Effective Shared Care Agreement (ESCA)

Methotrexate

ESCA: For the treatment of rheumatoid arthritis or psoriatic arthritis

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of methotrexate for rheumatoid arthritis or psoriatic arthritis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with rheumatoid arthritis or psoriatic arthritis are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of rheumatoid arthritis or psoriatic arthritis
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made
4. Do baseline monitoring prior to initiation of methotrexate
5. Initiate treatment and stabilise dose of methotrexate **using 2.5 mg increments and only as a once weekly dose** and issue a methotrexate monitoring booklet as per NPSA alert**.** **Please note: Oral methotrexate 10 mg tablets are not recommended for use in the BSSE health economy.** **Please note: Parenteral methotrexate – ensure that the patient** • **has had the appropriate training to self-administer methotrexate** • **has been advised about safe disposal using a purple lidded shapes bin** • **has been advised about steps to take to in an event of a spillage (leaflet or the provision of a spillage kit)**
6. Review the patient's condition and monitor response to treatment regularly
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay
8. Report serious adverse events to the MHRA
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below)

General Practitioner responsibilities
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days
2. Prescribe methotrexate at the dose recommended **using 2.5 mg increments and only as a once weekly dose.** **Please note: Oral methotrexate 10 mg tablets are not recommended for use in the BSSE health economy.** **Please note: Parenteral methotrexate – ensure that the patient** • **has had the appropriate training to self-administer methotrexate** • **has been advised about safe disposal using a purple lidded shapes bin. Prescribe a Sharpsafe purple lidded shapes bin or a Sharpsguard purple lidded shapes bin or follow locally agreed process** • **has been advised about steps to take to in an event of a spillage (leaflet or the provision of a spillage kit) or follow locally agreed process**
3. Adjust the dose as advised by the specialist and document in the patients methotrexate monitoring booklet
4. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement

GP Prescribing System	Read Code	Description		GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care

5. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist
6. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment
7. Refer back to specialist if condition deteriorates
8. Report serious adverse events to specialist and MHRA
9. Stop treatment on advice of specialist

Patient's role
1. Report to the specialist, clinical nurse 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 with the specialist, clinical nurse specialist or GP
3. Keep and present your methotrexate monitoring booklet at each appointment
4. Report any adverse effects to the specialist or GP whilst taking methotrexate
5. Attend regular outpatient appointments with the specialist

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

Based on MTRAC template
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Birmingham CrossCity CCG

SUPPORTING INFORMATION

<table>
<tr><td>Indication</td><td colspan="3">Methotrexate is used in the treatment of adults with severe, active, classical or definite rheumatoid arthritis who are unresponsive or intolerant to conventional therapy and psoriatic arthritis (unlicensed)</td></tr>
<tr><td rowspan="8">Dosage and Administration</td><td colspan="3">Supply only 2.5 mg strength tablets, as it reduces the risk of accidental overdose (see National Patient Safety Agency Web site). Issue the methotrexate monitoring booklet to all patients. Update with any dose changes
Please note: Oral methotrexate 10 mg strength is not recommended for use in the BSSE health economy.</td></tr>
<tr><td>BSR recommendation</td><td colspan="2">Typical dose: 7.5–25 mg ONCE weekly; starting dose may vary depending on the severity of the condition and patient characteristics such as age, renal function and other comorbid conditions.

The initial dose may be 5–10 mg once weekly, increasing by 2.5–5 mg every 2–6 weeks until disease stabilised.

The maximum licensed dose in RA is 25 mg/week. Rarely, the maximum dose can be 30 mg/week.

Lower doses should be considered for frail elderly patients who often have poor renal function. If maximum oral dose is not effective or causes intolerance, consider i.m. or subcutaneous route of administration before discontinuation of the drug.</td></tr>
<tr><td colspan="3">Suggested regimen</td></tr>
<tr><td>Starting dose</td><td colspan="2">7.5 mg – 10 mg per week for two weeks</td></tr>
<tr><td>Titration</td><td colspan="2">Dependent on tolerability and blood picture:
• 10 mg per week for four weeks
• Then 12.5 mg per week for four weeks
Subsequent dosing in increments 2.5 mg every two to four weeks depending on response</td></tr>
<tr><td>Range</td><td colspan="2">2.5 mg to 20 mg as a single dose taken on the same day once a week. Spreading the dose over 24 hours helps reduce the risk of nausea
NB: Dose can be increased to a maximum of 25 mg per week under specialist guidance (unlicensed)</td></tr>
<tr><td>Folic acid</td><td colspan="2">5 mg once a week taken 24 hours after dose of MTX can help reduce some minor side effects</td></tr>
<tr><td>By injection</td><td colspan="2">Subcutaneous self injection by patient or carer may be used - hospital protocol applies</td></tr>
<tr><td>Renal Impairment
Hepatic impairment</td><td colspan="3">Methotrexate is contraindicated in the presence of severe/significant renal or significant hepatic impairment.</td></tr>
<tr><td>Contra-indications / Special precautions</td><td colspan="3">Contraindications
• Patients with a known allergic hypersensitivity to methotrexate should not receive methotrexate.
• severe/significant renal renal impairment.
• significant hepatic impairment. Liver disease including fibrosis, cirrhosis, recent or active hepatitis; active infectious disease; and overt or laboratory evidence of immunodeficiency syndrome(s)
• Serious cases of anaemia, leucopenia or thrombocytopenia.
• Concomitant administration of folate antagonists such as trimethoprim, co-trimoxazole and nitrous oxide should be avoided. Hepatic and nephrotoxic drugs should be avoided. Methotrexate is teratogenic and should not be given during pregnancy or to mothers who are breast feeding.
Cautions
• Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, diarrhoea, and ulcerative disorders of the GI tract and psychiatric disorders
• Hepatic toxicity has been observed, usually associated with chronic hepatic disease. The administration of low doses of methotrexate for prolonged periods may give rise, in particular, to hepatic toxicity. Liver function should be closely monitored
• Renal lesions may develop if the urinary flow is impeded and urinary pH is low, especially if large doses have been administered. Renal function should be closely monitored before, during and after treatment. Reduce dose of methotrexate in patients with renal impairment</td></tr>
</table>

		• Particular care and possible cessation of treatment are indicated if stomatitis or GI toxicity occurs as haemorrhagic enteritis and intestinal perforation may result. • Haematopoietic suppression caused by methotrexate may occur abruptly and with apparently safe dosages. Full blood counts should be closely monitored before, during and after treatment. • Malignant lymphomas may occur in patients receiving low dose methotrexate, in which case therapy must be discontinued • Methotrexate has some immunosuppressive activity and therefore the immunological response to concurrent vaccination may be decreased. In addition, concomitant use of a live vaccine could cause severe antigenic reaction • Patients with pleural effusions and ascites should be drained prior to initiation of methotrexate therapy or treatment should be withdrawn • Pleuropulmonary manifestation of rheumatoid arthritis has been reported in patients with rheumatoid arthritis. Patients should be advised to contact their physicians immediately should they develop a cough or dyspnoea • Lung manifestations of RA and other connective tissue disorders are recognised to occur. In patients with RA, the physician should be specifically alerted to the potential for methotrexate induced adverse effects on the pulmonary system • Methotrexate is extensively protein bound and may displace, or be displaced by, other acidic drugs. The concurrent administration of agents such as p-aminobenzoic acid, chloramphenicol, penicillines, ciprofloxacin, diphenylhydantoins, phenytoin, acidic anti-inflammatory agents, salicylates, sulphonamides, tetracyclines, thiazide diuretics, probenicid or sulfinpyrazone or oral hypoglycaemics will decrease the methotrexate transport function of renal tubules, thereby reducing excretion and almost certainly increasing methotrexate toxicity • Methotrexate dosage should be monitored if concomitant treatment with aspirin, ibuprofen or indometacin (NSAID's) is commenced, as concomitant use of NSAID's has been associated with fatal methotrexate toxicity • Vitamin preparations containing folic acid or its derivatives may alter response to methotrexate. • Following administration to a man or woman conception should be avoided by using an effective contraceptive method for at least 3 months after using methotrexate
Side Effects	Common	Nausea (spreading the dose over 24 hours helps), mouth ulcers, diarrhoea, hair loss
	Less Common	• Leucopenia • Thromobocytopoenia • Pneumonitis • Increased nodule formation • Malaise • Abnormal LFTs • Modest rise in MCV is common - check B12 and folate • Watch for adverse effects if changing NSAIDs or consider reducing • methotrexate dose temporarily

Monitoring **BSR Recommendations**	Pretreatment Assessment	FBC, U&E, LFT and CXR (unless CXR done within the last 6 months). Pulmonary function tests should be considered in selected patients
	After commencing treatment	FBC, U&E, LFT every 2 weeks until dose of methotrexate and monitoring stable for 6 weeks; thereafter monthly until the dose and disease is stable for 1 yr. Thereafter the monitoring may be reduced in frequency, based on clinical judgement with due consideration for risk factors including age, comorbidity, renal impairment, etc when monthly monitoring is to continue. Re: Serum pro-collagen III in patients with psoriatic arthritis
	Disease monitoring	Occasional ESR/CRP helps assessment

Actions to be taken:	
WBC<3.5x10^9/l	Withhold until discussed with specialist team.
Neutrophils<2.0x10^9/l	Withhold until discussed with specialist team.
Platelets<150x10^9/l	Withhold until discussed with specialist team.
AST, ALT>twice upper limit of reference range	Withhold until discussed with specialist team
Albumin-unexplained fall (in absence of active disease)	Withhold until discussed with specialist team.
Rash or oral ulceration, nausea and vomiting, diarrhoea	Withhold until discussed with specialist team.
New or increasing dyspnoea or dry cough	Withhold and discuss urgently with specialist team.
MCV>105 fl	Withhold and check serum B12, Folate and TFT and discuss with specialist team if necessary.
Mild to moderate renal impairment	Withhold until discussed with specialist team
Severe sore throat, abnormal bruising	Immediate FBC and withhold until the result of FBC is available

Dose reduction	Side effects, e.g.: • mouth ulcers • rash • nausea • diarrhoea Depending on the severity of these a small dose reduction e.g. 2.5 mg per week may be sufficient. Alternatively temporary cessation and restarting at a lower dose or increasing the dose of folic acid (e.g. 5 mg six days per week except the day of methotrexate) may be effective.
Important notes	• Live vaccines should **not** be administered • Influenza and pneumovax vaccines are recommended • Contraception during treatment is recommended

Drug Interactions

Methotrexate has the following interaction information:

Acetazolamide	excretion of methotrexate increased by alkaline urine due to acetazolamide
Acitretin	plasma concentration of methotrexate increased by acitretin(also increased risk of hepatotoxicity)—avoid concomitant use
Aminophylline	methotrexate possibly increases plasma concentration of aminophylline
Aspirin	excretion of methotrexate reduced by aspirin (increased risk of toxicity)
Ciclosporin	risk of toxicity when methotrexate given with ciclosporin
Ciprofloxacin	excretion of methotrexate possibly reduced by ciprofloxacin(increased risk of toxicity)
Cisplatin	increased pulmonary toxicity when methotrexate given with cisplatin
Dexamethasone	possible increased risk of hepatoxicity when *high-dose* methotrexate given with dexamethasone
Diclofenac	excretion of methotrexate reduced by diclofenac (increased risk of toxicity)

Digoxin	methotrexate possibly reduces absorption of digoxin *tablets*
Doxycycline	increased risk of methotrexate toxicity when given with doxycycline
Fosphenytoin	antifolate effect of methotrexate increased by fosphenytoin
Ibuprofen	excretion of methotrexate reduced by ibuprofen (increased risk of toxicity)
Indometacin	excretion of methotrexate reduced by indometacin (increased risk of toxicity)
Ketoprofen	excretion of methotrexate reduced by ketoprofen (increased risk of toxicity)
Leflunomide	risk of toxicity when methotrexate given with leflunomide **Note:** Increased risk of toxicity with other haematotoxic and hepatotoxic drugs
Meloxicam	excretion of methotrexate reduced by meloxicam (increased risk of toxicity)
NSAIDs	excretion of methotrexate probably reduced by NSAIDs(increased risk of toxicity) **Note:***See also* Aspirin. Interactions do not generally apply to topical NSAIDs
Naproxen	excretion of methotrexate reduced by naproxen (increased risk of toxicity)
Neomycin	absorption of methotrexate possibly reduced by neomycin
Nitrous Oxide	antifolate effect of methotrexate increased by nitrous oxide—avoid concomitant use
Penicillins	excretion of methotrexate reduced by penicillins (increased risk of toxicity)
Phenytoin	antifolate effect of methotrexate increased by phenytoin
Proton Pump Inhibitors	excretion of methotrexate possibly reduced by proton pump inhibitors (increased risk of toxicity)
Pyrimethamine	antifolate effect of methotrexate increased by pyrimethamine
Sulfamethoxazole	increased risk of haematological toxicity when methotrexategiven with sulfamethoxazole (as co-trimoxazole)
Sulfonamides	increased risk of methotrexate toxicity when given with sulfonamides
Tetracycline	increased risk of methotrexate toxicity when given with tetracycline
Theophylline	methotrexate possibly increases plasma concentration of theophylline
Trimethoprim	increased risk of haematological toxicity when methotrexate given with trimethoprim (also with co-trimoxazole)

Methotrexate belongs to **Antimetabolites** but **Antimetabolites** has no interactions information
Methotrexate belongs to **Cytotoxics** and will have the following interactions:

Clozapine	avoid concomitant use of cytotoxics with clozapine (increased risk of agranulocytosis) **Note:** Avoid concomitant use of clozapine with drugs that have a substantial potential for causing agranulocytosis

References

- British Society for Rheumatology (BSR) guidelines
- National Patient Safety Agency Web site
- Maxtrex Tablets SmPC
- Methotrexate BNF

I agree to participate in this shared care agreement for the treatment of the below named patient with methotrexate for rheumatoid arthritis or psoriatic arthritis

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: