AZATHIOPRINE for use in rheumatic diseases

Background
This sheet provides guidance on monitoring of azathioprine in primary care. These recommendations have primarily been taken from current BSR guidance on DMARD monitoring. Some rheumatology departments may have slight variations in their monitoring practices. For the full shared care protocol and responsibilities for primary care refer to www.bnssgformulary.nhs.uk/Shared-Care-Protocols

Treatment schedule
Azathioprine is given daily by mouth and is available as 25mg, 50mg and 100mg tablets. Increasingly, the activity of TPMT (thiopurine methytransferase, the key enzyme metabolising azathioprine) is measured prior to treatment, to identify those patients likely to experience serious adverse effects. A typical dose regimen is to commence 50 to 100mg oral daily and to increase by 50mg every 2 weeks to a maximum dose of 2.5mg per kg per day (usually 150 to 200mg daily). This should be continued as long as clinically indicated unless there is a serious side effect or the drug becomes ineffective.

Cautions and special recommendations
Cautions
- TPMT deficiency (heterozygous state): may be associated with delayed haematotoxicity
- Sunscreens and protective covering should be encouraged to reduce sunlight exposure
- Localised or systemic infection (including hepatitis B or C and TB)
- Pregnancy and breast feeding should be avoided in patients taking azathioprine. However azathioprine has been widely used as immunosuppression in pregnant patients when clinically indicated and a careful assessment of the risk versus benefit is advised.

Contra-indications
- TPMT deficiency (homozygous state): avoid, can be fatal.
- Lesch-Nyhan syndrome

Side-effects
The most common side effects are nausea, vomiting and heartburn. These can be reduced by taking the drug with meals and an H2-blocker or proton pump inhibitor may also be helpful. Rashes, hepatitis and alopecia may also occur. The most serious side effect is bone marrow suppression.

Drug interactions
- Allopurinol: azathioprine has increased toxicity. Therefore the azathioprine dose should be reduced to a quarter of the usual dose.
- Aminosalicylates: may increase the risk of leukopaenia when given with azathioprine.
- Warfarin: azathioprine reduces the effect of warfarin.
- Co-trimoxazole and trimethoprim: can cause life threatening haematotoxicity when co-prescribed with azathioprine.
- ACE-inhibitors: may cause anaemia
- Febuxostat: co-prescription of azathioprine with febuxostat is not recommended by the manufacturer.

Monitoring

Pre-treatment assessment: FBC, renal function, LFT and TPMT level. This will be done by the rheumatology department.

Monitoring: FBC and LFT's weekly for 6 weeks and then continue every 2 weeks until dose stable for 6 weeks; then monthly. In people heterozygote for TPMT, monitoring should continue at monthly intervals. Renal function should be repeated 6-monthly.

Actions to be taken: Azathioprine should be WITHHELD if any of the following occur. Please repeat monitoring bloods in 1 week and if still low/high then discuss with the rheumatology team. Falling trends may also prompt discussion.

- Neutrophils <1.5 $x10^9$/L
- Platelets <100 $x10^9$/L
- ALT >twice upper limit of reference range
- Rash or oral ulceration
- Severe sore throat, abnormal bruising: immediate FBC and withhold until the result of FBC is available.

February 2015 Dr Matthew Roy on behalf of Bristol & Weston rheumatology consultants

Rheumatology Departments' contact details

Trust / Hospital	Contact	Telephone / Fax	On call service	Availability
University Hospitals Bristol Foundation Trust, Bristol Royal Infirmary	Rheumatology Telephone Advice Line	T: 0117 3424881 F: 0117 3423841	Registrar pager: 07623972925	**Mon – Thu 9am to 5pm** **Fri 9am to 1pm**
North Bristol Trust, Southmead Hospital	Consultant secretary as per clinic letter OR Rheumatology Telephone Advice Line	T: 0117 4140600 F: 0117 4140570 For clinicians only T: 07894800989	T: 07894800989 Sat/Sun 9am-noon (GP service for existing NBT rheum patients only)	**Mon – Fri 9am to 5pm**
Weston Area Health Trust, Weston General Hospital	Rheumatology Telephone Advice Line	T:01934 881075 F: 01934 647025	01934 636363 Bleep 279	**Mon – Fri 9am to 5pm**