Sussex Community Dermatology Service NHS

EFFECTIVE SHARED CARE AGREEMENT (ESCA)

DRUG NAME: METHOTREXATE

INDICATION/S COVERED: **FOR RHEUMATOLOGY AND DERMATOLOGY**

Coastal West Sussex Traffic Light system classification: Amber

N.B. The eligibility criteria included here apply to new patients commencing treatment under this agreement & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the primary care prescriber

Amber drugs: Prescribing to be initiated by a consultant / specialist but with the potential to transfer to primary care. The expectation is that this agreement should provide sufficient information to enable primary care prescribers to be confident to take clinical and legal responsibility for prescribing these drugs**.**

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care agreement?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this ESCA), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of the final page to the requesting consultant / specialist. Until the requesting consultant / specialist has received a signed copy of the final page indicating that shared care has been agreed all care (including prescribing) remains with the consultant / specialist.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant / specialist within 14 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, which will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your Medicines Management pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The primary care prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

Information

This page should include general information relevant to the specific drug and indication/s. It should include information on the dose of the drug for the indication, cautions, contraindications, common side effects and interactions to look out for. This section should have input from a specialist consultant in the field.

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. **Link to the relevant SPC website**:

http://www.medicines.org.uk/emc/medicine/6003/SPC

2. **Background to use for the indication/s, including licence status**

Licensed indications: Treatment of adult patients with moderate to severe active rheumatoid arthritis, and in patients with psoriatic arthritis who are unresponsive or intolerant to conventional therapy. It is also licensed for use in chronic plaque psoriasis. It has both immunomodulatory and anti-inflammatory effects.

Unlicensed uses include Crohn's disease, inflammatory myositis, SLE and as a steroid-sparing drug in polymyalgia rheumatica and giant cell arteritis, atopic eczema, sarcoidosis, dermatomyositis, scleroderma, pemphigoid, pemphigus, pyoderma

3. **Dose & administration**

Recommended starting dose is 7.5 mg orally **once weekly** and the dose gradually adjusted, according to response. The maximum licensed dose is 20mg **once weekly**; however doses up to 25mg **once weekly** are sometimes prescribed on the advice of a consultant. Therapeutic effects take 4 to 12 weeks to occur. Folic acid should also be given at a minimum dose of 5mg per week **on a different day** to methotrexate. **Dermatology: recommended starting dose 2.5/5/mg orally or subcutaneously once a week, gradually increased up to 20mg once a week, Folic Acid 5mg once a week to 6 days a week except day of methotrexate.**

We recommend prescribing methotrexate **only as 2.5mg tablets.** This avoids patients taking too high a dose e.g. when increasing the dose from 7.5mg to 10mg. It should be noted that 2.5mg and 10mg tablets are similar in appearance and are also similar to folic acid tablets (small yellow). The dose of methotrexate is occasionally split to reduce adverse effects e.g. 5mg on two days per week rather than 10mg once weekly.

Route: Methotrexate is usually administered orally. Tablets are swallowed whole with a glass of water. It is occasionally given by subcutaneous or intramuscular injection, usually using a pre-filled syringe such as Metoject® (see below).

4. **Cautions (including for pregnancy and lactation where relevant)**

- The drug is **teratogenic** and both men and women should take contraceptive precautions for 6 months after stopping. It should be avoided whilst breast-feeding. It may reduce male fertility (maybe reversible after discontinuing therapy)
- Interstitial lung disease
- Acute porphyria
- Localised or systemic infection including hepatitis B or C and history of tuberculosis

5. **Contraindications**

- Pregnancy and lactation
- Severe / significant hepatic or renal impairment (avoid if creatinine clearance <20ml/min)
- Liver disease e.g. cirrhosis, fibrosis, hepatitis
- Severe cases of anaemia, leucopenia, or thrombocytopenia
- Hypersensitivity to methotrexate
- Acute infectious disease, particularly viral
- Overt or laboratory evidence of immunodeficiency syndrome(s)

6. Side effects

Skin: Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary changes, alopecia, ecchymosis, telangiectasia, acne, furunculosis.

Haematopoietic: Bone marrow suppression is most frequently manifested by leucopenia, thrombocytopenia (which are usually reversible) and anaemia, or any combination may occur. Macrocytosis.

Gastrointestinal: Mucositis (most frequently stomatitis although gingivitis, pharyngitis and even enteritis, intestinal ulceration and bleeding) may occur. Nausea, anorexia and vomiting and/or diarrhoea common, but often improve with repeated doses.

Hepatic: Raised liver transaminases, necrosis, fatty infiltration, periportal fibrosis or cirrhosis usually following chronic administration.

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. This effect appears to be reversible after discontinuation of therapy.

Pulmonary System: Infrequently an acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Acute pulmonary oedema has also been reported after oral and intrathecal use. Pulmonary fibrosis is rare. 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. It is not always fully reversible. Pulmonary symptoms (especially a dry, non productive cough) may require interruption of treatment and careful investigation.

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. There have been reports of leucoencephalopathy following intravenous methotrexate in high doses, or low doses following cranial-spinal radiation.

Immunological: Reduced resistance to infection. Also opportunistic infections, particularly herpes zoster. Although very rare, anaphylactic reactions to methotrexate have been reported.

7. Interactions

- Avoid folate antagonist drugs especially co-trimoxazole, trimethoprim and nitrous oxide.
- NSAIDs, salicylates, sulphonamides, phenytoin, hypoglycaemics, diuretics & tetracyclines may increase blood levels of methotrexate. NSAIDs can continue, but monitor U&E closely, esp. in elderly
- Probenecid, penicillins and NSAID reduce renal excretion of methotrexate. Patients stabilised on methotrexate need the dose of methotrexate halved if prescribed penicillins and twice weekly FBC's conducted.
- Low dose aspirin for antiplatelet effect can be continued
- Alcohol intake should be very cautious during treatment with methotrexate and well within national guidelines
- Vitamin preparations containing folic acid or its derivatives may alter response to methotrexate
- Acitretin
- Pyrimethamine
- Clozapine
- Ciclosporin
- Cisplatin
- Leflunomide

8. Criteria for use

As given under licensed and unlicensed indications. Should only be initiated by clinicians experienced in the treatment of chronic inflammatory rheumatic and dermatological disease.

9. Any further information (e.g. supporting therapies)

Folic acid is co-prescribed at a dose of 5mg once weekly, taken on a different day to methotrexate, to reduce adverse effects (particularly gastrointestinal ADR). Occasionally the dose of folic acid is increased to 10mg once weekly or 5mg daily (except the day methotrexate is taken) to improve tolerability of methotrexate. Folic acid tablets are used, although a syrup is also available. Adverse effects to folic acid are very rare, but occasionally gastrointestinal disturbance can occur.

In cases of severe toxicity e.g. pancytopenia or overdose, methotrexate can be reversed by folinic acid rescue (folinic acid 15mg qds IV or PO for 2 days).

Methotrexate by injection is available as a pre-filled syringe Metoject® in doses of 7.5mg to 30mg in 2.5mg increments. This is usually self-administered by the patient once weekly and requires the same monitoring and co-prescription of folic acid as the oral formulation. Metoject® is prescribed only in secondary care by the consultant, using a Central Homecare Ltd prescription. This company provides nurse training for the patient and supplies the drug direct to their home. Very occasionally Metoject® is supplied to GP surgeries for administration by the practice nurse.

10. References

Summary of Product Characteristics – Maxtrex® 2.5mg tablets; Pharmacia Limited (last updated June 2012) http://www.medicines.org.uk/EMC/medicine/6003/SPC/Maxtrex+Tablets+2.5+mg

Chakravarty K *et al*. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatology. *Rheumatology* 2008; 47: 924-5 http://rheumatology.oxfordjournals.org/content/suppl/2008/05/31/kel216a.DC1/kel216b.pdf

11. Information given to patient and their primary care prescriber

INFORMATION TO PATIENTS

The patient will receive a WSHT Rheumatology Shared Care or NPSA Patient Booklet, Arthritis Research UK methotrexate information leaflet and appropriate counselling.

Dermatology patients will receive a shared care NPSA or WSHT patient booklet.

The patient will be informed to contact their primary care prescriber or Hospital Rheumatology Clinic or Dermatology Nurse Specialist immediately if any of the following occur: fever, sore throat, cough, shortness of breath, skin rash or mouth ulcers, unexplained bruising or bleeding.

INFORMATION TO BE RECEIVED BY THE PRIMARY CARE PRESCRIBER FROM THE CONSULTANT

The Consultant's review letter will be sent after initial assessment and following each further appointment.

INFORMATION TO BE RECEIVED BY THE CONSULTANT FROM THE PRIMARY CARE PRESCRIBER

It is recommended that the prescribing of methotrexate by a primary care prescriber should be done under an effective shared care agreement between primary care prescriber and consultant. In the rare event that the primary care prescriber is unwilling to assume prescribing responsibility for the patient the consultant should be informed within 2 weeks of receipt of the consultant's letter. In such cases the primary care prescriber must inform the consultant of all relevant medical information regarding the patient and any changes to the patient's medication regime irrespective of indication.

RESPONSIBILITIES and ROLES

	Consultant / Specialist responsibilities
1	Confirmation of diagnosis and identification of suitable patients
2	Request agreement of shared care with primary care prescriber
3	Initiation of appropriate therapy
4	Discussion of risks and benefits with patients, outline possible side effects
5	To ensure and take responsibility for baseline and ongoing monitoring, act on the results appropriately and communicate these results to the primary care prescriber. **Monitoring requirements and appropriate dose adjustments:** *Before treatment:* Exclude pregnancy Liver Function Tests (LFTs) (including AST / ALT) CXR within 6 months (and consider PFTs with transfer factor in selected patients) Full blood count (FBC) (including differential white blood cell count and platelet count) Electrolytes, including creatinine Dermatology: Procollagen 3, consider HIV test *During treatment: (repeat fortnightly for 6 weeks, then monthly until the disease and dose are stable for 1 yr; monitoring thereafter is based on clinical judgement, typically 3 monthly):* Liver Function Tests (LFTs), including AST/ALT, & Creatinine Full blood count (including differential white blood cell count and platelet count) Dermatology: Procollagen 3 3 monthly if raised over a period of a year may need referral to gastroenterology for possible liver biopsy or fibroscan The consultant will stop, reduce dose, or advise to stop methotrexate treatment if any of the following occur: White blood cell count < 3.5×10^9/l Neutrophils < 2.0×10^9/l Platelets < 150×10^9/l AST / ALT > 2 times normal range MCV > 105fl Unusual bruising or bleeding, sore throat or mouth ulcers Pruritis or rash (rare possibility of Stevens – Johnson syndrome) Significant alopecia, abdominal pain, nausea, diarrhoea, fever or weight loss. Shortness of breath or cough Albumin-unexplained fall (in absence of active disease) Blood tests will be monitored by the Rheumatology/Dermatology team and results fed back to primary care prescribers by letter or fax, together with advised action to continue as before or to adjust or stop prescribing, as necessary. The Rheumatology/Dermatology team will provide patients with blood forms to present to their primary care prescriber/Phlebotomist or hospital Pathology Department for fortnightly blood tests during initiation or 3 monthly as a minimum in patients on stable doses. The Rheumatology/Dermatology team will ensure that the consultants name is on the form and that a copy of the result is sent to the patient's primary care prescriber.
6	Issuing initial prescription(s) until the patient is stabilised (minimum of **ONE month**) and until ESCA is in place
7	Ensure that all newly treated patients (and/or their carers) receive appropriate education and advice regarding their drug therapy and shared care arrangements. This should include written information where appropriate and provision of the NPSA or WSHT methotrexate treatment booklet
8	Providing primary care prescriber with clinic letter stating planned introduction and reviews
9	Provide outpatient reviews, monitor effectiveness/side effects
10	Give a copy of the information sheet to the patient / carer and explain their roles
11	Notify the primary care prescriber of the patient's failure to attend for clinical review or drug monitoring
12	Timely communication with primary care regarding changes in therapy

Primary care prescriber responsibilities	
1	Initial referral to secondary care.
2	To inform the consultant if unwilling to enter into shared-care arrangements.
3	To provide repeat prescriptions once ESCA is agreed and in place and the patient is stabilised (not before initial **ONE month** stabilisation period). A demonstrable system should be in place to ensure that prescribing is reviewed by the primary care prescriber if there is no record of the fact that monitoring has taken place within the agreed time scales.
4	To record any changes in therapy in the prescribing record on receipt of such communication from secondary care.
5	To monitor patients overall health and well-being and to report any adverse drug reactions or interactions to secondary care.
6	Liaise with Rheumatology/Dermatology if any cause for concern or drug discontinued.
7	To provide a copy of this ESCA to the patient to ensure that they are familiar with all roles and responsibilities
8	To review the appropriateness of prescribing for patients who have not been seen by a specialist for over 6 months.

Patient's / Carer's role	
1	Ask the rheumatologist/dermatologist or primary care prescriber for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with methotrexate.
3	Tell the rheumatologist/dermatologist or primary care prescriber of any other medication being taken, including over-the-counter products.
4	Read the patient information leaflet included with the medication and report any side effects or concerns to the rheumatologist or primary care prescriber.
5	Arrange blood tests as per rheumatologist/dermatologist request
6	Report to their GP/specialist any symptoms described in patient methotrexate booklet.

BACK-UP ADVICE AND SUPPORT

	Name / position	Telephone	Email
Medicine Management Lead:	Dr Andrew Morris Consultant Dermatologist	For further information & advice, please contact Grace Hancock (Assistant Service Manager): 01903 703281	grace.hancock@nhs.net
Hospital Pharmacy:	Worthing Hospital St Richards Hospital	01903 205 111, ext 5698 01243 788 122, ext 3347	pharmacy@wsht.nhs.uk
Out of hours (e.g. medical team on call):	On call physicians On call	Bleep 118 or 119 01903 205 111	

Version History			
Document Name:		Methotrexate	
Document Type:		Effective Shared Care Agreement	
Relevant to:		All primary care prescribers working within Coastal West Sussex and all relevant clinicians at Western Sussex Hospitals NHS Trust.	
Version No.	Date	Author of original development or review	Details of document development
1	June 2008	Julie Sadler, Prescribing Support Pharmacist	Original development
2	05/10/12	Gloria Omisakin, Medicines Management Pharmacist	Full review and re-draft
3	30/11/12	Gloria Omisakin, Medicines Management Pharmacist	Re-draft to include dermatological indications
5	01/08/14	Chris Emerson	Modified for use within Sussex Community Dermatology Service

Approval for organisational use	
ESCA authorised for use in Coastal West Sussex by	**Medicine Management Lead:** Dr Andrew Morris

EFFECTIVE SHARED CARE AGREEMENT (ESCA)

DRUG NAME: METHOTREXATE
INDICATION: **FOR RHEUMATOLOGY AND DERMATOLOGY**

Agreement for transfer of prescribing to PRIMARY CARE PRESCRIBER

Patient details:

Name:

Address:

DoB:

NHS No:

Hospital No:

Drug name and dose:

The following tests and investigations have been carried out:
Details of Tests:

Date treatment initiated:

At the last patient review the drug appeared to be effectively controlling symptoms / providing benefit:
Yes/No

The patients has now been stabilised on a dose of:

I will arrange to review this patient regularly. Date of next clinic appointment:

Title of specialist:
Name:
Department:
Hospital Address:

Contact Number:

Primary care prescriber:
Address:

Contact Number:

Main Carer:
Contact Number:

Key worker if appropriate:
Contact Number:

Agreement to shared care, to be signed by primary care prescriber and Medicine Management Lead:

Medicine Management Lead signature:

Date:

Primary care prescriber signature:

Date:

If shared care is agreed and the primary care prescriber has signed above please return a copy of this page to the requesting consultant or alternatively fax to: 01903 340849