Shared Care Guideline for Methotrexate (GP Summary)

It is essential that a transfer of care only takes place with agreement of the GP and when sufficient information has been received. If the GP does not agree to share care they will inform the Consultant responsible for the patient's care.

Basingstoke, Southampton & Winchester District Prescribing Committee

Indications	Active rheumatoid arthritis or other inflammatory arthritis conditions. Severe psoriasis & off-license in Crohn's disease. Used as steroid sparing agent in giant cell arteritis, polymyalgia rheumatica, uveitis and vasculitis.
Dose & response	• **Variable dose**. Usual range 5-25mg ONCE a WEEK on a fixed day. Usual starting dose 10-15mg & increased by 2.5mg per week (or as directed by specialist). Consider lower doses if renal or hepatic impairment or older person. • **Time to response is variable**. In psoriasis significant effect may not be seen before a month or more. In other indications a response should not be expected before two or three months and in some cases may not occur until six months of treatment.
Specialist Responsibilities	• **Prescribe initial treatment until dose stable (usually 2-3 months).** • **Request blood tests and monitor results for the first 2-3 months and when dose is increased.** • **Counsel patients about possible side effects.** • **Request chest-x-ray and pulmonary function tests if indicated.**
GP Responsibilities	**Methotrexate tablets:** 1. Prescribe as **methotrexate 2.5 mg tablets** and state number of tablets "to be taken once a week as a single dose" and total quantity of tablets to supply. 2. Prescribe supporting therapy "folic acid 5mg ONCE a WEEK to be taken on a different day to methotrexate". Consider increasing frequency to 3 or 6 times weekly if GI side effects such as nausea or sore mouth troublesome. **Methotrexate injection:** 3. Prescribe **Metoject® PEN** "to be injected sub-cutaneously ONCE a week as a single dose". 4. Prescribe 1 litre purple-lidded cytotoxic sharps bin and mediswabs as required. 5. Ensure systems are in place for the patient to receive their weekly injection if they are not self-administering. **For both:** 6. Ensure the patient understands that dosing is ONCE a WEEK and which warning symptoms to report. 7. Request blood tests at the recommended frequencies once asked to take over shared care (usually 2-3 months) and review results before prescribing. 8. Report any adverse events to the specialist and stop treatment on their advice or immediately if an urgent need arises (see monitoring section). 9. Report any worsening of control of the condition to the specialist. **Recommended monitoring for new DMARDs** • **FBC, Cr (or GFR), ALT, albumin every 2 weeks until stable dose for 6 weeks.** • **Then monthly FBC, Cr or GFR, ALT, albumin for 3 months.** • **Then FBC, Cr or GFR, ALT, albumin at least every 12 weeks.** • **For dose increases -FBC, Cr or GFR, ALT, albumin every 2 weeks until stable dose for 6 weeks then back to previous schedule.** **For patients on methotrexate and leflunomide in combination, long-term monthly monitoring is needed** • Pneumococcal vaccination every 10 years and annual influenza vaccinations are recommended for patients with inflammatory arthritis • Although the shingles (Zostavax) vaccine is a live attenuated vaccine, treatment with low dose methotrexate (<0.4mg/kg/week) is not considered sufficiently immunosuppressive and is not a

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	contraindication to administering the vaccine. • Passive immunisation may be given with varicella zoster immunoglobulin (VZIg) in non-immune patients exposed to chicken pox or shingles. Contact specialist for advice.
Actions to be taken in response to monitoring	**Thresholds at which to discontinue treatment and contact Rheumatology for urgent review:** • **WCC<3.5 x10^9/L** • **Neutrophils<1.6 x10^9/L** • **Unexplained eosinophilia>0.5 x10^9/L** • **Platelets<140 x10^9/L** • **MCV>105** • **ALT>100 units/L** • **Unexplained fall in albumin** • **Creatinine>30% above baseline +/- GFR<60**

Contra-indications	• **Hepatic Impairment** • **Alcohol abuse** • **Acutely unwell older person -** acute renal failure likely (see monitoring section). • **Pregnancy & breast feeding** – patients (both sexes) of reproductive age should be advised to use contraception during treatment and for at least 3 months after stopping. • **Active infection and immunodeficiency syndromes** • **Bone marrow failure** indicated by cytopenia, anaemia. • **Immunisations** - avoid live immunisations.
Cautions	• **Elective surgery** - continue, but consider infection risk & drug interactions. • **Chronic renal failure (stable)** - avoid if eGFR< 20 ml/minute. • **Ascites and pleural effusions** – reduced elimination of methotrexate. • **Avoid dehydration** – increased risk of toxicity.
Important adverse effects & management	Serious side effects can occur acutely at any time during treatment • **Nausea, vomiting & acute minor GI upsets or mucosal side effects** - can occur at any stage. Advise patient to take methotrexate with food. May resolve with methotrexate dose reduction or increasing dose of folic acid. Withhold treatment if does not resolve or is severe and discuss with specialist. • **Alopecia, rash & diarrhoea –** may be encountered, but if severe withhold treatment and discuss with specialist. • **Pulmonary symptoms -** a small minority of patients develop symptoms of interstitial pneumonitis, often soon after starting treatment, indicated by persistent dry cough, shortness of breath or fever. Withhold treatment and refer urgently to specialist or A&E. • **Severe sore throat, abnormal bruising -** request urgent FBC & withhold treatment until results known. • **Haematopoetic suppression -** may occur abruptly; factors likely to increase toxicity include advanced age, renal impairment and concomitant anti-folate medication. Any profound drop in white cell or platelet count calls for immediate withdrawal of treatment and urgent referral for supportive treatment. • **Patient develops significant infection or is systemically unwell -** withhold treatment & discuss with specialist. • **Hepatotoxicity**
Important Drug Interactions	• **Acitretin - avoid**. May increase serum concentration of methotrexate & increase risk of toxicity. • **Alcohol -** advise patients to stay within 4-6 units per week. • **Aspirin, NSAIDs** – reduced methotrexate excretion. Clinically significant interaction with NSAIDs is rare, continue standard doses advised by specialist, but patients should be advised to avoid self-medication with over the counter aspirin or ibuprofen. Low dose aspirin can be continued. • **Azathioprine** – increased risk of toxicity. • **Ciclosporin -** monitor closely**.** Risk of toxicity. • **Ciprofloxacin -** monitor closely. Reduced methotrexate clearance may increase toxicity. • **Clozapine - avoid.** Increased risk agranulocytosis. • **Co-trimoxazole - avoid**. Increased anti-folate effect of methotrexate which increases risk of marrow

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	aplasia. • **Digoxin - caution.** Methotrexate possibly reduces adsorption. • **Fluorouracil topical - avoid.** Risk of toxic skin reaction. • **Leflunomide**- monitor closely. Increased risk of liver/haematoxicity. • **Penicillins** - monitor closely. Some penicillins can reduce methotrexate clearance, but methotrexate toxicity has only rarely been reported. • **Phenytoin -** caution. Increases anti-folate effect of methotrexate. • **Probenecid - avoid.** Reduces methotrexate excretion & increases toxicity. • **Proton pump inhibitors -** monitor closely**.** Possibly reduce methotrexate excretion. • **Sulfonamides** – risk of increased toxicity. • **Tetracyclines/Doxycycline -** monitor carefully- increased risk methotrexate toxicity. • **Tolbutamide -** monitor closely. Increases serum concentration of methotrexate. • **Trimethoprim - avoid**. Increased anti-folate effect of methotrexate which increases risk of marrow aplasia. • **Warfarin** - monitor INR closely.
Patient information	General :**http://www.patient.co.uk/medicine/methotrexate-maxtrex-metoject** Specific to Metoject PEN: **http://metoject.co.uk/healthcare-professionals/metoject-is-switching/**

This guidance should be read in conjunction with the BNF

Contact numbers for urgent GP advice

Southampton - Nurse specialist advice line 023 8120 5352 or bleep SpR 1801 (Mon-Fri 9-5). Out of hours – on-call consultant via hospital switchboard

Southampton – (Ophthalmology) Dr Nigel Hall Contact: 023 8120 4761

Basingstoke - Administration team 01256 312768, fax 01256 313653, advice line (answerphone) 01256 313117 or on-call consultant via switchboard

Winchester – Administration team 01964 824150, Advice line 01962 824256, on-call SpR bleep 3425 via switchboard.