Shared Care Agreement: Methotrexate (oral and subcutaneous) for patients in adult services (non-cancer indications)

This Shared Care Protocol sets out details for the sharing of care for patients prescribed oral or subcutaneous Methotrexate. This protocol is for use within adult services for non-cancer indications.

It should be read in conjunction with the latest Summary of Product Characteristics (SPC) available at www.medicines.org.uk/emc/.

As outlined in NHS England Guidance 2018 "Responsibility for Prescribing between Primary & Secondary/Tertiary Care. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP concerned (and the patient) to share their care.

This document provides information on drug treatment for the shared commitment between the consultant and primary care clinician concerned. The primary care clinician may accept or decline shared care. If shared care is declined the primary care clinician practice must discuss the reason for refusal with the consultant within 14 days. Where appropriate, the clinical responsibility will then remain with the consultant.

Introduction

This shared care guideline sets out details to support the transfer of responsibility for prescribing Methotrexate for any of the indications listed in section 2, from specialist to primary care. For further information please click on the links below:

British National Formulary

http://www.medicines.org.uk/emc/

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Authored by:	Cambridgeshire and Peterborough Integrated Care System
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Cambridgeshire & Peterborough Integrated Care System

NHS Cambridgeshire & Peterborough

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Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber) 22

Appendix 2: Shared Care Refusal Letter (Primary Care Prescriber to Specialist) ..... **Error! Bookmark not defined.**

The content of this shared care protocol was correct as of March 2025. As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Ensure the patient and/or carer understands and can follow the once-weekly dose regimen.
- If prescribing subcutaneous methotrexate ensure the patient/carer is trained to administer safely, or liaise with primary care to arrange safe administration by a healthcare professional. Ensure that there are local arrangements for safe supply and disposal of ancillary products.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Initiate and optimise treatment as outlined in section 5. Transfer to primary care is normally after the patient has been treated for 3 months and with satisfactory investigation results for at least 4 weeks.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose of methotrexate and folic acid, any relevant test results, which day of the week the patient takes their methotrexate and folic acid, and when the next monitoring is required. Include contact information (section 13). If subcutaneous methotrexate is prescribed, include the brand.
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Review treatment and reassume prescribing responsibility if a patient becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required

Primary care responsibilities

- If accepted, prescribe methotrexate and folic acid as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.

- If refusing, refuse the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- Adjust the dose of methotrexate and folic acid prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- 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.
- Discuss with the specialist if the patient plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Take or administer methotrexate as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. If provided, they should bring their monitoring booklet to each appointment. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter (OTC) medications to primary care and specialist and be aware they should discuss the use of methotrexate with their pharmacist before purchasing any OTC medicines.
- Moderate their alcohol intake to no more than 14 units per week.
- Not to drive or operate heavy machinery if methotrexate affects their ability to do so safely.
- All patients should use appropriate contraception. Those of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant. See section 12.

1. Background

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Methotrexate is a cytotoxic folic acid antagonist used to treat chronic inflammatory conditions and certain cancers. It inhibits the enzyme dihydrofolate reductase and inhibits synthesis of DNA, RNA and proteins.

Methotrexate is licensed for the treatment of certain cancers, as well as some chronic inflammatory disorders. It is not licensed for all the conditions it is used to treat. However, its use for the indications below are well established and supported by clinical specialists.

This shared care protocol does not cover treatment of cancer, or treatment of people less than 18 years old.

2. Indications

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The licensed indications for methotrexate include:

- Active rheumatoid arthritis
- Mild to moderate Crohn's disease in patients refractory or intolerant to thiopurines (licensed indication of subcutaneous preparations)
- Severe psoriasis
- Severe psoriatic arthritis

Licensed indications vary with brand. See relevant summary of product characteristics for full details.

This shared care protocol also includes treatment of chronic inflammatory conditions where off-label use of methotrexate is appropriate, including, but not limited to, the following specialities and conditions:

- Rheumatology (e.g. inflammatory arthritis, connective tissue disease, vasculitis)
- Dermatology (e.g., severe eczema, bullous conditions)
- Gastroenterology (e.g. severe Crohn's disease or other inflammatory bowel disease)
- Neurology (e.g. myasthenia gravis, inflammatory neuropathies)
- Ophthalmology (e.g. uveitis, scleritis)
- Respiratory disease (e.g. sarcoidosis, interstitial lung disease)

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

This shared care protocol applies to adults aged 18 and over. It does not include use of methotrexate for cancer indications.

3. Locally agreed off-label use

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See above.

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC), and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

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 (CrCl) less than 30 mL/min.
- Severe infections (acute or chronic) or immunodeficiency syndromes.
- Known active peptic ulceration.
- Pregnancy and breast-feeding.
- Vaccination with live vaccines during treatment with methotrexate at immunosuppressive doses. See section 7 for further detail.
- Concomitant use of medicines with anti-folate properties, e.g. trimethoprim, co-trimoxazole (see section 7).

Cautions:

- Renal impairment: dose reduction required (section 5).
- Alcohol dependence.
- Hepatic impairment, particularly if due to alcohol use.
- Pre-existing blood dyscrasias or disorders, including bone marrow hypoplasia, leucopenia, thrombocytopenia, or significant anaemia. Confirm to primary care that any underlying dyscrasias have been considered, and whether any change to standard monitoring in section 9 is required.
- Respiratory disease.
- Concomitant use with hepatotoxic or haematotoxic medicines (see section 7).
- History of ulcers of the oral cavity, ulcerative stomatitis, gastrointestinal ulcers or ulcerative colitis.
- History of chronic or recurrent infection (e.g. frequent infective COPD exacerbations, or recurrent urinary tract infection).
- Frail or elderly – consider reduced dose.
- Conditions which increase the risk of dehydration (e.g. vomiting) may increase the risk of toxicity. Consider interrupting treatment until symptoms cease.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for 3 months, the dose has been optimised, and with satisfactory investigation results for at least 4 weeks
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

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.**

Maintenance dose (following initial stabilisation):

Usual dose range**: 7.5 mg – 25 mg weekly**, adjusted according to response. Please note for rheumatology conditions a patient may be initiated on more than one DMARD. To reduce dosing errors ***only the 2.5 mg tablets should be prescribed***. The dose should be taken ***once weekly*** on the same day each week, and that day should be clearly communicated to the patient.
All patients should be prescribed folic acid at a dose of 5 mg at least once weekly, to be taken on a different day than their methotrexate dose. The specialist should include clear details of the folic acid regimen in their communication with the patient and primary care.

The initial maintenance dose must be prescribed by the initiating specialist.
Transfer of monitoring and prescribing to primary care is usually after 3 months. The duration of treatment will be determined by the specialist based on clinical response and tolerability.

Conditions requiring dose adjustment:

- Renal impairment: in patients with CrCl less than 60 mL/min the dose should be reduced by 50%. If CrCl is less than 30mL/min discontinuation may be indicated. See section 10.

6. Pharmaceutical aspects

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Route of administration:	Oral tablets, or subcutaneous injections
Formulation:	***Methotrexate tablets***

	Other strengths are available but, to reduce dosing errors, ***only the 2.5 mg tablets should be prescribed***. The dose should be taken ***once weekly*** on the same day each week, and that day should be clearly communicated to the patient. Methotrexate 2.5 mg tablets ***Methotrexate subcutaneous injection*** Solution for injection available in 2.5 mg increments ranging from 7.5 mg – 30 mg and varying with brand: • 50 mg/mL in pre-filled injector or syringe (Methofill®): 7.5 mg to 30 mg • 50 mg/mL in pre-filled pen (Metoject®): 7.5 mg to 30 mg • 25 mg/mL in pre-filled pen (Nordimet®): 7.5 mg to 25 mg • 25 mg/mL in pre-filled syringe (Zlatal®): 7.5 mg to 25 mg If subcutaneous methotrexate is prescribed, secondary care must specify the brand and the patient should be maintained on that brand due to device familiarity. Brand should be specified on clinical systems. See SPCs for full details of available products. Local, pre-existing arrangements for the supply of methotrexate injection and ancillary products, and for the disposal of cytotoxic waste, should be observed. When deciding which formulation to prescribe, the specialist should consider the patient's circumstances and overall polypharmacy burden, especially for patients with a high pill burden. See MHRA advice on preventing inadvertent daily dosing. 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.
Administration details:	Tablets should not be split or crushed for administration. Review formulation if patient is unable to swallow tablets. Carers should wear single-use gloves to handle methotrexate tablets. Anyone handling the tablets should wash their hands immediately afterwards. Pregnant people, including patients and carers, should avoid handling methotrexate. 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 taken as soon as remembered, within one or two days. Doses which are three or more days late should be skipped entirely. Take the next dose as scheduled, on the usual day. *A double dose should not be taken to make up for a missed dose.*
Other important information:	Methotrexate is taken *once weekly*, and there is a significant risk of toxicity if it is taken more frequently. Prescribers should follow the MHRA advice on preventing inadvertent daily dosing, including ensuring that the patient and/or carer understands the dosing schedule and is able to follow it. All patients should be prescribed folic acid at a dose of at least 5 mg once weekly, to be taken on a different day than their methotrexate dose. The specialist should include clear details of the folic acid regimen in their initial communication with primary care. In areas where methotrexate monitoring booklets are in use, the patient should receive a monitoring booklet from the specialist upon initiation of treatment. They should bring this 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 to any health professional involved in other aspects of their care e.g. pharmacists and dentists.

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

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 (see section 4). Additional interactions which become relevant at higher doses (e.g. those used in oncology) are not included.

- Co-administration of medicinal products which cause folate deficiency (e.g. **trimethoprim** and **co-trimoxazole**) can lead to increased methotrexate toxicity and is contraindicated (see section 4). Particular caution should therefore also be exercised in the presence of existing folic acid deficiency.
- **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.
- **Drugs with hepatotoxic, haematotoxic or nephrotoxic effects:** Increased frequency of monitoring may be recommended.
- **Live vaccines** (e.g. oral polio, oral typhoid, MMR, BCG, Zostavax®) are advised in line with the national schedule for all patients, unless the patient is taking a dose of methotrexate or other immunosuppressive drug that exceeds those specified in the Green Book. Doses below this level are not considered sufficiently immunosuppressive and these patients *can* receive live vaccines. Clinician discretion is advised. Please refer to the Green Book Chapter 6 for current advice.
- Avoid concomitant use of **cytotoxics, clozapine, and olanzapine:** increased risk of agranulocytosis.
- **Retinoids**: increased risk of hepatotoxicity, and may increase plasma levels of methotrexate.
- **Levetiracetam:** may increase plasma levels of methotrexate.
- **Nitrous oxide and pyrimethamine**: increased antifolate effect of methotrexate.
- **Lomitapide:** increased risk of hepatotoxicity.
- **Probenecid:** excretion of methotrexate reduced.
- **Phenytoin:** possible increased methotrexate toxicity, and decreased phenytoin effect.
- **NSAIDs**, **COX-2 inhibitors, aspirin:** may reduce excretion of methotrexate, increasing risk of toxicity. 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.
- **Antibiotics** may alter methotrexate levels. Methotrexate should be interrupted during periods of acute infection (see section 10).
- **Theophylline and other methylxanthines:** may reduce methotrexate efficacy. Methotrexate may reduce theophylline clearance.
- **Anticonvulsants:** may reduce methotrexate levels.
- **Colestyramine**: may increase elimination of methotrexate.
- **Alcohol:** consumption of alcohol increases the risk of hepatotoxicity. Patients should moderate their alcohol intake to no more than 14 units per week.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations:

- Height and weight
- Blood pressure
- Full blood count (FBC)
- Urea and electrolytes (U&Es) including creatinine and creatinine clearance (CrCl)
- LFTs
- Screening for HIV and hepatitis B and C
- Screening for lung disease, including interstitial lung disease and tuberculosis, should be undertaken at clinician discretion on a case by case basis
- Provide or request appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, shingles, influenza, COVID-19)
- Psoriasis patients: FIB-4 (in line with the Eastern Hepatology guideline for methotrexate)

Initial monitoring and at dose change:

- To be repeated every 2 weeks until the dose has been stable for 6 weeks, then monthly for 3 months. Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for 3 months, the dose has been optimised, and with satisfactory investigation results for at least 4 weeks.
- FBC
- U&Es, including creatinine and CrCl
- LFTs
- Rheumatology patients: CRP &/or ESR
- Psoriasis patients: FIB-4 (in line with the Eastern Hepatology guideline for methotrexate)

Following a dose change repeat every 2 weeks until the dose has been stable for 6 weeks, then revert to previous schedule.

More frequent monitoring is appropriate in patients at higher risk of toxicity.

At initiation of shared care, communication to primary care should include current and ongoing dose, any relevant test results, and date the next monitoring is required. The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment, and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually. When a patient is reviewed, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
• FBC • U&Es including creatinine and CrCl • LFTs • Rheumatology patients: CRP &/or ESR; specialist to confirm	At least every 12 weeks, and more frequently in patients at higher risk of toxicity, as advised by the specialist team. **The exact frequency of monitoring to be communicated by the specialist in all cases**.
• Patients aged 60-79 years old could be eligible for the shingles vaccine (herpes zoster). For patients on immunosuppressive therapy, a non-live vaccine may be indicated and specialist input may be required. Refer to Green Book Chapter 6 (Contraindications and special considerations) and Green Book Chapter 28a (Shingles) for further details. • **Annual** influenza (The Green Book, Chapter 19) vaccinations are recommended. • COVID-19 vaccination (The Green Book, Chapter 14a) is safe and recommended. • Repeat pneumococcal vaccine may be indicated. See Green Book Chapter 25 for advice.	• Shingles vaccination: one-off course of two doses. • Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list. • Other vaccinations as per national schedule.

(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care. Secondary care should inform primary care of actions taken.

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance

Result	Action for primary care
• Full blood count: • White blood cells less than $3.5x10^9$/L • Lymphocytes less than $0.5x10^9$/L • Neutrophils less than $1.6x10^9$/L • Platelets less than $140x10^9$/L • Eosinophilia greater than $0.5x10^9$/L	Withhold and discuss with specialist team.
Mean cell volume >105 fL	Consider interruption in treatment. Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal discuss with specialist team urgently.
Signs or symptoms of bone marrow suppression, e.g. unexplained bleeding or bruising with or without sore throat, purpura, mouth ulcers.	Check FBC immediately, withhold treatment while awaiting results, and discuss with the specialist team. See haematological monitoring above.
Infections: Infection requiring antibiotics	Temporarily withhold methotrexate until the patient has recovered. Consider additional investigations (e.g. FBC), if clinically appropriate.
Liver function tests: ALT or AST >100 units/L, or any sudden increases (e.g. double of baseline), OR Unexplained fall in serum albumin <30g/L Jaundice	Withhold and discuss with specialist team. Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication.
Psoriasis patients: FIB-4 (in line with the Eastern Hepatology guideline for methotrexate)	Discuss with specialist team
Renal function: Creatinine increase of greater than 30% from baseline in the last 12 months, or CrCl reduces to <60ml/min	Withhold and discuss with specialist team.
Gastrointestinal disorders: Nausea	Review for reversible causes and treat as appropriate. Enquire which day of the week the patient takes their methotrexate, and which day(s) they take folic acid and confirm against the patient's records. Discuss with specialist team if persistent or severe. Switch to subcutaneous therapy may be indicated, under specialist advice.

Diarrhoea, ulcerative stomatitis, haematemesis, black or bloody stools, or suspected pancreatitis	Withhold and discuss with specialist team.
Symptoms of interstitial lung disease e.g. persistent cough, dyspnoea, fever	If methotrexate-induced lung disease is suspected, discuss with specialist team urgently and withhold treatment. Treat with corticosteroids as directed by a specialist and do not restart methotrexate.
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, stop methotrexate immediately and prescribe folic acid 5 mg/day. Discuss with specialist team urgently. See section 12. • In pregnancies with paternal exposure, see section 12.

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Symptoms of chickenpox, or contact with a person with chickenpox or shingles.
- Persistent cough, shortness of breath, or any other problems with breathing.
- Sore throat, 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.
- Swelling of the hands, feet, or ankles
- Unexplained bleeding or bruising, black stools, or blood in the vomit or stools.
- Suspected or confirmed pregnancy.

The patient and/or carer should be advised:

- What shared care means for their treatment, what to expect, and their responsibilities under shared care.

- Methotrexate is taken ***once weekly***, and taking it more frequently can be dangerous. If a patient thinks they have taken too much methotrexate they should immediately seek advice from their prescriber, or NHS 111.
- For patients taking tablets, that they will only ever be prescribed methotrexate 2.5 mg tablets. ***Patients who receive 10 mg tablets should always question the discrepancy***.
- Which day or days they should take their folic acid, with emphasis that methotrexate and folic acid should not be taken on the same day.
- Moderate their alcohol intake to no more than 14 units per week while taking methotrexate. More information can be found at https://www.nhs.uk/live-well/alcohol-support/calculating-alcohol-units/. Taking alcohol and methotrexate together increases the risk of liver injury.
- Tell anyone who prescribes them a medicine that they are taking methotrexate. Always ask a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.
- Skin may be more sensitive to exposure to UV light while taking methotrexate. If this occurs 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 use effective contraception, and to take a pregnancy test if they think they could be pregnant. Patients should inform the specialist or GP immediately if they become pregnant. All patients, both men and women, should inform their specialist well in advance if they are planning a pregnancy so that changes can be made to their treatment regime.
- Not to drive or operate heavy machinery if methotrexate affects their ability to do so safely, e.g. due to fatigue or dizziness.
- That vaccination in line with current national advice (e.g. for COVID-19, influenza) is safe and recommended.
- For patients taking 20mg/week or more: to avoid contact with people with chicken pox or shingles and report any such contact urgently to their primary care prescriber. If the patient is exposed, contact the specialist for advice. 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

Patient information:
General information: https://www.nhs.uk/medicines/methotrexate/

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Methotrexate is contraindicated in pregnancy. It is cytotoxic, and is used for termination of pregnancy and to treat ectopic pregnancy. Pregnancy should be excluded prior to starting treatment.

The BNF and SPC states that patients of childbearing potential should use effective contraception during treatment and for at least 6 months afterwards. If a patient becomes pregnant within 6 months of treatment with methotrexate, folic acid 5 mg daily should be continued throughout the pregnancy. Those who wish to become pregnant should speak to their prescriber to discuss the possibility of switching to an alternative medicine.

The British Society of Rheumatology (BSR) guidance on pregnancy states that methotrexate can be stopped at least one month prior to conception, and this difference between the BNF, SPC and BSR guidance has been acknowledged. Therefore patients should be assessed on a case-by-case basis, and a shared decision should be made after the patient has been provided with all relevant information.

Information for healthcare professionals: https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-METHOTREXATE-IN-PREGNANCY/

Information for patients and carers: https://www.medicinesinpregnancy.org/Medicine--pregnancy/Methotrexate/

Breastfeeding:

The manufacturers contraindicate use of methotrexate while breastfeeding. The UK Drugs in Lactation Advisory Service recommends caution, and advises that breastfeeding should be avoided until at least 24 hours after a weekly dose not exceeding 25 mg. Infant blood counts should be monitored. Limited evidence indicates that small amounts are found in breast milk after weekly administration.

Information for healthcare professionals: https://www.sps.nhs.uk/medicines/methotrexate/

***Paternal exposure**:*

There are hypothetical risks of genetic abnormalities in sperm which could potentially affect offspring conceived during treatment. 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). Where a couple wishes to attempt conception and the male partner's condition is well-controlled with methotrexate, the UK Teratology Information Service recommends an assessment and discussion of the potential benefits and risks of continuing paternal treatment vs. discontinuation. This should be undertaken by the specialist, using a shared decision making approach. The risks to the fetus are theoretical rather than established. Paternal methotrexate use at the time of conception is not an indication for additional fetal 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.

Information for healthcare professionals:
https://www.medicinesinpregnancy.org/bumps/monographs/PATERNAL-USE-OF-METHOTREXATE/

***Fertility**:*
Methotrexate affects spermatogenesis and oogenesis and may decrease fertility. In humans, methotrexate has been reported to cause oligospermia, menstrual dysfunction and amenorrhoea. These effects appear to be reversible after discontinuation of therapy in most cases.

13. Specialist contact information

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Cambridge University Hospitals NHS Foundation Trust

CUH Dermatology Department:

Name	Role	Contact details
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Dr Shiu Kwan Chan	Consultant Dermatologist	01223 216501
Dr Niamh Flanagan	Consultant Dermatologist	01223 586678
Dr Julia Gass	Consultant Dermatologist	01223 216501
Dr Thomas Ha	Consultant Dermatologist	01223 216459
Dr Shaheen Haque	Consultant Dermatologist	01223 586678
Dr Andre Khoo	Consultant Dermatologist	01223 216501
Dr Paul Norris	Consultant Dermatologist	01223 216459
Dr Natasha Stembridge	Consultant Dermatologist	01223 216501
Dr Justyn Thomas	Consultant Dermatologist	01223 216459
Dr Pamela Todd	Consultant Dermatologist	01223 216459

Dr Vanessa Van de Velde	Consultant Dermatologist	01223 216459
Dr Marc Wallace	Consultant Dermatologist	01223 216459
Dermatology Specialist Nurses	Dermatology CNS team	Add-tr.dermnurses@nhs.net

CUH Rheumatology Department:

Decisions to alter or discontinue treatment are usually discussed via the Rheumatology Helpline on 01223 217398. The on-call rheumatology specialist registrar (SpR) may also be contacted via the Addenbrooke's Contact Centre.

Name	Role	Contact details
Dr Frances Hall	Consultant Rheumatologist	01223 349674
Dr Anoop Kuttikat	Consultant Rheumatologist	01223 349674
Dr Shipa	Consultant Rheumatologist	01223 349674
Dr Maliha Shaikh	Consultant Rheumatologist	01223 256883
Dr Mark Lillicrap	Consultant Rheumatologist	01223 256883
Dr Chris Chan	Consultant Rheumatologist	01223 216774
Prof Kenneth Poole	Consultant Rheumatologist	01223 216774
Dr Nicholas Shenker	Consultant Rheumatologist	01223 216774
Dr Gaffar Massawi	Consultant Rheumatologist	01223 349675
Dr Ei Ei Phyu Htut	Consultant Rheumatologist	01223 349675
Dr Qutab Shah	Locum Consultant Rheumatologist	01223 349675
Dr Andra Negoescu	Consultant Rheumatologist	01223 274561
Dr Anshuman Malaviya	Consultant Rheumatologist	01223 274561
Dr Carmel Stober	Consultant Rheumatologist	01223 274561
Dr Paivi Miettunen	Consultant Rheumatologist	01223 349674

CUH Paediatric Rheumatology Department

Name	Role	Contact details
Dr Kate Armon	Consultant Paediatric Rheumatologist	01223 348577
Dr Peter Bale	Consultant Paediatric Rheumatologist	01223 348577
Lennina Alban; Claire Ede	Nurse Specialist	01223 254988

CUH Lupus and Vasculitis Department

Name	Role	Contact details

Prof David Jayne	Consultant in nephrology & vasculitis	01223 217259
Dr Frances Hall	Consultant rheumatologist	01223 217316
Stella Burns	Specialist vasculitis sister	01223 586796
Jane Hollis	Lupus nurse specialist	01223 217050

CUH Ophthalmology department

Name	Role	Contact details
Dr Erika Damato	Consultant medical ophthalmologist	01223 217904
Mr Gerry Clare	Consultant ophthalmologist	01223 217904

CUH Gastroenterology Department

Inflammatory Bowel Disease Helpline 01223 257212 (voicemail)

Name	Role	Contact details
Dr Duncan Massey	Consultant Gastroenterologist	01223 254650
Dr Miles Parkes	Consultant Gastroenterologist	01223 348265
Dr Jeremy Woodward	Consultant Gastroenterologist	01223 596231
Dr Stephen Middleton	Consultant Gastroenterologist	01223 256582
Dr Timothy Raine	Consultant Gastroenterologist	01223 216226
Dr Ewen Cameron	Consultant Gastroenterologist	01223 348718
Dr Gareth Corbett	Consultant Gastroenterologist	01223 348718
Dr Ines Modolell	Consultant Gastroenterologist	01223 348718
Dr James Lee	Consultant Gastroenterologist	01223 216226
Dr Lisa Sharkey	Consultant Gastroenterologist	01223 254650
Dr Massi Di Pietro	Consultant Gastroenterologist	01223 256582
Dr Nicholas Carroll	Consultant Gastroenterologist	01223 216226
Dr Nicole Kaneider-Kaser	Consultant Gastroenterologist	01223 256582
Dr Sibu Varghese	Consultant Gastroenterologist	01223 216226
Dr Juan De La Revilla Nero	Consultant Gastroenterologist	01223 216226
Dr Jo Rimmer	Consultant Gastroenterologist	01223 348718
Dr Edel McDermott	Consultant Gastroenterologist	01223 348265
Professor Rebecca Fitzgerald	Consultant Gastroenterologist	01223 256582
Prof Arthur Kaser	Consultant Gastroenterologist	01223 768308
Sr Allison Nightingale	Inflammatory Bowel Disease Nurse Specialist	01223 217990 **(for GPs to contact for advice)**

Royal Papworth Hospital NHS Foundation Trust
Medicines Information department telephone: 01480 364179

RPH Respiratory Medicine Department

Name	Role	Contact details
Dr Muhunthan Thillai	Consultant Respiratory Physician and Clinical Lead for Methotrexate Shared Care	01223 639524
Dr Christine Fiddler	Consultant Respiratory Physician	01223 638423
Dr Helen Parfrey	Consultant Respiratory Physician	01223 639517
Dr Nicola Simler	Consultant Respiratory Physician	01223 639522
Emma Harris Katie Harding	Specialist Nurses (**Usual first point of contact for GP queries)**	01223 638017 or 01223 638000 and ask for pager 109
Duncan Grady	Thoracic Directorate Pharmacist	01223 638179 or 01223 638000 and ask for pager 845
Pharmacy Department	Non-Urgent Medicines Information for Clinicians engaging in Methotrexate Shared Care	01223 638179
Medicines Helpline	Non-urgent Medicines Information for Patients receiving methotrexate via a shared care agreement	01223 638777

North West Anglia NHS Foundation Trust

NWAFT Rheumatology Department

Name	Role	Contact details
Dr Wiranthi Gunasekera	Consultant Rheumatologist	01733 676762
Dr Poonam Sharma	Consultant Rheumatologist	01480 416744
Dr Sandeep Dahiya	Consultant Rheumatologist	01733 676764
Dr John Pradeep	Consultant Rheumatologist	01480 442824
Dr Maeve Fifield	Consultant Rheumatologist	01733 676762
Rheumatology advice line		01733 676766

NWAFT Neurology Department

Name	Role	Contact details
Dr Dirk Baumer	Consultant Neurologist	01733 673549
Dr Sybil Stacpoole	Consultant Neurologist	01733 673549
Dr Tom Stoker	Consultant Neurologist	01733 673549

Dr John Thorpe	Consultant Neurologist	01733 673549
Dr Tejal Mitchell	Consultant Neurologist	01733 673549
Dr Tracey Graves	Consultant Neurologist	01480 847533

NWAFT Gastroenterology Department

Name	Role	Contact details
Dr Irfan Amin	Consultant Gastroenterologist	01733 677525
Dr Tapas Kumar Das	Consultant Gastroenterologist	01733 677526
Dr Anita Gibbons	Consultant Gastroenterologist	01480 442853
Dr Mohamed Habieb	Consultant Gastroenterologist	01480 416416
Dr Rizwan Kassam	Consultant Gastroenterologist	01480 418742
Dr Mary Ninkovic	Consultant Gastroenterologist	01733 677527
Dr Philip Roberts	Consultant Gastroenterologist	01480 442852
Dr Syed Shaukat	Consultant Gastroenterologist	01480 442854

NWAFT Dermatology Department

Name	Role	Contact details
Nicki Errington Rachel Casbon	Dermatology Nurses	01733 673581 nwangliaft.dermnurses@nhs.net
Dr Onoshoke Abiola Dr Ayesha Khokhar Dr Richard Mallett Dr Kerry Shalders Dr Vanessa Smith Dr Mahmood Tabra Dr Cedric Banfield	Consultant Dermatologists	01733 673586 nwangliaft.dermatologysecretaries@nhs.net

14. Additional information

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It is anticipated that each area will continue to adhere to pre-existing local arrangements for the supply of methotrexate injection and ancillary products, and for the disposal of cytotoxic waste.

In Cambridgeshire and Peterborough, this service is provided by the District Councils and Peterborough City Council. For information on participating pharmacies, please use the links below:

- Cambridge: Domestic clinical and hygiene waste - Cambridge City Council
- East Cambridgeshire: Clinical collections | East Cambridgeshire District Council
- Fenland: Clinical Waste - Fenland District Council
- Huntingdonshire: Clinical Waste - Huntingdonshire.gov.uk
- South Cambridgeshire: Clinical waste - South Cambs District Council
- Peterborough: Medical and hygiene waste | Peterborough City Council

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

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- eBNF. Methotrexate. Accessed via https://bnf.nice.org.uk/drug/methotrexate.html on 13/08/2021.
- Methotrexate 2.5 mg tablets (Maxtrex®). Date of revision of the text 12/2020. Accessed via https://www.medicines.org.uk/emc/product/1376/ on 13/08/21.
- Methotrexate 10 mg solution for injection in pre-filled injector (Methofill®). Date of revision of the text 01/03/21. Accessed via https://www.medicines.org.uk/emc/product/9057/smpc on 13/08/21.
- Methotrexate 10 mg solution for injection in pre-filled pen (Metoject®). Date of revision of the text 07/2020. Accessed via https://www.medicines.org.uk/emc/product/11351/ on 13/08/21.
- Methotrexate 10 mg solution for injection in pre-filled pen (Nordimet®). Date of revision of the text Dec 2020. Accessed via https://www.medicines.org.uk/emc/product/7721/ on 13/08/21.
- Methotrexate 10 mg solution for injection in pre-filled pen (Zlatal®). Date of revision of the text 25/09/2020. Accessed via https://www.medicines.org.uk/emc/product/7270/ on 13/08/21.
- Methotrexate 2 mg/mL oral solution (Jylamvo®). Date of r/evision of the text 01/01/2021. Accessed via https://www.medicines.org.uk/emc/product/8599/ on 13/08/21.
- British Society of Rheumatology and British Health Professionals in Rheumatology. 2017. Guidelines for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Accessed via https://academic.oup.com/rheumatology/article/56/6/865/3053478.
- British Society of Dermatologists' guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. Accessed via https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.14816.
- British Society of Rheumatology and British Health Professionals in Rheumatology. 2016. Guideline on prescribing drugs in pregnancy and breastfeeding – Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Accessed via https://academic.oup.com/rheumatology/article/55/9/1693/1744535.

MHRA 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. September 2020. Accessed via 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.

16. Other relevant national guidance

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- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

If there are any concerns in relation to the patient or their condition changes, primary care prescribers should contact the relevant initiating specialist using the **Specialist contact information** detailed above.

Specialist teams should contact primary care prescribers via the usual communication routes agreed locally.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]*shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

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

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

If you would like to refuse, please respond to this request for shared care, in writing, within 14 days of the request being made where possible.