Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

CUH
Ospidéal Ollscoile Chorcaí
Cork University Hospital

Department of Rheumatology

Methotrexate
GP Information Sheet

Methotrexate
Methotrexate is a folic acid antagonist. Its main therapeutic effect is inhibition of DNA synthesis but it also impairs RNA and protein synthesis.

Pre Treatment Assessment
FBC, U&E, Creatinine, LFT and in selected patients chest X-Ray.

Typical Dose Regimen
7.5/10mg weekly, increasing to a maximum of 20mg. Occasionally the schedule may be adjusted gradually to achieve an optimal response but should not exceed a total weekly dose of 25mg.

Patients should be prescribed folic acid 5mgs at least one day a week, not to be taken the day they take their Methotrexate.

Precautions and Contraindications
As Methotrexate is highly protein-based and excreted unchanged in urine, it may interact with other drugs. Cotrimoxazole or Trimethoprim must be avoided in patients taking Methotrexate. Live vaccines should also be avoided in patients taking Methotrexate but **Flu, pneumonia and covid-19 vaccines are safe and should be given however methotrexate should be held for 1 week after the vaccine.**

Non-steroidal anti-inflammatory drugs may reduce the excretion of Methotrexate, they are not contraindicated but patients on this combination should be monitored carefully.

Alcoholism is an absolute contraindication, but one or two glasses of wine or two pints of beer a week are permitted. Methotrexate is contraindicated in patients with severe anemia, leucopenia and thrombocytopenia. Methotrexate is teratogenic, so effective contraception is required in treated women of childbearing age and for 1 month after discontinuing the drug. Methotrexate may also temporarily decrease fertility. According to the recent studies, paternal exposure to Methotrexate is not contra indicated. Probenecid can severely inhibit renal excretion of Methotrexate and so is contraindicated. Lower doses should be used in the frail elderly or if there is significant renal impairment. Phenytoin and Theophylline should be avoided as they may increase Methotrexate blood levels.

Time to Response
6 weeks to 3 months

Monitoring
FBC and LFT's monthly for 3 months.
Once the patient is stable with no alteration in drug dose, reports of side effects, or co-morbidities every 3 months thereafter with a renal profile every 6 months.

Actions to be taken

If significant deterioration in renal function occurs reduce dose of Methotrexate and discuss with Rheumatologist.

If abnormal bruising occurs ensure platelets are normal.

Neutrophils <1.5* 10^9/1	Hold drug and repeat in 2 weeks
Platelets <120* 10^9/1	
Significant deterioration in renal function	Reduce dose and discuss with Rheumatologist
>2 but <3 fold rise in AST or ALT from upper limit of reference range	Reduce dose and repeat LFT
>3 fold rise in AST or ALT from upper limit of reference range	Hold Methotrexate and repeat LFT within 2-4 weeks.
2-3 fold fall in albumin	Discuss with Rheumatologist
MCV>105 fl	Investigate and if B12 or folate low- start appropriate supplementation.

Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Side Effects

Haematological: Neutropenia, thrombocytopenia, macrocytosis, rarely aplastic anemia

Hepatic: Cirrhosis and fibrosis, risk factors are alcohol abuse, obesity and previous liver disease.

Gastro-intestinal: Nausea, vomiting, abdominal pain, ulcerative stomatitis and diarrhoea.

Pulmonary: An allergically medicated pneumonitis is a rare early complication, manifesting as a progressive dyspnoea. This requires Methotrexate to be stopped and investigations undertaken. This is more likely to occur in smokers.

Mucocutaneous: Rashes, urticaria, erythematous pruritis, oral ulceration, skin pain and alopecia.

Renal: Acute tubular necrosis is a rare complication. Renal impairment is a relative contraindication, but therapy may still be used if serum creatinine is monitored and dosage adjusted accordingly.

Other: Headaches, depression, irritability and enteritis. Toxic epidermal necrolysis, Stevens- Johnson syndrome. Opportunistic infections may occur. Suppression of ovarian and testicular function may occur. There have been rare reports of lymphomas and other malignancies in patients being treated with Methotrexate. Methotrexate therapy increases the risk of developing lymphomas, Skin cancer and other malignancies. While taking Methotrexate patients are advised to avoid direct sun light and the use of tanning beds. They should use SPF 30 or higher when out in the sun.

Contact Details

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Please consult up to date relevant literature (data sheets) or BNF when prescribing this agent. Please contact the Rheumatology team if you have any other queries regarding the prescribed medication.