SHARED CARE AGREEMENT: METHOTREXATE S/C (RHEUMATOLOGY)

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 https://www.rheumatology.org.uk/practice-quality/guidelines/)

DRUG AND INDICATION:

Generic drug name:	**Methotrexate**
Formulations:	**Metoject® PEN 50mg/ml for Subcutaneous injection** **Methofill® Pre-filled Injector 50mg/ml for Subcutaneous injection** **Nordimet® Pre-filled Pen 25mg/ml for Subcutaneous injection**
Intended indication:	**Adult Patients with Rheumatoid Arthritis, Severe Psoriatic Arthritis**
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 arrangements are in place.
- Counsel patients on pregnancy prevention during treatment and for at least 6 months thereafter.

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 ' 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 (or training of family member/ carer).
- 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/ PARENT/ CARER:

- 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).
- Acute infections – withhold methotrexate until resolved.

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 – usual recommended initial dose 10mg – 15mg once weekly, 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 six 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 – monthly monitoring required.
- 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.

Please note this list is not exhaustive, for further details of drug interactions, see BNF or Summary of Product Characteristics.

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 ALT, AST >100u/L then withhold and discuss with specialist team.
Thrombocytopenia, leucopenia, anaemia, eosinophilia	If WCC <3.5x10^9/L or Neutrophils<1.6x10^9/L or Platelets<140x10^9/L or unexplained eosinophilia >0.5x10^9/L then withhold and discuss with specialist team
MCV	If MCV >105fl 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 when on stable dose – monthly for 3 months then thereafter at least every 12 weeks. For dose adjustments – 2 weekly until dose stable for 6 weeks then revert to previous schedule. If on concomitant leflunomide treatment then monthly monitoring required.	WCC Neutrophils Platelets Eosinophils MCV	WCC<3.5x10^9/L Neutrophils<1.6x10^9/L Platelets<140x10^9/L Unexplained eosinophilia - eosinophils >0.5x10^9/L MCV>105fl Withhold and discuss with specialist team
U&E's		Mild to moderate Creatinine increased by >30% in one year, or eGFR decreased to <50ml/min	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 >100u/L Unexplained drop in albumin <30g/L without active disease Withhold and discuss with specialist team

In certain circumstances, such as a pandemic, this monitoring schedule may be altered as per local or national guidance to allow less frequent monitoring. See modified covid NPT here.

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.

COST:

- Based on a dose 15mg/week £ 862 pa (BNF 76)

INFORMATION FOR COMMUNITY PHARMACIST:

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION:

Name	Designation	Acute Site	Department phone number
Dr Sarah Saunders	Consultant Rheumatologist, North	Glasgow Royal Infirmary	0141 211 4965
Dr David Crosbie	Consultant Rheumatologist, South	Queen Elizabeth University Hospital	0141 451 6170
Dr Gillian Roberts	Consultant Rheumatologist, Clyde	Royal Alexandra Hospital	0141 314 6134
Pamela Everitt	Advanced Clinical Pharmacist - Rheumatology, North	Glasgow Royal Infirmary	pamela.everitt@ggc.scot.nhs.uk
Deborah Russell	Advanced Clinical Pharmacist - Rheumatology, Clyde	Royal Alexandra Hospital	deborah.russell@ggc.scot.nhs.uk

- 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 NHS GGC communication sheet 'Methotrexate Injection for Self Administration'.