BNSSG Health Community's Traffic Light System
Shared Care Guidance

Section 1: Heading

Trust: North Bristol NHS Trust

Specialty / Department: Neurosciences

Drug:Methotrexate

Section 2: Treatment schedule

Immune suppression may be required for a variety of neurological conditions such as Myasthenia Gravis and CIDP. These are unlicensed indications.
Generally clinical improvement is normally seen within 2 to 3 months after starting treatment.
Methotrexate is usually given orally for these patients.

Dose Regimen
Test dose of 5 to 10 mg orally, then progressively increase to optimum response with a maintenance dose of 10 to 25 mg once per week.
Most patients can be maintained on 15mg to 17.5 mg once weekly but particular specialities may offer their own guidance for specific indications.
Folic acid 5 mg given once a week may reduce the incidence of toxicity. Give on a day different to the day of administration of methotrexate.
Lower doses of methotrexate should be used in the frail elderly or if there is significant renal impairment.

Section 3: Monitoring

Before treatment check:FBCs, U&Es, LFTs, creatinine, chest x-ray and folate. A physical examination including routine examination of lymph nodes should be carried out before starting treatment.
FBC, U&Es & LFTs should be checked weekly until therapy is stabilised, thereafter monitor every 2-3 months throughout treatment.
If liver function abnormalities occur treatment should be suspended for at least 2 weeks. It is only appropriate to restart methotrexate provided the abnormalities return to normal and re-exposure is deemed appropriate.
Renal function should be closely monitored before, during and after treatment. Reduce dose of methotrexate in patients with renal impairment.
Haematopoietic suppression caused by Methotrexate may occur abruptly and with apparently safe dosages.
Ask patient about and monitor for fever, rash, oral ulceration, sore throat or unexplained dyspnoea/cough (especially a dry, non-productive cough) at each visit.

If aspirin or other NSAIDs are given concurrently the dose of methotrexate should be carefully monitored. It is understood that the anti-inflamatory agents reduce excretion and increase risk of methotrexate toxicity. Dosage of methotrexate may therefore need to be reduced.

Section 4: Side-effects

Acute or chronic interstitial pneumonitis (pulmonary toxicity) may occur. Particular care and possible cessation of treatment are indicated if stomatitis or GI toxicity occurs as haemorrhagic enteritis and intestinal perforation may result.
If acute toxicity occurs patients may require treatment with folinic acid.
Side-effects and their management:
GI side-effects (loss of appetite, nausea, diarrhoea) -should subside, if troublesome nausea prescribe prochlorperizine. Folic acid 5mg once weekly (day before methotrexate dose) should reduce effects.
Hair loss-usually mild, rarely significant

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Abnormal bruising/sore throat-withold until FBC available
Rash/oral ulceration/stomatitis-withold and discuss with consultant
Macrocytosis: check B12, TSH and folate-treat accordingly if low
Bone marrow depression, manifesting usually as leucopenia, thrombocytopenia and anaemia, or any combination may occur. Withold and discuss with consultant if the following occurs:
WBC <3.5 x 109/l
Neutrophils < 2.0 x109/l
Platelets <150 x 109/l
Hepatotoxicity and liver cirrhosis reported. Treatment should not be started or should be discontinued if any abnormality of liver function tests or liver biopsy is present or develops during therapy. If there is a 2-fold rise in AST, ALT above upper reference values withold and discuss with consultant
Unexplained fall in albumin-withold and discuss with consultant
Significant (20%) reduction in renal function-withold and discuss with consultant
New or increasing dyspnoea/dry cough-withold and discuss with consultant
CNS disturbances-Headaches, drowsiness, blurred vision
Abnormal bleeding or bruising-check FBC and discuss with consultant
Severe or persistent infection/sore throat-withold, check FBC and discuss with consultant
Ask about side effects at every consultation.
Please note that in addition to absolute values for haematological indices a rapid fall or consistent downward trend in any values should prompt caution and extra vigilance.
Chicken pox/shingles infection - stop and commence aciclovir.

Section 5: Drug interactions

For clinically significant drug interactions see BNF (Appendix 1).

Methotrexate has some immunosuppressive activity and therefore the immunological response to concurrent vaccination may be decreased. In addition, concomitant use of a live vaccine could cause severe antigenic reaction and should therefore be avoided.
Excretion may be reduced and the risk of toxicity increased if given with: p-aminobenzoic acid, chloramphenicol, diphenylhydantoins, acidic anti-inflammatory agents, salicylates, sulphonamides, tetracyclines, thiazide diuretics, acitretin, probenicid or sulfinpyrazone or oral hypoglycaemics.
Methotrexate dose should be monitored with concurrent treatment with NSAIDs. Care should be taken with other anti-folate drugs due an increased risk of adverse effects.
Concomitant administration with trimethoprim, co-trimoxazole and nitrous oxide should be avoided.
Hepatic and nephrotoxic drugs should be avoided.

Section 6: Cautions and special recommendations

Pregnancy and breastfeeding are contraindications to methotrexate therapy. Effective contraception should be used during therapy in either men or women during and for 3 months after cessation of therapy.
Bone marrow suppression can occur abruptly; factors likely to increase toxicity include advanced age, renal impairment, and concomitant use with another anti-folate drug. Use with extreme caution in patients with liver or renal impairment, haematological depression, diarrhoea, GI ulceration and psychiatric disorders.
Patients should avoid contact with people who have active chickenpox or shingles and report any contact to their GP and hospital specialist. If immunosuppressed patients are exposed to chickenpox or shingles, they will need to be assessed for susceptibility and the need for aciclovir post exposure prophylaxis, see: UKHSA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles and the Green Book Chapter 34.

Section 7: Advice to the patient

A Methotrexate NPSA advice booklet must be given to patients started on treatment. Patients will be counselled on the dose and possible adverse effects of treatment. The patient will be warned to report

immediately the onset of any feature of blood disorders (e.g. infection, especially sore throat, bruising, and mouth ulcers), liver toxicity (e.g. nausea, vomiting, abdominal discomfort and dark urine), and respiratory effects (e.g. shortness of breath).
Patients will be advised to avoid self-medication with over-the-counter aspirin or ibuprofen.

Patients will be advised to contact their physician if they develop a cough or dyspnoea.
Following administration to a man or woman conception should be avoided by using an effective contraceptive method during treatment and for at least 3 months after using methotrexate. Fertility may be reduced during therapy but this may be reversible.
The patient should be carefully advised of the dose and frequency and the reason for taking methotrexate and any other prescribed medication (folic acid).

Section 8: Responsibilities for Secondary Care

Initiation of methotrexate treatment and prescribing remains with specialist for 3 months
Provide the patient with an NPSA methotrexate advice booklet.
Initial blood tests as recommended above.
Specialist teams to offer guidance to GP of time scale of treatment, doses and action if abnormal results occur.
Report adverse effects to MHRA via Yellow Card Reporting Scheme.

Section 9: Responsibilities for Primary Care

Prescribe methotrexate on an ongoing basis following initiation and 3 months prescription from Secondary Care.
Note: Within BSSNG only one strength of methotrexate tablet (2.5mg) should be prescribed and dispensed.
Monitoring FBC, platelets and LFTs ensuring they are within guided ranges, as discussed above
Report adverse events to the Consultant and MHRA
Reporting to and seeking advice from the consultant and/or specialist nurse on any aspect of patient care which is of concern to the GP and may affect disease treatment

Section 10: Contact details

Name	Organisation	Telephone number	Fax number	E-mail address	Availability
Consultant Neurologist	North Bristol NHS Trust	0117 9701212 access via switchboard			
Neurology registrar	North Bristol NHS Trust	0117 9701212 access via switchboard			

Section 11: Document details

Date prepared:	21/10/2011
Prepared by:	Emily Widdicombe and Kirsty Newton Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.
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Section 12: Collaboration

Document circulated to secondary care consultant Neurologists for their input. Document circulated to GP colleagues and Primary care lead pharmacists and senior NBT pharmacists.

Section 13: References

Summary of product characteristics. Maxtrex tablets 2.5mg. Available at www.medicines.org.uk/EMC/medicine Accessed December 2010
Stockley's Drug Interactions. Available at www.medicinescomplete.com Accessed December 2010
British National Formulary 60.
NHS Clinical Knowledge Summaries. Available at www.cks.nhs.uk