

**South East London Integrated Medicines Optimisation Committee
(SEL IMOC, formerly the SEL Area Prescribing Committee)
Position Statement**

Reference	PS-028
Intervention:	Methotrexate 10mg tablets (including Matrex™) in patients prescribed 'low dose' methotrexate (i.e. ≤ 25mg)
Date of Decision:	August 2021
Date of Issue:	August 2021
Recommendation:	GREY – not recommended for routine prescribing
Further information	<p>Methotrexate is a folate antagonist that is prescribed to manage several conditions including rheumatoid arthritis, psoriasis and eczema. In overdose, methotrexate carries potentially life-threatening adverse effects, including bone marrow suppression, liver toxicity, pulmonary toxicity, and death. Between 1993 and 2017 there have been 21 reported deaths classified as poisoning with methotrexate as the sole drug associated [1]. Methotrexate overdoses are featured on the NHS Never Events list [2].</p> <p>Oral methotrexate is available as 2.5 mg tablets or 10 mg tablets. Both strengths are similar in size and colour. The prescription of 10mg tablets, or mixed strength prescriptions, has been identified as a key ongoing issue that can increase the risk of harm from errors. Patients who mistakenly take higher strength methotrexate tablets are at risk of fatal overdoses [3]. For these reasons, national recommendation is to give single-strength prescriptions of 2.5mg tablets of oral methotrexate (when patients are prescribed 'low dose' methotrexate (i.e. ≤ 25mg)).</p> <p>There are a few other important recommendations that prescribers must follow to reduce the risk of an accidental overdose and ensure safe prescription and administration of oral methotrexate [4,5]:</p> <ul style="list-style-type: none"> ● Ensure the patient understands why they are taking the medication and the dosage is clear to the patient, in milligrams and the number of tablets to be taken ● As oral methotrexate is taken once weekly, this unusual frequency can lead to confusion for some patients, who may take the medication daily. Care must therefore be taken to explain the weekly frequency of the medication to the patient or carer, ensuring that this is understood, and set up a day that the patient will be able to regularly take the medication, which should then be noted on the prescription. ● Ensure the patient <u>is not</u> co-prescribed any other pharmaceutical forms of methotrexate e.g. subcutaneous or oral solutions or brand of methotrexate ● Explain to the patient and carer the potential risk of fatal outcomes with accidental overdoses ● Ensure the dosage, frequency, which specific day of the week and reason for taking folic acid supplements is also explained clearly. The

	<p>folic acid supplement should be taken on a different day to the methotrexate.</p> <ul style="list-style-type: none"> ● Prescription of methotrexate with either co-trimoxazole or trimethoprim is absolutely contraindicated
Cost Impact for agreed patient group	Across NHS SEL CCG spend for Methotrexate 10mg tablets for April 2020 to March 2021 was ~£8K.
Usage Monitoring & Impact Assessment	Trusts: Monitor non-formulary requests
	SEL CCG Borough Medicines Optimisation Teams: Monitor EPACT2 data and exception reports from GPs if inappropriate requests to prescribe are made to primary care
Evidence reviewed.	<ol style="list-style-type: none"> 1. MacKenna B. Methotrexate [Internet]. figshare; 2019. Available at: <https://figshare.com/collections/Methotrexate/4542308/1> [Accessed 9 April 2021] 2. England N. <i>NHS England</i> [Internet]. England.nhs.uk. 2020. Available at: <https://www.england.nhs.uk/publication/never-events/> [Accessed 9 April 2021] 3. MacKenna B. et al <i>Trends and variation in unsafe prescribing of methotrexate: a cohort study in English NHS primary care</i>. <i>British Journal of General Practice</i> 2020; 70 (696): e481-e488. Available at: <https://doi.org/10.3399/bjgp20X710993> [Accessed 8 July 2021] 4. Joint Formulary Committee. <i>British National Formulary</i>. 2021. <i>METHOTREXATE Drug BNF content published by NICE</i>. [online] Bnf.nice.org.uk. Available at: <https://bnf.nice.org.uk/drug/methotrexate.html#importantSafetyInformations> [Accessed 8 April 2021]. 5. National Patient Safety Agency. NPSA alert: improving compliance with oral methotrexate guidelines 2006. 2006. <https://www.sps.nhs.uk/articles/npsa-alert-improving-compliance-with-oral-methotrexate-guidelines-2006/> (Accessed 10 April 2021). 6. OpenPrescribing, 2021. <i>Methotrexate 10 mg tablets by all CCGs OpenPrescribing</i>. [online] Openprescribing.net. Available at: <https://openprescribing.net/measure/methotrexate/> [Accessed 8 July 2021].

NOTES:

- a) SEL Integrated Medicines Optimisation Committee recommendations, position statements and minutes are available publicly via the SEL IMOC website.
- b) This SEL IMOC position statement has been made on the cost effectiveness, patient outcome and safety data available at the time. The position statement will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**

Appendix 1:

Suggested Template Letter from General Practice/ Specialist to Patients within the NHS SEL CCG, on changing 10mg methotrexate tablets to 2.5 mg tablets (for patients on 'low dose' i.e. $\leq 25\text{mg}$) to improve on the safety of methotrexate prescriptions

[Practice name]
[Address]
[Tel]
[Email]
[Date]
[Title/Initial/Surname]
[Patient Address Block]

Dear [Title] [Surname],

Re: Change to the strength of your prescribed methotrexate tablets

As your practice GP, we have recently reviewed your medicines and are making a change to the strength of methotrexate tablets we prescribe you. You have been receiving a total dose of **xxxxx** prescribed as 10mg strength tablets [and 2.5mg tablets **delete as appropriate**]. When your next prescription is issued, we will prescribe the same dose as 2.5mg strength tablets. This means, to make up the same dose, you will need to take **xxxxx** of the 2.5mg tablets on the same day as you are used to taking your Methotrexate tablets. Your specialist/ GP **delete as appropriate** is fully aware of this change.

In summary:

Old prescription (no longer applicable)	NEW prescription (what you will receive from now on)
[insert total dose] as [insert number of tablets] of Methotrexate 10mg tablets [and 2.5mg tablets <i>*delete as appropriate*</i>]	[insert total dose] as [insert new number of tablets] of Methotrexate 2.5mg tablets

Please note we are not making any changes to the total dose of your methotrexate prescription.

The 2.5mg tablets need **to be taken ONCE a week** on the same day as you used to take your 10mg tablets. The changes are being made in all GP practices in South East London and will help with patient safety.

We advise that you always check the label on your methotrexate box/ bottle to make sure you are taking the correct dose, as stated on your prescription.

If you are concerned and wish to discuss the matter further, please speak to your specialist at the hospital, doctor at the surgery, practice pharmacist at the surgery or your local community pharmacist, who will also know of this change.

Yours sincerely, [GP Name]