Heatherwood and Wexham Park Hospitals NHS
NHS Foundation Trust

Department of Rheumatology

Azathioprine
Oxford and Berkshire Regional Rheumatology Guidelines

To be read in conjunction with the shared care agreement between Oxfordshire and Berkshire Primary Care Trusts and the Rheumatology Department

Background for use
Azathioprine is a cytotoxic immunosuppressive drug used as a disease modifying drug in the treatment of rheumatoid arthritis and other connective tissue diseases. It may also be used as a steroid-sparing agent.
Azathioprine should only be initiated on the recommendation of a rheumatologist.

Dosage
Azathioprine is given orally starting at a dose of up to 1mg per kg / per day increasing if necessary up to 2- 3mg per kg /per day. Dosage will be advised by the rheumatologist dependent on the results of the TPMT genotype.
Azathioprine may need to be given for 3 months before therapeutic benefit is seen.

Pre treatment assessment by Rheumatologist
FBC, including platelets and differential, U& E's, ESR , CRP and TPMT assay

Monitoring
- FBC weekly for 6 weeks
- Continue fortnightly until dose stable for 6 weeks thereafter monthly.
- LFTs, U&E's, ESR, CRP monthly
- Frequency of monitoring may be reduced on the advice of the rheumatologist

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

Side Effects	Action
WBC < 3.5 X 10 ^ 9 / l Neutrophils <2.0 X 10^ 9/l	Withhold, and repeat WBC, if normal continue, if abnormal discuss with specialist team
Platelets < 150 X 10^ 9/l	Withhold, and repeat. If normal continue,
Liver function > 2.0 fold rise in AST/ALT from upper limit of reference range.	Withhold. Look for alternative cause, repeat LFT's, if abnormal discuss with specialist team
MCV > 105 fl	Check B12, folate and TFT. If low, start appropriate supplementation.

A S Zakari / M Cox / Verified by Dr Paul Bowness / WPH Rheumatology Team / Version 5 (Oct 2012) For Review Nov 2014

	Check alcohol status.
Rash or oral ulceration	Withhold until symptoms clear. Consider re-challenging at a lower dose. If rash recurs stop azathioprine and discuss with specialist team. Treat oral ulceration.
Hypersensitivity reactions	Fever, malaise, rash, vomiting, muscle/bone pain, dizziness. Stop azathioprine.
Abnormal bruising or sore throat	Withhold until FBC result available
Nausea, vomiting, diarrhoea	Administer tablets after meals to reduce nausea. An anti-emetic or dose reduction may help. If symptoms persist stop azathioprine.

Note:

- Azathioprine can be withheld for several days without causing a flare.
- Pnuemovax and annual flu vaccinations are recommended

Contraindications and Precautions

TPMT assay	Provides information of risks related to treatment. Both homozygous and heterozygous deficiency are associated with serious and fatal toxicity
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	Effective contraception is advised. However there may be some circumstances where the benefits of continuing treatment outweigh the possible risks to the unborn child Breast feeding should be avoided.

Notable Drug Interactions (refer to BNF and SPC)

- 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 reduces the absorption of these drugs
- ACE inhibitors: co-prescription may cause anaemia
- Aminosalicilates: co-prescription may contribute to bone marrow toxicity
- Co-trimomazole /Trimethoprim: can cause life threatening haemotoxicity
- NSAIDs may be continued

Contact Telephone Numbers

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