Whittington Health NHS

Rheumatology Department
Magdala Avenue
London N19 5NF

Consultants:
Prof. J. Dacre
Dr. I. Wamuo
Dr L. Congi
Dr A. Nuttall
Dr E. Nikiphorou

Switchboard 020 7272 3070
Main Appts: 020 7288 5511
Secretaries: 020 7288 5259/5740

Rheumatology Nurse 02072885257

Rheumatology Clinic 3D: Ext: 5708

British Society of Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR); (Feb, 2017) recommends harmonisation of monitoring schedules, for all DMARDs that require laboratory monitoring. These should follow the same frequency of testing.

PROTOCOL FOR THE ADMINISTRATION OF AZATHIOPRINE – INFORMATION FOR GENERAL PRACTITIONERS

BACKGROUND FOR USE:

Azathioprine is a cytotoxic immunosuppressive drug used as a disease modifying drug in the treatment of rheumatoid arthritis, connective tissue diseases and other chronic inflammatory conditions. It may also be used as a steroid-sparing agent. Azathioprine should only be initiated on the recommendation of a rheumatologist or relevant specialist.

DOSAGE REGIME:

Azathioprine is given orally starting at a dose of up to 1mg/kg daily increasing after 4-6 weeks to 2-3mg per kg /per day. Azathioprine may need to be given for 3 months before therapeutic benefit is seen. It is best taken with or after food to reduce nausea.

PRE TREATMENT ASSESSMENT BY RHEUMATOLOGIST:

• FBC, U& E's, Creatinine, eGFR, LFTs, ESR and CRP
• Check TPMT

TPMT (thiopurine methyl transferase) genotype must be checked. TPMT is a key enzyme in azathioprine metabolism which is inherited in autosomal dominant pattern. Up to 12% of population has reduced or very low TPMT activity and these individuals can be very sensitive to standard doses of azathioprine.

MONITORING:

- FBC, Creatinine, Calculated GFR, ALT, AST ; two weekly for six weeks then, once on stable dose, monthly for three months.
- Thereafter, FBC, Creatinine, Calculated GFR, ALT, AST and Albumin, at least every 12 weeks.

- More frequent monitoring is appropriate in patients at higher risk of toxicity

In addition to absolute values for haematological or biochemical indices a rapid fall/rise or consistent downward/upward trend in any value should prompt caution and extra vigilance.

• Azathioprine can be withheld for several days without causing a flare.
• Sunscreens and protective covering should be encouraged to reduce sunlight exposure

SIDE EFFECTS	ACTION
WBC < 3.5 X 10 ^ 9 / l Neutrophils <1.5 X 10^ 9/l	Withhold, and repeat WBC. If normal continue, if abnormal discuss with rheumatologist
Platelets < 150 X 10^ 9/l	Withhold, and repeat. If low discuss with Rheumatologist.
AST/ALT > 2 upper limit of normal reference range.	Withhold. Look for alternative cause, repeat LFT's, if abnormal discuss with rheumatologist
MCV > 105 fl	Check B12, folate and TFT. If low, start appropriate supplementation. Check alcohol status. If no cause found discuss with a rheumatologist
Rash or oral ulceration	Withhold until symptoms clear. Consider challenge at lower dose,if rash re appears stop azathioprine and discuss with Rheumatologist.
Hypersensitivity reactions	Fever, malaise, rash, vomiting, muscle/bone pain, dizziness. Stop azathioprine.
Abnormal bruising or sore throat	Withhold until FBC result available. Discuss with Rheumatologist.
Nausea, vomiting, diarrhoea	Administer tablets after meals to reduce nausea. An anti-emetic or dose reduction may help. If symptoms persist stop azathioprine and discuss with rheumatologist

CONTRAINDICATIONS AND PRECAUTIONS

Immunization with LIVE vaccines	Patients receiving azathioprine must NOT receive immunization with LIVE vaccines. Inactivated polio is available although sub-optimal response may be seen
Chicken pox /Shingles	Patients suffering from chickenpox or active skin lesions in shingles; withhold azathioprine and inform rheumatologist. Exposure to chickenpox or shingles; passive immunization should be carried out using VZIG

Pregnancy and breast feeding	Azathioprine is compatible with pregnancy at a daily dose not exceeding 2mg/kg per day. It is compatible with breast feeding and paternal exposure.
Renal impairment Hepatic impairment	Dose reduction necessary. Please discuss with rheumatologist.

NOTABLE DRUG INTERACTIONS (Refer to British National Formulary and Summary Product Characterisitcs)

• Sulphamethoxazole (as Co-trimoxazole) /Trimethoprim: can cause life threatening marrow toxicity

• Allopurinol: Dose of azathioprine must be reduced to 25% of original dose.

• Warfarin: azathioprine inhibits the anti-coagulant effect of warfarin

• Phenytoin/sodium valproate/carbamezapine: azathioprine possibly reduces the absorption of these drugs

• Captopril: co-prescription increases risk of leucopenia

• Aminosalicilates: co-prescription possibly increases risk of leucopenia
• NSAIDs may be continued

- **FLU AND PNEUMOCOCOCCAL VACCINES ARE RECOMMENDED FOR PATIENTS ON IMMUNOSUPRESSIVE THERAPY**

REFERENCE:

http://www.rheumatology.org.uk/about_bsr/press_releases/bsr_publishes_updated_guideline_nonbiologic_dmards.aspx

http://www.rheumatology.org.uk/about_bsr/press_releases/bsr_publishes_new_guidelines_on_prescribing_antirheumatic_drugs_in_pregnancy_and_breastfeeding