NHS West Essex Clinical Commissioning Group

The Princess Alexandra Hospital NHS NHS Trust

Shared Care Agreement

Methotrexate

Oral and Subcutaneous

For the use in gastroenterology, dermatology and rheumatology

Principles of Shared Care

- Shared care is the mechanism of sharing patient care between primary and secondary care providers and assumes good communication between the patient, GP and hospital consultant and pharmacists.
- The aim of these shared care guidelines is to provide sufficient information to the GP to be confident to take on the clinical and legal responsibility for prescribing the drug treatment.
- The shared care guidelines will clearly outline the responsibilities of the GP, hospital consultant/specialist and the patient.
- The intention to share care with the GP should be explained to the patient / carer by the specialist initiating treatment and an outline of responsibilities provided.
- The doctor who prescribed the medication legally assumes clinical responsibility for the drug and the consequences of its use.
- It would not be expected that a GP would decline to share prescribing on the basis of cost.
- The patient's best interest and the safe management of their treatment are paramount.
- These guidelines are for patients over 18 years of age
- 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
- Safe prescribing must be accompanied by effective monitoring

Shared Care Responsibilities

Consultant

- Undertake the necessary testing to confirm a diagnosis for which methotrexate treatment is recommended.
- Ensure the patient's concurrent drug therapy is stabilised and there are no contra-indications to treatment with methotrexate.
- Perform pre-treatment screening (see monitoring section) and provide results to GP
- Ensure the patient is aware of risks and benefits of medication and has read the appropriate information leaflet
- Ensure the patient understands the shared care agreement and has signed the Patient Agreement Letter (see page 9-10)
- Ensure patient understands that dosing is **ONCE WEEKLY** and which warning symptoms to report
- Administration of test dose where appropriate, initiation of treatment and prescribe until the GP takes on the prescribing.
- Send a letter to the GP requesting shared care for this patient.
- Initiate treatment and prescribe until the patient has been on a stable dose for minimum of SIX weeks
- Always prescribe oral methotrexate using multiples of the 2.5mg strength tablet, DO NOT use 10mg strength tablet.
- Initiate folic acid tablets and advise on anti-emetics as appropriate (see support medicines section)
- Where subcutaneous methotrexate is used ensure that the patient is trained and able to administer their injections or alternative appropriate arrangements for administration are in place.
- To provide the patient with a monitoring and dosage record booklet and ensure the patient knows when and where to attend for monitoring. Encourage the patient to take responsibility for ensuring that the results of tests are entered in the monitoring booklet.
- To provide the patient's GP with a full summary letter indicating dose and frequency before implementation of shared care, including results of baseline tests.
- To detail in the patient's methotrexate booklet that they are now under shared care.

- Review the patient in outpatients as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the specialist.
- Inform the GP by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Evaluate any reported adverse effects by GP or patient
- To report any adverse events to the CHM and GP (see link)
- https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
- Inform GP of patients who do not attend clinic appointments
- Ensure clear arrangements for back-up, advice and support is available at all times

General Practitioner

- To monitor overall health and well-being of the patient
- Consider request to prescribe under shared care arrangements and reply only if you do not agree to share care, in a timely manner within 14 days as outlined on page 8 with clinical reasons and return to Consultant and Pharmacy department.
- To prescribe methotrexate at the recommended dose and formulation.
- Adjust the dose as advised by the specialist.
- Always prescribe oral methotrexate using multiples of the 2.5mg strength tablet, DO NOT use 10mg strength tablet.
- Prescribe folic acid tablets and anti-emetics as appropriate (see support medicines section)
- Ensure patient understands that dosing is **ONCE WEEKLY** and which warning symptoms to report.
- To report any adverse events to the specialist team and the CHM and stop treatment on their advice or immediately if an urgent needs arises.
- Arrange on-going monitoring at the recommended frequencies (see monitoring section) and ensure that test results are recorded in the monitoring booklet.
- Ensure compatibility with other concomitant medication.
- To report any worsening of control of the condition to the consultant or specialist nurse
- Ensure the patient is offered an annual flu vaccination and one off pneumococcal vaccination
- Whenever DMARD prescribing is undertaken by someone not in the GP practice, it is expected that the DMARD will be added to the patients repeat screen as zero dispensed to ensure all prescribers are aware when issuing other prescriptions.

Patient

- Report to specialist or GP if there is not a clear understanding of their treatment and discuss any concerns in relation to treatment
- Report any adverse effects to the Specialist whilst taking Methotrexate, especially unexplained bruising/bleeding, mouth ulcers, sore throat or cough which should be reported immediately.
- Report any changes in disease symptoms to Specialist whilst taking Methotrexate.
- Inform GP or specialist of any other medicines being taken including over-the-counter products.
- Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy
- Try to avoid contact with chickenpox or shingles if no definite history of chickenpox and report any such contact urgently to their GP and/or specialist
- Carry and present their methotrexate booklet to their GP, Consultant and community pharmacy at each prescribing and dispensing activity
- Attend for regular reviews and blood monitoring tests

Monitoring Standards for Methotrexate based on BSR BHPR Standards 2017

The following standards have been agreed for the monitoring of methotrexate in all patients at Princess Alexandra Hospital NHS Trust.

Pre-treatment by Specialist	Height, weight, blood pressure, FBC, U&Es, LFTs, calculated GFR and albumin chest X-ray (may not be necessary in some dermatology patients) (Dermatology: P III N P assay)	
Initial monitoring by Specialist	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Every 2 weeks until on stable dose for 6 weeks.
Ongoing monitoring by GP	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Then once on stable dose monitor monthly for 3 months.
	FBC Creatinine / calculated GFR ALT +/- AST Albumin	At least every 12 weeks. Dermatology patients – PIIINP assay every 3 months
Dose increase	FBC Creatinine / calculated GFR ALT +/- AST Albumin	Every 2 weeks until on stable dose for 6 weeks, then revert to previous schedule
Specialist and GP at every visit	Rash/Oral ulceration	Patient should be asked about these symptoms at each visit.

Action and Advice

If a GP has taken blood tests for the general medical management of a patient and blood test results fall into the categories below or the patient reports one of the adverse events below, these are recommendations for considering the withdrawal of Methotrexate therapy:

Blood Test Results	
WBC < 3.5 x 10^9/l	Withhold until discussed with specialist team
Neutrophils < 2.0 x 10^9/l	Withhold until discussed with specialist team
Platelets < 150 x 10^9/l	Withhold until discussed with specialist team
> 2-fold rise in AST, ALT (from upper limit of reference range)	Withhold until discussed with specialist team
MCV > 105fl	Check B12, serum folate and TSH. Treat any underlying abnormality. If results normal, discuss with specialist team
Unexplained reduction in albumin <30 g/l	Discuss with specialist team
Creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min	Withhold until discussed with specialist team
Elevation of Type 3procollagen above normal range (1.7 -4.2ug/l) in three samples over a 12 month period, or above 8.0ug/l in two consecutive samples	Discuss with specialist dermatology team
Symptoms	
Unexplained acute widespread rash	Withhold and seek urgent specialist (preferably dermatological) advice.
Abnormal bruising, cough or sever sore throat	Withhold until FBC results available & discuss with specialist team
Oral ulceration	Withhold discuss with specialist team
Nausea/dizziness/headache	If possible continue, may have to reduce dose or stop if symptoms are severe. Discuss with specialist team, if necessary.

- Consider NICE recommendations regarding screening for hepatitis B and C in patients at increased risk of infection

Availability of Consultant and senior hospital staff

PAH switchboard: 01279 444455

Rheumatology

Consultant via switchboard:		Ext 7420 / 7434
Reena Robin	Rheumatology Clinical Nurse Specialist	Ext 7434
Nicola McCutcheon	Specialist Rheumatology Pharmacist	Direct dial 01279 827819 (voicemail)

Gastroenterology

Bridget Frazer	IBD Clinical Nurse Specialist	Ext 3364
Consultant via switchboard:		Ext 7424 / 7821
Clare Macpherson	Specialist Gastroenterology Pharmacist	Bleep 272 Direct dial: 01279 278224 (voicemail if not answered)

Dermatology

Dr R Verdolini	Consultant Dermatologist	Ext 7431
Dr K Wolpert	Consultant Dermatologist	Ext 7421
Lynn Hodgson	Dermatology Clinical Nurse Specialist	Ext 7431 / 7421
Medicines Information		01279 827054

Clinical Information

Methotrexate is an anti-metabolite cytotoxic drug, which inhibits DNA synthesis and cellular replication. It belongs to the group of DMARDs alongside sulphasalazine, hydroxychloroquine, leflunomide and azathioprine.
Two large meta-analyses favorably compared the efficacy and safety of methotrexate with other DMARDs and showed that efficacy is maintained for up to 5 years treatment.

Methotrexate is licensed for the treatment of rheumatoid arthritis, and psoriasis that has failed to respond to conventional therapy. It is also used for connective tissue disease and vasculitis (dermatology unlicensed indications) and Crohn's Disease and ulcerative colitis (gastroenterology unlicensed indications).

For complete product information please see SPC
http://www.medicines.org.uk/emc/

Dose

Adults
Use lower doses if patient renally impaired or frail elderly (see SPC)

Rheumatoid arthritis: (unlicensed – see reference 1)
Treatment is started at 7.5mg-10mg **orally** *once weekly*. The dose will usually be adjusted to a target to achieve an optimal response but does not usually exceed 20 mg *once weekly*, but occasionally a patient may require 25mg *once weekly*.
Methotrexate injection is indicated for the treatment of active Rheumatoid arthritis. Patients commenced on methotrexate are usually commenced on oral methotrexate. They may be switched to methotrexate injection if their response is suboptimal or they suffer from intractable nausea on oral methotrexate. The pre-filled syringes are licensed for subcutaneous administration. The dose usually starts at 7.5mg *once weekly* increasing in increments to a maximum of 20mg *once weekly* depending on patient response.

All increase and dose adjustments will be done in outpatient department and the GP should not be asked to take over prescribing on a shared care basis until the dosage is stabilized.

Psoriasis:
Treatment is started at doses of 5 -15mg **orally** *once weekly* and adjusted according to the patient's response, to a usual maximum of 25mg *once weekly*. Doses above 25mg *once weekly* are to be recommended by a consultant dermatologist

only. An initial test dose one week prior to initiation of therapy is recommended to detect any idiosyncrasy. Recommended test dose is 5mg.

Crohn's Disease

Treatment is usually started at 7.5mg orally *once weekly* and adjusted according to response up to a maximum of 20mg once weekly.

Ulcerative Colitis is not a licensed indication and methotrexate is not usually effective

Support Medicines

Folic acid

Ensure adequate folic acid supplementation to improve tolerability and compliance. A starting dose is generally 5mg once weekly, usually 2-3 days after methotrexate. However, the dose could be increased on advice from the specialist. Folic acid also reduces the risk of hepatotoxicity, though the effect on efficacy of methotrexate is still unclear

If nausea limits use of oral methotrexate consider use of anti-emetics.

Supply

Oral methotrexate is available in 2.5mg tablets from Wyeth, Mayne, Pharmacia (Maxtrex) and Wockhardt.

The prescriptions should only be written in multiples 2.5mg and should be dispensed as 2.5mg tablets.

Injectable methotrexate is available in pre-filled syringes as 7.5mg, 10mg, 12.5mg, 15mg, 17.5mg, 20mg, 22.5mg, and 25mg strengths.

A sudden change in dose must be noted and clarified with the patient and the prescribing practitioner

Adverse effects

In general, the incidence and severity of side effects are considered to be dose-related.

Common non-life threatening adverse effects of low-dose methotrexate mainly affects the gastrointestinal system (nausea, diarrhoea and stomatitis). Less commonly, the central nervous system may be affected (headaches, drowsiness and blurred vision).

Serious effects include hepatic, pulmonary and bone-marrow toxicity and can occur acutely at any time during therapy. As with most other DMARD agents, there is a risk of bone-marrow depletion with methotrexate. A low neutrophil count is of most concern and can present with high fever and sore throat. Rarely, serious pulmonary adverse effects with acute breathlessness have been recorded.

Other side effects include GU ulceration, alopecia, erythematous skin reactions and suppression of ovarian and testicular function.

If serious reaction is suspected: stop the drug immediately, check tests and contact specialist team for advice/or review.

Some adverse effects, namely mucosal or GI side effects may be reduced by the addition of folic acid 5mg, usually once weekly (although this may be increased to 6 days a week). Folic acid should not be taken within 24 hours of Methotrexate.

Contraindications

- Known allergic hypersensitivity to methotrexate
- Severe renal impairment (eGFR 15 - 29ml/min, CKD 4)
- Hepatic impairment
- Liver disease (fibrosis, cirrhosis, recent or active hepatitis)
- High alcohol consumption
- Active infection
- Immunodeficiency syndrome
- Severe anaemia, leucopenia or thrombocytopenia
- Pregnancy
- Breastfeeding
- Concomitant use of acitretin

Methotrexate should not be used concomitantly with drugs with anti-folate properties (eg trimethoprim). An exception to this is the combination of Sulfasalazine with Methotrexate.

Guidance for patients of child-bearing age: All patients, male and female, should be advised against conception and pregnancy during treatment with methotrexate as it is an abortificient as well as a teratogenic drug. If patients become pregnant inadvertently, it is appropriate to refer the patient to an obstetrician. Breast feeding should not be allowed as the drug may be excreted in the breast milk. Patients should be advised to continue contraception for at least 3 months and possibly up to 6 months after stopping methotrexate
BSR Guidelines (2008)
https://academic.oup.com/rheumatology/article/55/9/1693/1744535

Drug Interactions

NSAIDs and salicylates can reduce excretion of methotrexate. This potential interaction is seldom of clinical importance in the doses used in rheumatology and dermatology as opposed to the much higher doses used in oncology. The majority of patients who still need an anti-inflammatory agent can therefore safely take the two agents together.
Ciclosporin can increase Methotrexate toxicity. Specific advice should be given to patients by the specialist department if used together.
Concurrent use of trimethoprim or co-trimoxazole should be avoided due to a risk of severe bone marrow depression.
Probenecid markedly increases serum methotrexate levels and dosage reductions are needed to avoid toxicity. There may be a small risk of increased methotrexate levels with other antibiotics e.g. penicillin. Existing monitoring guidelines are adequate and should be followed as usual if antibiotics are used.
Concurrent use of acitretin and methotrexate can lead to methotrexate toxicity and risk of hepatotoxicity. This combination is best to be avoided. Alcohol should be avoided but small amounts are unlikely to be a problem.
For more details for drug interactions refer to a current BNF.

Immunizations

(1) Patients receiving methotrexate must not receive immunization with live vaccines. The advice of the physician or immunologist in charge should be sought for at least six months after treatment. Inactivated polio is available although suboptimal response may be seen.
(2) Annual flu vaccination and one off pneumococcal vaccination is recommended.
(3) In patients receiving methotrexate exposed to chickenpox or shingles, passive immunization should be carried out using VZIG. The Herpes Zoster immunoglobulins can be obtained from Health Protection Agency. Tel. No: 020 8200 6868 London or 0345 1550 069
https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book
Chapters 6 and 34

Overdose

Calcium folinate (Calcium Leucovorin) is a potent agent for neutralizing the immediate toxic effects of methotrexate on the haematopoietic system. In general, where overdosage is suspected, the dose of calcium folinate should be equal to or higher than, the offending dose of methotrexate and should be administered as soon as possible; preferably within the first hour and certainly within 4 hours after which it may not be effective. Treatment should be continued until the serum levels of methotrexate are below 10^{-7}M. This is only a guide. Please **always** contact the poisons help line. UK National Poisons Information Service (directs caller to relevant local centre) - 0870 600 6266 and/or the Summary of Product Characteristics (SPC) of the methotrexate product (via www.emc.medicines.org.uk)

Abbreviation Key

BAD	British Association of Dermatologists		
BNF	British National Formulary		
CHM	Committee on Human Medicines (yellow card scheme)		
CKD 3	Chronic Kidney Disease stage 3	= Moderate renal impairment	eGFR 30 - 59ml/min
CKD 4	Chronic Kidney Disease stage 4	=Severe renal impairment	eGFR 15 -29ml/min
NSAIDs	Non-steroidal anti-inflammatory drugs		
SPC	Summary Product Characteristics		
C&E	Creatinine and electrolytes Sodium, Potassium Creatinine		
eGFR	Estimated glomerular filtration rate	LFT	Liver function test
FBC	Full blood count	ALT	Alanine aminotransferase

Hb	Haemaglobin	AST	Aspartate aminotransferase
MCV	Mean corpuscular volume	TFT	Thyroid function test
WBC	White blood cells	PIIINP	Type 3 procollagen
mg/kg/day	milligrams per kilogram per day		

Additional sources of advice

Pharmacy Medicines Information 01279 827054 (Mon-Fri 9-5)

Useful sources of information

- BNF (current edition)
- MIMS
- SPC for methotrexate (via www.emc.medicines.org.uk)

Acknowledgements

With acknowledgment to Mid Essex Hospital Services NHS Trust on whose shared-care guidelines this document is based

Useful information

BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs 2017 https://academic.oup.com/rheumatology/article/3053478/BSR-and-BHPR-guideline-for-the-prescription-and?searchresult=1

CKS DMARDs http://cks.nice.org.uk/dmards#!scenario:8

West Essex CCG Shared Care Webpage Shared Care Letter - West Essex CCG

Arthritis Research UK Patient information letter
http://www.arthritisresearchuk.org/arthritis-information/drugs/methotrexate.aspx

GMC Prescribing Guidance: Shared Care: https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices/shared-care

References

1. BSR/BHPR guidelines for disease-modifying antirheumatic drug therapy in consultation with the BAD
2. NICE CG 152 Oct 2012 Crohn's disease: management

GP response to Shared Care Agreement

(only complete & send if NOT participating in shared care)

This shared care agreement has been approved by the Medicines Management Optimisation Programme Board March 2015

Patient Name:	NHS No:
Consultant:	Medicine requested for shared care: **Methotrexate**

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care agreement. 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. **ANONYMISED COPY OF THIS FORM ONLY** to the E-MAIL: **tpa-tr.ClinicalPharmacy@nhs.net**

(sending a copy of this form to the PAH pharmacy 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 Medicines Optimisation Team of the reasons shared care is not being undertaken by GPs allowing for changes to be made in future updates to improve patient safety)

P14064

The Princess Alexandra Hospital NHS
NHS Trust

Hamstel Road
Harlow, Essex
CM20 1QX

Tel: 01279 444455

Information for patients:

SHARED CARE:
Agreement information and confirmation

Patient name:

.....

Medicine:

.....

We would be grateful if you would take time to read this information as it will help us work with you to manage your condition and ensure safe prescribing of the specific medicine listed above.

What is a Shared Care Agreement?

A Shared Care Agreement (SCA) enables the care you have for a specific condition to be shared between the hospital and your GP.

The agreement means that the medicine the hospital has started, can be continued by your GP, so you won't have to visit the hospital to collect your medicine.

The SCA gives information on your medicine, guidance on the prescribing and monitoring responsibilities for your consultant (in the hospital), your GP and you. For an SCA to work everyone involved must understand it and communicate effectively.

Your consultant and your GP will need to sign the agreement and if you agree to this approach we would ask you to sign this letter, to indicate your agreement to have your care managed in this way.

How does Shared Care work?

Your consultant and GP share responsibility for your care.

The consultant is a specialist in your condition and will start prescribing your medicine, making sure it is suitable for you. There will come a point in your treatment when you may not need to be monitored by the consultant as often and this monitoring can be done by your GP.

Once your GP has agreed to the SCA, they will be able to prescribe the same medicine for you at the dose recommended by the consultant.

The organisation which regulates GPs, the General Medical Council, says that 'when a GP prescribes a medicine, the GP needs to satisfy themselves that the prescription is needed, appropriate for the patient and within the limits of their competence'.

So, your GP can only issue a prescription if the consultant and you keep to the responsibilities you have agreed (see below). If responsibilities are not kept or if the GP no longer feels it is safe to prescribe the medicine he/she will explain the reasons to you and your consultant, then prescribing responsibilities will be transferred back to the hospital.

What do I need to do to ensure the SCA can continue?

- **Attend hospital outpatients**
  You must still attend the hospital for regular reviews as directed by your consultant (these maybe less frequent than before). If you do not attend your hospital appointments your GP will not be able to continue issuing prescriptions for this medication.
- **Attend GP appointments**
  You must attend any appointments you have with your GP in relation to this medicine, so they can look after you effectively

continued overleaf

- **Have blood tests as you have been advised to** Your consultant should have informed you if and how often you need to have blood monitoring tests. You can usually have your blood taken at an appropriate clinic and not need to go to the hospital.

  If you do not have the blood monitoring tests as advised by your consultant, your GP will no longer be able to issue you with prescriptions as it would not be safe to do so.

What do I do if I am having side effects to the medicine?

Your consultant should have informed you of the common side effects to expect and what to do if you experience them. If you think you may be having side effects from a medicine discuss these with your pharmacist and GP. Your GP may need to seek advice from your consultant before issuing you with another prescription; this is to ensure it is safe for you to continue on the medication.

What if my disease symptoms change or get worse?

Report any changes in disease symptoms or circumstances that could affect management of your disease to your GP.

What about the other medicines I take?

Inform your GP and the consultant of all other medicines you are taking, including those you may have bought yourself. Do not take new medicines (including those you could buy) until you have discussed this with your pharmacist, GP or consultant.

If you would like to go ahead with a shared care agreement for the specific medication identified on page 1, please sign below to confirm that you:

- Understand the shared care agreement
- Are happy to have your care for this aspect of your health managed by a shared care agreement
- You agree to attend regular review appointments as requested
- You agree to have blood tests as required

Patient's signature .....

Date .....

Print name .....

If at any point in time you would like this shared care agreement to stop, please talk to your GP.