These guidelines should be used in conjunction with the METHOTREXATE Summary of Product Characteristics (SmPC) and the recommendations of the rheumatology consultant.

BACKGROUND AND PHARMACOLOGY
METHOTREXATE decreases the immune response in rheumatoid arthritis and other inflammatory conditions. Recommended starting dose is between 5mg and 15mg ORALLY once per week (this should be on the same day each week) and the dose is adjusted, according to response, up to a maximum of 30 mg per week. Therapeutic effects take 4 to 12 weeks to occur. Folic Acid should also be given at a dose of 5mg per week on the day after the METHOTREXATE.

METHOTREXATE SHOULD ONLY BE PRESCRIBED AS 2.5 MG TABLETS (THIS AVOIDS CONFUSION BETWEEN 2.5 MG AND 10 MG TABLETS WHICH LOOK SIMILAR)

METHOTREXATE INJECTIONS
Occasional patients will be changed from oral METHOTREXATE to METOJECT (METHOTREXATE sub cutaneous injections) because of gastric intolerance or suspected poor bioavailability. Patients will be taught how to self administer these injections over a two to four week period by the nurses on the chemotherapy suite (ESH) or the nurses on Comet ward (Crawley Hospital). METOJECT _will thereafter be prescribed and monitored by their GP. The monitoring of METOJECT is exactly the same as that of oral METHOTREXATE. However, if a patient is swapped from a stable dose of oral METHOTREXATE to METOJECT then, this is counted as a “dose increase”. Patients will need fortnightly monitoring for 6 weeks and then monthly monitoring for a couple of months before resuming two monthly monitoring. Patients will also need to be provided with a sharps bin suitable for the disposal of “cytotoxic waste”. There will need to be a clear pathway for the disposal of this waste (please contact local area pharmacy advisor for help with this). All other precautions are the same as for oral METHOTREXATE.

INDICATIONS
METHOTREXATE is indicated for the treatment of patients with active rheumatoid arthritis and psoriatic arthritis as a disease modifying anti-rheumatic drug (DMARD) and in the control of connective tissue diseases and vasculitis.
### AREAS OF RESPONSIBILITY

#### GP responsibilities

1. Initial referral to secondary care.
2. To inform the consultant if unwilling to enter into shared-care arrangements according to the LES.
3. To provide prescriptions. A demonstrable system should be in place to ensure that prescribing is reviewed by the GP 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. To review the appropriateness of prescribing for patients who have not been seen by a specialist for over 12 months.

#### Consultant responsibilities

1. Confirmation of diagnosis.
2. Recommends appropriate therapy.
3. To ensure that all newly treated patients (and/or their carers) receive appropriate education and advice regarding their drug therapy. This should include written information and the purple NPSA booklet.
4. To ensure and take responsibility for baseline investigations and advise on future problems appropriately.
5. Timely communication with primary care regarding changes in therapy. Changes of METHOTREXATE dose should be recorded in the purple NPSA booklet carried by the patient.
6. Clinical review and to report any adverse drug reactions or interactions to primary care.
7. Notify the GP of the patient's failure to attend for clinical review

#### Patient responsibilities

1. To attend appointments and organize blood tests as advised.
2. To inform the GP if health problems arise
3. To be aware of side effects and report any relevant symptoms
4. To carry the purple NPSA booklet and ensure that changes of METHOTREXATE dose and dates of blood test results are entered into this.
5. To show the purple NPSA booklet to community pharmacist

### DOSAGE AND ADMINISTRATION

**Route:** Oral. Tablets are swallowed whole with a glass of water  
**Dose:** 5-15 mg one day per week (AS 2.5MG TABLETS) increasing slowly to 30 mg per week depending on response.

Reduce dose in renal impairment. Avoid in severe impairment (refer BNF).

### INFORMATION TO PATIENTS

The patient will receive a purple NPSA METHOTREXATE booklet, METHOTREXATE information leaflet from the Arthritis Research Council (via hospital clinic) and appropriate counselling. The patient will be asked to contact their GP or rheumatology consultant immediately if any of the following occur: fever, sore throat, cough, shortness of breath, diarrhoea, skin rash or mouth ulcers, unexplained bruising or bleeding.
BASELINE DATA AND ROUTINE MONITORING

<table>
<thead>
<tr>
<th>Monitoring criteria</th>
<th>Responsibility: CONSULTANT</th>
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<tbody>
<tr>
<td>Before Treatment</td>
<td>Exclude pregnancy</td>
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<tr>
<td></td>
<td>Liver Function Tests (LFTs) (including AST / ALT)</td>
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<td></td>
<td>Chest X-ray</td>
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<td></td>
<td>FBC</td>
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<td>U &amp; Es and Renal Function</td>
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**Pharmacist screening and Pre-Treatment assessment:**

- **Every TWO weeks**: FBC, LFTs, U&Es & Renal Function
- **Until 6 weeks after last dose increase**, thereafter
- (if no problems) once **every two months**

Note: ESR and/or CRP will be monitored 2 monthly by GP/ Rheumatology Team

The prescribing doctor will stop METHOTREXATE treatment (and discuss with Rheumatologist) if any of the following occur:

- White blood cell count < 3.5x 10^9/l
- Neutrophils ≤ 1.5 x 10^9/l
- Platelets < 150 x 10^9/l
- ALT > 3 x ULN
- *(CrCl (ml/min) >50 : Give 100% dose)*
- *(D/W consultant) 20-50 : Give 50% dose (moderate renal impairment))*
- <20 : Avoid (severe renal impairment)

- Albumin – unexpected fall in the absence of active disease
- Rash or oral ulceration, nausea and vomiting, diarrhoea
- New or increasing dyspnoea or dry cough
- MCV > 105 fl (check B12, folate, TSH)
- Severe sore throat, abnormal bruising (check immediate FBC)

**ADVERSE EFFECTS** – see Statement of Product Characteristics for details:

- Photosensitivity, marrow suppression, GI disturbances, hepatic dysfunction, infertility, teratogenicity, pulmonary toxicity, renal failure (rare).
- Patients with known allergy to Methotrexate should not receive the drug.

**CONTRA-INDICATIONS**

The drug is teratogenic and both men and women must take contraceptive precautions during treatment and for 3-6 months after stopping. It must be avoided whilst breast feeding. It may reduce male fertility.

**DRUG INTERACTIONS** – see Statement of Product Characteristics for details

- Avoid folate antagonist drugs especially **Co-trimoxazole and Trimethoprim**.
- NSAID’s and aspirin used concurrently are not contraindicated but may increase toxicity.
- Alcohol should ideally be reduced to three units per week during treatment with METHOTREXATE
VACCINATION ADVICE

1. Patients receiving METHOTREXATE must not receive immunizations with live vaccines. Inactivated polio is available although suboptimal response may be seen.
2. Pneumovax and annual flu vaccine is recommended
3. In patients receiving METHOTREXATE exposed to chicken pox or shingles (who have not had prior exposure to these viruses), passive immunisation should be carried out using VZIG. The Herpes Zoster immunoglobulins can be obtained from the Health Protection Agency tel: 020 8200 6868

INFORMATION TO BE RECEIVED BY THE GP FROM THE CONSULTANT
The consultant’s review letter will be sent after initial assessment and following each further appointment. If a GP needs to contact the Consultant for advice about a patient’s METHOTREXATE the call should be returned whenever possible within 24 hours.

INFORMATION TO BE RECEIVED BY THE CONSULTANT FROM THE GP
Recent NPSA guidance suggests shared care between specialist clinic and GP. In the rare event that the GP is unwilling to assume prescribing responsibility for the patient the consultant should be informed within 1 week of receipt of the consultant’s letter. In such cases the GP must inform the consultant of all relevant medical information regarding the patient and any changes to the patient’s medication regime irrespective of indication.

THE GP SHOULD INFORM THE CONSULTANT OF ANY ADVERSE EFFECTS EXPERIENCED BY THE PATIENT. LIKEWISE THE CONSULTANT SHOULD INFORM THE GP OF ANY ADVERSE EFFECTS EXPERIENCED BY THE PATIENT.

CONTACT NAMES AND DETAILS:
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DThomas / L Abudy, Rheumatology Nurse Specialist, East Surrey Hospital ext 2118 / 1798

Support groups and information websites
Arthritis Research Campaign www.arc.org.uk
Arthritis Care www.arthritiscare.org.uk
NRAS www.rheumatoid.org.uk
BSR www.rheumatology.org.uk

Approved by
Dr Patrick Kerr
Lead of East Surrey Clinical Governance Group
Date of guidance 31.3.09
Date Reviewed: January 2014

Dr Sian Griffith
Consultant Rheumatologist
Surrey and Sussex Healthcare NHS Trust
Date Reviewed: December 2015

METHOTREXATE Shared Care Guideline
4
Date of Guidance: March 2009
Next Review: January 2018