Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Shared care agreement for the prescribing of once weekly oral methotrexate

See shared care monitoring of DMARDS document for further information.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of oral once weekly methotrexate can be shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. The consultant should prescribe the initial four week dose of oral, once weekly methotrexate, complete the appropriate sections in the NPSA methotrexate monitoring handbook and , write to the GP. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

	Hospital Clinician / Specialist responsibilities
1	Perform baseline tests FBC, LFTs, UEC, chest X-ray (P3NP, Hepatitis B&C, antimitochondrial autobodies, for Dermatology patients only).
2	Initiate and stabilise treatment with methotrexate.
3	Discuss the benefits and side effects of treatment with the patient. Ensure that the patient understands that dosing is at weekly intervals.
4	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient, and who will provide the patient with a monitoring and dosage record.
5	Provide results of baseline tests and recommend frequency of monitoring as per monitoring schedule .
6	Recommend dose and timing of any concomitant folic acid.
7	Periodically review the patient's condition and communicate promptly with the GP when treatment is changed.
8	Advise the GP on when to adjust the dose, stop treatment, or consult with specialist.
9	Report adverse events to the MHRA (Yellow card scheme) and GP.
10	Ensure that clear backup arrangements exist for GPs to obtain advice and support.
11	Ensure the patient has a NPSA methotrexate monitoring booklet.

	General Practitioner responsibilities
	Also see shared care monitoring of DMARDS document for further information
1	Reply to the request for shared care as soon as practicable.
2	Prescribe methotrexate at recommended dose. **Always prescribe 2.5mg tabs not 10 mg tabs for oral use**
3	Ensure compatibility with other concomitant medication.
4	Ensure that the patient understands that dosing is at weekly intervals, and which warning symptoms to report.
5	Monitor blood counts, hepatic and renal function at recommended frequencies, and refer if abnormal.
6	Adjust the dose as advised by the specialist.
7	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
8	Report adverse events to the specialist and MHRA (Yellow card scheme).

	Patient's role
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with methotrexate.
3	Inform specialist or GP of any other medication being taken, including over-the-counter products..
4	Report any adverse effects or warning symptoms to the specialist or GP whilst taking methotrexate
5	To bring the NPSA methotrexate monitoring booklet to any GP/Hospital appointment along with a printout of latest blood results.
6	Present NPSA methotrexate monitoring booklet to the Pharmacist when dispensing the methotrexate.

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Updated March 2017 to include Gastroenterology and Respiratory medicine

Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

BACK-UP ADVICE AND SUPPORT

(see contacts section in appendices 2-5)

SUPPORTING INFORMATION

DERMATOLOGY

Methotrexate is licensed for the treatment of adults with severe psoriasis unresponsive to conventional therapy.

RHEUMATOLOGY

Methotrexate is licensed for the treatment of adults with severe, active, classical or definite rheumatoid arthritis who are unresponsive to or intolerant of conventional therapy.

Methotrexate is also prescribed for other rheumatic conditions including psoriatic arthritis, early undifferentiated arthritis, juvenile idiopathic arthritis (JIA), spondylarthropathies, SLE, myositis, mixed connective tissue disease, scleroderma, vasculitis and polymyalgia rheumatica. Use in these conditions is unlicensed and recommended by the British Society of Rheumatology.

GASTROENTEROLOGY

Inflammatory bowel disease (unlicensed). Its use is recommended by the British Society of Gastroenterology

RESPIRATORY MEDICINE

Interstitial lung diseases, sarcoidosis and pulmonary vasculitis (unlicensed uses). Its use in these conditions is recommended by the British Thoracic Society.

Dosage and Administration

Psoriasis

Methotrexate is started at a dose of 2.5mg orally once weekly. The schedule is adjusted gradually to achieve an optimal response but will not usually exceed a total weekly dose of 25 mg. The lowest possible effective dose should be used.

Rheumatology indications

Methotrexate is started at a dose of 7.5mg orally once weekly, or divided oral doses of 2.5mg at 12 hour intervals for 3 doses (7.5mg) as a course once weekly. The schedule may be adjusted gradually to achieve an optimal response but should not exceed a total weekly dose of 25mg . The lowest possible effective dose should be used. Methotrexate should be used with extreme caution in elderly patients.

There may occasionally be patients in whom Methotrexate will need to be administered subcutaneously or intra-muscularly (see shared care agreement for subcutaneous methotrexate

Inflammatory bowel disease

Usual dose 15 to 25mg orally once weekly.

Respiratory indications

Initial dose 7.5 mg orally once weekly. The dosing schedule may be adjusted gradually to achieve an optimal response but should not exceed a total weekly dose of 25mg. The lowest possible effective dose should be used. Methotrexate should be used with extreme caution in elderly patients.

Contra-indications and precautions for use

- Patients receiving anti-folate drugs e.g trimethoprim, sulphonamides.
- Severe or significant renal impairment
- Significant hepatic impairment, or liver disease including fibrosis, cirrhosis, recent active hepatitis
- Active localised or systemic infectious disease e.g tuberculosis, hepatitis A, B C
- Overt or laboratory evidence of immunodeficiency syndrome(s)
- Serious cases of anaemia, leucopenia, or thrombocytopenia
- Pregnancy. Women of childbearing potential should use effective contraception during treatment. A pregnancy test should be done to rule out pregnancy prior to initiating treatment.
- As methotrexate can be genotoxic, this should be discussed with patients prior to initiation as per SPC.
- Breast-feeding
- Patients with a known allergic hypersensitivity to methotrexate or excipients of the formulation

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Adverse effects
Patients must urgently report mouth ulcers, sore throat, fever, epistaxis, jaundice, unexpected bruising or bleeding, any unexplained illness/infection and should be seen urgently for clinical assessment, FBC and LFT.
New onset of shortness of breath should also be reported.

The incidence and severity of adverse effects are considered to be dose related
Commonly these include: nausea, stomach pains, mucositis / stomatitis mouth ulcers, hair loss
Rarely these include: vomiting, diarrhoea, loss of appetite, headache, tiredness, dizziness, blurred vision, eye irritation, fever, chills, joint / muscle pain, allergic reaction, rash, acne, mood changes.

Serious adverse effects include:

Blood	Bone marrow depression – leucopenia, thrombocytopenia and anaemia
Skin	Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary, changes, alopecia, ecchymosis, telangiectasia,, furunculosis
Lungs	Acute or chronic interstitial pneumonitis, acute pulmonary oedema, pulmonary fibrosis
Liver	Hepatic toxicity / significant elevations in LFTs (> 2-3 times ULN), fibrosis or cirrhosis
Kidney	Severe Renal failure and uraemia
Neurological	Aphasia, paresis, hemiparesis, and convulsions
Other	Malignant lymphomas

Immunisation
Influenza vaccination is recommended PRIOR to the first dose of methotrexate and then annually (due to immunosuppression). A pneumococcal vaccine may also be recommended. Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles. A list of safe vaccinations prior to travel is also available via the following links:

http://www.bad.org.uk/for-the-public/patient-information-leaflets/immunisation/?showmore=1&returnlink=http%3a%2f%2fwww.bad.org.uk%2ffor-the-public%2fpatient-information-leaflets

http://www.bad.org.uk/for-the-public/patient-information-leaflets/methotrexate/?showmore=1&returnlink=http%3a%2f%2fwww.bad.org.uk%2ffor-the-public%2fpatient-information-leaflets%3fl%3d0%26group%3d00016001000200010003

Pregnancy and Lactation
Because methotrexate is both abortifacient and teratogenic it is strictly contraindicated in pregnancy and during breastfeeding. Adequate contraceptive measures must be taken by women of childbearing potential during methotrexate therapy, and for at least **3 months** after treatment discontinued. Although methotrexate is not mutagenic, the drug may affect spermatogenesis. It is customary to advise men to avoid fathering children during therapy and for at least **3 months** after stopping

Interactions
Methotrexate is extensively protein-bound and may be displaced by other protein-bound drugs (e.g. diuretics, salicylates, hypoglycaemics), with a potential for increased toxicity. Concomitant use of other drugs with nephrotoxic or hepatotoxic potential (including alcohol) should be avoided.

- Always avoid trimethoprim, co-trimoxazole and sulphonamides (increases anti-folate effect) risk of pancytopenia
- Avoid concomitant use of cytotoxics with clozapine (increased risk of agranulocytosis)
- Live vaccines should not be administered (may cause strong antigenic reaction)
- Avoid aspirin (but low-dose regular aspirin is acceptable)
- NSAIDs can be prescribed, but patients will need to be carefully monitored for any side effects, particularly at higher methotrexate doses.
- Phenytoin can increase the antifolate effect of methotrexate.
- Excretion of methotrexate possibly reduced by ciprofloxacin, penicillins
- Increased risk of toxicity when given with doxycycline, ciclosporin, probenecid, and lefluomide
- Avoid concomitant use of acitretin

Monitoring - Also see shared care monitoring of DMARDS document for further information
Regular monitoring during treatment is essential to detect adverse reactions at an early stage and patients should be counselled about the risk factors and to report all signs and symptoms of toxicity. Carry out full blood count (FBC) and renal and liver function tests (including ALT and/or AST and albumin) before starting treatment and repeat every 2 weeks until patient is on stable dose for 6 weeks. Once on stable dose carry out monthly FBC, renal and liver function tests for 3 months. Thereafter carry out FBC, renal and liver function tests at least every 12 weeks. If there is a dose increase or unstable bloods repeat monitoring every 2 weeks until dose of methotrexate and monitoring stable for 6 weeks.
Threshold laboratory values and symptoms that need discussion with the specialist are: wbc $<3.5x10^9$/l, neutrophils $<1.6x10^9$/l, platelets $<140x10^9$/l, ALT &/or AST>100u/L, unexplained fall in albumin, rash or oral ulceration, new or increasing dyspnoea or cough. Also rapid fall or consistent downward trend in haematological values should prompt caution and extra vigilance.

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Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Cost

At current prices one year's treatment with methotrexate 7.5 mg per week costs £16.

References

- eMC, Methotrexate 2.5mg tablets, 2015 http://www.medicines.org.uk/emc/medicine/29190
- National Patient Safety Agency, 2006 www.npsa.nhs.uk
- Patient held booklet NPSA http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800
- Methotrexate treatment books available from www.nhsforms.co.uk SEE BNF for details
- Carter M J, Lobo A J & Travis S P L on behalf of the IBD Section of the British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. Gut 2004; **53** (Suppl V); v1-v16.
- British Thoracic Society Interstitial Lung Disease guidelines. http://www.brit-thoracic.org.uk/Portals/0/Guidelines/DPLDGuidelines/Thorax%20Sept%2008.pdf
- BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs: Rheumatology 2017;56:865-868

Appendices

Appendix 1	Rheumatology department request to GP to participate in shared care
Appendix 2	Contact details for Salisbury district hospital Rheumatology department
Appendix 3	Dermatology department request to GP to participate in shared care
Appendix 4	Gastroenterology department request to GP to participate in shared care
Appendix 5	Respiratory Medicines department request to GP to participate in shared care

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Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Appendix 1

The **Rheumatology** Department, Salisbury NHS Foundation Trust, would like to request your participation in the Shared Care Agreement (attached), for Oral Methotrexate, for the named patient below.

Patient Label	GP Label

Contact Tel: 01722 429217

Consultant Name	Consultant Signature	Date
Dr. S. Bartram		
Dr. Z. Cole		
Dr. A. Coy		
Dr. G.A. Smith		
Locum Consultant Dr A. Litwic		
PLEASE INDICATE NAMED CONSULTANT RHEUMATOLOGIST		
Specialist Registrar Dr. G .Dulay		
Senior Clinical Nurse Specialist S. Carvalho		

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Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Appendix 2

Contact details for the Salisbury Rheumatology Department.

Consultants	Dr S. Bartram, Dr Z. Cole, Dr A. Coy, Dr GR. Smith
Locum Consultant	Dr. A. Litwic
Specialist Registrar	Dr. G. Dulay
	Please contact via the consultants secretaries/office
Consultant Secretaries	01722 345556
	Di Graham, Rachael Thompson, Claire Young
	di.graham@salisbury.nhs.uk
	rachael.thompson(rheumatology)@salisbury.nhs.uk
	claire.young@salisbury.nhs.uk
Senior Nurse Specialist	Sam Carvalho
Nurse Specialists	Jackie Bradford, Teresa Donaldson, Cathy Gulliver
Nurse Secretaries	Diana Collinson, Sandra Loader
	diana.collinson@salisbury.nhs.uk
	sandra.loader@salisbury.nhs.uk
	01722 336262 ext 2669
Patient Adviceline	01722 429137 (limited manned hours each week)
Rheumatology Reception	01722 429217 (08.30 – 17.00)
Rheumatology Fax No.	01722 337912 (08.30 – 17.00)

Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Appendix 3

The **Dermatology** Department, Salisbury NHS Foundation Trust, would like to request your participation in the Shared Care Agreement (attached), for Oral Methotrexate, for the named patient below.

Patient Label	GP Label

Contact Tel: 01722 425206

Consultant Name	Consultant Signature	Date
Dr. N. Nayak		
Dr. S. Mellor		
Dr. V. Smith		
Dr. B. Kay		
Locum Consultant Dr .D. Jones		
PLEASE INDICATE NAMED CONSULTANT DERMATOLOGIST		

Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Appendix 4

The **Gastroenterology** Department, Salisbury NHS Foundation Trust, would like to request your participation in the Shared Care Agreement (attached), for Oral Methotrexate, for the named patient below.

Patient Label	GP Label

Contact Tel: 01722 429227

Consultant Name	Consultant Signature	Date
Dr. J. Loehry		
Dr. A. Jamil		
Dr. D. Sheppard		
Dr. A. Tanner		
Dr.S.Vyas		
PLEASE INDICATE NAMED CONSULTANT GASTROENTEROLOGIST		

Salisbury NHS Foundation Trust, Shared Care Agreement
Once Weekly Oral Methotrexate

Appendix 5

The **Respiratory Medicine** Department, Salisbury NHS Foundation Trust, would like to request your participation in the Shared Care Agreement (attached), for Oral Methotrexate, for the named patient below.

Patient Label	GP Label

Contact Tel: 01722 429220

Consultant Name	Consultant Signature	Date
Dr. R. Mehta		
Dr. C. Thompson		
Dr. S. Evans		
PLEASE INDICATE NAMED CONSULTANT RESPIRATORY MEDICINE		
Respiratory Nurse Specialist T. Flower		
Respiratory Nurse Specialist C. Maule / K. Nash		