

Methotrexate Shared Care Agreement

Introduction

Rheumatoid Arthritis (RA) is a chronic, incurable, progressive inflammatory disease of the synovial lining of peripheral joints. The goals of management of RA are to relieve pain and inflammation, to prevent joint destruction and to preserve or improve a patients function. First-line treatment starts with simple analgesics and/or non-steroidal anti-inflammatory drugs (NSAIDs) but since they do not affect disease progression, slow-acting disease modifying anti-rheumatic drugs (DMARDs) are added at increasingly early stages of the disease to suppress the processes responsible for the chronic inflammation of RA.

Therapeutic Use

Methotrexate is an anti-metabolite cytotoxic drug which inhibits DNA synthesis and cellular replication. It belongs to the group of DMARDs alongside gold, penicillamine, hydroxychloroquine, azathioprine, leflunomide, and sulphasalazine.

Two large meta-analyses favourably compared the efficacy and safety of methotrexate with other DMARDs and showed that efficacy is maintained with up to 5 years treatment.

Criteria for Patient Selection for Methotrexate therapy

Patients with acute, classical or definite rheumatoid arthritis who are unresponsive or intolerant to conventional therapy with analgesics or NSAIDs and require ongoing drug management.

Presentation and Availability

Tablets in strengths 2.5mg and 10mg-(only the 2.5mg is licensed for rheumatoid arthritis).

[NB: Methotrexate is also available as injection and there is a Regional IM policy for administration by specified District Nurses for those patients who cannot tolerate oral dosing. Methotrexate can also be given by the subcutaneous route if requested by the clinic team.]

Dosage and Administration

The doses of Methotrexate used are 2.5-7.5mg orally once weekly increased to 15-20mg (max 25mg) weekly depending on patient response. All increases and dose adjustments will be done in Out-patients unless directions have been specified in the medical letter to the GP.

Folic acid 5mg once a week (on a different day to methotrexate) should be co-prescribed to minimise the risk of minor effects.

Side-Effects

Common non-life threatening adverse effects of low-dose methotrexate mainly affect the gastrointestinal system (nausea, diarrhoea, and stomatitis), and the central nervous system (headaches, drowsiness and blurred vision).

Serious effects include hepatic, pulmonary, and bone-marrow toxicity, and can occur acutely at any time during therapy.

If a serious reaction is suspected: stop the drug, check tests and contact Rheumatology team for advice and/or review.

Guidance for Women of child-bearing age

Methotrexate is teratogenic and female patients of child-bearing age should be prescribed or offered contraception.

If a patient wishes to start a family, it is advised that they stop the methotrexate for 3 to 6 months before conception.

Drug Interactions

NSAIDs and salicyclates can reduce excretion of methotrexate, and although it is advised not to use these drugs together, the Rheumatology department have many years experience of co-prescribing these drugs without additional problems, as the majority of patients will still need an anti-inflammatory agent. Monitoring would continue as normal.

Cyclosporin can increase methotrexate toxicity and the dept will co-prescribe these drugs, but the majority of those patients will be monitored by the Rheumatology Nurse Specialist.

Other interactions which can increase toxicity are co-trimoxazole, trimethoprim, sulphonamides, penicillin, acitretin, and probenecid. Concomitant alcohol consumption may increase the risk of liver damage.

Monitoring

FBC and platelets should be tested monthly and LFTs tested every 3 months; these should be performed in the primary care setting. Bloods will also be checked at every out-patient appointment.

If one or more of the following changes are seen in the results, the dose should be withheld and the situation discussed with the Rheumatology Department:-

WBC $<3.0 \times 10^9$ E/L Platelets $<100 \times 10^9$ E/L AST or Alk Phos > 2 fold rise

Cost

At current prices, one years treatment with methotrexate 15mg/weekly costs approximately £35.60 per year.

Aspects of Care for which Hospital Responsible

- Initiation of methotrexate treatment
- Initial tests at discretion of medical team
- Guidance to GP of time scale of treatment, doses, action if abnormal result
- Regular out-patient appointments to monitor progress
 - * 3 monthly till patients stabilised then every 6 months
- Reporting of adverse effects to CSM
- Rheumatology Nurse Specialist for patient contact

Aspects of Care for which GP Responsible

- Prescribing of methotrexate
- Monitoring FBC, platelets and LFTs ensuring they are within guided ranges, and entering results in the patients Shared Care Booklet supplied by the Rheumatology Department
- Reporting adverse events to the Consultant and CSM
- Reporting to and seeking advice from the consultant and/or specialist nurse on any aspect of patient care which is of concern to the GP and may affect disease treatment

*****Recommendation to GP*****

It is advised that due to the cytotoxic nature and once weekly dosing of this drug, that prescriptions for Methotrexate should not be issued by the computer repeat system, but should be handwritten by the prescribers themselves. The prescription can then be issued when the patient attends for their blood test.

Aspects of Care for which the Patient is responsible

- Reporting of any side-effects to their GP whilst taking Methotrexate
- Informing their GP and Consultant of any other medication they may be taking including OTC products
- To ensure they have a clear understanding of their treatment

Availability of Back-up Advice and Support

Walsall Manor Hospital	01922-721172
Dr Constable	ext. 6337 or bleep/mobile through switchboard
Vicki Oakley - answerphone checked regularly (If answerphone message states Vicki on annual leave for more than 3 days, please ring secretary on 6337)	ext. 7318
Drug Information Service/Interface Pharmacist	01922-656610

These guidelines have been written in collaboration by the Walsall Manor Hospital NHS Trust Rheumatology Department and Pharmacy Department, and approved by Walsall Health Authority, Local Medical Committee, and Walsall Primary Care Groups.

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Other Useful Contacts

Arthritis Care
18 Stephenson Way
London
NW1 2HD
0171-9161500

Arthritis Research Campaign
Copeman House
St. Mary's Court
St. Mary's Gate
Chesterfield
S41 7TO

References

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Felson, DT, Anderson, JT, & Meena, RF. Use of short-term efficacy/toxicity trade off's to select second-line drugs in rheumatoid arthritis: A meta-analysis of published clinical trials. *Arthritis Rheum* 1992;35(10):1117-1125.
Weinblatt, ME, Kaplan, H, Germain, BF et al. Methotrexate in rheumatoid arthritis: A five year prospective multicentre study. *Arthritis Rheum* 1994;37:1492-1498.
ABPI Data Sheet Compendium 1999-2000