Berkshire West Integrated Care System
Representing
Berkshire West Clinical Commisioning Group
Royal Berkshire NHS Foundation Trust
Berkshire Healthcare NHS Foundation Trust
Berkshire West Primary Care Alliance

Prescribing Guidelines

Prescribing arrangement for the management of patients transferring from ***Secondary Care to Primary Care***

Rheumatology Department DMARD Monitoring Guidelines for Methotrexate

APC PG 025

For the latest information on interactions and adverse effects, always consult the latest version of the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Approval and Authorisation

Approved by	Job Title	Date
RBH Drugs and Therapeutics Committee	S Hussain, Chair	September 2017
BW GP Medicines Optimisation Committee	W Beecham, Chair	Nov 2014

Change History

Version	Date	Author	Reason
v.2.0	September 2017		
v.2.0	October 2017	n/a	Update to APC category

This prescribing guideline remains open to review considering any new evidence.

This guideline should only be viewed online and will no longer be valid if printed off or saved locally

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Job Title	Commissioning Pharmacist, NHS Central Southern CSU	Review Date	September 2020
Protocol Lead	Dr Antoni Chan, Royal Berkshire Foundation Trust Hospital	Version	v.2.0

Rheumatology Department DMARD Monitoring Guidelines for Methotrexate

For the latest information on interactions and adverse effects, consult the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Information

Summary of GP responsibilities

General Practitioner responsibilities
1. Prescribe dose in line with hospital recommendation (dose to be made up of 2.5mg tablets only for oral or Metoject® subcutaneous injection as outlined on page 5). Folic acid must be prescribed alongside methotrexate for both oral and subcutaneous doses. 2. Ensure the patient understands weekly dosing interval, and which warning symptoms to report. 3. Request blood tests (these will be monitored via the DAWN database). 4. For patients commencing subcutaneous Metoject® (as advised by the rheumatology consultants) ensure Metoject® subcutaneous injection and a sharpsguard purple container 1L are put onto the repeat system. The patient will require a sharpsguard purple container every month. 5. Ensure patient is scheduled for and attends reviews in secondary care. 6. Monitor for drug interactions. 7. Adjust dose/ stop treatment as advised by specialist. 8. Monitor the patient's overall health status and report adverse events to the rheumatology team.

Information

Methotrexate is a folic acid antagonist and is classified as an antimetabolite cytotoxic agent. It is prescribed in multiples of 2.5mg tablets (this avoids confusion between the 2.5mg and 10mg dose which look similar). Methotrexate can also be administered subcutaneously by Injection as Metoject subcutaneous injection.

All patients should have a drug information booklet on methotrexate given at the start of the treatment by the rheumatology department**.**

Methotrexate is given **ONCE** weekly on the same day each week, swallowed whole with a glass of water one hour after food while sitting or standing. The therapeutic range is normally between 5mg - 25mg weekly. Time to a therapeutic response is approximately 4 – 12 weeks.

Dose for Inflammatory Arthritis

Folic acid should be prescribed routinely alongside methotrexate (both for oral and subcutaneous doses) in an equivalent mg weekly dose, to be taken at least 24 hours after the methotrexate. Folic acid can be given at an increased dose or more frequently but **NOT** on the day of methotrexate. Folic acid reduces the risk of hepatotoxicity and gastrointestinal side effects and improves compliance.

Methotrexate is commenced initially between 7.5mg to 15mg orally once a week then adjusted gradually to achieve optimal response and minimise side effects with maintenance dose varying between 5mg to 25mg once a week. Once a response has been achieved, the dose is maintained or reduced to achieve disease clinical remission. (range 2.5mg - 25mg per week).

Dose for Psoriasis

Treatment of severe psoriasis is managed by the Dermatology Department. The methotrexate dose is 10 - 25 mg orally, once weekly. Dosage should be adjusted according to the patient's response and the haematological toxicity. Monitoring is not done through the DAWN service.

Drug Interactions – see SPC and BNF for further details

- Avoid folate antagonist drugs especially **co-trimoxazole** and **trimethoprim**. NSAID's and aspirin used concurrently are not contraindicated but may increase toxicity.
- Refer to BNF before prescribing antibiotics
- Alcohol should be reduced to three units per week during treatment with methotrexate.

Adverse Effects

- Photosensitivity, marrow suppression, GI disturbances, hepatic fibrosis, infertility, teratogenicity, pulmonary toxicity, renal failure (rare).

Contraindications and cautions

- **Conception and pregnancy** – Methotrexate is teratogenic. For men and women, contraceptive advice should be given, as pregnancy should be prevented for a minimum of 4 months after discontinuation of treatment. Male fertility may be reduced.
- **Breastfeeding** is contraindicated.
- **Vaccinations**
- LIVE vaccines - must NOT be given whilst on Methotrexate. This includes the yellow fever vaccine. Inactivated polio is available although sub-optimal response may be seen. The herpes zoster vaccine can be given to patients with low dose Methotrexate (<0.4/kg/week).
- Pneumovax and annual influenza vaccination is recommended**.**
- Patients exposed to chicken pox or shingles (who have not had prior exposure to these viruses), passive immunisation should be carried out using VZIG.
- **NSAIDs** - Can continue, if taken regularly and monitored, may increase risk of toxicity but is considered appropriate in most patients providing patient is monitored for toxicity. Avoid over the counter NSAIDs/aspirin.
- **Low dose aspirin-** The opinion of clinicians locally is that there may be some patients in whom the benefit of co-prescribing of low dose aspirin and low dose methotrexate outweighs the risks involved, provided that regular monitoring is carried out. **Vitamins -** some preparations containing folic acid or its derivatives may alter response to methotrexate. Patients should be advised to avoid the use of over-the-counter products without consulting their GP, hospital consultant, Community or Hospital Pharmacist.

Monitoring and Actions

Blood Test Results	**Actions**
WBC < 3.5 X 10^9 /l	Withhold treatment and discuss with rheumatology team
Neutrophils < 2 X10^9/l	Withhold treatment and discuss with rheumatology team
Platelets <150 X10^9/l	Withhold treatment and discuss with rheumatology team
Abnormal liver function ALT & AST > 2 x upper normal reference range	Withhold treatment and discuss with rheumatology team
MCV > 105fl	Investigate if B12 or folate low commence supplements
Albumin (unexplained fall)	If disease not active, withhold treatment and discuss with rheumatology team
Significant deterioration of renal function	Reduce dose and discuss with rheumatology team
Adverse events	**Action**
Nausea	Ensure patient is on similar dose of folic acid as with Methotrexate. Split methotrexate dose over one evening and the next morning. If the nausea is severe, consider increasing the folic acid up to 5mg 6 days per week, omitting day methotrexate is taken. An anti-emetic can be prescribed.
Mouth ulcers	May respond to 5mg folic acid daily (except the day taking methotrexate)

Rash or severe oral ulceration	Urgent FBC for WCC. Withhold treatment until discussed with rheumatology team. Look for alternative causes. Re-challenge with lower dose once symptoms settle.
Menstrual dysfunction/ Amenorrhoea	May occur during treatment and for a short time following cessation.
Otherwise unexplained dyspnoea/cough	Pneumonitis may occur. Withhold treatment and discuss urgently with rheumatology team. Urgent CXR required.
Severe sore throat, abnormal bruising	Immediate FBC and withhold treatment until result of FBC available

Monitoring requirements
Baseline tests will be performed by the specialist and an initial prescription for 2 weeks issued. **Blood tests done via surgery or hospital. Monitoring to be done through the DAWN monitoring service for patients in Berkshire West:-** For the first 2 months: Two-weekly blood tests including, FBC, LFT, U&E, ESR, CRP then monthly thereafter. **After 12 months**: If results remain stable, monitoring can be reduced to every 2 months (follow advice from specialist). **Dose increases**: Perform 2 - 4 weekly monitoring for at least 6 weeks after final dose change before considering changing to monthly monitoring (follow advice from specialist).

Methotrexate Subcutaneous Injection

Patients unable to tolerate oral methotrexate may be considered for transfer to parenteral methotrexate, by subcutaneous injection, using **METOJECT®** prefilled syringes. Metoject® is a licensed product of methotrexate 50mg/ml.

For transfer to Primary Care patients MUST be able to self administer. Methotrexate is a cytotoxic drug and patients will be taught how to self administer these injections by community specialist nurses trained in the handling of cytotoxic drugs.

- Training for the patient will be provided by BHFT high tech community nursing team. They must ensure that the patient will be supervised for a minimum of two injections or until competent prior to transfer to primary care.
- Training will include risk assessment, safe storage, handling and disposal, including spillage. Spillage kits will be available at time of training.
- In addition to the methotrexate treatment booklet the patient should be offered the Metoject® patient's guide.
- Patients can have their technique reviewed at least yearly by the BHFT community specialist nurse and have a named contact.
- Once patients have had their training for self administration of subcutaneous methotrexate, GPs will switch the prescription of oral to subcutaneous methotrexate. The prescription of Metoject® subcutaneous injection is on a monthly basis (4 injections).

Monitoring: If a patient is changed from a stable dose of oral methotrexate to Metoject® then, this is treated as a "dose increase". Patients will need fortnightly monitoring for 6 weeks as per any other dose increase. **All other precautions are the same as for oral methotrexate**.

Metoject® Pre-filled Syringes

DOSE	VOLUME	
7.5mg	0.15 ml	Metoject® should be stored at room temperature and out of the sight and reach of children
10mg	0.20 ml	
15mg	0.30 ml	
20mg	0.40 ml	
25mg	0.50 ml	

Waste disposal

Metoject® is a cytotoxic drug and is therefore classified as 'hazadous waste' and must be disposed of in a sharpsguard purple container. Patients should return used sharps bin to their GP practice or to the community pharmacy for disposal. New sharpsguard purple containers will be issued monthly for patients on FP10 prescriptions.

Back up advice and support

Contact details	Database	Telephone No.	Email address:
Rheumatology	DAWN DMARD	01183226574	Dawn.dmard@royalberkshire.nhs.uk

RESPONSIBILITIES and ROLES

Rheumatology team responsibilities

1.Pre-treatment checks:-

a) Confirmation of diagnosis, check patient's history of exposure to varicella zoster virus and exclude pregnancy (if female).
b) Consider possible drug interactions.
c) Conduct baseline tests (FBC, U&E, LFT (including AST/ALT), ESR, CPR, Chest X-ray (CXR). Also include pulmonary function tests for selected patients (e.g. underlying lung disease) d) Advise patients to have an annual flu vaccine and the pneumovax inoculation.

2. **Patient education:-**

a) Discuss benefits versus risks with patient.
b) Provide written information and give the patient a copy of the methotrexate treatment booklet and explain the importance of showing this to all healthcare professionals.
c) Explain dose (in mgs and number of 2.5mg tablets) and once weekly administration.
d) Ask patient to contact GP practice after one week to inform the practice that methotrexate has been started.
e) If changing to self-administered injectable methotrexate discuss cautions and benefits versu

precautions. Also discuss self-administration training. Send a referral to the Hub for device training by BHFT IV tech team.
f) Issue the patient with a 2 week prescription for Metoject® subcutaneous injections as well as a sharpsguard purple container 1L. Advise the patient to return the sharpsguard container to the GP p for safe disposal

3. Starting of treatment:-
a) Review baseline blood tests and record this
b) Issue hospital prescription for a minimum 2 weeks supply for patients starting methotrexate for the first time.
c) Ask GP to continue prescribing and providing baseline test results, a copy of this shared care agreement, details of methotrexate dose, its frequency, together with dose and timing of any folic acid.
d) Monitor efficacy, inform GP of any dose changes as well as any relevant or significant abnormal blood tests (DAWN service) and also report adverse event.

General Practitioner responsibilities
1. Prescribe dose in line with hospital recommendation (dose to be made up of 2.5mg tablets only for oral or subcutaneous injection as outlined on page 5). 2. Ensure the patient understands weekly dosing interval, and which warning symptoms to report. 3. Request blood tests which will be monitored via the DAWN database. 4. For patients commencing subcutaneous methotrexate (as advised by the rheumatology consultants) refer patients to the Hub for device training by BHFT IV tech team. In addition, order a sharpsguard purple container 1L and advise patient to return this to the GP practice once full for safe disposal. 5. Ensure patient is scheduled for and attends reviews in secondary care. 6. Monitor for drug interactions. 7. Adjust dose/ stop treatment as advised by specialist. 8. Monitor the patient's overall health status and report adverse events to the rheumatology team.

Patient's / Carer's role and responsibilities
1 Ask for information when the patient does not have a clear understanding of the treatment and share any concerns in relation to treatment with methotrexate. 2 Tell the Consultant, GP or Pharmacist of any other medication being taken, including over-the-counter products. 3 Read the patient information leaflets given to them by the rheumatology team. 4 Report any side effects or concerns to the Consultant, CNS or GP. 5. Read the methotrexate information booklet, attend appointments and blood tests. 5 For patient's being prescribed subcutaneous methotrexate to agree to attend training on self-administration and return the sharpsguard container.