Specialised Medicines Service (SMS) Guideline ~

Once-weekly subcutaneous methotrexate for patients within adult dermatology services (West Devon only)

Specialist: Please complete the shared care agreement letter at the end of this document and send together with the guideline to the GP.

GP: GPs are invited to participate. Please indicate whether you wish to share patient's care by completing the relevant letter at the end of this document and returning to the specialist.

Responsibilities remain with the specialist service until formally accepted by the GP. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

If the GP agrees to share the care of the patient, the patient should not be discharged from the care of their specialist, but rather the care of the patient is shared between the patient, GP and specialist in accordance with the responsibilities outlined in this guideline.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

Introduction and aims of treatment

This west Devon SMS guideline covers the use of once-weekly subcutaneous methotrexate for the treatment of the following indications in patients within adult dermatology services (excluding cancer care):

- **Psoriasis**
- **Sarcoidosis**
- **Connective tissue diseases**
- **Atopic dermatitis**
- **Pemphigoid**
- **Pemphigus**
- **Nodular prurigo**

This guideline excludes patients unable to self-administer subcutaneous methotrexate – in such cases an alternative DMARD should be prescribed.

Subcutaneous methotrexate is licensed for the treatment of moderate - severe, psoriasis. The precise licensing definition varies with brand. Treatment of other indications included in this guideline is off-label but well established and supported by local specialists.

The specialist must specify the indication for each patient when initiating shared care and clearly state when use is off-label.

Use of methotrexate for indications not listed above and use of oral methotrexate falls outside the scope of this guideline. For other shared care / SMS guidelines on the use of methotrexate, refer to the NHS Devon website (https://onedevon.org.uk/our-work/services-and-support/medicines-and-treatments/clinical-guidancefor-prescribers/) or the Devon Formulary website (https://devonformularyguidance.nhs.uk/).

This guideline details the responsibilities for the ongoing prescribing and monitoring required to enable a shared care agreement to be arranged between the primary and secondary care interface. Refer to the online British National Formulary (BNF), Summary of Product Characteristics (SmPCs) or the Medicines and Healthcare products Regulatory Agency (MHRA) for full and up-to-date prescribing data.

Methotrexate is a folic acid antagonist; an antimetabolite cytotoxic agent. Its major site of action is the enzyme dihydrofolate reductase. Its main effect is inhibition of DNA synthesis but it also acts directly both on RNA and protein synthesis.

Important safety information

Methotrexate should only be prescribed by clinicians who have a full understanding of the characteristics of the drug, its mode of action and risks of therapy. Dosage errors in the use of methotrexate can result in serious adverse effects, including death.

MHRA/CHM advice: Methotrexate once-weekly for autoimmune diseases: new measures to reduce risk of fatal overdose due to inadvertent daily instead of weekly dosing (September 2020)

Methotrexate should be taken once a week in autoimmune conditions and, less commonly, in some cancer therapy regimens. A European review highlighted continued reports of inadvertent overdose due to more frequent dosing (including daily administration), which has resulted in some fatalities. Subsequently, new measures have been implemented by the MHRA.

Prescribers are advised to:

- ensure patient and/ or the patient's carer can understand and comply with once-weekly dosing before prescribing methotrexate
- decide with the patient and/ or the patient's carer which day of the week they will take their dose, and note this down in full on the prescription
- consider the patient's overall polypharmacy burden when deciding which formulation to prescribe, especially in those with a high pill burden;
- inform patient and/ or the patient's carer of the potentially fatal risk of accidental overdose if methotrexate is taken more frequently than once a week, and reaffirm that it should not be taken daily;
- advise patient and/ or the patient's carer to seek immediate medical attention if overdose is suspected.

The MHRA further advises that patient and/ or the patient's carer should be encouraged to write the day of the week for dosing in their patient alert card and carry it with them. Instruct patient and/ or the patient's carer to use it to alert any healthcare professionals they consult who are not familiar with their methotrexate treatment about their once-weekly dosing schedule (for example, on hospital admission, change of care).

NHS Never Event: Overdose of methotrexate for non-cancer treatment (January 2018)

Patients given methotrexate, by any route, for non-cancer treatment should not be given more than their intended weekly dose.

National Patient Safety Agency: Patient safety alert (2006)

Includes recommended actions to help reduce the number of drug errors associated with methotrexate which reinforce the guidance above.

Specialist responsibilities

Specialists may decide to delegate some of these tasks to members of their team, however the responsibility for ensuring the following are undertaken remains with the named specialist overseeing the care of the individual patient:

- Assess the patient, establish diagnosis and the need for treatment with methotrexate. Ensure the diagnosis is within scope of this SMS guideline.
- Provide appropriate counselling to ensure the patient and/ or the patient's carer is involved in making an informed choice about their treatment.
- Provide the patient and/ or the patient's carer with suitable written and verbal information about the medication prior to starting treatment, including benefits and risks, side effects, cautions, frequency of dosing, monitoring requirements and treatment reviews (timing and by whom).
- Provide methotrexate monitoring booklet and patient alert card.
- Ensure the patient and/or the patient's carer understands and can follow the once-weekly dose regimen.
- Inform the patient and/or the patient's carer if the use of methotrexate is unlicensed.
- Confirm patient and/or the patient's carer understands the treatment and record consent (including off-label use) and agreement to associated patient responsibilities in the patient's medical records.
- Update records with list of existing drugs from available resources and ensure there are no drug interactions of clinical significance with current medication, recreational drugs, or over the counter (OTC) drugs or herbal remedies. Recommend the patient and/ or the patient's carer consults a pharmacist before using OTC treatments or herbal remedies.
- Provide advice on the need for contraception, and the risks of pregnancy to individuals on initiation and at each review; the ongoing responsibility for providing this advice rests with both the specialist and the GP.
- Advise the patient and GP regarding the need for appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19). Refer to The Green Book for latest vaccination schedules and guidance.
- Ensure the patient and/ or the patient's carer understands that treatment may be stopped if they do not attend for monitoring & treatment review.
- Undertake pre-treatment screening and required baseline monitoring before initiating methotrexate.
- **Initiate once-weekly methotrexate. Specialist to confirm day of the week with patient and specify on prescription. Prescribe subcutaneous methotrexate by brand.**
- **Prescribe oral folic acid at least 5mg once weekly. The dose to be taken at least 24 hours after methotrexate dose.** Include clear directions for the folic acid regimen in the initial communication with GP.
- **Prescribe treatment and monitor the patient; transfer to primary care is normally after the patient has been treated for 3 months.** The condition should be stable and the dose optimised (with no anticipated further changes expected in the immediate future).
- Ensure the patient is trained in the proper injection technique to self-administer subcutaneous methotrexate – the first injection should be performed under direct medical supervision.
- Counsel the patient on safe disposal of cytotoxic medication and explain relevant local waste collection arrangements
- Once treatment is optimised, ask the GP in writing whether they are willing to participate in shared care for a particular patient using the shared care agreement letter below. Include all relevant test results (GPs may not have access to these results in primary care).
- Prescribing and monitoring will remain in secondary care until the patient is stable and the GP agrees to share care.
- Following the request to the patient's GP to participate in a shared care agreement, the specialist must ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued by the specialist if, for unforeseen reasons, arrangements for shared care are not in place at the end of this period.
- The duration of treatment will be determined by the specialist, based on clinical response and tolerability.
- Review the patient at agreed specified clinically appropriate intervals - assess patient's ongoing response to treatment. NHS England recommends that this should usually be undertaken annually.

- Ensure prompt written summary is sent to the GP whenever the patient is reviewed including any changes in treatment or monitoring requirements, results of monitoring undertaken, assessment of adverse events, or guidance on when to stop treatment if indicated. Confirm ongoing dose.
- Urgent changes to treatment should be communicated electronically and directly to the GP surgery (and followed up by telephone as required) to ensure prompt and immediate update.
- Provide the GP with relevant contact information and clear arrangements for back-up advice and support (including weekend and bank holidays).
- Ensure that the GP is informed in writing of any changes to the patient's specialist or their contact details.
- Where patient care is transferred from one specialist service to another, and/or the patient is initiated on a different treatment with associated SMS guidelines a new shared care agreement must be completed between the specialist, the GP and the patient.
- Respond promptly to GP or patient queries and advise on action required when abnormal monitoring results are identified or adverse effects signs or symptoms are detected and flagged.
- Any individual who becomes pregnant or wishes to become pregnant will be referred back to the specialist for an individualised review and discussion of ongoing management plans to provide the best outcome for the individual patient. The specialist will reassume prescribing responsibility, ending the shared care agreement.
- Report suspected side effects to MHRA via yellow card scheme.

General practitioner responsibilities

GPs may decide to delegate some of these tasks to members of their team; however, the responsibility for ensuring the following are undertaken remains with the GP overseeing the care of the individual patient:

- Ensure a timely reply is sent to the specialist in response to the request for shared care using the shared care agreement letters below. Where possible this should be undertaken within 14 days of the request being made.

If GP has agreed to share care:

- Continue to prescribe once-weekly **subcutaneous methotrexate by brand**.
- Continue to prescribe **folic acid** 5mg once weekly (unless a higher dose has been advised by the specialist), to be taken at least 24 hours after methotrexate.
- Continue to monitor treatment in accordance with these guidelines.
- Ensure the patient is vaccinated in accordance with national vaccination programmes – seek guidance from initiating specialist where required e.g. where treatment with methotrexate has already commenced:
  - Influenza vaccination (The Green Book Chapter 19)
  - Pneumococcal vaccination (The Green Book Chapter 25)
  - COVID-19 vaccination (The Green Book Chapter 14a)
  - Shingles (herpes zoster) (The Green Book Chapter 28a)
- Review monitoring results and take any necessary action (see monitoring requirements below).
- Be alert to the possibility of interactions when initiating new medicines, recommending over the counter (OTC) treatments or herbal remedies, or disclosure of the use of recreational drugs.
- It is the responsibility of the specialist to provide advice on the need for contraception to individuals on initiation and at each review however the ongoing responsibility for providing this advice rests with both the specialist and the GP.
- Be alert to the possibility of adverse effects at every contact. Manage patient in accordance with guidance below. Ensure prompt action in the case of a severe adverse effect or signs or symptoms.
- **Stop methotrexate and discuss urgently with the specialist if the patient develops signs of severe infection, liver or respiratory disease, unexplained bleeding or bruising, becomes pregnant, or if immunosuppressed patients are exposed to chickenpox or shingles.** See monitoring guidance below for further details.
- Ensure advice sought promptly from the specialist if there is a change in the patient's physical or mental health status which is of concern to the GP and may affect treatment.
- Any individual who becomes pregnant should be referred back to the specialist. The specialist will reassume prescribing responsibility, ending the shared care agreement.

- Discuss with the specialist if the patient plans to become pregnant.
- Respond promptly to advice from specialist regarding any changes in treatment or monitoring requirements.
- Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.
- Where patient care is transferred from one GP practice to another a new shared care agreement must be completed.
- Report suspected side effects to specialist and to MHRA via yellow card scheme.

Patient and/ or carer responsibilities

- **Methotrexate is injected once weekly on the same day each week; injecting it more frequently can be dangerous. If a patient thinks they have injected too much methotrexate they should immediately seek advice from their prescriber, or NHS 111.**
- Understand the importance of monitoring treatment and attend specialist and GP appointments to ensure timely monitoring and reviews can be completed in accordance with the guideline.
- Understand that treatment will be stopped if they do not attend for monitoring and treatment review.
- Bring the methotrexate monitoring booklet to all specialist and GP appointments where it will be updated by the health professional conducting the appointment. The patient should also produce the booklet and/or alert card to any health professional involved in other aspects of their care e.g. pharmacists, dentists, medical teams during hospital admissions.
- Ensure contact details are kept up to date with both the GP and the Specialist.
- Read the methotrexate patient information leaflet. Request information in different format(s) if required to aid understanding. Understand treatment, expected benefits and potential side effects. Links to patient information resources can be found in the supporting information section below.
- Ensure methotrexate brand/formulation is as expected due to differences between injection devices. ~~Take~~ Inject (or support administration of) methotrexate and take folic acid as directed by the prescriber. Methotrexate and folic acid should not be taken on the same day.
- Patients wishing to reduce their dose or stop methotrexate treatment should discuss with their specialist before doing so. Avoid abrupt withdrawal unless advised by the GP or specialist.
- Tell anyone who prescribes them a medicine that they are prescribed methotrexate
- Avoid self-medication with over-the-counter aspirin or ibuprofen. Seek guidance from a pharmacist, GP or specialist on medication safety and potential interaction with methotrexate if engaging in recreational drug use, or using herbal remedies or over the counter (OTC) treatments.
- Report any adverse effects or newly presenting signs or symptoms to the GP and/or specialist.
- **Report the following signs and symptoms to the GP without delay (out of hours contact NHS 111):**
  - 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, mouth ulcers, 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, abdominal discomfort, dark urine
  - Swelling of the hands, feet, or ankles
  - Unexplained bleeding or bruising, epistaxis, black stools, or blood in the vomit or stools.
  - Suspected or confirmed pregnancy.
- **Individuals must not get pregnant during methotrexate therapy. Individuals should take a pregnancy test if they think there is a possibility they may be pregnant, and inform the GP or specialist immediately if they become pregnant or wish to become pregnant.**
- Female patient: Effective contraception must be used during methotrexate treatment and continued for at least 6 months thereafter.
- Male patient (or their female partners): Reliable contraception is recommended during treatment with methotrexate and for at least 6 months after cessation. Men should not donate semen during therapy or for 6 months following discontinuation of methotrexate.
- Abstain from alcohol during treatment – taking alcohol and methotrexate together increases the risk of liver injury.

- Avoid excessive consumption of beverages containing caffeine or theophylline (coffee, soft drinks containing caffeine, black tea)
- Skin may be more sensitive to exposure to sun while using methotrexate. Avoid exposure to intense sunlight especially between 11am and 3pm, and avoid UV rays (e.g. sunbeds and sunlamps). Purchase and use a sunscreen with a high sun protection factor (SPF) and wear a hat and clothes that cover your arms and legs when in the sun; speak to a healthcare professional if they have concerns about a skin reaction.
- For patients prescribed 20mg/week or more of methotrexate: avoid contact with people with chicken pox or shingles and report any such contact urgently to their GP.
- Maintain adequate hydration during treatment.
- Store medicines safely and securely; it must not be shared with anyone else. Dispose of any unused medication appropriately.
- Do not drive or operate machinery if methotrexate affects their ability to do so safely, e.g. by causing fatigue or dizziness.
- Report suspected side effects to the GP or specialist and the MHRA via yellow card scheme.

Monitoring requirements

Baseline assessment to be completed by the specialist before initiating methotrexate in adults:

Full history and physical examination and laboratory tests to include:

- Medical history and current medication
- Height, weight, blood pressure
- Consideration of cautions and contraindications associated with methotrexate
  - Confirm to GP that any underlying blood dyscrasias have been considered
- Chest x-ray and additional screening for lung disease, including interstitial lung disease and tuberculosis, will be undertaken at clinician discretion on a case-by-case basis
- Assessment of renal function, liver function and FBC.
- Check levels of vitamin B12 prior to initiating folic acid supplementation, particularly in adults aged over 50 years, as folic acid intake may mask a vitamin B12 deficiency.
- Ascertain immune status by enquiring about history of chickenpox. If chicken pox immune status is unclear then consider checking antibodies to varicella zoster.
- Any infections should be attended to before initiation of methotrexate therapy.
- Ensure patient is vaccinated in line with recommendations in The Green Book.
- Discuss contraception in all patients and the risks of pregnancy. It is important to exclude pregnancy prior to starting treatment
- Consider screening (and treatment) for inactive chronic infections (e.g. herpes zoster, tuberculosis, hepatitis B or C) and HIV because of their potential activation.
- Consider risk assessment for liver fibrosis such as Fibrosis-4 index (FIB-4)

Specialist should copy all baseline results to GP.

Monitoring Requirements:

The requirements outlined in the table below will be **completed by the specialist until the GP takes over prescribing and monitoring.**

The transfer to primary care is normally after the patient has been treated for 3 months. The condition should be stable and the dose optimised (with no anticipated further changes expected in the immediate future).

The exact frequency of monitoring to be communicated by the specialist in all cases.

Where abnormal results are identified during routine monitoring consider the actions in the table below, seeking advice from specialist for further support and guidance where required. **As well as responding to absolute values, a rapid change or a consistent trend in any value should prompt caution and extra vigilance**.

If monitoring results are forwarded to the specialist team, include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

<table>
<tr><th>Tests</th><th>Frequency of monitoring</th><th>Threshold for action</th><th>Action to be taken by GP</th></tr>
<tr><td>FBC</td><td rowspan="3">Every 1-2 weeks until on a stable dose for 6 weeks, then every month for 3 months, then at least every 12 weeks.

Following dose increases, monitor every 2 weeks until on a stable dose for 6 weeks, then revert to previous schedule.

Patient factors where continued monthly monitoring is recommended (unless otherwise specified)*:
• Previous toxicity or deranged FBC or LFTs while on DMARDs
• Chronic kidney disease (CKD 3 or worse)
• Pre-existing liver disease

Additional urgent monitoring tests should be carried out within 24 hours for any patient with acute kidney injury (AKI).</td><td>WCC < 3.5 x 10^9/L
Neutrophils < 1.6 x 10^9/L
Eosinophils >0.5 x 10^9/L
Platelets < 140 x 10^9/L
Lymphocytes < 0.5x10^9/L
MCV > 105fl (if samples are being analysed by Derriford Hospital lab, MCV >108fl)</td><td rowspan="3">If results meet specified criteria, stop treatment and refer to specialist.
If isolated MCV rise, check for other causes (B12, folate, thyroid function and alcohol consumption). If results are normal, refer to specialist.
If concerned about sequential drops in FBC indices (possibly still within normal range), consider an early re-test/seek specialist advice.
If deterioration in renal function, dose adjustment may be necessary; if toxicity suspected or dosing advice required refer to specialist team.
Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including over the counter (OTC) treatments or complementary medication.</td></tr>
<tr><td>Creatinine / eGFR</td><td>Creatinine increase >30% over 12 months and/or eGFR <60ml/min/1.73m^2</td></tr>
<tr><td>ALT and/or AST and albumin</td><td>ALT and/or AST >100 U/L

Albumin unexplained reduction to <30g/L</td></tr>
<tr><td>Adverse effects</td><td>At every contact</td><td>See table below</td><td></td></tr>
<tr><td colspan="4">*Other factors that may increase risk of toxicity include moderate renal impairment, extremes of body weight, polypharmacy (especially other haematotoxic/ hepatotoxic/ nephrotoxic drugs), comorbidities, age > 80 years. Where more frequent ongoing monitoring is required due to a combination of patient factors this will be advised by the specialist prescriber.</td></tr>
</table>

Presentation of the following adverse effects, signs or symptoms and associated actions should be noted. Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. See also adverse effects in supporting information below.

Adverse effects, signs and symptoms	Action to be taken by GP
Interstitial pneumonitits; often associated with eosinophillia Symptoms may include: dyspnoea, cough (especially a dry non-productive cough) and fever	**Withhold methotrexate** and discuss with initiating specialist urgently. Specialist will advise on investigations and treatment plan. GP to arrange chest x-ray. The manufacturer states that if methotrexate induced lung disease is suspected, treatment with methotrexate should not be restarted.
Infections	During a serious infection **withhold methotrexate** until the patient has recovered. Discuss with specialist if required and consider additional investigations e.g. FBC if clinically appropriate. During minor infections (e.g. uncomplicated UTI treated with a short antibiotic course) treatment can be continued. If patient requires antibiotics ensure potential interaction risk has been considered.
Bone marrow suppression Symptoms may include: unexplained bleeding or bruising with or without sore throat, purpura, mouth ulcers	**Withhold methotrexate**. Check FBC immediately and discuss with the initiating specialist. See also haematological monitoring advice above.
Jaundice	**Withhold methotrexate** and discuss with initiating specialist. Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication. See also hepatic monitoring advice above.
Nausea	Review for reversible causes and treat as appropriate. Enquire which day of the week the patient injects their methotrexate, and which day(s) they take folic acid and confirm against the patient's records. Discuss with initiating specialist if persistent or severe.
Diarrhoea, ulcerative stomatitis, haematemesis, black or bloody stools, or suspected pancreatitis	**Withhold methotrexate** and discuss with initiating specialist.
Conditions which increase the risk of dehydration (e.g. vomiting)	Temporarily **withhold methotrexate** until patient has recovered.
Photosensitivity	Continue methotrexate. Reinforce appropriate self-care e.g. sun avoidance and purchasing of a broad spectrum sunscreen (at least SPF30).
Pregnancy	In pregnant patients **withhold methotrexate** immediately and prescribe folic acid 5mg/day. Discuss with initiating specialist urgently. In pregnancies with paternal exposure, discuss with initiating specialist.
	Continued overleaf

Chickenpox or shingles	**Post exposure prophylaxis** Contact microbiology if a patient, not known to be immune to chickenpox, comes into contact with shingles or chickenpox, for advice on whether varicella-zoster immune globulin (VZIG) or other treatment is indicated. For detailed advice on risk assessment and post exposure prophylaxis following exposure to chicken pox and shingles, see: • the Green Book (Chapter 34) • UKSHA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles April 2022 **In patients suffering from chickenpox or active skin lesions from shingles** **Withhold methotrexate**. **Patients with chickenpox**: contact microbiologist for consideration of admission to hospital for IV antivirals. **Patients with shingles**: if any vesicles are still present (regardless of the time of onset), treat with aciclovir (800mg five times a day for 7 days).

Supporting Information

This section provides additional information regarding methotrexate. Refer to the online BNF, SmPCs, the MHRA or NICE websites for up-to-date information on any medicine.

Methotrexate must be prescribed by the specialist during initiation and dose stabilisation.

Formulation

Refer to Devon formulary for list of preparations approved for use locally.

Administration

Converting from an oral to a subcutaneous dosage form may be appropriate where patients experience intolerable gastrointestinal adverse effects and should only be undertaken by a specialist; a dose reduction may be required.

Pregnant people, including patients and carers, should avoid handling methotrexate.

Local, pre-existing arrangements for the safe supply of methotrexate injection and ancillary products, and for the disposal of cytotoxic waste, should be followed.

Avoid skin or mucosa contact with methotrexate solution for injection. Spillage kits should be available for patients on subcutaneous methotrexate.

If a dose of methotrexate is missed it should be injected as soon as remembered, within one or two days. Doses which are three or more days late should be skipped entirely. Inject the next dose as scheduled, on the usual day. **A double dose should not be taken to make up for a missed dose**.

Dosage and administration

All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the GP.

There is a wide dose range depending on the indication. The selected dose of methotrexate, and the folic acid regimen, will be tailored to the individual patient and decided by the specialist. The dose titration period must be prescribed by the initiating specialist. The initial maintenance dose must be prescribed by the initiating specialist.

Usual maintenance dose range 7.5mg – 25mg once a week. Dosage should be adjusted according to the patient's response.

Patients should be co-prescribed folic acid to prevent methotrexate-induced side-effects (off-label use). Prescribe 5mg once weekly (unless a higher dose has been advised by the specialists), to be taken at least 24 hours after methotrexate. Be aware that methotrexate and folic acid tablets look alike.

Elderly

Methotrexate should be used with caution in elderly patients. A reduction in dosage should be considered due to reduced liver and kidney function as well as lower folate reserves, which occur with increased age.

Renal impairment

Methotrexate is excreted to a significant extent by the kidneys, and therefore should be used with caution in patients with impaired renal function. Dose adjustments may be required to prevent accumulation. Refer to SmPCs for full guidance.

Hepatic Impairment

Methotrexate should be administered with great caution, if at all, to patients with significant current or previous liver disease, especially if due to alcohol.

Pleural effusion, ascites

The half-life of methotrexate can be prolonged to 4 times the normal length in patients who possess a third distribution space; dose reduction or, in some cases, discontinuation of methotrexate administration may be required.

Treatment review and discontinuation

Termination of treatment will be the responsibility of the specialist with exceptions due to adverse effects detailed in the table above. Treatment duration will be based on clinical response and tolerability.

The BNF recommends that treatment should be stopped if inadequate response after 3 months at the optimum dose.

Contraindications

- Hypersensitivity to methotrexate or any excipients.
- Significant hepatic impairment.
- Ascites or pleural effusion: drain prior to treatment to reduce the risk of methotrexate accumulation.
- Significant renal impairment (creatinine clearance less than 30 mL/min), and moderate renal impairment (creatinine clearance less than 60 ml/min) for methotrexate doses >100 mg/m2
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia or significant anaemia
- Alcoholism
- Severe infections (acute or chronic) or immunodeficiency syndrome.
- Stomatitis, ulcers of the oral cavity and known active gastrointestinal ulcer disease
- Pregnancy and breast-feeding.
- Live vaccines
  - The NHS England shared care protocol for methotrexate advises consultation with The Green Book which states “Live vaccines should not be administered to individuals who are receiving or have received in the past 3 months methotrexate at a dose of >25mg per week.”
  - Clinician discretion is advised when considering live vaccination.
- Concomitant use of medicines with anti-folate properties, e.g. trimethoprim, co-trimoxazole

Precautions

In addition to the points listed below, refer to the monitoring section above for further cautions to be noted during treatment depending on patient medical history and actions to take in the case of a severe adverse effect or patient reported signs or symptoms.

- Doses exceeding 20 mg week can be associated with a substantial increase in toxicity, especially bone marrow depression.

- The immunosuppressive effect of methotrexate should be taken into account when immune responses of patients are important or essential. Special attention should be paid in cases of inactive chronic infections (e.g. herpes zoster, tuberculosis, hepatitis B or C) because of their potential activation.
- Pre-existing blood dyscrasias or disorders, including bone marrow hypoplasia, leucopenia, thrombocytopenia, or significant anaemia.
- Renal impairment. If risk factors such as renal function disorders, including mild renal impairment, are present, combined administration with NSAIDs is not recommended. Dose adjustments may be required (see above)
- Hepatic impairment. Dose adjustments may be required (see above)
- Risk factors for hepatotoxicity during treatment e.g. previous liver disease, repeatedly abnormal liver function tests and alcohol consumption, family history of hereditary liver disorders, obesity and previous contact with hepatotoxic drugs or chemicals, prolonged methotrexate treatment, diabetic patients treated with insulin.
- Alcohol dependence
- Dehydration, diarrhoea, vomiting
- Photosensitivity (see below). Psoriasis lesions may be aggravated by UV radiation—skin ulceration has been reported. Radiation recall reaction has been reported in both radiation- and sun-damaged skin.
- Skin and mucosal contact with methotrexate injection solution is to be avoided.
- History of ulcers of the oral cavity, gastrointestinal ulcers, peptic ulcer, ulcerative colitis, ulcerative stomatitis
- Presence/history of infection (chronic or recurrent) e.g. frequent infective COPD exacerbations or recurrent UTI
- Frail or elderly. Dose adjustment may be required (see above)
- Psychiatric disorders.
- Respiratory disease
- Pleural effusions and ascites should be drained prior to initiation of methotrexate therapy or treatment should be withdrawn.
- Malignant lymphomas may occur in patients receiving low dose methotrexate, in which case therapy must be discontinued.
- When methotrexate is controlling an individual's skin disease, it can be continued during the perioperative period. However, where patients are due to undergo major surgery and have comorbidities such as diabetes, which may alter infection risk, the use of methotrexate may theoretically augment infection risk, and the decision to continue must be decided on a case-by-case basis.

MHRA/CHM advice: Methotrexate: advise patients to take precautions in the sun to avoid photosensitivity reactions (August 2023)

Photosensitivity reactions, including phototoxicity, are known side-effects of methotrexate that may occur with low- and high-dose treatment. These reactions are distinct from radiation recall reactions, and can appear as severe sunburn (e.g. rashes with papules or blistering, and sometimes swelling); rarely, photosensitivity reactions have contributed to deaths from secondary infections.

Healthcare professionals are reminded to inform patients and their carers of the risk and signs of photosensitivity reactions during methotrexate treatment.

Adverse effects

Folic acid should be prescribed alongside methotrexate to reduce side-effects. Folic acid decreases mucosal and gastrointestinal side-effects of methotrexate and may prevent hepatotoxicity; there is no evidence of a reduction in haematological side-effects.

The most serious adverse reactions of methotrexate include **bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, thromboembolic events, anaphylactic shock and Stevens-Johnson syndrome.**

The data below has been taken from the online BNF. **The list is not exhaustive.** Refer to the online BNF and SmPCs for full prescribing data. Seek specialist advice where necessary. See also adverse effects, signs and symptoms in monitoring requirements section above.

Very common (≥1/10) or common (**≥1/100 to <1/10):** Anaemia; appetite decreased; diarrhoea; drowsiness; fatigue; gastrointestinal discomfort; headache; leucopenia; nausea; oral disorders; respiratory disorders; skin reactions; throat ulcer; thrombocytopenia; vomiting

Uncommon (≥1/1000 to <1/100): Agranulocytosis; alopecia; arthralgia; bone marrow disorders; confusion; cystitis; depression; diabetes mellitus; drug toxicity; dysuria; gastrointestinal disorders; haemorrhage; healing impaired; hepatic disorders; increased risk of infection; local reaction; myalgia; neoplasms; osteoporosis; photosensitivity reaction; rheumatoid arthritis aggravated; seizure; severe cutaneous adverse reactions (SCARs); vasculitis; vertigo; vulvovaginal disorders

Rare (≥1/10,000 to <1/1,000) or very rare (<1/10,000): Apnoea; asthma-like conditions; azotaemia; conjunctivitis; cough; dyspnoea; embolism and thrombosis; eosinophilia; fever; gynaecomastia; hypotension; immune deficiency; infertility; insomnia; lymphadenopathy; meningism; meningitis aseptic; menstrual cycle irregularities; mood altered; muscle weakness; nail discolouration; neutropenia; pain; pericardial disorders; pericarditis; proteinuria; reactivation of infection; renal impairment; retinopathy; sensation abnormal; sepsis; sexual dysfunction; sperm abnormalities; stress fracture; taste altered; telangiectasia; vision disorders

Frequency not known: Aphasia; chills; cognitive disorder; defective oogenesis; dizziness; hemiparesis; injection site necrosis; leukoencephalopathy; metabolic change; mucositis; necrosis; nephropathy; oedema; pancreatitis; progressive multifocal leukoencephalopathy (PML); radiation injuries; skin ulcer; sudden death; tinnitus

Interactions

Methotrexate is associated with a large number of interactions, some of which are significant enough to contraindicate concurrent use, require dose adjustment and/or additional monitoring.

The following lists are not exhaustive. Consider interaction with prescription and recreational drugs. Refer to the online BNF and SmPCs for full prescribing data. Seek specialist advice where necessary and / or refer to specialist Medicines Information services for additional support (and reference to Stockley's Drug Interactions where paid subscription available) if concomitant administration of interacting medicines clinically indicated. Guidance on frequently asked questions on medicine interactions with low dose methotrexate has also been produced by the Specialist Pharmacy Service (SPS) and can be accessed here.

The following interactions are classified in the online BNF as **severe** (the result may be a life-threatening event or have a permanent detrimental effect):

- **NSAIDs, COX-2 inhibitors, aspirin** may reduce excretion of methotrexate (particularly high -dose), increasing risk of toxicity. The NHS England shared care protocol states that these drugs are frequently used with methotrexate without incident, and aspirin at antiplatelet doses is unlikely to interact to a significant degree. Be aware of trends in monitoring parameters. Concomitant use of methotrexate with NSAIDs, COX-2 inhibitors, aspirin increases the risk of nephrotoxicity.
- **Alcohol** induced liver disease increases the risk of hepatotoxicity in those taking methotrexate.
- **Live vaccines (e.g. cholera, dengue, herpes zoster, influenza, rotavirus, varicella zoster, yellow fever, MMR, BCG, oral polio and typhoid):** SmPC states that administration of live vaccines is contra-indicated during therapy; however the Green Book states "live vaccines should not be administered to individuals who are receiving or have received in the past 3 months methotrexate at a dose of >25mg per week." There is an increase in the risk of generalised infection (possibly life-threatening) when given with methotrexate (high-dose). Clinician discretion is advised.
- Co-administration of medicinal products which cause folate deficiency (e.g. **trimethoprim** and **co-trimoxazole**) can lead to increased methotrexate toxicity and is contraindicated. Increased risk of haematological side effects (sometimes fatal). Particular caution should therefore also be exercised in the presence of existing folic acid deficiency. Both methotrexate and trimethoprim can increase the risk of nephrotoxicity.
- **Sulfonamides including sulfadiazine, sulfadoxine, sulfamethoxazole** are predicted to increase the exposure to methotrexate. Manufacturer advises use with caution or avoid.

- **Proton pump inhibitors (PPIs)** and high dose methotrexate should be used with caution or avoided (SmpC states avoid), especially in patients with renal impairment. PPI decreases the clearance of methotrexate.
- **Penicillin antibiotics** increase the risk of toxicity when given with methotrexate, BNF advises monitoring. NHS England states that methotrexate should be interrupted during periods of acute infection.
- **Ciprofloxacin** potentially increases the risk of toxicity when given with methotrexate
- **Low molecular weight heparins (LMWH) (bemiparin, dalteparin, enoxaparin and tinzaparin):** methotrexate might increases the risk of hepatotoxicity when given concomitantly with high dose LMWH.
- **Antineoplastics (Asparaginase, Crisantaspase**, **Pegaspargase)** affect the efficacy of methotrexate. Manufacturer advises separating administration. Both can increase the risk of hepatotoxicity and myelosuppression.
- **Tegafur** (manufacturer recommends caution), **fluorouracil:** Methotrexate potentially increases the risk of severe skin reaction when given with topical fluorouracil. Methotrexate, fluorouracil and Tegafur increase the risk of myelosuppression. Fluoracurcil and methotrexate increase the risk of hepatotoxicity.
- **Nitrous oxide** (manufacturer recommends avoid) and **pyrimethamine**: increased antifolate effect of methotrexate.
- **Baricitinib** is predicted to enhance the risk of immunosuppression when given with methotrexate.
- **Levetiracetam** decreases the clearance of methotrexate. Manufacturer advises monitor levetiracetam and methotrexate concentrations.

The following interactions have been highlighted in the NHS England shared care protocol and SmPC:

- Drugs with **hepatotoxic, haematotoxic** or **nephrotoxic effects**: Increased frequency of monitoring may be recommended.
- Avoid concomitant use of **cytotoxics, clozapine,** and **olanzapine**: increased risk of agranulocytosis.
- **Diphenylhydantoins, acidic anti-inflammatory agents, salicylates, phenylbutazone, phenytoin, barbiturates, tranquilisers, oral contraceptives, amidopyrine derivatives, p-aminobenzoic acid, thiazide diuretics, oral hypoglycaemics, doxorubicin, tetracyclines, probenicid or sulfinpyrazone or oral hypoglycaemics** will decrease the methotrexate transport function of renal tubules, thereby reducing excretion and increasing methotrexate toxicity.
- **Leflunomide**: increased risk of bone marrow and liver toxicity; increased monitoring and vigilance required.
- **Ciclosporin**: increased risk of nephrotoxicity and methotrexate toxicity.
- **Azathioprine** and **mercaptopurine**: not advised due to increased risk of toxicity.
- **Sulfasalazine**: may increase risk of bone marrow and liver toxicity. However, this combination is used in clinical practice without incident. Be aware of trends in monitoring parameters.
- **Retinoids**: increased risk of hepatotoxicity, and may increase plasma levels of methotrexate.
- **Lomitapide**: increased risk of hepatotoxicity.
- **Probenecid**: excretion of methotrexate reduced.
- **Phenytoin**: possible increased methotrexate toxicity, and decreased phenytoin effect.
- **Theophylline** and other **methylxanthines**: may reduce methotrexate efficacy. Methotrexate may reduce theophylline clearance.
- **Anticonvulsants**: may reduce methotrexate levels.
- **Colestyramine**: may increase elimination of methotrexate.
- **Loop-diuretics** and **pyrazols** reduce tubular secretion; great caution should be exercised when these medicinal products are co-administered with methotrexate.
- Antibiotics, like **glycopeptides, sulfonamides,** and **cefalotin** can, in individual cases, reduce the renal clearance of methotrexate, so that increased serum concentrations of methotrexate with simultaneous haematological and gastro-intestinal toxicity may occur.
- Oral antibiotics such as **tetracyclines**, **chloramphenicol** and **non-absorbable broad-spectrum antibiotics** may reduce intestinal methotrexate absorption or interfere with the enterohepatic circulation, due to inhibition of the intestinal flora or suppression of bacterial metabolism.
- **Vitamin preparations or other products containing folic acid or its derivatives** may impair methotrexate efficacy.
- **Procarbazine** during high-dose methotrexate therapy increases the risk of impairment or renal function.
- **Triamterene:** Bone marrow suppression and decreased folate levels have been described

Pregnancy, lactation and paternal exposure

Before prescribing in this area seek specialist advice and check up-to-date sources of information.

Pregnancy (Maternal exposure)

The UK Teratology Information Service (UKTIS) provides a national service on all aspects of the toxicity of drugs and chemicals in pregnancy (Tel: 0344 892 0909), and provides the 'best use of medicines in pregnancy' (bumps) website for supportive patient information relating to individual treatments. A UKTIS abstract on the use of methotrexate is available here. A patient information leaflet from bumps is available here.

Methotrexate is **contra-indicated** during pregnancy in non-oncological indications. Pregnancy should be excluded prior to starting treatment. Methotrexate has been shown to be teratogenic; it causes embryotoxicity, abortion and foetal malformations in humans. The possible effects on reproduction, pregnancy loss and congenital malformations should be discussed with patients of childbearing potential prior to initiating treatment.

Patients of reproductive potential must be counselled regarding pregnancy prevention and planning. During treatment pregnancy tests should be repeated as clinically required (e.g. after any gap of contraception).

The manufacturer recommends that patients of childbearing potential must use effective contraception during treatment and for at least six months after (see below for contraception advice during paternal exposure).

If pregnancy occurs during treatment with methotrexate and up to six months thereafter, medical advice should be given regarding the risk of harmful effects on the child associated with treatment and ultrasonography examinations should be performed to confirm normal foetal development. The continued use and dose of folic acid during the pregnancy must be confirmed with the specialist.

Paternal exposure

A UKTIS abstract on the paternal use of methotrexate is available here. A bumps patient information leaflet for use of methotrexate in men is available here.

The manufacturer's SmPC states that it is not known if methotrexate is present in semen. Methotrexate has been shown to be genotoxic in animal studies, such that the risk of genotoxic effects on sperm cells cannot completely be excluded. Limited clinical evidence does not indicate an increased risk of malformations or miscarriage following paternal exposure to low-dose methotrexate (less than 30 mg/week). For higher doses, there is insufficient data to estimate the risks of malformations or miscarriage following paternal exposure.

Sexually active male patients or their female partners are recommended to use reliable contraception during treatment of the male patient and for at least 6 months after cessation of methotrexate. Men should not donate semen during therapy or for 6 months following discontinuation of methotrexate.

Where a couple wishes to attempt conception and the male partner's condition is well-controlled with methotrexate, the UKTIS recommends an assessment and discussion of the potential benefits and risks of continuing paternal treatment versus discontinuation. This should be undertaken by the specialist, using a shared decision making approach. The risks to the foetus are theoretical rather than established.

UKTIS also states paternal methotrexate use at the time of conception is not an indication for additional foetal monitoring. However, other risk factors may be present in individual cases which may independently increase the risk of adverse pregnancy outcome. Clinicians are reminded of the importance of consideration of such factors when performing case-specific risk assessments.

Lactation

UK Drugs in Lactation Advisory Service (UKDILAS) provides evidence based information on the use of drugs during the breastfeeding period to all UK healthcare professionals. Information relating to methotrexate can be found here.

Methotrexate is **contra-indicated** during breast-feeding however the UKDILAS guidance states "very limited published evidence indicates negligible amounts in breast milk. For doses of 25mg weekly or less, breastfeeding may continue with caution. However, breastfeeding should be withheld for a period of 24 hours after each dose."

“Monitor the infant for signs of immunosuppression and gastro-intestinal disturbances; the infant’s blood count should also be checked regularly.”

Fertility

The manufacturer’s SmPC states that methotrexate affects spermatogenesis and oogenesis and may decrease fertility. Methotrexate has been reported to cause oligospermia, menstrual dysfunction and amenorrhoea. These effects appear to be reversible on discontinuing therapy in most cases.

Support

Dermatology Services Contact Details
University Hospitals Plymouth NHS Trust Contact initiating specialist using contact details provided at outset or via hospital switchboard, telephone: 01752 202082

For further support and information in relation to individual shared care agreements please contact your practice pharmacist or alternatively please contact the Medicines Optimisation Team.

Email: D-ICB.medicinesoptimisation@nhs.net

Version 1

Date ratified: June 2024

This guideline has been reviewed by stakeholders across Devon and is intended for use in accordance with locally commissioned services.

This guideline has been developed with consideration and local adaptation of the national shared care protocol; “Methotrexate (oral and subcutaneous) for patients in adult services (excluding cancer care)” 4 July 2022 Version 1 (available here). Development of the national guideline was led by the Regional Medicines Optimisation Committee (RMOC) (north) with approval for publication on the NHS England website.

Shared Care Agreement Letter - Specialist Request to GP

To	**GP name**	
	Practice address	
Patient name		
Hospital number		
NHS number		
Date of birth		
Address		

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

I have discussed and agreed the following treatment with the patient:

Once-weekly subcutaneous methotrexate (state dose and day of the week to be administered)

……

Folic acid 5mg tablets; at least 5mg once weekly. The dose to be taken at least 24 hours after methotrexate dose (confirm regimen)

……

For the treatment of:

Indication	Select applicable indication
Psoriasis	
Sarcoidosis	
Connective tissue diseases	
Atopic dermatitis	
Pemphigoid	
Pemphigus	
Nodular prurigo	

Treatment was started on ……

The patient has been on the optimised dose stated for ……..

This patient is now suitable for prescribing to move to primary care. The patient fulfils criteria for shared care therefore I am writing to request your agreement to continue the care of this patient according to the Specialised Medicines Service (SMS) Guideline.

In accordance with the SMS Guideline the transfer of monitoring and prescribing to the GP is normally after the patient has been treated for 3 months. The condition should be stable and the dose optimised (with no anticipated further changes expected in the immediate future).

I have provided the patient with sufficient medication to last until ……

Please undertake prescribing and monitoring from …… in line with the SMS Guideline.

The next monitoring is due on ……

I have arranged a follow up with this patient in ……..

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete (YES/NO)
Baseline investigation and monitoring as set out in the SMS Guideline have been completed and were satisfactory	
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	
The risks and benefits of treatment have been explained to the patient	
The roles of the Specialist / GP / Patient have been explained and agreed	
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	
I have enclosed a copy of the SMS Guideline which covers this treatment. The guideline can also be found here	
I have included with this letter copies of the information the patient has received	

The results of baseline tests, early monitoring and any additional supportive information are included below and/or attached:

GP please sign response letter and return promptly (where possible this should be within 14 days of the request being made).

Specialist signature		**Date**	
Specialist name, role, speciality			
Daytime telephone number			
Email address			
Alternative contact **e.g. clinic or specialist nurse**			
Out of hours contact details **e.g. duty doctor**			

Remember to keep a copy of this letter for the patient's records.

Shared Care Agreement Letter – GP Acceptance Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment:

Medicine	Formulation	Route	Dose and frequency
Methotrexate	injection	Subcutaneous	
Folic acid	5mg tablets	Oral	

I can confirm that **I am willing to take on this responsibility** from …….. and will maintain the prescribing and monitoring responsibilities as set out in the Specialised Medicines Service (SMS) Guideline.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

Shared Care Agreement Letter – GP Refusal Letter to Specialist

To	Specialist name	

Patient name	
Hospital number	
NHS number	
Date of birth	
Address	

GPs are invited to participate in shared care agreements, but if the GP is not confident to undertake these roles then they are under no obligation to do so. If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

The prescriber has the clinical and legal responsibility for the drug and the consequences of its use. Responsibility for drug monitoring and acting on results remains with the prescriber.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs."

In the interest of patient safety NHS Devon, in conjunction with local acute trusts have classified methotrexate as a "shared care" drug which requires a number of conditions to be met before transfer can be made to primary care.

Thank you for your request for me to accept prescribing responsibility for this patient. I regret to inform you that in this instance **I am unable to take on responsibility** due to the following:	**Tick all applicable**
The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care. As the patients GP I do not feel clinically confident to manage this patient's condition. I have consulted with other GPs in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given below.**	

The condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement. As the condition requested to be treated is not included on the locally recognised list of indications for shared care for methotrexate I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this condition is identified locally as requiring shared care with methotrexate the responsibility for providing this patient with their medication remains with you.**	
A minimum duration of supply by the initiating specialist. As the patient has not had the minimum supply of medication to be provided by the initiating specialist (28 days) I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.**	
Initiation and optimisation by the initiating specialist. Transfer to primary care is normally after the patient has been treated for 3 months. The condition should be stable and the dose optimised (with no anticipated further changes expected in the immediate future). As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. **Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.**	
Other (GP to complete if there are other reasons why shared care cannot be accepted):	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

GP signature		**Date**	
GP name			
Practice address			
Telephone number			
Email address			

Remember to keep a copy of this letter for the patient's records.