SHARED CARE AGREEMENT: METHOTREXATE S/C

NHS GREATER GLASGOW AND CLYDE

NB: This document should be read in conjunction with the current Summary of Product Characteristics (SPC) and BSR Guideline for disease-modifying anti-rheumatic drug (DMARD) therapy
(available at www.rheumatology.org.uk/resources/guidelines/bsr_guidelines.aspx)

DRUG AND INDICATION:

Generic drug name:	**Methotrexate**
Formulations:	**Metoject® Pre-filled Syringe 50mg/ml for Subcutaneous injection**
Intended indication:	**Adult Patients with Rheumatoid Arthritis, Severe Psoriatic Arthritis, Severe Active Juvenile Idiopathic Arthritis (age 3 to 16 years old)**
Status of medicine or treatment:	Licensed indication for licensed medicine

RESPONSIBILITIES OF ACUTE CARE/SPECIALIST SERVICE (CONSULTANT):

- Undertake baseline investigations/monitoring and initiate treatment
- Dose adjustments
- If appropriate, ensure that the patient has an adequate supply of medication (usually minimum of 28 days, but local variations may apply) until the shared care arrangement are in place

Acute care/specialist service will provide the GP with:

- An initiation letter (which includes diagnosis, relevant clinical information, baseline results, treatment to date, treatment plan, duration of treatment before consultant review)
- Details of outpatient consultations, ideally within 14 days of seeing the patient
- A standard NHS GGC communication sheet ' Metoject PEN® (Methotrexate) Injection for Self Administration' will be sent from secondary care to the GP

Acute care will provide the patient with relevant drug information to enable:

- Informed consent to therapy
- Understanding of potential side effects and appropriate action
- Understanding of the role of monitoring
- Monitoring booklet where appropriate

RESPONSIBILITIES OF ACUTE CARE/SPECIALIST SERVICE (SPECIALIST NURSE):

- Training of patient in administration of methotrexate by the subcutaneous route
- Education of the patient on importance of monitoring
- Specialist advice during therapy when required by patient including appropriate referral back to medical staff when required.
- Training of patient to deal with spillage and disposal of injections.
- A Patient Information Booklet will be provided to the patient, and discussed with the Specialist Nurse.

RESPONSIBILITIES OF PRIMARY CARE (GENERAL PRACTITIONER):

- To monitor and prescribe in collaboration with the specialist according to this agreement
- To ensure that the monitoring and dosage record is kept up to date
- Symptoms or results are appropriately actioned, recorded and communicated to acute care when necessary

Provision of near-patient testing is in accordance with the service outline of the GMS contract

RESPONSIBILITIES OF PATIENT:

- To attend hospital and GP clinic appointments and bring monitoring booklet (if issued)
- Failure to attend appointments will result in medication being stopped
- To report adverse effects to their specialist or GP

ADDITIONAL RESPONSIBILITIES:

- Any serious reaction to an established drug should be reported to the CHM

CAUTIONS:

- Renal Impairment
- Hepatic Impairment
- Patients with third distribution space (e.g. pleural effusions, ascites)

CONTRAINDICATIONS:

Relative

- Liver insufficiency
- Alcohol abuse
- Pre-existing blood dyscrasias (Note - Anaemia and lymphopenia is not uncommon in this patient group and may not exclude the patient from treatment.)
- Ulcers of the oral cavity or active gastrointestinal ulcer disease. (Many patients have a history of ulceration due to methotrexate, both s/c and oral or gastrointestinal ulcer disease, due to NSAID use – this may not exclude them from treatment or may require increased folic acid dosages – see Undesirable Effects.)

Absolute

- Hypersensitivity to methotrexate
- Serious acute or chronic infection (e.g. TB, HIV or other immunodeficiency syndromes)
- Pregnancy and breast feeding
- Concurrent vaccination with live vaccines
- Severe renal insufficiency (Creatinine Clearance less than 20ml/min)

TYPICAL DOSAGE REGIMENS:

Route of administration:	Subcutaneous injection
Recommended starting dose:	Will vary - recommended initial dose 7.5mg once weekly, or for direct switch from oral because of inefficacy, then 15mg/wk. For toxicity, starting dose will probably depend on dose tolerated orally
Titration of dose:	May not need to be titrated, but where started at less than 10mg/wk, increments of 5mg every month-6 weeks
Maximum dose:	There is evidence that escalating beyond 15mg/wk may not increase efficacy, but 20-25mg not infrequently used
Adjunctive treatment regimen:	May be on NSAIDs, other DMARDs, analgesics. Occasionally patients still require anti-emetics for post-dose nausea. Folic acid should be prescribed for all patients, the commonest regimes are 5mg once a week (typically 3-4 days after methotrexate) or 5mg 6 days per week excluding the day of methotrexate.
Conditions requiring dose adjustment:	Renal impairment
Usual response time:	6-12 weeks
Duration of treatment	Indefinite

All dose adjustments will be done in acute care unless directions have been specified in a medical letter to the GP

SIGNIFICANT DRUG INTERACTIONS:

- Trimethoprim - avoid - increased risk of haematological toxicity
- Co-trimoxazole – avoid - increased risk of haematological toxicity
- NSAID's – avoid over the counter medications (use with prescribed NSAID's safe if methotrexate for above indications monitored correctly)
- Clozapine – avoid - increased risk of agranulocytosis
- Ciclosporin – risk of toxicity when given with methotrexate
- Leflunomide – risk of toxicity when given with methotrexate
- Probenecid – excretion of methotrexate reduced
- Acitretin – plasma concentration of methotrexate increased and increased risk of liver toxicity
- Cisplatin – Increased pulmonary toxicity
- Pyrimethamine – Antifolate activity of methotrexate increased

UNDESIRABLE EFFECTS:

- The following list should not be considered exhaustive. For further documented ADRs and details of likelihood etc, see Summary of Product Characteristics or BNF.

- Methotrexate has been shown to be teratogenic to humans. In women of child-bearing age, any existing pregnancy must be excluded with certainty by taking appropriate measures, e.g. pregnancy test, prior to initiating therapy. Patients of a sexually mature age (women and men) must use effective contraception during treatment with methotrexate and at least 6 months thereafter

ADR details (where possible indicate if common, rare or serious)	Management of ADR
Nausea – very common	Use of antiemetics where necessary, discuss with specialist team
Stomatitis – very common Oral Ulcers – common	Prophylactic folic acid 5mg should be given up to 6 times per week (avoid on day of methotrexate) discuss with specialist team if occurs
Elevated transaminases – very common	If over 2xULN then withhold and discuss with specialist team
Thrombocytopenia, leucopenia, anaemia	If WCC <4.0x10^9/L or Neutrophils<2.0x10^9/L or Platelets<150x10^9/L then withhold and discuss with specialist team
Dyspnoea – new or increasing or dry cough	Withhold and discuss urgently with specialist team
Severe sore throat or abnormal bruising	Immediate FBC and withhold until result of FBC available

BASELINE INVESTIGATIONS:

- Baseline investigation should have been completed for the initiation of oral methotrexate. If patient has not been on oral methotrexate then :-
- FBC,U&E's,LFT's and CXR (unless previous CXR within 6 months).
- Pulmonary function tests in selected patients (see BSR guidelines)

MONITORING (PRIMARY CARE):

- The following monitoring is to be undertaken in Primary Care

Monitoring Parameters	Frequency	Laboratory results	Action to be taken
FBC	2 weekly until dose stable for 6 weeks then monthly until dose stable for 1 year then based on clinical judgement	WCC Neutrophils Platelets	WCC<4.0x10^9/L Neutrophils<2.0x10^9/L Platelets<150x10^9/L Withhold and discuss with specialist team
U&E's		Mild to moderate (CKD stage 2 or 3)	Withhold and discuss with specialist team. Please weigh patient and report weight when seeking advice for accurate calculation of creatinine clearance.
LFT's		ALT AST Albumin	ALT,AST more than twice upper limit of normal Unexplained drop in albumin without active disease Withhold and discuss with specialist team

MONITORING (ACUTE SECTOR):

- The following monitoring is to be undertaken in Acute Care

Monitoring Parameters	Frequency	Laboratory results	Action to be taken
DAS 28 or DAS-44	Dependent on stage of therapy	ESR or CRP (used in DAS score)	Dosage adjustment or escalation to anti TNF therapy according to BSR guidelines
Review of primary care monitoring	Dependent on stage of therapy	FBC, LFT's, U+E's	May include dosage reduction, withholding or cessation of therapy.

PHARMACEUTICAL ASPECTS:

- Sharps containers will be supplied by secondary care at patient's clinic appointments or when a full box is presented. These should be returned to secondary care when full for disposal in line with previous processes. This process will be discussed with the patient during injection training by the specialist nursing staff.
- Methotrexate is a cytotoxic drug, however, in line with the current RCN guidelines (2nd edition, 2013) on subcutaneous methotrexate administration it is unnecessary to treat it as such due to the very small volumes involved. Guidance on spillage should also be referred to this document.

COST:

PLEASE NOTE: All medicines included in a shared care agreement that meet the criteria for a "high cost expensive medicine" and are prescribed in accordance with the shared care agreement are automatically accounted for in the "high cost/ expensive medicines list" for budget-setting purposes. No additional action is therefore required by GPs to request funding. For those medicines which are the subject of a shared care agreement but which do not meet the high cost expensive medicines criteria, transfer of prescribing costs will be considered if this is appropriate.

- Based on a dose 15mg/week £ 862 pa (BNF 69)

INFORMATION FOR COMMUNITY PHARMACIST:

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION:

Name	Designation	Acute Site	Department phone number
Dr Anne McEntegart	Consultant Rheumatologist, Clinical Lead Rheumatology Managed Clinical Network	Glasgow Royal Infirmary	0141 800 1908
Dr David McCarey	Consultant Rheumatologist, North	Glasgow Royal Infirmary	0141 211 4965
Dr David Crosbie	Consultant Rheumatologist, South	Queen Elizabeth University Hospital	0141 451 6170
Dr David Marshall	Consultant Rheumatologist, Clyde	Inverclyde Royal Hospital	01475 505106
Robert Puckett	Lead Clinical Pharmacist for Medical Specialities	Queen Elizabeth University Hospital	0141 452 5701

- Contact details for suitable persons within acute care to get further information from (including the likely consultants who will be initiating the treatment)
- All departments involved in the use of s/c methotrexate for rheumatology patients issue the patient with a card with contact details of the medical staff, specialist nurses and other staff involved in their care, including emergency advice.

SUPPORTING DOCUMENTATION:

- Patient information leaflet
- Standard NGS GGC communication sheet ' Metoject PEN® (Methotrexate) Injection for Self Administration'
- Administering subcutaneous methotrexate for inflammatory arthritis RCN guidance 2nd edition 2013 available at http://www.rcn.org.uk/__data/assets/pdf_file/0006/513339/004377.pdf