SHARED CARE GUIDELINES FOR THE PRESCRIBING OF LOW DOSE ORAL AND SUBCUTANEOUS METHOTREXATE FOR RHEUMATOID ARTHRITIS

INDICATION

This shared care guideline has been prepared to support healthcare professionals in the implementation of shared care management of patients who have been prescribed methotrexate for the treatment of rheumatoid arthritis.

Methotrexate can be used as sole therapy on in combination with other disease modifying drugs (DMARDS). Regular folic acid supplementation is considered to reduce the likelihood of methotrexate toxicity. It is therefore recommended that individuals are co-prescribed folic acid. The exact regime will vary from patient to patient but it should be noted that patients should not take their folic acid on the same day as they take their methotrexate.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of methotrexate can be shared between the rheumatology 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 GP is required to inform the rheumatology specialist, in writing, that they do not wish to participate in shared care and, in this instance, total clinical responsibility for the patient for the diagnosed condition will remain with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the specialist team initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

Shared care is only appropriate if it provides the optimum solution for the patient.

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

Specialist Responsibilities	
1	To assess the patient and establish/confirm the diagnosis,
2	To determine a management strategy and ensure appropriate follow-up in conjunction with the GP
3	To initiate methotrexate treatment including: • Ensuring the suitability of the patient for methotrexate treatment including performing all relevant pre-treatment assessments (baseline chest x-ray, blood tests to include: FBC, LFTs, U&Es and pregnancy screen if appropriate) • Discussing and agreeing the management strategy with the patient including: o informing them of possible side-effects to the treatment and ensuring they are aware of who to contact in this instance o ensuring they understand the once weekly dosage instructions of both methotrexate (always prescribed as multiples of 2.5mg tablets or subcut injection) and folic acid and the importance of using effective contraception o issuing a patient held monitoring and dosage booklet in accordance with the National Patient Safety Agency requirements • Prescribing at least the first 28 days of methotrexate • Ensuring the patient understands the proposed plan for follow-up Writing to the patient's GP advising them of the treatment commenced, including appropriate prescribing information, dosing increments, the intention to 'share care' unless the specialist team are informed otherwise, ongoing blood monitoring requirements (including who is responsible for checking the results) and arrangements for follow-up.
4	To be available for advice if the patient's condition changes and to arrange for the

	patient to be followed up in the rheumatology out-patient clinic as necessary.

General Practitioner Responsibilities	
1	To confirm in writing, without delay, if they do not wish to participate in shared care.
2	After initial 28 day supply, to continue to supply methotrexate as per dose specified by specialist team
3	To prevent ongoing prescription of methotrexate if patient is not compliant with blood testing
4	To ensure practice system is in place to recall patient for monitoring blood tests where relevant unless the GP is assured that secondary care have a recall system in place.
5	To monitor side effects/complications of treatment and seek advice from the specialist team as necessary
6	To deal with general health issues of the patient.
7	To check for possible drug interactions when newly prescribing concurrent medications (in particular other folate antagonists such as trimethoprim or co-trimoxazole)

Patient's role (or that of carer)	
1	To report to the specialist or GP if he/she does not have a clear understanding of the treatment and to report any concerns
2	To attend appropriate hospital and GP appointments
3	To have required monitoring/tests carried out at regular intervals
4	To report any adverse events to the doctor who is prescribing their treatment
5	To read the drug information given to them and to bring their monitoring and dosage booklet to the out-patient rheumatology clinic
6	To take responsibility for appropriate contraceptive precautions
7	To restrict alcohol intake as advised in the patient information literature

Role of community pharmacist	
1	Ensure that dispensing is in accordance with the safe dispensing practice checklist in the NPSA Alert.
2	Provide patients with information about methotrexate and ensure access to medicines management support to encourage concordance, where appropriate through a Medication Use Review.

SUPPORTING INFORMATION

Dosage and Administration

NB: Only multiples of 2.5mg tablets or pre-filled, pre-dosed syringes (Ebetrex® or Metoject®) are considered appropriate for prescribing in accordance with NPSA Alert from June 2006 and local guidance and formulary.

Dosage adjustments in specific populations

Dosage and rate of dose increments will vary from patient to patient. This will therefore be advised by the specialist team. The usual range is between 7.5mg once weekly and 25mg once weekly.

Contraindications

On account of teratogenic effects, methotrexate is contraindicated in conception, pregnancy and breastfeeding. Contraception is therefore mandatory in both men and women of childbearing age and must be continued for at least 6 months after stopping treatment.

Methotrexate is contraindicated for those with severe renal or hepatic impairment.

Special warnings
Methotrexate should be used with caution in those with underlying pulmonary disease and the prescribing physician should be specifically alerted to the potential for methotrexate induced adverse effects on the pulmonary system.

Extreme caution should be exercised in patients with haematological depression.
Extreme caution should be exercised in patients with a history of liver disease or who are at high risk of liver disease. The patient should be advised that excess alcohol should be avoided.

Caution is also needed in the presence of inactive, chronic infections (e.g. herpes zoster, tuberculosis, hepatitis B or C) due to possible activation.

Cotrimoxazole, trimethoprim and other folate anatagonists must not be prescribed for patients taking methotrexate.

Live vaccines are contraindicated for patients taking methotrexate. However, the annual flu and pneumonia vaccination **should** be given.

NSAIDs in addition to the above doses of methotrexate are **not** contraindicated. However, patients should be advised to avoid self-medication with OTC aspirin or ibuprofen.

Side Effects
Common side effects include: nausea, mouth ulcers and headaches, mild to moderate derangement of LFTs, alopecia. These side effects can usually be ameliorated by increasing the folic acid dose or switching to sub cutaneous administration.

Rare but serious side effects include: Methotrexate induced lung disease. This 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 including repeat chest x-ray in the first instance. Hepatic toxicity resulting in significant elevations of liver enzymes (in particular ALT >3x upper limit of normal range).
Pancytopaenia, leucopoenia, thrombocytopenia can occur. These are usually reversible, however, prompt action is necessary.

This list is not exhaustive – the manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary (BNF) should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

Monitoring
Blood monitoring incorporating FBC, LFTs and ESR/CRP should be performed fortnightly for the first 8 weeks of treatment or until the maximum dose recommended by the specialist has been achieved. Thereafter, blood monitoring can be performed monthly. In the case of a subsequent increase in dose, a blood test should be performed after 2 weeks. Providing this is satisfactory, monthly blood tests can be resumed thereafter.
Where patients are stable on treatment and monitoring results have been satisfactory for 12 months, FBC, LFTs and ESR/CRP can be performed every 2-3 months.
U&Es should be monitored every 3/6 months.

References
1. NPSA Alert June 2006
2. NPSA Patient-held blood monitoring and dosage record booklet for methotrexate

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