

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

METHOTREXATE for patients 16+ years
(Oral/subcutaneous preparations for Chesterfield Royal Hospital & oral only preparations for University Hospitals of Derby and Burton)

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring
- When transfer agreed the patient will be given a supply of methotrexate sufficient for at least 4 weeks maintenance therapy.

2. AREAS OF RESPONSIBILITY

[Methotrexate once-weekly for autoimmune diseases: new measures to reduce risk of fatal overdose due to inadvertent daily instead of weekly dosing \(MHRA Sept 2020\)](#)

Advice for prescribers:

- before prescribing methotrexate, make sure that the patient is able to understand and comply with once-weekly dosing
- consider the patient's overall polypharmacy burden when deciding which formulation prescribe, especially for a patient with a high pill burden
- decide with the patient which day of the week they will take their methotrexate and note this day down in full on the prescription
- inform the patient and their caregivers of the potentially fatal risk of accidental overdose if methotrexate is taken more frequently than once a week; specifically, that it should not be taken daily
- advise patients of the need to promptly seek medical advice if they think they have taken too much

GP responsibilities	Consultant responsibilities
<p>a) If NOT participating in shared care reply to the request from the consultant/specialist as soon as practicable (see appendix 1)</p> <p>b) Ensure compatibility with other concomitant medication</p> <p>c) Prescribe the dose and formulation recommended. (Reminder – prescribe SC injection by brand), specifying date of taking methotrexate on the prescription</p> <p>d) Supplies for parenteral methotrexate prescriptions are usually issued via homecare service (e.g. healthnet). In situations where a GP issues a FP10, they are reminded that ancillary equipment will need to be supplied. (See section x)</p> <p>e) Continue to prescribe folic acid 5mg at least once weekly, avoiding the day of methotrexate, as recommended by the specialist</p> <p>f) Perform monitoring tests as specified in section vii.</p> <p>g) Adjust the dose as advised by the specialist.</p> <p>h) Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arises.</p> <p>i) Update the patient's methotrexate booklet</p> <p>j) Always prescribe oral methotrexate using multiples of the 2.5mg strength tablet, AVOID USING THE 10mg STRENGTH.</p> <p>k) Ensure the patient is offered an annual flu vaccination and a one off pneumococcal vaccination. Live vaccinations can be used with caution in patients taking methotrexate up to a</p>	<p>a) Discuss the possible benefits and side effects of treatment with the patient.</p> <p>b) Perform baseline tests (as recommended in section vii)</p> <p>c) Provide results of baseline tests</p> <p>d) Prescribe methotrexate for the first three months or until medication monitoring is stable.</p> <p>e) Initiate folic acid 5mg at least once weekly, avoiding the day the methotrexate.</p> <p>f) To contact patient's GP to request prescribing under shared care and send a link to or copy of the shared care protocol.</p> <p>g) Recommend dose of the drug and frequency of monitoring.</p> <p>h) Annually review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist.</p> <p>i) Ensure that clear backup arrangements exist for GPs to obtain advice and support.</p> <p>j) Provide the patient with the NPSA hand held methotrexate booklet</p> <p>k) Report any adverse effects to the MHRA yellow card scheme and GP</p> <p>l) Advise on the suitability for herpes zoster vaccination in accordance with national screening programme</p> <p>m) For parenteral methotrexate (CRHFT only): Notify the GP of arrangements for supply via "home care" and waste collection. Ensure the patient is trained for the device and brand recommended.</p> <p>n) Communicate any dose increase to the GP and transfer monitoring to GP when the patient's condition is stable or predictable following 6 weeks period of titration.</p> <p>o) Advise and respond to GP queries on live vaccination.</p>

<p>dose of 25mg, if not on any other immunosuppressant – See section vi</p> <p>i) Report any adverse effects to the referring specialist and the MHRA yellow card scheme</p>	
Patient responsibilities	
<ul style="list-style-type: none"> • Report to the specialist or GP if there is not a clear understanding of the treatment and share any concerns in relation to treatment. • Inform specialist or GP of any other medication being taken including over-the-counter products. • Report any adverse effects or warning symptoms to the specialist or GP whilst taking the drug for example sore throat, bruising, mouth ulcers, breathlessness, dry persistent cough, vomiting and diarrhoea. • Carry and present their methotrexate booklet/ patient card to their GP and community pharmacy at each prescribing and dispensing activity • For parenteral methotrexate contacting either GP or homecare company for ancillaries/ administrative issues. 	

3. COMMUNICATION AND SUPPORT

<p>i. Hospital contacts:</p> <p>Chesterfield Royal Hospital NHS Foundation Trust Contact the referring consultant/nurse via switchboard: 01246 277271 Nurse advice line: 01246 513097 Available Monday-Thursday 9am-4:30pm, Friday 9am- 12:30pm IBD advice line 01246 512884 (answerphone) and GP mobile contact 07717700489</p> <p>University Hospitals of Derby and Burton NHS Foundation Trust</p> <p>Derby Hospitals Rheumatology - Rheumatology helpline: 01332 787710 Gastroenterology - IBD helpline: 01332 785504 Consultant/specialist nurse via switchboard: 01332 340131 Dermatology - Consultant/specialist nurse via switchboard: 01332 265500 Respiratory - Consultant via switchboard: 01332 340131 Neurology - Consultant via switchboard: 01332 340131/Neurology secretaries 01332 786478/783548 dhft.neurologysecretaries@nhs.net</p> <p>Burton Hospitals 01283 511511 / 566333</p> <p>Rheumatology Dr R Laximinarayan ext. 3167 Dr S Das ext. 3211 Dr D Ray ext. 3247 Clinical Rheumatology Nurse Specialist ext. 4112 Bleep 274 available during office hours.</p> <p>Dermatology Dr Beswick and Dr Cartwright secretary ext. 4061 Dr Elston and Dr Tudor secretary 5202</p> <p>Gastroenterology Dr Palejwala secretary ext. 4221 Dr Watmough secretary ext. 4008 IBD Nurse Specialist ext. 5854</p>	<p>ii. Out of hours contacts and procedures:</p> <p>Chesterfield Contact the CRH on-call Medic for the relevant speciality via switchboard: 01246 277271</p> <p>Derby Pharmacy, DTHFT, ask for on-call pharmacist via switchboard: 01332 340131 Messages can be left on the Derby Rheumatology nurse advice line: 01332 787710 The aim is to address these next working day</p> <p>Burton 01283 511511 / 566333 ask for on-call pharmacist via switchboard</p> <p>Burton Rheumatology Messages can be left on the nurse advice line out of hours. 01283 511511 ext. 4112.</p> <p>If the advice line is not staffed, messages may be left 24 hours a day. The team aim to respond at latest within two working days. The specialist nurses may also be bleeped via switchboard for urgent enquiries.</p>
<p>iii. Specialist support/resources available to GP including patient information:</p> <p><u>Rheumatology</u> British Society of Rheumatology Specialist website: http://www.rheumatology.org.uk/resources/guidelines/default.aspx Versus Arthritis Patient Information https://www.versusarthritis.org/media/1354/methotrexate-information-booklet.pdf</p> <p>Patient information leaflet:- http://www.medicines.org.uk/emc/medicine/15727</p> <p>Improving Compliance with oral methotrexate guidance http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800</p> <p><u>Renal</u> Kidney Transplant Guideline, Transplant Unit, Nottingham University Hospital Vasculitis and Immunosuppressive Protocol, Renal Unit, UHDB</p>	

4. CLINICAL INFORMATION

<p>i. Prescribed indications</p>	<p>Licensed oral Rheumatoid arthritis (RA) Psoriasis Parenteral (in addition to above) Crohn's disease</p>	<p>Unlicensed Psoriatic arthritis Crohn's disease (oral) Connective Tissue Disease (SLE, myositis, & vasculitis) Felty's syndrome Asthma Sarcoidosis</p>
<p>ii. Therapeutic summary</p>	<p>It is speculated that methotrexate produces its effects via anti-folate activity immunosuppressive and other anti-inflammatory actions.</p>	
<p>iii. Dose & Route of administration</p>	<p>ALWAYS PRESCRIBE ORAL DOSE USING 2.5mg TABLETS</p> <p>Orally or subcutaneously (CRH hospital only- parenteral routes may be used where the patient fails to respond to or is intolerant of oral administration)</p> <p>Licensed indications Rheumatoid arthritis - 7.5mg – 25mg orally or subcutaneous injection ONCE WEEKLY</p> <p>Severe psoriasis unresponsive to conventional therapy. Initially 2.5mg-10mg once weekly. Then increased in steps of 2.5mg-5mg, adjusted according to response, dose to be adjusted at intervals of at least one week; usual dose 7.5-15mg once weekly. Maximum 30mg per week</p> <p>Unlicensed indications Crohn's Disease - maintenance of remission of severe Crohn's disease 10 – 25mg orally ONCE WEEKLY</p> <p>Psoriatic arthritis 7.5mg – 25mg orally or subcutaneous injection ONCE WEEKLY</p> <p><u>For other indication see BNF or as per specialist advice</u></p> <p>Doses outside the recommended range may be considered with prior agreement with the specialist team and GP involved.</p> <p>Lower doses should be considered for frail elderly and patients with renal impairment.</p> <p>Folic Acid 5mg at least once weekly should be prescribed whilst patient remains on Methotrexate.</p>	
<p>iv. Duration of treatment</p>	<p>Indefinite but may be withdrawn after a prolonged period of disease remission in selected cases.</p> <p>Surgery DMARD therapy should not routinely be stopped in the perioperative period, although individualised decisions should be made for high-risk procedures (BSR) on the advice of a consultant.</p>	
<p>v. Adverse effects See BNF/SPC for full list</p>	<p>The most common adverse reactions include: Leucopaenia, Increased risk of infection (especially in respiratory, urinary tract and shingles/ chickenpox- Temporarily withhold / advise stopping if patient is systemically unwell with significant infection requiring anti-microbial treatment) Headache, dizziness, fatigue Ulcerative stomatitis, anorexia, nausea, vomiting, diarrhoea, abdominal discomfort Skin reactions, alopecia</p> <p>Other adverse effects include: Mouth ulcers (these are usually responsive to a temporary cessation of the drug and re-introduction at a lower dose) Vasculitis Eye irritation Loss of libido/impotence Thrombocytopenia (withdraw methotrexate and inform specialist team/haematologist) Pulmonary Symptoms (seek medical attention if dyspnoea, cough or fever develops- discontinue if pneumonitis suspected) In general, the incidence and severity of side effects are considered to be dose-related.</p> <p>Alcohol should be kept to a minimum as the risk of liver damage from alcohol is increased in patients taking Methotrexate.</p>	
<p>vi. Immunisation</p>	<ul style="list-style-type: none"> • Live vaccinations- Individuals who are on or have recently received high doses of certain immunosuppressive or biological therapies should not be given live 	

	<p>vaccines because of the risk of severe or fatal infections. In patients receiving methotrexate exposed to chickenpox or shingles, passive immunisation should be carried out using VZIG</p> <p>JCVI Green book recommends that low dose corticosteroid (prednisolone <20mg daily) and oral DMARD therapy at standard doses (methotrexate <25mg per week in adults) are not considered sufficiently immunosuppressive and these patients can receive live vaccines, although clinician discretion is advised.</p> <ul style="list-style-type: none"> • Annual flu vaccination is recommended. • One-off Pneumococcal vaccination recommended unless <u>severely</u> immunocompromised where a different schedule is needed. See JCVI for more information.
<p>vii. Monitoring Requirements</p>	<p><u>Before commencing immunosuppressant therapy</u></p> <ul style="list-style-type: none"> • Record patient's blood pressure, weight and height if clinically indicated. • Screening for lung disease should be undertaken at clinician discretion on a case-by-case basis. The extent of screening should be influenced more by a patient's clinical features and risk factors for lung disease (e.g. underlying autoimmune disease or smoking history) rather than subsequent immunomodulating choice. Pre-existing lung disease should not be considered an absolute contraindication to any immunomodulating medication. • Consultant to consider ECG where appropriate <i>especially when commencing medications associated with hypertension</i> • Screen for viral hepatitis B&C and HIV in all patients • Investigate patient medical history including co-morbidities and previous immunomodulating medication use. <hr/> <p>Consultant/specialist monitoring schedule Baseline followed by 2 weekly monitoring until on a stable dose for at least 6 weeks</p> <ul style="list-style-type: none"> • FBC • ALT and/or AST and albumin • U&E including creatinine/ eGFR • Serum Pro Collagen III measured only in Psoriasis (<i>not Psoriatic arthritis</i>) <p>Annually review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist.</p> <p>GP responsibility monitoring schedule In patients following the 6 weeks of dose stability conduct monthly monitoring for three months followed by three monthly monitoring thereafter of:</p> <ul style="list-style-type: none"> • FBC • ALT and/or AST and albumin • U&E including creatinine/eGFR <p>For rheumatic patients CRP/ESR may be done every 3 months (this is not done for dermatology patients). These tests are part of the assessment of the underlying rheumatic disease rather than a requirement for monitoring of immunomodulating therapy. The monitoring CRP/ESR may be coordinated between secondary and primary care on an individual basis.</p> <p>Leflunomide in combination with MTX requires extended monthly monitoring for at least 12 months. Patients who have been stable for 12 months can be considered for reduced frequency of monitoring on an individual patient basis.</p> <p><u>Dosage increase</u> For dose increase, monitor fortnightly until stable for 6 weeks. Dose and monitoring to be agreed with consultant.</p> <ul style="list-style-type: none"> • FBC • ALT and/or and albumin • U&E including Creatinine/eGFR <p>Monitoring to then revert to previous schedule.</p> <p>When restarting treatment after an abnormality has been detected repeat bloods in 2 weeks and then monthly for 3 months. Following this resume monitoring frequency to what it was prior to the abnormality.</p> <p>Actions to be taken</p> <ol style="list-style-type: none"> 1. Immunosuppressants prescribed to prevent transplant rejection should not be

stopped without discussion with a member of the specialist team.

- In addition to responding to absolute values in laboratory tests, it is also relevant to **observe trends in results** (e.g gradual decreases in white blood cells (WBC) or albumin, or increasing liver enzymes)
- Parameters below are to be used as a guide for clinicians rather than absolute values, where monitoring should be based on individualised basis. It is important to consider alternative explanations other than the immunomodulation agents, especially in patients who have been stable for prolonged periods

NB – a rapidly increasing or decreasing trend in any value should prompt caution irrespective of actual value.

WBC <3.5 x10 ⁹ /l	Contact Specialist urgently and consider interruption
Neutrophils <1.6 x 10 ⁹ /l	Contact Specialist urgently and consider interruption
Platelets <140 x 10 ⁹ /l	Contact Specialist urgently and consider interruption
ALT and/or AST >100 U/l	Contact Specialist urgently and consider interruption
Unexplained fall in albumin (<30g/l)	Contact Specialist urgently and consider interruption
Mean cell volume >105 f/l	Withhold and check serum B12, folate & TFT and discuss with specialist team.
Creatinine increase >30% over 12 months and/or eGFR <60ml/min	Contact Specialist urgently and consider interruption

Drug specific: Methotrexate

Rash or oral ulceration, nausea & vomiting, diarrhoea	Contact Specialist urgently and consider interruption
New or increasing dyspnoea or dry cough	Contact Specialist urgently and consider interruption
Breathlessness	Contact Specialist urgently and consider interruption <i>and Consider emergency care if necessary</i>
Severe sore throat, abnormal bruising	Immediate /urgent FBC & withhold until the result of FBC is available.
CRP/ESR	Measured to allow disease activity evaluation

Note: specific monitoring of eosinophil counts has been removed, as historically eosinophilia was an important marker for identifying toxicity from only gold therapy. This has been agreed with local specialists.

viii. Clinically relevant drug interactions

For a full list of interactions please refer to the BNF

- Analgesics- aspirin & NSAIDS e.g. diclofenac, ibuprofen, naproxen
- Antibacterials- e.g. ciprofloxacin, doxycycline, penicillins, **trimethoprim, co-trimoxazole**
- Antiepileptics – e.g. phenytoin
- Antipsychotics- e.g. clozapine
- Cardiac glycosides e.g. digoxin
- Theophylline
- PPI's – There appears to be limited evidence involving the doses of methotrexate used for inflammatory diseases. Local consultants advise that there are no concerns for this interaction at methotrexate doses used in this guideline.
- Co-prescription of drugs with potential hepatotoxic and nephrotoxic effects is not recommended.

ix. Contraindications and cautions

- Contraindications**
- Pregnancy: Women of childbearing age and men should not plan to conceive whilst on methotrexate. Following administration to a man or woman conception should be avoided by using an effective contraceptive method for at least 6 months (SPC) In case of accidental pregnancy stop methotrexate and discuss with the specialist team.
 - Women receiving Methotrexate should not breastfeed as the drug may be excreted in the breast milk.
 - Suspected serious infection (requiring IV antibiotics or hospitalisation) treatment should be discontinued.
 - Bone marrow failure indicated by cytopenia, anaemia; Significant leuopenia or thrombocytopenia
 - Severe renal or hepatic impairment (SPC)
 - Active infectious disease/ Severe acute or chronic infections and immunodeficiency

	<p>syndrome (SPC)</p> <ul style="list-style-type: none"> • Untreated folate deficiency <p>Cautions</p> <ul style="list-style-type: none"> • Patients with clinically significant renal impairment from any cause • Localised or systemic infection including hepatitis B or C and a history of TB. • Appropriate to continue with therapy in patients with minor infections (EG. Uncomplicated urinary tract infections treated with a short course of antibiotics) seek advice from specialist • Unexplained anaemia and/or cytopenia associated with marrow failure. • Patients with deranged liver biochemistry or synthetic function • Patients with Chronic Kidney disease • Any patient suspected of alcohol abuse is usually unsuitable for Methotrexate therapy. Patients should be advised to stay well within national limits. Patients with psoriasis should be strongly advised to stay within 4-6 units /week. Excessive alcohol consumption should be discussed with the specialist team.
x. Supply of ancillary equipment	CRH- For patients receiving parenteral methotrexate therapy supplies of the drug, waste management products and collection of cytotoxic waste can be arranged through a home care provider.
xi. Supply, storage and reconstitution instructions	Injections can be stored at room temperature
Prepared by	The Shared Care Guidelines Group, Derby Hospitals Martin Shepherd, Head of Medicines Management, Chesterfield Royal Hospital Derbyshire Medicines Management Clinical Effectiveness Team
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This does not replace the SPC, which should be read in conjunction with it
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References

1. EMC Summary of Product Characteristics for Methotrexate accessed online 08/03/2017, 2/7/2019
2. British National Formulary accessed online 2/7/2019
3. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, The British Society for Rheumatology, February 2017
4. The Green book, Immunisation against infection disease, September 2014, accessed online 08/03/2017, 2/7/2019

Sample Transfer Letter

Hospital No: «HOSPITAL_NUMBER»

NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL

«GP_TITLE» «GP_INITIALS» «GP_SURNAME»

«GP_ADDRESS_1»

«GP_ADDRESS_2»

«GP_ADDRESS_3»

«GP_ADDRESS_4»

«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»

«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»

«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on *{Insert date}* with a diagnosis of *{Insert diagnosis}*. I have initiated the following medication *{Insert drug name}* and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date <i>{Insert medicine name}</i> started	Date for GP to start prescribing <i>{Insert medicine name}</i> from
The baseline test results are (if applicable): See overleaf for initiation criteria.		

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted the need for monitoring, how monitoring will be arranged, and the roles of the consultant / nurse specialist, GP and the patient in shared care. I confirm the patient has understood and is satisfied with this shared care arrangement at this time.

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care)

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

Yours sincerely

{GP name}

{Surgery}

Please send a copy of this response to:

1. The specialist/consultant requesting shared care
2. **AN ANONYMISED COPY OF THIS FORM ONLY** to the Medicines Management and Clinical Policies and Decisions Team , 1st Floor East Point, Cardinal Square, 10 Nottingham Road, Derby, DE1 3QT or E-MAIL: ddccg.medicinesmanagement@nhs.net

(Sending a copy of this form to the Medicines Management and Clinical Policies and Decisions Team will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG prescribing group of the reasons shared care is not being undertaken allowing for changes to be made in future updates to improve patient care).