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Waitemata District Health Board
Best Care for Everyone

METHOTREXATE - SAFE PRESCRIBING - ONCE A WEEK!

- 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, taken as a single dose **once a week**, is generally safe for severe psoriasis and rheumatoid arthritis. Methotrexate is usually well tolerated and its side-effects are predictable.

ALWAYS DOUBLE-CHECK PRESCRIPTIONS - PRESCRIBING AND DISPENSING ERRORS CAUSE THE MOST HARM

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) when the dose should be taken **and** the **strength** to be dispensed. The day of the week should be printed on the label.

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. 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. Methotrexate should be avoided during pregnancy and breastfeeding. Ensure women of child-bearing age are not pregnant before starting methotrexate. Effective contraception should be used during, and for at least 3 months after treatment in both men and women.

BE AWARE OF INTERACTIONS THAT CAN INCREASE THE RISK OF TOXICITY

Methotrexate can be hepatotoxic. Concomitant use with other hepatoxic 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

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(such as non-steroidal anti-inflammatories (NSAIDs) and diuretics), dehydration, or kidney disease.Encourage patients to ask for advice before self-medicating with NSAIDs.

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

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 toxicities identified. Repeat prescriptions should not be provided without a full blood count and liver function test having been performed within the previous 4 to 8 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.

An agreed management plan should specify who takes responsibility for changes to dosing, and for arranging, reviewing and acting upon laboratory investigations.

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REFERENCES

1. Health Quality and Safety Commission. Methotrexate - once weekly dosing. Medication alert 14, April 2012. http://www.hqsc.govt.nz/assets/Medication-Safety/Alerts-PR/Oral-methotrexate-Alert-final.pdf (Accessed 04-05-12)
2. Best Practice Advisory Centre. Recommended Investigations for some commonly used DMARDs. Best Practice Journal 2008;17:29-32 http://www.bpac.org.nz/magazine/2008/october/docs/bpj17_dmards_pages_29-32_pf.pdf (Accessed 19-04-13)
3. Hospira New Zealand Limited. DBL Methotrexate injection and tablets data sheet 14-09-12. http://www.medsafe.govt.nz/profs/datasheet/d/dblmethotrexateinjmayne.pdf (Accessed 18-04-13)
4. The New Zealand Formulary, methotrexate. http://www.nzf.org.nz/nzf_4548.html?searchterm=methotrexate (Accessed 18-04-13)

CLICK HERE FOR FURTHER INFORMATION ON METHOTREXATE AND A FULL REFERENCE LIST

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Table 1

Methotrexate Monitoring Recommendations

(Adapted from BPAC 2008;17:29)

Monitoring	Frequency	Parameters	Action
Complete blood count (CBC)	Baseline, then every 2 weeks until stable for 6 weeks; thereafter every 4-8 weeks	WBC <3.5 x 10^9/L Neutrophils <2.0 x 10^9/L Platelets <150 x 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 stable for 6 weeks; thereafter every 4-8 weeks	AST, ALT > twice the upper limit of reference range	Withhold, discuss with specialist and check: alcohol intake NSAID intake and other medication
		Unexplained decrease in albumin (in absence of active disease)	Withhold and discuss with specialist
Serum creatinine	Baseline, then every 2 weeks until stable for 6 weeks; thereafter every 4-8 weeks	Significant deterioration in renal function	Reduce dose
Rash or oral ulceration	Inform patient to report immediately if occurs		Withhold, discuss with specialist. Try folinic acid mouthwash for mucositis
Nausea and vomiting, diarrhoea	Inform patient to report immediately if occurs		Consider subcutaneous route to avoid nausea if other causes excluded
Dyspnoea or dry cough (pneumonitis)	Baseline chest X-ray and respiratory function tests may be advised		Discuss URGENTLY with specialist. Arrange chest X-ray and respiratory function tests
Severe sore throat, abnormal bruising	Inform patient to report immediately if occurs		Immediate CBC, withhold methotrexate until results available. Discuss abnormal results with specialist

WBC = White blood cells

MCV = Mean cell volume

TSH = Thyroid stimulating hormone

NSAID = Non-steroidal anti-inflammatory drugs

AST = Aspartate transaminase

ALT = Alanine transaminase