

Effective Shared Care Agreement (ESCA)
Methotrexate (oral only)

ESCA: For the treatment of Interstitial lung disease

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of of Methotrexate for the treatment of Interstitial lung disease 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 Interstitial lung disease 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 Interstitial lung disease	
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient	
3. Ensure all patients receive an oral methotrexate patient information leaflet & dosage record booklet – as per NPSA alert	
4. Following agreement with the patient, initiate (using 2.5mg strength and only as a once weekly dose) and supply methotrexate. Titrate to an effective dose and stabilise the patient on an appropriate maintenance dose before seeking to initiate shared care	
5. 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	
6. Do baseline monitoring prior to initiation of Methotrexate	
7. Initiate treatment and stabilise dose of Methotrexate	
8. Review the patient's condition and monitor response to treatment regularly	
9. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay	
10. Report serious adverse events to the MHRA	
11. 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 2.5mg strength and only as a once weekly dose)					
3. Adjust the dose as advised by the specialist and update the oral methotrexate patient information leaflet & dosage record booklet – as per NPSA alert					
4. Prescribe Methotrexate at the dose recommended					
5. 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	SystemOne	XaB58	Shared care
6. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist					
7. 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					
8. Refer back to specialist if condition deteriorates					
9. Report serious adverse events to specialist and MHRA					
10. 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. Ensure that the methotrexate patient information leaflet & dosage record booklet is presented to the consultant, GP and community pharmacists	
3. Share any concerns in relation to treatment with methotrexate with the specialist, clinical nurse specialist or GP	
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		

SUPPORTING INFORMATION

Indication	Interstitial lung diseases, sarcoidosis & pulmonary vasculitis (unlicensed uses). Its use in these conditions is recommended by the British Thoracic Society	
Dosage and Administration	Important note regarding the preparation Supply only 2.5mg strength tablets, as it reduces the risk of accidental overdose (see National Patient Safety Agency Web site). Please note: Oral methotrexate 10 mg tablets are not recommended for use in the BSSE health economy.	
	Starting dose	7.5mg – 10mg per week for two weeks
	Range	7.5mg to 20mg as a single dose taken on the same day once a week. NB: Dose can be increased to a maximum of 25mg per week under specialist guidance (unlicensed)
	Titration	Dependent on tolerability and blood picture: <ul style="list-style-type: none"> • 10mg per week for four weeks • Then 12.5 mg per week for four weeks Subsequent dosing in increments 2.5mg every two to four weeks depending on response
	Folic acid	5mg once a week taken 24 hours after dose of MTX can help reduce some minor side effects but is not routinely prescribed
	By injection	Injection preparations not routinely used for pulmonary disease.
Renal Impairment	Methotrexate is contra-indicated in the presence of severe/significant renal impairment	
Hepatic impairment	Methotrexate is contra-indicated in the presence of significant hepatic impairment.	
Contra-indications / Special precautions	<p>Contraindications</p> <ul style="list-style-type: none"> • Patients with a known allergic hypersensitivity to methotrexate should not receive methotrexate. • Severe/significant renal • 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, cotrimoxazole 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. <p>Cautions</p> <ul style="list-style-type: none"> • 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 • 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 	

	<ul style="list-style-type: none"> • 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, diphenylhydantoin, phenytoin, acidic anti-inflammatory agents, salicylates, sulphonamides, tetracyclines, thiazide diuretics, probenecid 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	<p>Skin: Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary changes, alopecia, ecchymosis, telangiectasia, acne, furunculosis.</p> <p>Haematopoietic: Bone marrow depression is most frequently manifested by leucopenia, thrombocytopenia (which are usually reversible) and anaemia, or any combination may occur. Infection or Hypogammaglobulinaemia has been reported.</p> <p>Alimentary System: Mucositis (most frequently stomatitis although gingivitis, pharyngitis and even enteritis, intestinal ulceration and bleeding) may occur.</p> <p>Hepatic: Hepatic toxicity resulting in significant elevations of liver enzymes, acute liver atrophy, necrosis, fatty metamorphosis, periportal fibrosis or cirrhosis or death may occur, usually following chronic administration.</p> <p>Urogenital System: Renal failure and uraemia may follow Methotrexate administration, particularly after high doses or prolonged administration. Vaginitis, vaginal ulcers, cystitis, haematuria and nephropathy have also been reported. Methotrexate can decrease fertility.</p> <p>Pulmonary System: In the treatment of rheumatoid arthritis, Methotrexate induced lung disease is a potentially serious adverse drug reaction which may occur acutely at any time during therapy. Pulmonary symptoms (especially a dry, non productive cough) may require interruption of treatment and careful investigation.</p> <p>Central Nervous System: Headaches, drowsiness, ataxia and blurred vision have occurred following low doses of Methotrexate, transient subtle cognitive dysfunction, mood alteration, or unusual cranial sensations have been reported occasionally. Aphasia, paresis, hemiparesis, and convulsions have also occurred following administration of higher doses.</p> <p>Other reports include eye irritation, malaise, undue fatigue, vasculitis, sepsis, arthralgia/myalgia, chills and fever, dizziness, loss of libido/impotence and decreased resistance to infection. Also opportunistic infections such as herpes zoster. Osteoporosis, abnormal (usually "megaloblastic") red cell morphology, precipitation of diabetes, other metabolic changes, and sudden death in relation to or attributed to the use of Methotrexate.</p>

Monitoring	Baseline screening	FBC, renal and LFTs CXR and pulmonary function tests as a baseline																														
	Routine monitoring	FBC, U&E and LFTs every two weeks for six weeks. Then monthly for four to 12 months until stable dose Every eight weeks thereafter Ask patient to report respiratory symptoms, e.g. dyspnoea or persistent cough																														
	Disease monitoring	<ul style="list-style-type: none"> Occasional ESR/CRP helps assessment 																														
	Cessation of treatment (seek advice)	Platelets <120.000 WBC <3.5 N <2.0 LFTs 2x upper normal limit Temporary cessation, if concomitant respiratory or other infections																														
	Dose reduction	Side effects, e.g.: <ul style="list-style-type: none"> mouth ulcers rash nausea diarrhoea 																														
	Important notes	<ul style="list-style-type: none"> Live vaccines should not be administered Influenza and Pneumovax vaccines are recommended Contraception during treatment is recommended 																														
	Drug interaction (significant interaction as outlined in BNF, please see BNF and SPC for more detail)	Methotrexate has the following interaction information: <table border="1"> <tr> <td>Acitretin</td> <td>plasma concentration of methotrexate increased by acitretin (also increased risk of hepatotoxicity)—avoid concomitant use</td> </tr> <tr> <td>Aspirin</td> <td>excretion of methotrexate reduced by aspirin (increased risk of toxicity)</td> </tr> <tr> <td>Ciclosporin</td> <td>risk of toxicity when methotrexate given with ciclosporin</td> </tr> <tr> <td>Cisplatin</td> <td>increased pulmonary toxicity when methotrexate given with cisplatin</td> </tr> <tr> <td>Diclofenac</td> <td>excretion of methotrexate reduced by diclofenac (increased risk of toxicity)</td> </tr> <tr> <td>Ibuprofen</td> <td>excretion of methotrexate reduced by ibuprofen (increased risk of toxicity)</td> </tr> <tr> <td>Indometacin</td> <td>excretion of methotrexate reduced by indometacin (increased risk of toxicity)</td> </tr> <tr> <td>Ketoprofen</td> <td>excretion of methotrexate reduced by ketoprofen (increased risk of toxicity)</td> </tr> <tr> <td>Leflunomide</td> <td>risk of toxicity when methotrexate given with leflunomide Note: Increased risk of toxicity with other haematotoxic and hepatotoxic drugs</td> </tr> <tr> <td>Meloxicam</td> <td>excretion of methotrexate reduced by meloxicam (increased risk of toxicity)</td> </tr> <tr> <td>NSAIDs</td> <td>excretion of methotrexate probably reduced by NSAIDs(increased risk of toxicity) Note:See also Aspirin. Interactions do not generally apply to topical NSAIDs</td> </tr> <tr> <td>Naproxen</td> <td>excretion of methotrexate reduced by naproxen (increased risk of toxicity)</td> </tr> <tr> <td>Nitrous Oxide</td> <td>antifolate effect of methotrexate increased by nitrous oxide—avoid concomitant use</td> </tr> <tr> <td>Pyrimethamine</td> <td>antifolate effect of methotrexate increased by pyrimethamine</td> </tr> <tr> <td>Sulfamethoxazole</td> <td>increased risk of haematological toxicity when methotrexate given</td> </tr> </table>		Acitretin	plasma concentration of methotrexate increased by acitretin (also increased risk of hepatotoxicity)—avoid concomitant use	Aspirin	excretion of methotrexate reduced by aspirin (increased risk of toxicity)	Ciclosporin	risk of toxicity when methotrexate given with ciclosporin	Cisplatin	increased pulmonary toxicity when methotrexate given with cisplatin	Diclofenac	excretion of methotrexate reduced by diclofenac (increased risk of toxicity)	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)	Nitrous Oxide	antifolate effect of methotrexate increased by nitrous oxide—avoid concomitant use	Pyrimethamine	antifolate effect of methotrexate increased by pyrimethamine	Sulfamethoxazole
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		with sulfamethoxazole (as co-trimoxazole)
	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

Maxtrex SmPC

Methotrexate BNF

Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax 2008

I agree to participate in this shared care agreement for the treatment of the below named patient with of methotrexate for the treatment of interstitial lung disease

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: