

METHOTREXATE - SAFE PRESCRIBING – ONCE A WEEK!

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- ▶ ALWAYS DOUBLE-CHECK PRESCRIPTIONS - PRESCRIBING AND DISPENSING ERRORS CAUSE THE MOST HARM
- ▶ CLEARLY EXPLAIN THE DOSING SCHEDULE TO PATIENTS
- ▶ TELL PATIENTS TO REPORT ADVERSE REACTIONS AND CONTRAINDICATIONS
- ▶ BE AWARE OF INTERACTIONS THAT INCREASE THE RISK OF TOXICITY
- ▶ ENSURE THERE IS A MONITORING PLAN

Low-dose (less than 25mg) oral methotrexate therapy, taken as a single dose once a week, is a safe and effective treatment when prescribed for inflammatory conditions such as severe psoriasis and rheumatoid arthritis.

Methotrexate is usually well tolerated and its side-effects are predictable.

ALWAYS DOUBLE-CHECK PRESCRIPTIONS

The most common cause of significant patient harm occurs when methotrexate is unintentionally prescribed and dispensed **daily** rather than **once a week**. Harm may also occur when the wrong strength is dispensed.

Please double-check prescriptions:

right strength right dose right frequency (weekly)

Prescribers are advised to specify a **day of the week** (written in full) on which the dose should be taken and to recommend the **strength** to be dispensed. Consider specifying only 2.5mg tablets to be dispensed. The day of the week in full, should also be printed on the label by the pharmacy.

CLEARLY EXPLAIN THE DOSING SCHEDULE TO PATIENTS

The unusual weekly dosing schedule has promoted medication errors, some of which have been fatal. Always ensure patients know how to take their dose; written resources may help. See the patient guide available on www.saferx.co.nz

TELL PATIENTS TO REPORT ADVERSE REACTIONS AND CONTRAINDICATIONS

Adverse reactions

Many of the side-effects are due to the inhibition of folate metabolism and include nausea, stomatitis and bone marrow suppression. These symptoms can be reduced with oral folic acid tablets (5mg once a week, on a different day to methotrexate) without affecting the efficacy of methotrexate and should be prescribed for all patients. A simple mnemonic tool is used by some patients 'Methotrexate on Monday and

Folic acid on Friday' to help them remember which day to take their tablets.

Advise patients to report **any** symptoms of toxicity to their GP or specialist immediately. Toxicity may present as symptoms of bone marrow suppression (eg fever, sore throat, mouth ulcers), hepatotoxicity (eg abdominal pain, jaundice), or pulmonary toxicity (eg new or increasing dyspnoea, chest pain, hypoxaemia, dry cough). Pulmonary toxicity can progress rapidly; it may not be fully reversible and is potentially fatal. Diarrhoea and ulcerative stomatitis can progress to potentially fatal haemorrhagic enteritis and intestinal perforation if methotrexate is continued.

Contraindications

Contraindications to treatment include active infection, alcoholism, peptic ulcer disease, poor nutritional status and recent exposure to chicken pox or herpes zoster infection. Advise patients to inform their GP or specialist if these conditions occur.

Women of child bearing potential should have pregnancy excluded before starting methotrexate. Women or men taking methotrexate whose partner is of child bearing potential should use effective contraception during treatment and for three months after cessation.

BE AWARE OF INTERACTIONS THAT CAN INCREASE THE RISK OF TOXICITY

Methotrexate can be hepatotoxic, concomitant use with other hepatotoxic agents (including alcohol) will increase the risk of toxicity, which can progress to cirrhosis in severe cases. One to two standard alcoholic drinks once or twice a week is unlikely to cause a problem, but more than four standard drinks on any one occasion are strongly discouraged.

Doses of methotrexate should be reduced in cases of poor renal function, whether caused by concomitant medications, such as non-steroidal anti-inflammatories (NSAIDs) and diuretics, dehydration, or kidney disease. Encourage patients to ask for advice before taking NSAIDs.

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The risk of toxicity can be increased if methotrexate is taken with some antibiotics such as penicillins and tetracycline. **Trimethoprim and cotrimoxazole significantly increase the risk of bone marrow aplasia and should be avoided.** Live vaccines should be avoided; however inactivated vaccines such as the annual influenza vaccination may be given.

For more information, consult the data sheet or the 'Interaction' function on the *New Zealand Formulary* www.nzf.org.nz.

ENSURE THERE IS A MONITORING PLAN

Inadequate monitoring can also result in harm. A full blood count, renal and liver function tests, and in some cases chest X-ray and respiratory function, need to be checked before treatment is started. Monitoring should be repeated at regular intervals so the patient can be evaluated, and any toxicity identified. Repeat prescriptions should not be provided without a full blood count and liver function test having been performed within the previous 4 to 12 weeks.

See Table 1 for more details, but please note that **local guidelines may vary;** follow the advice of the treating specialist about the frequency of testing.

In all cases, an agreed management plan should be in place for each patient specifying the doctor (GP or specialist) who will take primary responsibility for changes to dosing, and for arranging, reviewing and acting upon laboratory investigations.

ACKNOWLEDGEMENTS

We wish to thank Hugh de Lautour, Rheumatologist and Elizabeth Brookbanks, Pharmacist Team Leader, Medicine, at Waitemata District Health Board, for their valuable contribution to this bulletin.

KEY REFERENCES

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2. Best Practice Advisory Centre. Recommended Investigations for some commonly used DMARDs. Best Practice Journal 2008;17:29-32 www.bpac.org.nz/magazine/2008/october/docs/bpj17_dmards_pages_29-32_pf.pdf (Accessed 04-10-18)
3. Hospira New Zealand Limited. DBL Methotrexate injection and tablets data sheet 25-08-2017. www.medsafe.govt.nz/profs/datasheet/d/dblmethotrexateinjmayne.pdf (Accessed 08-10-18)
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METHOTREXATE

Methotrexate Monitoring Recommendations (Adapted from BPAC 2008;17:29)

Monitoring	Frequency	Parameters	Action
Full blood count (FBC)	Baseline, then every 2 weeks until dose and monitoring has been stable for 6 weeks Thereafter every 4-12 weeks	WBC $<3.5 \times 10^9/L$ Neutrophils $<2.0 \times 10^9/L$ Platelets $<150 \times 10^9/L$	Discuss with specialist team immediately
		MCV $> 105 fL$	Check vitamin B ₁₂ , folate, TSH and treat abnormalities
Liver function tests (LFTs)	Baseline, then every 2 weeks until dose and monitoring has been stable for 6 weeks Thereafter every 4 to 12 weeks	AST, ALT $>$ twice the upper limit of reference range	Withhold, discuss with specialist and check: Alcohol intake NSAID intake - may cause liver dysfunction Other medication
		Unexplained decrease in albumin (in absence of active disease)	Withhold and discuss with specialist
Serum creatinine	Baseline, then every 2 weeks until dose and monitoring has been stable for 6 weeks Thereafter every 4-12 weeks	Significant deterioration in renal function	Reduce dose
Rash or oral ulceration	Inform patient to report immediately if occurs		Withhold, discuss with specialist. Try folic acid mouthwash for mucositis.
Nausea and vomiting, diarrhoea	Inform patient to report immediately if occurs		Consider subcutaneous use to avoid nausea
Dyspnoea or dry cough (pneumonitis)	Baseline chest X-ray and respiratory function tests may be advised		Withhold and discuss URGENTLY with specialist team. Arrange chest X-ray and respiratory function tests
Severe sore throat, abnormal bruising	Inform patient to report immediately if occurs		Immediate FBC, withhold methotrexate until results available. Discuss abnormal results with specialist

ALT = Alanine transaminase

AST = Aspartate transaminase

MCV = Mean cell volume

NSAID = Non-steroidal anti-inflammatory drug

TSH = Thyroid stimulating hormone

WBC = White blood cells

[CLICK HERE FOR FURTHER INFORMATION ON METHOTREXATE AND A FULL REFERENCE LIST](#)

For further information on other high-risk medicines visit our website at : www.saferx.co.nz