Name: Attach Banda Label here
Address:

Date of Birth:
NHS number:

Coventry & Warwickshire
Area Prescribing Committee

# SHARED CARE AGREEMENT

# Methotrexate oral / Metoject subcutaneous

SCA: *For treatment of Rheumatoid arthritis, psoriatic arthritis, psoriasis and Unresponsive or chronically active Crohn's disease (unlicensed)*

## AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of methotrexate can be shared between the 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 total clinical responsibility for the patient for the diagnosed condition remains with the specialist. **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

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 initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

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

### Specialist responsibilities

1. To discuss the benefits, side effects and expected outcomes of treatment with the patient.
2. To supply the drug information leaflet, booklet, counsel the patient and obtain informed consent.
3. To ensure that the patient understands the WEEKLY dosing regimen.
4. To obtain patient consent to shared care arrangement and agreement to hold personal and treatment details on computerised blood monitoring database.
5. To undertake appropriate baseline tests (i.e. Height, weight, blood pressure, FBC, LFTs, albumin, U&Es, eGFR, CRP, chest X-ray and VZV) and provide results of baseline blood tests and recommend frequency of monitoring to the GP.
6. To monitor blood counts, hepatic and renal function at recommended frequencies, and take action if abnormal.
7. When considering subcutaneous methotrexate the initial dose will be administered in clinic with the clinical nurse specialist. All patients will be asked to sign a competency sheet and a copy will be kept in the patient's case notes. Notify GP of arrangements to supply via "homecare" and waste collection, brand supplied.
8. To recommend the dose and timing of any concomitant folic acid.
9. The initial 3-month prescription (in instalments as appropriate) will be issued by the consultant / nurse prescriber outlining dose and timing of any concomitant medications.
10. Ensure a written request to GP offering to participate in shared care by faxing the shared care template letter.
11. To ensure that for both oral and subcutaneous methotrexate, dosages on all correspondence between secondary and primary care will be written in milligram (mg) and for patients on oral methotrexate will include the number of tablets to be taken. Dosage changes will be recorded within methotrexate dosage booklet in **mg** and number of tablets to be taken.
12. To periodically review the patient's condition and communicate promptly with the GP when treatment is changed, providing a copy of most up to date blood tests with clinical letter.
13. To advise the GP on when to adjust the dose, stop treatment, or consult with specialist.
14. To ensure that clear backup arrangements exist for GPs to obtain advice and support.

Report adverse events to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard, and to the GP and appropriate Medicines Optimisation team.

### General Practitioner responsibilities

1. To reply in writing, to the request for shared care as soon as practicable by faxing back the completed shared care template form.
2. To prescribe methotrexate oral/ sc at the dose recommended.
3. To ensure blood forms issued by secondary care are used for routine blood test monitoring and if necessary patient to attend surgery for blood tests as specified on pre-printed blood form.
4. Patients living 'out of area' will have their blood results faxed by their surgery to the rheumatology database staff who will manually enter results onto the rheumatology blood monitoring database.
5. To ensure compatibility with other concomitant medication.
6. To adjust the dose as advised by the specialist.
7. To stop treatment on the advice of the specialist, or immediately if an urgent need to stop treatment arises.
8. Ensure, that due to the cytotoxic nature and once weekly dosing of this drug, that there is a practice process which ensures that prescriptions are issued safely and not issued in duplicate or subject to error during computer generation

Report adverse events to the MHRA on a Yellow Card (www.mhra.gov.uk/yellowcard), the specialist, and the appropriate Medicines Optimisation team.

### Patient/carer's role

1. To attend all appointments with GP and specialist.
2. To attend for bloods as discussed/ advised by rheumatology team.
3. To report to the specialist or GP if he or she does not have a clear understanding of the treatment.
4. To keep the patient–held monitoring and dosage record booklet safe and bring to all clinic and GP appointments.
5. To share any concerns in relation to treatment.
6. To inform specialist or GP of any other medication being taken, including over-the-counter products.

Report any adverse effects or warning symptoms to the specialist or GP. The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card , available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours).
The form can also be downloaded from www.mhra.gov.uk/yellowcard.

*This SCA should be read in conjunction with the Summary of Product Characteristics (SPC) and the current edition of the British National Formulary*

**Back-up Advice and Support:** See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care.

**SUPPORTING INFORMATION** *(see SPC for complete details/specific guidance http://emc.medicines.org.uk )*

**Licensed indications**: [SC Metoject] - rheumatoid arthritis, psoriatic arthritis and psoriasis, unlicensed SC Baxter preparation time to response 8 - 12 weeks.

Methotrexate is used in the treatment of adults with severe, active, classical or definite rheumatoid arthritis who are unresponsive or intolerant to conventional therapy.
Methotrexate has also been used in the treatment of severe, uncontrolled psoriasis, which is not responsive to other therapy.

**Dosage and administration:** Dosage for Rheumatoid and psoriatic arthritis
*Adults:* Starting dose usually 15 mg weekly [6 x 2.5 mg tablets]. NOTE – ONLY 2.5 MG TABLETS SHOULD BE PRESCRIBED AND DISPENSED
Quantity to be supplied initially from secondary care (maximum of 3 months)
Folic Acid 5 mg – 10 mg day after methotrexate should be co-prescribed to minimise the risk of side effects.

All practitioners must adhere to the Arden Cancer Network policy on SC cytotoxic chemotherapy disposal.

Methotrexate is usually taken in tablet form almost always once a week on the same day(s) of each week (occasionally methotrexate may be taken twice a week). It should be swallowed whole, not crushed or chewed and taken with food. Some patients take methotrexate once a week by subcutaneous or intramuscular injection.
The patient-held Methotrexate alert card details the patient's dose. This should be kept up to date, and the patient should take it with them to all appointments and when collecting their prescription.

*Prescribing records must state:* dose and number of methotrexate tablets to be taken.

*Elderly:* Methotrexate should be used with extreme caution in elderly patients, a reduction in dosage should be considered.

**Monitoring:** Single therapy
*Baseline:* Bloods, Height, weight, BP, FBC, U&E, LFT, albumin, creatinine/calculated GFR, CRP, VZV CXR

*During treatment:* Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity

Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Combination with any DMARD i.e. leflunomide – monitor monthly for 12 months then continue monthly afterwards. For patient on methotrexate and leflunomide combination, consider a reduced frequency monitoring schedule on an individual basis.

*Interruption of Treatment:* During a serious infection, temporarily discontinue until the patient has recovered from the infection.

Contact rheumatology team urgently and withhold treatment if any of the following develop:
white cell count <3.5 x $10^9$/l; mean cell volume >105 Fl and if B12 or folate low start supplementation; neutrophils <1.6 X $10^9$/l; creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min; unexplained eosinophilia >0.5 X$10^9$/l; ALT and/or AST >100 U/l; platelet count <140 X$10^9$/l; unexplained reduction in albumin <30 g/l.

*Rash:* Withhold until discussed with speciality team
*Oral ulceration:* Prescribe mouth rinse 5 -7 days. If no improvement contact rheumatology
Abnormal bruising or sore throat. Withhold until FBC result available and discuss with speciality team

As well as responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g. gradual decreases in white blood cells or albumin, or increasing liver enzymes).

**Cautions:** Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, diarrhoea, and ulcerative disorders of the GI tract and psychiatric disorders. Hepatic toxicity has been observed, usually associated with chronic hepatic disease. The administration of low doses of methotrexate for prolonged periods may give rise, in particular, to hepatic toxicity. Liver function should be closely monitored. If hepatic function abnormalities develop, methotrexate dosing should be suspended for at least two weeks. It is only appropriate to restart methotrexate provided the abnormalities return to normal and the re-exposure is deemed appropriate.

Particular care and possible cessation of treatment are indicated if stomatitis or GI toxicity occurs as haemorrhagic enteritis and intestinal perforation may result.

Reversible eosinophilic pulmonary reactions and treatment-resistant, interstitial fibrosis may occur, particularly after long-term treatment.

Renal lesions may develop if the urinary flow is impeded and urinary pH is low, especially if large doses have been administered. Renal function should be closely monitored before, during and after treatment. Reduce dose of methotrexate in patients with renal impairment. High doses may cause the precipitation of methotrexate or its metabolites in the renal tubules. A high fluid throughput and alkalinisation of the urine to pH 6.5 – 7 by oral or intravenous administration of sodium bicarbonate (5x625mg tablets every three hours) is recommended as a preventative measure.

Haematopoietic suppression caused by Methotrexate may occur abruptly and with apparently safe dosages. Full blood counts should be closely monitored before, during and after treatment. If a clinically significant drop in white cell or platelet count develops, methotrexate therapy should be withdrawn immediately and appropriate supportive therapy given (see Undesirable Effects section). Patients should be advised to report all symptoms or signs suggestive of infection.

Malignant lymphomas may occur in patients receiving low dose methotrexate, in which case therapy must be discontinued. Failure of the lymphoma to show signs of spontaneous regression requires the initiation of cytotoxic therapy.

Methotrexate has been shown to be teratogenic; it has been reported to cause foetal death and/or congenital abnormalities. Therefore, it is not recommended in women of childbearing potential unless the benefits can be expected to outweigh the considered risks. If this drug is used during pregnancy for antineoplastic indications, or if the patient becomes pregnant while taking this drug, the patient should be appraised of the potential hazard to the foetus.

Following administration to a man or woman conception should be avoided by using an effective contraceptive method for at least 3 months after using methotrexate tablets.

Methotrexate has some immunosuppressive activity and therefore the immunological response to concurrent vaccination may be decreased. In addition, concomitant use of a live vaccine could cause severe antigenic reaction.

If acute methotrexate toxicity occurs, patients may require treatment with folinic acid.
The disappearance of methotrexate from plasma should be monitored, if possible. This is recommended in particular when high, or very high doses are administered in order to permit calculation of an adequate dose of leucovorin (folinic acid) rescue.
Patients with pleural effusions and ascites should be drained prior to initiation of methotrexate therapy or treatment should be withdrawn.
When to perform a liver biopsy in rheumatoid arthritis patients has not been established either in terms of a cumulative Methotrexate dose or duration of therapy.

Pleuropulmonary manifestation of rheumatoid arthritis has been reported in the literature. In patients with rheumatoid arthritis, the physician should be specifically alerted to the potential for Methotrexate induced adverse effects in the pulmonary system. Patients should be advised to contact their physicians immediately should they develop a cough or dyspnoea (see Undesirable Effects section).
Methotrexate given concomitantly with radiotherapy may increase the risk of soft tissue necrosis and osteonecrosis.
Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Symptoms typically include dyspnoea, cough (especially a dry non-productive cough) and fever for which patients should be monitored at each follow-up visit. Patients should be informed of the risk of pneumonitis and advised to contact their doctor immediately should they develop persistent cough or dyspnoea. Methotrexate should be withdrawn from patients with pulmonary symptoms, and a thorough investigation should be made to exclude infection. If methotrexate induced lung disease is suspected, treatment with corticosteroids should be initiated and treatment with methotrexate should not be restarted.

Lung manifestations of RA and other connective tissue disorders are recognised to occur. In patients with RA, the physician should be specifically alerted to the potential for methotrexate induced adverse effects on the pulmonary system.

Always avoid trimethoprim and co-trimoxazole (increases anti-folate effect)

- Live vaccines should not be administered
- Avoid aspirin (with the exception of low-dose aspirin)

**Note:** NSAIDs can be prescribed, but patients will need to be carefully monitored for any side effects, particularly at higher methotrexate doses.

**Contra-indications: Profound impairment of renal or hepatic function or haematological impairment.**

Methotrexate is contra-indicated in the presence of severe/significant renal or significant hepatic impairment. Liver disease including fibrosis, cirrhosis, recent or active hepatitis; active infectious disease; and overt or laboratory evidence of immunodeficiency syndrome(s). Serious cases of anaemia, leucopenia or thrombocytopenia. Methotrexate should not be used concomitantly with drugs with antifolate properties (eg co-trimoxazole). Methotrexate is teratogenic and should not be given during pregnancy or to mothers who are breast feeding.

Following administration to a man or woman conception should be avoided by using an effective contraceptive method for at least 3 months after using Methotrexate Tablets 2.5mg Patients with a known allergic hypersensitivity to methotrexate should not receive methotrexate.

Methotrexate should be used with extreme caution in patients with haematological depression, renal impairment, diarrhoea, and ulcerative disorders of the GI tract and psychiatric disorders. Hepatic toxicity has been observed, usually associated with chronic hepatic disease. The administration of low doses of methotrexate for prolonged periods may give rise, in particular, to hepatic toxicity. Liver function should be closely monitored. If hepatic function abnormalities develop, methotrexate dosing should be suspended for at least two weeks. It is only appropriate to restart methotrexate provided the abnormalities return to normal and the re-exposure is deemed appropriate

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**Side effects:** In general, the incidence and severity of side effects are considered to be dose-related. Adverse reactions for the various systems are as follows:
*Skin:* Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary changes, alopecia, ecchymosis, telangiectasia, acne, furunculosis. Lesions of psoriasis may be aggravated by concomitant exposure to ultraviolet radiation. Skin ulceration in psoriatic patients and rarely painful erosion of psoriatic plaques has been reported. The recall phenomenon has been reported in both radiation and solar damaged skin.

*Haematopoietic:* Bone marrow depression is most frequently manifested by leucopenia, thrombocytopenia (which are usually reversible) and anaemia, or any combination may occur. Infection or Hypogammaglobulinaemia has been reported.

*Alimentary System:* Mucositis (most frequently stomatitis although gingivitis, pharyngitis and even enteritis, intestinal ulceration and bleeding) may occur. In rare cases the effect of Methotrexate on the intestinal mucosa has led to malabsorption or toxic megacolon. Nausea, anorexia and vomiting and/or diarrhoea may also occur.

*Hepatic:* Hepatic toxicity resulting in significant elevations of liver enzymes, acute liver atrophy, necrosis, fatty metamorphosis, periportal fibrosis or cirrhosis or death may occur, usually following chronic administration.

*Urogenital System:* Renal failure and uraemia may follow Methotrexate administration, particularly after high doses or prolonged administration. Vaginitis, vaginal ulcers, cystitis, haematuria and nephropathy have also been reported. Methotrexate can decrease fertility. This effect appears to be reversible after discontinuation of therapy (see Pregnancy and Lactation section).

*Pulmonary System:* Infrequently an acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Acute pulmonary oedema has also been reported after oral and intrathecal use. Pulmonary fibrosis is rare. A syndrome consisting of pleuritic pain and pleural thickening has been reported following high doses.

In the treatment of rheumatoid arthritis, Methotrexate induced lung disease is a potentially serious adverse drug reaction which 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.
Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported

*Central Nervous System:* Headaches, drowsiness, ataxia and blurred vision have occurred following low doses of Methotrexate, transient subtle cognitive dysfunction, mood alteration, or unusual cranial sensations have been reported occasionally. Aphasia, paresis, hemiparesis, and convulsions have also occurred following administration of higher doses.

There have been reports of leucoencephalopathy following intravenous Methotrexate in high doses, or low doses following cranial-spinal radiation. Other reports include eye irritation, malaise, undue fatigue, vasculitis, sepsis, arthralgia/myalgia, chills and fever, dizziness, loss of libido/impotence and decreased resistance to infection. Also opportunistic infections such as herpes zoster. Osteoporosis, abnormal (usually "megaloblastic") red cell morphology, precipitation of diabetes, other metabolic changes, and sudden death in relation to or attributed to the use of Methotrexate.
Although very rare, anaphylactic reactions to methotrexate have been reported.

Methotrexate does not have black triangle (▼) status. All serious suspected adverse reactions (even well recognised or causal link uncertain) should be reported to the MHRA.

**Drug interactions (see also above under cautions):** Methotrexate is extensively protein-bound and may be displaced by other protein-bound drugs (e.g. diuretics, salicylates, hypoglycaemics), with a potential for increased toxicity. Concomitant use of other drugs with nephrotoxic or hepatotoxic potential (including alcohol) should be avoided. Always avoid trimethoprim and co-trimoxazole (increases anti-folate effect).

**Cost:** At current prices one year's treatment of methotrexate 15 mg weekly will cost £16.37.
Accessed 6.3.18 via www.nhsbsa.nhs.uk (reference: Prescription Pricing Division (PPD). NHS Business Services Authority. Drug Tariff March 2018)

**References:**


1. Summary of Product Characteristics. Methotrexate 2.5 tablets. Last updated 15.4.16. Available via www.medicines.org.uk accessed 14/8/172.
2. Ledingham J, Gullick N, Irving N et al. on behalf of the BSR and BHPR Standards, Guidelines and Audit Working Group; BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, Rheumatology, Volume 56, Issue 6, 1 June 2017, Pages 865–868. Available at https://academic.oup.com/rheumatology/article/56/6/865/3053478/BSR-and-BHPR-guideline-for-the-prescription-and