SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR METHOTREXATE ORAL (ADULT RENAL)

N.B. This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Methotrexate

Formulation: Tablets

Strength: 2.5mg

STATUS OF MEDICINE

Licence status: Off-label (For Vasculitis)

Formulary status: Formulary

Black triangle medicine: NO

Risk minimisation materials: NO

CONDITION(S) TO BE TREATED

To Treat Vasculitis

TYPICAL DOSAGE REGIME (N.B. Once weekly dose, Folic acid 5mg should be given 72 hours after each dose)	
Licensed dose	See Renal Specialist for advice
Route of administration	Oral
Recommended starting dose	See Renal Specialist for advice
Titration dose/increment	See Renal Specialist for advice
Maximum dose	See Renal Specialist for advice
Situations requiring dose adjustment	See Renal Specialist for advice
Duration of treatment	See Renal Specialist for advice

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

1. **Baseline:**
   Chest X-ray, Full Blood Count (FBC); U&E and Liver Function Tests (LFTs).
2. Copy of results to be sent to GP.
3. Exclude pregnancy before starting therapy. **Advise men and women:**
   - To avoid conception during treatment and 6 months after discontinuation.
   - Of the potential adverse effect of methotrexate on reproduction.
4. Initiation of therapy and recommendations for dose increments. **This will be controlled by the Renal Specialist Consultant.**
5. The Renal Unit has primary responsibility for monitoring therapy according to the schedule below:
   - FBC, U&E and LFTs (including ALT and Alk Phos) every two weeks until dose and results stable for six weeks.
   - FBC, U&E and LFTs monthly while on stable dose, increasing to fortnightly after any dose changes.
   - If disease and dose stable for one year, monitoring frequency can be reduced if advised by specialist team.
   - Patients should be advised to report immediately any signs or symptoms of infection, especially sore throat, cough or dyspnoea.

RESPONSIBILITY OF PRIMARY CARE

To preserve vital venous access, monitoring will be done by the renal service at ARI unless otherwise notified or the patient develops an intercurrent illness which would require bloods to be taken in primary care.

A Practice agreeing to prescribe Methotrexate should:

1. Prescribe medication under the guidance of the Renal Specialist Consultant.
2. Ensure the GP is aware that the drug can cause:
   - Leucopenia
   - Thrombocytopenia
   - Stomatitis and GI ulceration
   - Suppression of ovarian and testicular function
   - New or increasing fever, dyspnoea or cough or the presence of rash or oral ulceration
   - Renal or Hepatic damage.
3. Ensure that the relevant monitoring requirements have been undertaken at the correct frequency.
4. Ensure when the patient has an intercurrent illness FBC, U+E and LFTs are done and make sure abnormal results are acted upon promptly.
5. Only continue to prescribe medication if it is being satisfactorily monitored.
6. Contact the Consultant/Renal Unit/On call Registrar in the event of a drug reaction, monitoring abnormality, or if you are concerned in any way regarding the current treatment regime.
7. Be alert for any of the known adverse reactions.

CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

1. Prescribe medication under guidance of consultant.
2. Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.
3. Ensure no interacting medications are prescribed in primary care.
4. Monitor for concordance with therapy.
5. Report any adverse events to Consultant and the MHRA using the Yellow Card System.
6. If an intercurrent illness occurs, when writing laboratory request forms always include details of the patient's medication.
7. If bloods are taken due to intercurrent illness, ensure they are monitored and contact hospital consultant to advise if results are out with range.
8. A single pneumococcal polysaccharide vaccine and annual influenza vaccine should be given.
9. Methotrexate is available in strengths of 2.5mg and 10mg – but **Grampian Policy is that only the 2.5mg strength be used to avoid the possibility of any confusion and potential unintentional overdose.**

N.B. In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

N.B. If something unexpected occurs contact Renal Unit, On Call Registrar or Consultant. Notify the Consultant if the drug is stopped.

RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- To minimise the risk of skin cancer, exposure to sunlight and Ultra Violet light should be limited by wearing protective clothing and using sunscreen with a high protection factor.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

CONTRAINDICATIONS

- Hypersensitivity to methotrexate or any excipients
- Significantly impaired hepatic function
- Severe/significantly impaired renal function
- Liver disease including fibrosis, cirrhosis, recent or active hepatitis
- Active infectious disease
- Pre-existing blood dyscrasias such as bone marrow hypoplasia, significant anaemia, leucopenia or thrombocytopenia
- Alcoholism
- Severe acute or chronic infections and immunodeficiency syndrome
- Avoid live vaccines
- Avoid concomitant use with drugs with antifolate properties
- Pregnancy should be avoided by using an effective contraceptive method for at least 6 months after using methotrexate.

PREGNANCY

Discuss with Consultant. Contraindicated in pregnancy. Effective contraception required during and for at least 6 months after discontinuation of treatment. Advise to contact their physician immediately should pregnancy occur. Advise men or women to avoid conception during and for at least three months after discontinuation.

BREAST-FEEDING

Not recommended. Discuss with Aberdeen Maternity Hospital.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

- Anorexia
- Nausea
- Vomiting
- Diarrhoea
- Ulcerative stomatitis (oral ulceration)
- Alopecia (usually minor).

Abnormal Monitoring Results	**Action To Be Taken**
• **WBC** < 4.0 x 10^9/L	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• **Neutrophils** < 2.0 x 10^9 /L	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• **> 2-fold rise in ALT or Alk Phos** (from upper limit of reference range) • Other significantly deranged LFT results	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant

Abnormal Monitoring Results	Action To Be Taken
• **Platelets** < 150x10^9 /L	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• MCV>105fl	Investigate and if B12 or folate low start appropriate supplementation
• Unexplained fever	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• Rash, oral ulceration	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• Unexplained fall in albumin	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• New or increasing dyspnoea or cough	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant
• Abnormal bruising or sore throat	Withhold until FBC result available. Discuss with Renal Unit/Registrar on call or Consultant
• Mild to moderate renal impairment	Withhold **until discussed** with Renal Unit/Registrar on call or Consultant

COMMON DRUG INTERACTIONS (for a full list see SmPC)

- Live vaccines should be avoided in patients taking methotrexate.
- NSAIDs and aspirin can reduce excretion of methotrexate. However **low dose aspirin and standard doses of NSAIDs may be continued, provided the GP/renal team are aware of their use.** The use of over the counter NSAIDs should be discouraged. Monitoring is essential if new prescriptions added.
- **Co-trimoxazole or trimethoprim must not** be co-administered with methotrexate as there is increased risk of haematological toxicity. Cases of severe bone marrow suppression have been reported.
- Acitretin may increase plasma concentration of methotrexate. Caution is advised.
- Probenecid will decrease the methotrexate transport function of renal tubules, thereby reducing excretion and almost certainly increasing methotrexate toxicity, monitoring essential.
- Vitamin preparations that contain folic acid should be avoided.

ADVERSE DRUG REPORTING

If an adverse reaction should occur, inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

https://www.medicines.org.uk/emc/product/9945/smpc

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of concern being raised, the primary care practitioner should contact the referring Consultant via the hospital switchboard, via their secretary, by e-mail or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call Renal Registrar may be contacted via switchboard.

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