Cardiff & Vale (C&V) UHB Corporate Medicines Management Group (c MMG)
SHARED CARE AND NEAR PATIENT TESTING

Drug: METHOTREXATE (SUBCUTANEOUS AND ORAL ROUTE)
Protocol number CV 55

Indications: Rheumatoid arthritis and various auto-immune conditions, usually when corticosteroid therapy alone provides inadequate control. Methotrexate has immunosuppressive and steroid-sparing properties.

General Guidance
This protocol sets out details for the shared care and near patient testing of patients taking **methotrexate** and should be read in conjunction with the General Guidelines for Shared Care. Sharing of care requires communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **The doctor who prescribes the medication legally assumes responsibility for the drug and the consequences of its use.** The prescriber has a duty to keep themselves informed about the medicines they prescribe, their appropriateness, effectiveness and cost. They should also keep up to date with the relevant guidance on the use of the medicines and on the management of the patient's condition.

Responsibilities

A. Consultant responsibilities

1. When treatment is **initiated** send Shared Care/ Near Patient Testing request form with Shared Care Protocol to GP.
2. Initiate therapy following full discussion with the patient of benefits and risks
3. Baseline and continued monitoring ,until patient is stabilised of biochemical parameters,(see page 2)
4. A patient information leaflet/monitoring booklet will be provided. The patient will be informed to report immediately to their GP the onset of any feature of blood disorders (e.g. sore throat, bruising and mouth ulcers), liver toxicity (e.g. nausea, vomiting, abdominal discomfort and dark urine) and respiratory effects (e.g. shortness of breath).
5. Titrate methotrexate dose according to schedule below, adjusting dose as appropriate and undertake monitoring of clinical response and side effects.
6. To provide training for patient or carer on administration of methotrexate (if subcutaneous methotrexate is initiated) and to ensure that there is a robust collection mechanism for the cytotoxic sharps from the patient's home.
7. When a GP positive response to SC / NPT has been received and patient has been stabilized send a letter to GP "handing over" the Shared Care / Near Patient Testing of the patient to the GP.
8. To counsel patients (male and female) to take contraceptive precautions during treatment and for at least 3 months after treatment has ceased (refer to special precautions). Record in GP referral letter that contraceptive advice has been given.
9. Check patient's immune status to *herpes zoster* and notify GP to enable coding to occur.
10. To counsel patients that a strictly limited alcohol intake is to be adhered to and advise on the combined use of methotrexate with NSAIDs and aspirin products.

11. Respond to any request from GP to review the patient due to adverse effects of therapy.
12. Advise the GP on continuing or stopping methotrexate therapy following medical review of the patient and associated drug therapy.
13. If Near Patient Testing not agreed notify GP if patient is failing to attend for appropriate monitoring and advise GP on appropriate action.

B. General practitioner responsibilities

1. Within one week of receipt return the completed Shared Care/Near Patient Testing request form to indicate whether or not willing to undertake Shared Care/Near Patient Testing.
2. Prescribe **methotrexate** as part of the Shared Care agreement.
3. Monitor the general health of the patient.
4. Where Near Patient Testing is agreed monitor the parameters indicated (see page 2), document results in the patient's monitoring booklet and report to and seek advice from the consultant on any aspect of patient care which is of concern.
5. Report adverse effects of therapy to the consultant and the Medicines and Health Care products Regulatory Agency (MHRA).
   Recommend that patient receives pneumococcal vaccination and yearly influenza vaccination as well as Zostavax as part of the national shingles immunisation programme. (see Special recommendations)
6. If Near Patient Testing not agreed, to act on advice provided by the Consultant if patient does not attend for appropriate monitoring.

C. Patient responsibilities

1. Consent to treatment with methotrexate.
2. Attend regular appointments with specialist centre and GP.
3. Report any side effects to the specialist or GP whilst taking methotrexate.
4. Provide monitoring booklet to be updated

Dosage Regimen

<u>Methotrexate</u>

Typical dose (depending on indication): 5-25mg ONCE weekly; starting dose may vary depending on the severity of the condition and patient characteristics such as age, renal function and co-morbid conditions.
MHRA Warning this is a ONCE WEEKLY dose.
Fatalities have been reported due to prescribing and dispensing errors
Methotrexate can be given subcutaneously in those patients who have malabsorption problems or those who are unable to tolerate therapeutic doses of oral methotrexate because of side effects.

<u>Folic acid</u>

Typical dose: 5mg once weekly, preferably the day after the methotrexate however it can be given any day as long as it is not on the same day as methotrexate. Folic acid reduces toxic effects and improves continuation and compliance and can be given more frequently (up to 5mg daily except for day that methotrexate is taken)

Monitoring in secondary care

Before treatment
FBC, creatinine & electrolytes, LFTs, and CXR (unless CXR done within the last 6 months). Lung function tests should be undertaken in patients with pre-existing lung disease or respiratory symptoms before starting treatment.

P111NP (type 111 procollagen peptide) (Range 1.7 – 4.2 mcg/l) (**Psoriasis indication only**)-monitoring done by hospital team.

During treatment

Initial monitoring in Secondary Care

FBC, LFTs and creatinine & electrolytes every 1- 2 weeks for first four to six weeks then monthly. This time period may vary depending on how quickly patient is titrated up to maintenance dose, bearing in mind that FBC and LFTs are required two weeks after any dose increase.

Monitoring by GP when patient is stable

FBC, LFTs monthly for the first year and then every 3 months
Creatinine and electrolytes every 3 months.
FBC and LFTs two weeks after any dose increase (should dose increase be required)

Monitoring by secondary care
PNIIINP (for psoriasis indication only) –every 3 months (measured by hospital team).

Withold methotrexate and discuss with specialist if any of the following occurs:

WBC	< 4.0 x 10^9/L
Neutrophils	< 1.5 x 10^9/L
Platelets	< 150 x 10^9/L
AST/ALT	> 2-fold rise (from upper limit of reference range)
Albumin	unexplained fall (in absence of active disease)
Rash or oral ulceration, nausea, vomiting, diarrhoea	
New or increasing dyspnoea or dry cough	
MCV	> 105fl (check serum B12 folate and TFT)
Mild to moderate renal impairment	
Abnormal bruising or severe sore throat (check FBC immediately)	

* patients may continue treatment if WBC is 3.0 - 4.0 x 10^9/L if the neutrophil count is above 1.5 x 10^9/L

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance

Adverse effects

Clinical condition	Management
Myelosuppression: (see above) Sore throat, fever malaise. Bleeding, bruising, purpura	Check FBC, stop drug until result available. (Specialist may consider recommencing at lower dose when parameters return to normal. Recurrence requires alternative therapy.)
Pulmonary : cough, dyspnoea or fever (Acute pneumonitis (clinical signs/symptoms e.g. crackles and cyanosis) and pulmonary fibrosis, rare but potentially life threatening.)	Stop and refer to secondary care immediately
Hepatic: (see above) Abnormalities of liver function (very common), hepatic fibrosis and cirrhosis. Clinically serious liver disease is rarely seen in patients receiving low dose methotrexate and routine liver biopsies are therefore not recommended	Stop if any abnormalities, monitor LFTs- abnormalities may resolve after 2 weeks. Consideration to recommencing therapy may be made.
Gastrointestinal: nausea, vomiting, anorexia (very common, may necessitate dose reduction) diarrhoea (common), haemorrhagic enteritis, ulcerative stomatitis (very common).	If ulcerative stomatitis develops stop and discuss. If persistent diarrhoea (possibility of enteritis)-withhold and discuss with specialist.
Skin: rash, alopecia, skin ulceration (common). Severe reactions may occur	Stop and discuss with specialist.
Renal: nephrotoxicity and renal failure	Stop and discuss with specialist
Reproductive: Reduced oogenesis and spermatogenesis during treatment. Teratogenic.	Avoid conception during and for 3 months after discontinuing treatment in male or female.

Contact Secondary Care prescriber if patient is experiencing repeated bacterial infections.

Drug interactions

- Clinically significant interaction between NSAID and low dose weekly methotrexate are rare and NSAIDs can be continued as long as monitoring regularly undertaken
- Co-trimoxazole and trimethoprim are contraindicated with methotrexate. Other antibiotics may interact.
- Avoid concomitant use with acitretin.
- Excess alcohol should be avoided
- Corticosteroids: increased risk of haematological toxicity
- Antiepileptics, (increased antifolate effect of methotrexate)
- Omeprazole: possible increased risk of methotrexate toxicity
- Live vaccines- should be avoided (a contraindication).

For Medicines Information please contact one of the rheumatology pharmacists or your local Medicines Information Dept.

Special Recommendations

- Patients who have not previously had chickenpox should be identified and advised to seek medical attention if they subsequently come into contact with somebody who has chickenpox or shingles.

- Live vaccines should generally be avoided in patients taking methotrexate. However Department of health guidelines advise that Zostavax may be given to patients taking low dose methotrexate **(≤ 25mg once a week**) **either alone or in combination with prednisolone** ≤ **20mg daily.** Specialist advice should be sought for other treatment regimes

- In patients receiving methotrexate exposed to chickenpox or shingles, whose immune status to *Herpes Zoster* is unknown or negative, prophylactic aciclovir (po) (unlicensed use) should be prescribed 40mg/kg daily in four divided doses for 7 days starting one week after exposure.

- If a patient on methotrexate develops chickenpox, aciclovir should be started urgently. If the rash is severe and extensive and the patient is systemically unwell then he/she will need to be admitted urgently via the medical assessment unit as intravenous acyclovir and possibly other support will be required. If the patient is well however and the rash is no worse than would usually be seen then there is no indication for urgent admission or referral. The patient can be treated at home with oral aciclovir and advised to seek medical advice if there is any worsening of their condition

- Patients receiving methotrexate should be advised to limit their alcohol intake well within national recommendations.

- All patients, male and female, should be advised against conception and pregnancy during treatment with methotrexate as it is an abortifacient as well as a teratogenic drug. Patients should be advised to continue contraception for at least 6 months after stopping methotrexate.

- Methotrexate must be avoided in breast-feeding as the drug may be secreted into the breast milk.

Contact information

If you suspect an adverse reaction has occurred please seek advice.
The Shared Care Request form and handover letter (when patient is stabilised) will include necessary contact details and indicate if methotrexate is being used for an unlicensed condition.

Date of next review December 2021