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Royal Cornwall Hospitals NHS Trust

Oral and Subcutaneous Methotrexate Shared Care Guideline

V3.0

March 2019

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of methotrexate in patients with inflammatory joint disease and psoriasis. This guideline provides additional limited information necessary to aid in the treatment of rheumatology and dermatology patients. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the BNF, ABPI summary of product characteristics and do not replace them.

1.2. **Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation**

The Trust has a duty under the DPA18 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed and documented. We can't rely on Opt out, it must be Opt in.

The DPA18 covers how the Trust obtains, hold, record, use and store all personal and special category (e.g. Health) information in a secure and confidential manner. This Act covers all data and information whether held electronically or on paper and extends to databases, videos and other automated media about living individuals including but not limited to Human Resources and payroll records, medical records, other manual files, microfilm/fiche, pathology results, images and other sensitive data.

DPA18 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the DPA18 please see the 'information use framework policy', or contact the Information Governance Team rch-tr.infogov@nhs.net

2. The Guidance.

2.1. The National Patient Safety Authority (NPSA) has highlighted the risks when prescribing methotrexate including failings from poor monitoring of therapy, which have led to fatalities. This Shared Care Guideline reflects these recommendations.

2.2. **Methotrexate must only be administered as a WEEKLY dose**. Serious errors have occurred as a result of ambiguous instructions.

2.3. Methotrexate requires careful monitoring to avoid toxicity. It is recommended that it is initiated in primary care only after consultant diagnosis and under consultant supervision. Patients may be switched from oral to subcutaneous methotrexate due to poor tolerance, particularly gastrointestinal side effects, or to improve efficacy.

2.4. This SCG covers the treatment of adults with inflammatory joint disease or connective tissue disease, and treatment of adults with psoriasis and other rare skin diseases.

2.5. Preparations and Dosage

- Methotrexate 2.5mg tablets
- Methotrexate Pre-Filled Pen – the Metoject brand is the preferred product that patients are trained to administer; there are differences in the preparation and administration technique between brands. Please prescribe by brand name.
- If Metoject is prescribed generically, the concentration will be 50mg/mL with different volumes used depending on the dose required:
- Parallel-Imported Metoject Pre-Filled Syringes are available and can be supplied against prescriptions that do not specify pens - this may cause difficulties for patients who have only been trained to administer from the pen.

2.5.1. Usual oral dose range 2.5mg – 25mg **once weekly**. **Methotrexate should be prescribed as multiples of 2.5mg tablets.**

2.5.2. The label on prescribed/dispensed methotrexate should state the instructions clearly, for example: **'methotrexate 2.5mg tablets:** (number of tablets) **to be taken as a single dose ONCE A WEEK on XXXDAY**'.

2.5.3. Usual subcutaneous dose 7.5mg – 25mg **once weekly. Methotrexate should be prescribed as complete pre-filled pens by brand name. The majority of patients will use Metoject but a small number may be on alternative brands if they are unable to operate the device.** Patients will be trained on the use of injectable methotrexate by their specialist nurse. RCHT will train patients to use the Metoject device. If GP practices opt to use a different device then it is the responsibility of the GP practice to ensure patients can use it safely and appropriately.

2.5.4. The label on prescribed/dispensed methotrexate should state the instructions clearly, for example: 'methotrexate ……..injection: (dose) to be injected subcutaneously ONCE A WEEK on XXXDAY'.

2.5.5. To limit the side effects of methotrexate, all patients should receive folic acid 10mg once a week on the day after they take/administer methotrexate. Higher doses (e.g. 5mg daily omitted on the day of methotrexate) may sometimes be used on the advice of the specialist team

2.6. Contraindications – Methotrexate Should Not Be Used In Patients:

- With severe / significant hepatic or renal impairment (e.g. eGFR < 30mL/min/m^2)
- Active acute infectious disease, evidence of immunodeficiency syndrome
- With serious cases of anaemia, leucopenia, thrombocytopenia
- Receiving drugs with antifolate properties e.g. co-trimoxazole, trimethoprim, sulphonamides
- Who are breastfeeding
- Pregnancy – Methotrexate can reversibly affect female fertility. It can also affect the development of the unborn child so women of childbearing potential should use a

reliable method of contraception to avoid the risk of an unplanned pregnancy during treatment and for at least three months after discontinuing methotrexate. When planning a pregnancy it is important that women on this drug discuss their medication with the relevant clinical team. They will need to stop treatment with methotrexate for at least three months before attempting to conceive.

2.7. Precautions - Caution Is Advised In Patients:

- Who are elderly (consider reduction in dose)
- With haematological depression
- Renal impairment – use a maximum dose of 12.5mg week in patients with an eGFR 30 -60mL/min
- Diarrhoea, ulcerative disorders of GI tract
- Psychiatric disorders
- Radiotherapy
- Alcohol consumption increases the risk of liver fibrosis so it is advisable not to drink. However an occasional drink will not usually cause significant side effects.

2.8. Monitoring

2.8.1. Prior To Starting Therapy - The Rheumatology / Dermatology Team To Undertake And Communicate To Gp, Results Of:

- Chest x-ray
- Baseline assessment of renal and liver function, and FBC
- Pulmonary function tests in selected patients.

2.8.2. Ongoing Monitoring - General Practice:

It is recommended that all blood counts are monitored and recorded in the patient record and patient booklet to comply with NPSA and GMS. The patient may be asked to show their methotrexate booklet when collecting prescriptions from a community pharmacy; this is an additional check to ensure that appropriate monitoring is being undertaken. DO NOT issue further prescriptions unless the patient is attending for the required blood monitoring.

- Then FBC, Electrolytes & LFTs every 2 weekly until on stable dose for 6 weeks, then monthly thereafter for 3 months, then at least every 12 weeks unless advised otherwise. Some patients at increased risk of toxicity may be advised to have monthly blood tests for longer by their specialist team.
- CRP and ESR should be measured at the same intervals, to assist specialist teams in monitoring response to treatment (as trends are more helpful than isolated results).
- Always look at the mean corpuscular volume (MCV). A rising value may precede marrow dysplasia BUT check for other causes before stopping treatment (eg B12, TFT, Folate and alcohol consumption).
- Note that Dermatology also request pro-collagen III (PIIINP) test at regular intervals – this will be carried out by secondary care if indicated.

2.8.3. If Any Of The Following Occur, Repeat The Test, Consider Interrupting Treatment And If Required Contact The Specialist Team For Advice:

- WCC < 3.5 x 10^9/L – particularly if falling trend
- Neutrophils < 1.6 x 10^9/L – particularly if falling trend
- Mean Cell Volume > 105 – particularly if rising trend
- Unexplained eosinophilia > 0.5 x 10^9/L
- Platelet count < 140 x 10^9/L
- ALT and/or AST > 100
- Unexplained reduction in albumin (below 30 g/L)
- Creatinine increased > 30% over 12 months
- eGFR decreases < 60mL/min/1.73m² and there is a significant falling trend. If eGFR deceases to between 30 and 60mL/min/1,73m² but is stable, reduce the dose to a maximum of 12.5mg weekly
- eGFR decreases < 30mL/min/1.73m², discontinue methotrexate and repeat the test 10-14 days later. If eGFR improves to > 30mL/min/1.73m², is stable, and the drop is due to a reversible cause (e.g. AKI), methotrexate can be restarted with fortnightly bloods for a month, then monthly. If eGFR does not improve, contact the specialist team for advice.
- ***Severe*** nausea or diarrhoea
- ***Severe*** mouth or genital ulceration

NB: Do not routinely stop treatment prior to surgery or if the patient has an infection, unless hospital admission or parenteral antibiotics are required.

2.9. SIDE EFECTS

2.9.1. Patients must report mouth ulcers, sore throat, fever, epistaxis, unexpected bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

2.9.2. If pulmonary symptoms are reported, these should be investigated urgently with a chest x-ray to exclude pneumonitis.

2.9.3. Beware of patients attending GP surgeries or pharmacies presenting with other symptoms; signs of methotrexate toxicity may present as, for example, breathlessness, dry persistent cough, vomiting and diarrhoea.

2.9.4. Very common/Common:

- Mouth ulcers, nausea and diarrhoea, hair loss

2.9.5. Uncommon:

- Headaches, bone marrow suppression, lung inflammation, liver inflammation, clinically significant renal failure

2.9.6. Very rare:

- Drowsiness

2.10. COMMON/SIGNIFICANT DRUG INTERACTIONS

- Folate antagonists should be avoided – nitrous oxide, co-trimoxazole, **trimethoprim,** sulphonamides, phenytoin and some antimalarials.
- NSAIDs – This is not considered to be a problem in patients with inflammatory arthritides as the doses used take this interaction into account. However it may be an issue with Dermatology patients and advice should be sought from the Dermatology Team
- Ciclosporin
- Acitretin
- Clozapine: increased risk of agranulocytosis
- Leflunomide: increased risk of liver toxicity
- Drugs affecting transport function of renal tubules – ciprofloxacin, penicillins, probenecid, aspirin (though low-dose aspirin can be used safely)
- Caution is needed when co-prescribing hepatic or nephrotoxic drugs

2.11. VACCINATIONS

2.11.1. The Green Book should be regarded as the definitive source of information regarding vaccination; chapter 7 deals specifically with immunosuppressed patients.
Recommended vaccines for all patients include influenza (annually) and pneumococcal pneumonia, as a single dose of Pneumovax. Ideally this should be administered before starting treatment, but if this is not possible it should be administered as soon as practicable.

2.11.2. Low levels of immunosuppression are not considered an absolute contraindication to the shingles vaccine (Zostavax) and the Green Book recommends that low-dose (≤ 25mg/week) methotrexate is not a contraindication in most patients, though clinician discretion is advised. Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles; this will need to be discussed with the on-call Consultant Medical Microbiologist.

2.11.3. Other live vaccinations *may* be permitted; Refer to the Green Book for advice re: other vaccinations/infections.

2.12. HANDLING AND DISPOSAL

2.11.1. The patient will be trained in safe self-administration of subcutaneous methotrexate by one of the lead nurses in an outpatient setting using Metoject. When the patient feels confident, and the nurse is satisfied that the patient is

able to self-administer, they can start to self administer at home. The hospital will supply the first cytotoxic sharps bin.

2.11.2. If the GP surgery decide to prescribe a different brand of methotrexate injections, they are responsible for patient training as above.

2.11.3. Should a nurse administer subcutaneous methotrexate, then it is advised they follow accepted good practice as described in the RCN guidance (see reference). Gloves and apron should be worn and methotrexate should not be administered by anyone who is, or suspects they may be, pregnant.

2.11.4. All waste contaminated with methotrexate is classed as a cytotoxic waste and therefore should be disposed in accordance with local policy for the disposal of hazardous waste. Disposal of full sharps bins is via Cornwall Council (see **http://ow.ly/IU8m30ds1ST** or call 0300 1234 141 for details).

2.11.5. For home use, purple lidded cytotoxic sharps bins can be prescribed on an FP10 as: Sharpsguard (Daniels) or Sharpsafe (Frontier) Cyto/Purple, 1 Litre. NB. Not all practice computer systems list the colour of the container and so prescribers may need to manually add the word 'purple' to the prescription to ensure a cytotoxic one is supplied.

2.13. Areas Of Responsibility For The Sharing Of Care

2.12.1. These are suggested ways in which the responsibilities for the management of patients with rheumatoid arthritis or psoriasis and other rare skin disorders who are prescribed oral or subcutaneous methotrexate can be shared between the specialist and the general practitioners. GPs are invited to participate. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

2.12.2. In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.12.3. Specialist:

- Decision to prescribe methotrexate.
- Discussion with the patient regarding the benefits and side effects of treatment and gain consent to treatment. Refer patient to specialist nurse service where appropriate (e.g. new patient) for advice on taking/administering the drug, its cautions, side effects associated with treatment, monitoring requirements and the timing of re-assessment and by whom.
- A patient information leaflet and booklet for recording test results must be issued.
- To remind patients to bring their monitoring booklet with them each time they see a healthcare professional (so results can be recorded appropriately) and each time they collect a prescription from the community pharmacy.

- Either start oral methotrexate treatment by providing the first prescription and ensuring the patient's condition is stabilized (usually requires two to three month's treatment prescribed by the specialist), or, if appropriate, ask the GP whether they are willing to participate in shared care using the shared care agreement letter, and initiate treatment. In general, Rheumatology ask primary care to initiate oral treatment, whereas Dermatology ask primary care to take over after about one to two months. **Subcutaneous treatment should always be initially prescribed by the specialist.**
- Prompt communication with GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- Specify review dates at clinically relevant time intervals for both the GP and the consultant.
- Advice to GPs on when to stop treatment.
- Ensure clear arrangements for back-up advice and support.
- Reporting adverse events to the MHRA.

2.12.4. General Practitioner:

- If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter.
- Prescribing of oral or subcutaneous methotrexate after communication with specialists regarding the need for treatment.
- If relevant, taking note of National Patient Safety Advice on methotrexate and on injectable medicines
- Monitoring as outlined in the shared care guideline, and stopping treatment if patients are non-compliant with monitoring requirements.
- Recording of the results of monitoring in GP system and encouraging the recording of results in the patient booklet.
- Ensure that the GP computer system has an alert flag in accordance with NPSA guidance.
- Prompt referral to a specialist if there is a change in the patient's status.
- Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Reporting adverse events to specialist and MHRA.
- Stopping treatment in the case of a severe adverse event or as per shared care guideline.
- Provision of replacement monitoring booklets when full or lost/damaged.

2.12.5. Patient: and parent / carer responsibilities

- Report any adverse effects to their GP and/or specialist whilst being treated with methotrexate.
- Ensure that they have a clear understanding of their treatment. The patient may need support from an appropriate health professional on how to complete the patient held record.
- Ensure they organise and attend for monitoring blood tests as per shared care guideline.
- Aware that treatment will be stopped if patient does not attend for monitoring
- Aware that a record of monitoring results should be entered in their booklet, and that they may be asked to show this record when collecting prescriptions from their pharmacy.

- Disposes of used syringes and full sharps bins appropriately and safely.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Diversity & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Oral and Subcutaneous Methotrexate Shared Care Guideline V3.0				
Date Issued/Approved:	January 2018				
Date Valid From:	March 2019				
Date Valid To:	March 2022				
Directorate / Department responsible (author/owner):	Rheumatology & Dermatology Team / Pharmacy - Head of Prescribing Support Unit				
Contact details:	01872 253548				
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists				
Suggested Keywords:	Methotrexate				
Target Audience	RCHT	CFT	KCCG		
	✓		✓		
Executive Director responsible for Policy:	Medical Director				
Date revised:	Jan'19				
This document replaces (exact title of previous version):	Shared care guideline for oral and subcutaneous methotrexate				
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee				
Divisional Manager confirming approval processes	Care Group General Manager				
Name and Post Title of additional signatories	Not required				
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}				
	Name: Kevin Wright				
Signature of Executive Director giving approval	{Original Copy Signed}				
Publication Location (refer to Policy on Policies – Approvals and	Internet & Intranet	✓	Intranet Only		

Ratification):				
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards				
Related Documents:	Summary of Product Characteristics. Flint J, Panchal S, Hurrell A, van de Venne M, Gayed M, Schreiber K, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: Standard and biologic disease modifying anti-rheumatic drugs and corticosteroids: Table 1. Rheumatology. 2016:55: 1693–1697. Joint Committee on Vaccination and Immunisation. Immunisation against infectious diseases. London: Public Health England; 2014. Available from: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book. Ledingham J, Gullick N, Irving K, Gorodkin R, Aris M, Burke J, et al. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology. 2017;56(6):865-8. Royal College of Nursing. Administering subcutaneous methotrexate for inflammatory arthritis. 3rd ed. London: Royal College of Nursing; 2016. https://webarchive.nationalarchives.gov.uk/20171030124143tf_/http://www.nrls.npsa.nhs.uk/resources/			
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
Sept 12	V1.0		M Wilcock, Head of Prescribing Support Unit

Nov 2015	V2.0	Minor revision	M Wilcock, Head of Prescribing Support Unit
Jan 2018	V2.1	Minor revision	M Wilcock, Head of Prescribing Support Unit
Jan 2019	V3.0	Minor revision with dosing in renal impairment	M Wilcock, Head of Prescribing Support Unit

Appendix 2. Initial Equality Impact Assessment Form

<table>
<tr><td colspan="6">Oral and Subcutaneous Methotrexate Shared Care Guideline V3.0</td></tr>
<tr><td colspan="3">Directorate and service area:
Pharmacy</td><td colspan="3">Is this a new or existing Policy:
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="3">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="5">To provide information on prescribing of methotrexate to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="5">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="5">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="5">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="5">General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td>Other</td></tr>
<tr><td>X</td><td></td><td>X</td><td></td><td></td></tr>
<tr><td colspan="5">Please record specific names of groups
Cornwall Area Prescribing Committee</td></tr>
<tr><td>What was the outcome of the consultation?</td><td colspan="5">Agreed</td></tr>
</table>

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:

Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No X**	

9. If you are **not** recommending a Full Impact assessment please explain why.

Not required

Signature of policy developer / lead manager / director M Wilcock		Date of completion and submission 28/11/18
Names and signatures of members carrying out the Screening Assessment	1. M Wilcock 2. Policy Review Group	**PRG APPROVED**

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead
c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

This EIA will not be uploaded to the Trust website without the signature of the Human Rights, Equality & Inclusion Lead.

A summary of the results will be published on the Trust's web site.

Signed __M Wilcock _____

Date _____28/11/18_____