**Request to Share Care and Agreement Form**

**Methotrexate (oral and subcutaneous) use in adults:**

**Rheumatology, Dermatology, Gastroenterology and Respiratory**

**Shared Care Protocol: Guideline Number 5; Version 2.2**

**For use in West Essex**

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)****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 shared care accepted, prescribe methotrexate once patient is clinically stable in line with protocol.
* Arrange, record and share ongoing monitoring.
* 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-iterate with 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.
* Ascertain the reason for non-completion of routine blood testing, if one test is missed.
* Prompt notification to the hospital specialist of any significant and relevant changes in the patient’s condition, medication dose, or adverse reaction, according to the protocol and if the patient fails to attend for blood monitoring.
* Ensure no drug interactions with other medicines.
* Administer inactivated influenza vaccine annually unless otherwise advised by the initiating specialist.
* Check patient has had ONE DOSE of pneumococcal vaccine. Administer a single dose of the pneumococcal vaccination (Pneumovax®) to all patients if previously not vaccinated.
* 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 or varicella zoster immunoglobulin (VZIG) <https://www.gov.uk/government/publications/varicella-zoster-immunoglobulin>. Also inform specialist. Varicella zoster virus (VZV) serology can be obtained urgently (within 24 hours) on discussion with microbiology if required.
* Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding at every consultation.
* Prescribe methotrexate (using multiples of the 2.5mg strength tablet only and clearly state the day of administration) and folic acid as advised by the specialist after the initial stabilisation period (usually 12 weeks) and only after blood test results have been reviewed (in line with the shared care protocol). Do not use the dosage instruction ‘as directed’ when prescribing; a specific dose must be applied to each prescription.
* Record blood test results and medicine dosages in the patient notes. Recording of on-going results and medicine dosages in the NPSA monitoring booklet is optional. For patients who are out-of-area (i.e. no common electronic results system), print results and give to patient.
* Change dose or stop treatment in line with protocol and as advised by specialist.
* Organise urgent referral to the specialist team or A&E if severe side effects or potential overdose is apparent.
* Liaise with the initiating clinician if the medicine becomes less effective and patient complains of symptoms.
* Ensure that all GP practice staff involved in the provision of this service have the relevant knowledge and skills.

**MONITORING ANDACTIONS 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 treatment initiation** | **Following treatment initiation** | **Ongoing**  | **Annual review** |
| FBCU&E eGFRLFTsAlbumin \*\*\* | Baselineassessmentand fordrug toxicity monitoring | ✓ | **Phase I**Every 2 weeks until on stable dose for 6 weeks | **Phase II**Every 4 weeks for next 12 weeksHospital specialist will undertake the first 4-week testGP will undertake the second and third 4-week test | **Phase III**At least every 12 weeks unless indicated otherwise by specialist (e.g. in patients with high risk of toxicity) | As part of routine clinical review or more frequently if indicated |
| ESRCRP | Disease activity -assessment | ✓ | As indicated by disease activity | Not routinely required | Every 12 weeks on specialist advice | As part of routine clinical review or more frequently if indicated |
| HeightWeightBlood pressure | Baseline assessment  | ✓ | x | x | If clinically indicated |
| HIV, Hepatitis B Core Ab & Surface Ag, Hepatitis C serologyVZV serology | Baseline viral screeningBaseline if no history of varicella | ✓ | x | x | If clinically indicated |
| Chest X-Ray | Baseline if not done within 6 months in patients with suspected parenchymal lung disease  | ✓ | If clinically indicated | If clinically indicated | If clinically indicated |
| Lung function tests+/-HRCT chest(rheumatology patients only) | Baseline if suspicion of underlying parenchymal lung disease | ✓ | If clinically indicated |  | x | If clinically indicated |
| Pregnancy screening (via test or questioning) for females of child bearing age  | Baseline assessment | ü | x | x | x |
| Blood test for Procollagen III peptide level (P3NP) \*\*\* or Fibroscan**(dermatology patients only)** | Baseline assessment and ongoing monitoring of P3NP or Fibroscan undertaken by specialist. |
| \*Any dose increase requires blood test monitoring every 2 weeks until the dose is stable for 6 weeks, then revert back to previous schedule. The specialist would be responsible for organising and checking the blood tests.  \*\*Methotrexate/ leflunomide combination therapy requires monthly monitoring of routine blood tests long term due to the risk of hepatotoxicity unless specialist indicates otherwise.\*\*\* P3NP is a vetted test therefore clinical details are required (e.g. to assess liver fibrosis for dermatology patient prescribed methotrexate). Please also note that samples must reach the laboratory on day they are drawn. |

**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.

|  |  |
| --- | --- |
| **Abnormal result** | **Action to be taken by GP** |
| WBC <3.5 x 109/L | Withhold and contact specialist urgently |
| Lymphocytes under lower limit normal | Common in rheumatic disease but if concern discuss with specialist |
| Neutrophils <1.6 x 109/L | Withhold and contact specialist urgently |
| Unexplained eosinophilia >0.5 X 109/L | Withhold and contact specialist urgently |
| Platelets 110-140 x 109/LPlatelets <110 x 109/L | Discuss with specialist.Withhold and discuss with specialist urgently |
| MCV >105 fL | Check B12, folate, thyroid function and start treatment as necessary. Review alcohol consumption. If all within normal limits, contact specialist urgently and consider interruption of treatment.  |
| ALT and/ or AST rise <100 U/LALT and/ or AST rise > 100 U/L | Check if any other medication started recently e.g. statin, antibiotics, NSAIDs. Review OTC medications and alcohol intake. Repeat in 1-2 weeks and if still abnormal, discuss with specialist.Withhold and discuss with specialist urgently |
| Elevated GGT and Alkaline phosphatase | Should be investigated like in any other patient. Review alcohol intake. If no abnormality found contact specialist. |
| Albumin – unexplained fall to <30 g/L | Discuss with specialist |
| Creatinine rise >30% over 12 months and/ or calculated GFR <60 | Review hydration status and any change in medications especially addition of ACE inhibitors, angiotensin 2 receptor blockers, diuretics and NSAIDs. Withhold and discuss with specialist as dose adjustment likely to be required. |
| ESR/ CRP rise above baseline | Screen for infection and contact specialist if not found |
| P3NP >4.2mg/l on 3 occasions in 12 month period**OR**P3NP >8.0mg/l on 2 occasions **OR**P3NP >10mg/l on 1 occasion  | The Dermatologist will advise GP and patient if dose needs to STOP or reduction in dose; and seek advice from Hepatologist as required. |

 |

* 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**

**Shared Care Protocol: Guideline No 5; Version 2.2**

**Methotrexate (oral and subcutaneous) use in adults:**

**Rheumatology, Dermatology, Gastroenterology and Respiratory**

**This full protocol provides prescribing and monitoring guidance-** [**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**

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. It can be used in a wide range of conditions.

Indications not specified below are not covered by this Shared Care Protocol.

**Rheumatology**

Methotrexate is used as a disease modifying anti-rheumatic drug (DMARD) and as a steroid-sparing agent.

Licensed indication – rheumatoid arthritis (RA).

Unlicensed indications but recommended by the British Society of Rheumatology (BSR) – psoriatic arthritis (PsA), undifferentiated inflammatory arthritis, juvenile idiopathic arthritis (JIA), systemic lupus erythematosis, inflammatory myositis, scleroderma, vasculitis and polymyalgia rheumatica.

**Dermatology**

Licensed indication – Psoriasis.

Unlicensed indications – Eczema, cutaneous sarcoidosis, systemic sclerosis, Bullous Pemphigoid, Pemphigus, cutaneous lupus erythematosis, cutaneous T cell lymphoma, cutaneous vasculitis and several other skin diseases (see Reference 3 for full list).

**Gastroenterology**

Unlicensed indication – Crohn’s disease.

**Respiratory**

Unlicensed indication – pulmonary sarcoidosis.

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

**Adult dosage and administration**

**Oral Methotrexate:** 2.5mg and 10mg tablets are available but **ONLY multiples of the 2.5mg tablet** should be prescribed and dispensed for patients covered by this guideline and this should remain consistent to avoid confusion and to allow flexibility in dosing**. The day of administration must be specified on the prescription.**

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.

**Subcutaneous Methotrexate:** The specialist will specify which brand of methotrexate subcutaneous injection should be prescribed. The brand **must** be stated on prescriptions written in both primary and secondary care. GPs should not switch to an alternative brand without discussion with the specialist team. Pre-filled syringes of methotrexate are available in 7.5mg, 10mg, 12.5mg, 15mg, 17.5mg, 20mg, 22.5mg and 25mg strengths. Subcutaneous methotrexate can be used to overcome severe gastrointestinal side effects despite regular folic acid on 6 days a week or in non-responders to oral therapy in order to improve drug bioavailability. It should only be prescribed on advice of the specialist. The hospital specialist nurse will provide training in self-administration.

The hospital specialist nurse will advise on how to dispose methotrexate pre-filled syringes and provide a mauve top cytotoxic sharps bin. Once ready for disposal, the bin should be shut properly, the top wiped clean and returned to the relevant place as instructed by the specialist team.

**Rheumatology**

Typically commenced at 7.5 to 15mg **ONCE WEEKLY** and increased by 2.5mg every 1 to 4 weeks until 15 to 25mg once weekly depending on response**.** Dosing and toxicity risks are usually similar in oral and subcutaneous therapy. Lower doses are used in the elderly or in significant renal impairment. Methotrexate can take 6 weeks to 3 months to have full therapeutic effect. Treatment is long term. The specialist will advise the duration.

**Dermatology**

As for Rheumatology but initial doses of between 5 and 15 mg **ONCE WEEKLY.**

**Gastroenterology**

Typically commenced at 25mg **ONCE WEEKLY** for 3 months induction and thereafter maintained on 15mg **ONCE WEEKLY**.

**Respiratory**

Starting dose as for rheumatology with all the monitoring and exclusion criteria but ceiling of therapy for pulmonary sarcoidosis is usually **15mg ONCE WEEKLY**

Mode of administration is discussed with patient. For induction subcutaneous route is preferred. For maintenance can be switched to oral if patient preference.

**Folic Acid**

Co-prescribe a minimum of 5mg once weekly on a **DIFFERENT** day to methotrexate (preferably the day after) to minimise the risk of minor side effects and thereby improve compliance, and to minimise the risk of abnormal liver biochemistry. It can be increased to 5mg on 6 days a week to overcome certain side effects (see page 8/9) but it should not be taken on the same day as methotrexate.

|  |
| --- |
| **SPECIALIST RESPONSIBILITIES INCLUDING PRE-TREATMENT ASSESSMENT*** Confirm diagnosis, indication for methotrexate and ensure there are no contra-indications to start drug.
* If treatment is off-label, advise the patient.
* Undertake pre-treatment assessment and screening (see table on page 2-3).
* Recommend yearly influenza vaccination and a one off pneumoccal vaccination (Pneumovax®) if not previously administered.
* Offer smoking cessation to any patient currently smoking.
* Undertake pre-treatment counselling and document discussion in patient’s records including patient preferences, the rationale and benefits of treatment and time to expected response.
* Discuss the side effects of treatment with the patient, the need to report them promptly and to whom.
* When appropriate, patients should be advised on the impact of methotrexate on fertility, pregnancy and breastfeeding.
* Advise the patient their skin may be more sensitive to exposure to UV light while taking methotrexate. Use appropriate self-care: e.g. sun avoidance, protective clothing, avoiding tanning (including tanning beds) and to purchase and use a broad spectrum sunscreen (at least SPF30).
* Before prescribing methotrexate, ensure the patient is able to understand and comply with once weekly dosing regimen, highlighting the potentially fatal risk of accidental overdose if methotrexate is taken more frequently. Advise the patient to promptly seek medical advice if they think they have taken too much.
* For patients taking tablets, advise that they will only ever be prescribed methotrexate 2.5 mg tablets. Patients who receive 10 mg tablets should always question the discrepancy
* Decide with the patient which day of the week they will take their methotrexate and note this day down in full on the prescription.
* Provide patient with the methotrexate information leaflet and NPSA drug monitoring booklet.
* Encourage the patient to carry the warning card that comes with each dispensing of oral methotrexate upon their person (e.g. in their wallet or purse). This will prompt patients to take methotrexate once a week and to record the day of intake. It will also help patients identify the signs and symptoms of overdose.
* Initiate and prescribe methotrexate and arrange appropriate blood test monitoring for the initial stabilisation period (usually for 12 weeks) and/or until the GP formally agrees to shared care.
* Record baseline and on-going results and medicine dosages in clinic communication to GP and patient’s hospital records. Recording of on-going results and medicine dosages in the NPSA monitoring booklet is optional. For patients who are out-of-area (i.e. no common electronic results system), print results and give to patient.
* Explain shared care arrangements and responsibilities to the patient including the need for regular clinical review and blood tests to allow continued prescription of drug.
* Obtain agreement and consent to shared care from patient. Obtain signature from patient on the shared care agreement form and complete and sign the specialist section. Provide any additional instructions on monitoring on page 1. NB This should include advice regarding whether GP is required to undertake regular ESR/CRP testing (i.e. which of these test(s) are required/frequency required).
* Request GP to confirm acceptance of shared care by sending the shared care protocol and completed agreement form by secure email, allowing 2 weeks for response. Record outcome in patient records. If accepted, transfer prescribing/blood monitoring to GP. If declined, retain prescribing/blood monitoring within hospital.
* Provide regular outpatient clinic review to assess disease activity, make dose adjustments, review adverse drug effects (both clinical and on blood tests) and to advise on when to stop treatment. Notify GP promptly via written clinic communication and for more important or more urgent changes by secure email or telephone.
* Notify GP if failure to attend specialist clinic review and advise on action(s) to take.
* Provide clear arrangements and contact telephone numbers for back-up advice and support for patients and GPs throughout.
* Support any training arrangements to ensure that GPs have the skills to ensure safe practice.
* For patients under the care of Princess Alexandra Hospital Rheumatology Consultant refer patients with stable disease markers and DAS S<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.
* Ensure patient understands that dosing is ONCE WEEKLY: inform the patient and their caregivers of the potentially fatal risk of accidental overdose if methotrexate is taken more frequently than once a week; specifically, that it should not be taken daily
* Advise patients of the need to promptly seek medical advice if they think they have taken too much
* 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 1&2 and GP Considerations for Shared Care page 12.

|  |
| --- |
| **PATIENT RESPONSIBILITIES IN COOPERATION WITH SPECIALIST AND GP*** Confirm their agreement with the decision to move to a shared care model for their ongoing care and their understanding of the shared care agreement.
* Consent to share care and complete/sign specialist and patient agreement section of Shared Care Agreement form.
* Confirm their understanding of the treatment and agreeing to contact the specialist/GP if they subsequently do not have a clear understanding of the treatment (patient to be provided with relevant contact details for GP/specialist in and out of hours).
* For patients taking tablets, confirm their understanding that they will only ever be prescribed methotrexate 2.5 mg tablets and patients who receive 10 mg tablets should always question the discrepancy.
* Attending for blood monitoring and follow up hospital or GP appointments.
* Ensuring a list of all medications are brought to all GP surgery, outpatient and A&E consultations.
* When GP and hospital are unable to view blood results on a shared electronic system, ensure the printed blood results from specialist and GP are kept up to date and bought to all GP and outpatient consultations.
* Reporting any change in symptoms and adverse effects promptly to the clinician who is currently prescribing.
* Confirm that no new medicines are started (including over the counter preparations) unless this has been discussed with the GP, specialist or pharmacist.
* Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy; plans to move/change GP practice.
* Patients should take adequate precautions to avoid pregnancy.
* Be aware skin may be more sensitive to exposure to UV light while taking methotrexate. Use appropriate self-care: e.g. sun avoidance, protective clothing, avoiding tanning (including tanning beds) and to purchase and use a broad spectrum sunscreen (at least SPF30).
* To reduce alcohol to lowest possible intake and remain within maximum national allowed weekly limit
 |

|  |
| --- |
| **DISPENSING PHARMACIST RESPONSIBILITIES*** Confirming that the patient has received verbal and written patient counselling / information and provide additional counselling should this be required.
* Check the patient is being monitored regularly, e.g. using the patient held monitoring booklet where available, to ensure that it is safe before issuing or dispensing prescriptions.
 |

|  |
| --- |
| **MONITORING AND ACTIONS TO BE TAKEN*** Refer to page 2-4.
 |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 Effect** | **Action to be taken by GP** |
| Nausea, diarrhoea, headache | Can increase folic acid to 5mg daily up to 6 days a week except on the day of methotrexate  |
| Mouth ulcers, mucositis | Increase folic acid as for nausea but if persists stop methotrexate and contact specialist |
| Abnormal bruising, high fever or severe sore throat | Stop until urgent FBC result available and discuss with specialist if abnormal |
| Unexplained cough or breathlessness | Withhold methotrexate, arrange urgent chest X-Ray and discuss urgently with specialist  |
| Unexplained rash | Withhold and discuss with specialist |
| Hair loss | Rarely significant but can increase folic acid as for nausea. If concern discuss with specialist |

 |

**CONTRAINDICATIONS AND PRECAUTIONS**  **(REFER TO** [**BNF**](http://www.bnf.org/bnf/index.htm) **AND** [**SPC**](http://www.medicines.org.uk/emc) **for full details)**

* Pregnancy – Methotrexate at any dose is contraindicated in pregnancy. There is differing advice between speciality societies; the SPC for methotrexate advises that women and men should stop methotrexate 6 months prior to attempting conception, however the specialist should discuss and agree the optimal timing to stop treatment with the individual patient.
* In women treated with low dose methotrexate (<20 mg/week), folic acid 5 mg/day orally should be commenced prior to conception (usually within 3 months) and continued throughout the pregnancy.
* In case of accidental pregnancy, methotrexate should be stopped immediately, folic acid 5mg/day supplementation commenced and the patient should be referred to local experts for careful evaluation of foetal risk.
* Breastfeeding – not recommended.
* Chronic kidney disease (CKD) – contra-indicated in stage IV and V CKD (eGFR <30 ml/min) including in patients on dialysis. In CKD stage III (eGFR 30 - 59 ml/min), a 50% dose reduction is recommended.
* Pre-existing blood dyscrasia such as significant anaemia, leucopenia, thrombocytopenia.
* Severe local or systemic infection (acute or chronic).
* Active tuberculosis or other infectious disease.
* Immunodeficiency syndrome.
* Live vaccinations – see below.
* Hypersensitivity to methotrexate or any of the excipients.
* Significant hepatic dysfunction/ disease, cirrhosis or recent/active hepatitis.
* Active peptic ulceration.
* Co-prescription with drugs with anti-folate properties e.g. trimethoprim.
* Pulmonary fibrosis or significantly reduced lung function.

**Relative Contra-indications**

* Chronic liver disease (if synthetic function is impaired).
* Alcoholism – should be used with extreme caution.
* Chronic hepatitis B and C – these patients should be discussed with gastroenterologists before initiation of treatment and to consider antiviral treatment if indicated.
* Active gastritis.
* CKD stage III (eGFR 30-59) – a 50% dose reduction is advised.
* Male partners of women wishing to conceive.

**Precautions**

* Alcohol intake - should be limited to lowest possible intake (maximum 4-6 units per week).
* Peri-operative management – methotrexate should NOT be routinely stopped in the peri-operative period. Attention to renal function is important and the dose might need to be adjusted accordingly. Individualised decisions in discussion with the specialist should be made for procedures that carry a high risk of infection as they may require methotrexate to be stopped 2 weeks before surgery and restarted once wound healing is satisfactory e.g. contaminated or dirty procedures or longer procedures (>60 minutes).
* Intercurrent infection – for serious infection (e.g. patients receiving intravenous antibiotics or hospitalisation), methotrexate should be temporarily stopped until the patient has recovered from the infection. For minor infection requiring a short oral course of antibiotic, depending on the circumstance methotrexate can be continued in patients (e.g. uncomplicated UTI).
* Chicken pox/ shingles – for proven infection stop methotrexate and treat according to BNF for immunosuppressed patients. 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 or varicella zoster immunoglobulin (VZIG) <https://www.gov.uk/government/publications/varicella-zoster-immunoglobulin>. Inform specialist. VZV serology can be obtained urgently (within 24 hours) on discussion with microbiology.

**Vaccination**

* Refer to Chapter 7 Green Book as the definitive source of information regarding vaccination in patients commencing immunosuppression.
* Annual influenza vaccination should be recommended to all patients on methotrexate.
* COVID-19 vaccination (The Green Book, [Chapter 14a)](https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a) is safe and recommended.
* A single pneumococcal vaccination (Pneumovax®) should be given to all patients if previously not vaccinated preferably prior to methotrexate initiation or as soon as possible after.
* Live vaccines (e.g. yellow fever) should not be given to patients on methotrexate or within 4 weeks of commencing treatment.
* Zostavax® the live attenuated shingles vaccine is relatively contraindicated in immunosuppressed individuals. In people over the age of 69 years, low levels of immunosuppression e.g. corticosteroids <20mg daily and methotrexate at standard doses (<0.4mg/kg/week) are not considered an absolute contraindication but clinical discretion is advised. This recommendation does not extend to younger patients in the rheumatic disease population due to lack of robust efficacy and safety data.

**Methotrexate Overdose**

**Folinic Acid Rescue**: Used in overdose or severe bone marrow toxicity under specialist direction.

**Contact UK National Poisons Information Service – 0344 892 0111** ([www.toxbase.org](http://www.toxbase.org))

The National Patient Safety Agency has published actions to reduce the risks associated with oral methotrexate: [LINK](https://www.sps.nhs.uk/articles/npsa-alert-improving-compliance-with-oral-methotrexate-guidelines-2006/). More recently, the MHRA has issued additional safety measures to reduce the risk of fatal overdose due to inadvertent daily dosing instead of weekly dosing. The MHRA guidance also contains educational materials for healthcare professionals to minimise the risk of overdose: [LINK](https://www.gov.uk/drug-safety-update/methotrexate-once-weekly-for-autoimmune-diseases-new-measures-to-reduce-risk-of-fatal-overdose-due-to-inadvertent-daily-instead-of-weekly-dosing).

**NOTABLE DRUG INTERACTIONS (REFER TO** [**BNF**](http://www.bnf.org/bnf/index.htm) **AND** [**SPC**](http://www.medicines.org.uk/emc) **for full details)**

NSAID’s and salicylates – excretion of methotrexate may be impaired leading to toxicity but co-prescription of methotrexate with NSAID’s is common in rheumatology practice and a clinically significant interaction is rare. NSAIDs should be discontinued if liver function derangement occurs.

• Co-trimoxazole and trimethoprim – anti-folate effect of methotrexate is increased and greatly increases the risk of bone marrow aplasia. DO NOT CO-PRESCRIBE.

• Clozapine – avoid concomitant use due to increased risk of agranulocytosis.

• Ciclosporin – can increase methotrexate toxicity. The specialty team will provide patient- specific advice on co-prescriptions.

• Probenecid – methotrexate excretion is reduced leading to toxicity.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CONTACT DETAILS for BACK-UP INFORMATION / ADVICE** **Princess Alexandra Hospital NHS trust**

|  |  |  |  |
| --- | --- | --- | --- |
| **Department** | **Contact number** | **Specialist Team designated nhs.net email** | **Out of hours contact / switchboard** |
| **Gastroenterology** | 01279 278223(IBD advice line – answer machine)01279 278224(Gastro Pharmacist) | Tpa-tr.gastroadminclinicalcorrespondence@nhs.netPaht.ibd@nhs.net - IBD Specialist Nurse | 01279 444455 |
| **Dermatology**  | 01279 827227Derm Secretaries | tpa-tr.dermatologyclinicalcorrespondence@nhs.net  |
| **Rheumatology** | 01279 827434 – DMARD helpline01279 827819Nurse helpline | tpa-tr.rheumatologyadminclinicalcorrespondence@nhs.net  |
| **Respiratory**  | via switchboard | tpa-tr.respiratoryadminclinicalcorrespondence@nhs.net  |

**Communication**For any queries relating to a patient’s treatment with methotrexate, 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. |

|  |
| --- |
| **SUPPORTING INFORMATION***Rheumatology** British Society of Rheumatology (BSR) guidelines <https://www.rheumatology.org.uk/practice-quality/guidelines/>

*Crohn’s disease** NICE NG 129. May 2019. Crohn’s disease: management <https://www.nice.org.uk/guidance/ng129>
* Lamb CA, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults, Gut 2019;0:1–106 <https://www.bsg.org.uk/resource/bsg-consensus-guidelines-ibd-in-adults.html>

*Systemic lupus erythematosus* * Gordon C, Amissah-Arthur M\_B, Gayed M, et al, for the British Society for Rheumatology Standards, Audit and Guidelines Working Group, The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults, Rheumatology 2018; 57: e1–e45, <https://doi.org/10.1093/rheumatology/kex286>
* Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Annals of the Rheumatic Diseases 2019;78:736-745) <https://ard.bmj.com/content/78/6/736>

*Pemphigus vulgaris, atopic dermatitis, bullous pemphigoid, chronic actinic dermatitis, pyoderma gangrenosum, dermatomyositis, polymyositis, cutaneous vasculitis** Harman KE, Brown D, Exton LS *et al*, British Association of Dermatologists guidelines for the management of pemphigus vulgaris 2017 Br J Dermatol 2017; 177: 1170-1201 <https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.15930>
* Venning VA, Taghipour K, Mohd Mustapa MF et al British Association of Dermatologists' guidelines for the management of bullous pemphigoid 2012. Br J Dermatol 2012; 167: 1200-1214. <https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.12072>
* R.B. Warren, S.C. Weatherhead, C.H. Smith, L.S. Exton, M.F. Mohd Mustapa, B. Kirby and P.D.Yesudian. British Association of Dermatologists’ guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. British Journal of Dermatology (2016) 175:23–44

*Systemic vasculitis: granulomatosis with polyangiitis (GPA: formerly Wegener’s granulomatosis), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (formerly Churg–Strauss syndrome)** Ntatsaki E et al, BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis, Rheumatology, Volume 53, Issue 12, December 2014, Pages 2306–2309, <https://doi.org/10.1093/rheumatology/ket445>
* Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Annals of the Rheumatic Diseases 2016;75:1583-1594 <https://ard.bmj.com/content/75/9/1583>

*Pulmonary Sarcoidosis** NHS England Clinical Commissioning Policy: Infliximab for Progressive Pulmonary Sarcoidosis in adults – (references use of methotrexate) <https://www.england.nhs.uk/wp-content/uploads/2018/11/infliximab-progressive-pulmonary-sarcoidosis-adults.pdf>
 |

**REFERENCES**

1. Ledingham J et al. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology 2017, 56(6): 865–868. <http://doi.org/10.1093/rheumatology/kew479>.
2. Flint et al, BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford) 2016; 55 (9): 1693-1697. <http://doi.org/10.1093/rheumatology/kev404>
3. R.B. Warren, S.C. Weatherhead, C.H. Smith, L.S. Exton, M.F. Mohd Mustapa, B. Kirby and P.D.Yesudian. British Association of Dermatologists’ guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. British Journal of Dermatology (2016) 175:23–44
4. Methotrexate SPC (Summary of product specification): Sept 2018 <https://www.medicines.org.uk/emc/product/511/smpc>
5. NICE CKS DMARDs: Last revised in July 2018; What monitoring is required for methotrexate? <https://cks.nice.org.uk/dmards#!scenarioRecommendation:3>
6. The Green Book Immunisation against infectious disease <https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>
7. Specialist Pharmacy Service: Suggestions for Drug Monitoring in Adults in Primary Care, October 2017: <https://www.sps.nhs.uk/wp-content/uploads/2017/12/Drug-monitoring_October-2017.pdf>
8. MHRA Drug Safety Update, September 2020 - Methotrexate once-weekly for autoimmune diseases: new measures to reduce risk of fatal overdose due to inadvertent daily instead of weekly dosing <https://www.gov.uk/drug-safety-update/methotrexate-once-weekly-for-autoimmune-diseases-new-measures-to-reduce-risk-of-fatal-overdose-due-to-inadvertent-daily-instead-of-weekly-dosing>
9. NHS England National Shared Care protocols <https://www.england.nhs.uk/publication/shared-care-protocols/#heading-13>
10. MHRA Aug 2023 Methotrexate: advise patients to take precautions in the sun to avoid photosensitivity reactions: <https://www.gov.uk/drug-safety-update/methotrexate-advise-patients-to-take-precautions-in-the-sun-to-avoid-photosensitivity-reactions> accessed 10/01/24
11. BNF Methotrexate Cautionary Labels: <https://bnf.nice.org.uk/drugs/methotrexate/medicinal-forms/#tablet> accessed 10/01/24

**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  | 2.2 Updated in line with new shared care protocol template, May 2025.2.1 Updated wording on swallowing difficulties September 20242. Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include:* Adoption of HWE template and Feb 2021 HMMC approved, updated HWE APC April 2024 methotrexate shared care protocol for west Essex place.
* Addition of responsibilities for GP with Special Interest in Rheumatology for West Essex patients under the care of Princess Alexandra Hospital from October 2017 WEMOPB approved shared care protocol
 |
| Developed by | Dr Leena Patel, Consultant Rheumatologist, West Hertfordshire Hospitals NHS Trust and relevant specialists supported by Hertfordshire CCGs Pharmacy and Medicines Optimisation Teams. |
| Approved by | HMMC, HWE APC |
| Date approved/updated  | HMMC Feb 2021, updated HWE APC April |
| 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 | 1.0Amendment of Phase II monitoring in line with wording agreed HWE APC February 2024Addition of sun protection and 10mg tablet adviceAddition of Covid-19 vaccination recommendationRevision of PIIINP monitoring responsibilities and actions taken |