m2** | | Normal, Stage I | >90 (other evidence of kidney damage) | | Mild, Stage II | 60-89 (other evidence of kidney damage) | | Moderate, Stage III | 30-59 | | Severe, Stage IV | 15-29 | | Established renal failure, Stage V | <15 |   **Table 2: Recommended dose adjustment in CKD by the BSR**   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | |  | | | Recommended adjustment  (% of standard dose) | | | | Drug | Accumulates in renal failure | Nephrotoxic | CKD III | CKD IV | CKD V | | Leflunomide | No | No | Normal dose | Use with caution | Use with caution |   **Adverse Effects**  Mild increase in blood pressure, leucopenia, paraesthesia, headache, dizziness, diarrhoea, nausea, vomiting, oral mucosal disorders (e.g. aphthous stomatitis, mouth ulceration), abdominal pain, increased hair loss, eczema, rash (including maculo-papular rash), pruritus, dry skin, tenosynovitis, CPK increased, anorexia, weight loss (usually insignificant), asthenia, mild allergic reactions. Hepatic impairment may occur through prolonged use (elevated transaminases is a common adverse effect).  **For a full list of adverse effects please consult either the current BNF or SPC:**  [**https://bnf.nice.org.uk/**](https://bnf.nice.org.uk/)  [**https://www.medicines.org.uk/emc**](https://www.medicines.org.uk/emc) | |
| Common Drug Interactions | **Interactions:**   * Warfarin and other coumarin anticoagulants * Paclitaxel * Repaglinide * Rifampicin * Pioglitazone * Duloxetine * Ciprofloxacin. * Pravastatin, rosuvastatin, simvastatin * Cholestyramine * Alcohol may be consumed in moderation, on average one unit per day but avoid binge drinking   **For a full list of interactions please consult either the current BNF or SPC:**  [**https://bnf.nice.org.uk/**](https://bnf.nice.org.uk/)  [**https://www.medicines.org.uk/emc**](https://www.medicines.org.uk/emc) | |
| Communication/ Contact Details | * For acute advice:   + Monday to Friday, 9.00 am to 5.00 pm, phone the on-call monitoring nurse, rheumatology registrar or rheumatology consultant on call via the switchboard on **(0191) 565 6256**. Please use the bleep number **53546** in order to contact the rheumatology monitoring nurse for routine queries.   + Out of hours, phone the on-call medical registrar on **(0191) 565 6256**. * For non-acute advice, send a letter to the consultant in charge of the patient’s care. | |

***This information is not inclusive of all prescribing information and potential adverse effects. Please refer to full prescribing data in the SPC or the BNF.***

## Shared Care Request/Confirmation Private and Confidential

**Patient information:  
*To be completed by specialist prescriber:***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Patient details (use hospital label if preferred)** | | | | |
| **Consultant** | …………………………………… | **Name** | …………………………………………… | | | |
| **Department** | …………………………………… | **Address** | …………………………………………… | | | |
| **Hospital** | …………………………………… |  | …………………………………………… | | | |
|  |  | **Postcode** | ................................. | | **Sex** | ………... |
|  |  | **NHS or Hosp. Reg. No.** | | ………………… | **DoB** | ………... |

**Treatment Requested for Prescribing in Accordance with Shared Care Arrangement:**

***To be completed by specialist prescriber:***

|  |  |
| --- | --- |
| **Drug name** |  |
| **Dose** |  |
| **Frequency** |  |
| **Indication** |  |
| **Other information** |  |

Name (print)……………………….… Signature (of specialist prescriber)…………………..……….. Date……..

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**Acceptance/rejection of treatment under Shared Care Agreement:  
*To be completed by GP:***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | Please tick one box | | |
| ***I ACCEPT the proposed shared care arrangement for this patient*** | | | **❑** | |
| or |  | |  | |
| ***I ACCEPT the proposed shared care arrangement with the caveats below*** | | | **❑** | |
| or |  | |  | |
| ***I DO NOT ACCEPT the proposed shared care arrangement for this patient*** | | | **❑** | |
| My caveats / reason(s) for not accepting include: …………………………………………………………………………………… ………………………………………………………………………………………………………………………………………  Name (print)…………………………..… Signature (of GP)………………………………..………….... Date……… | | | | . |

**N.B. Participation in this shared care arrangement implies that prescribing responsibility is shared between the specialist prescriber and the patient’s GP**