BNSSG Health Community's Traffic Light System
Shared Care Guidance

Please complete all sections.
Type in the grey shaded areas (deleting the prompts for information in each section).

Section 1: Heading

Trust: North Bristol NHS Trust

Specialty / Department: Renal

Drug:Azathioprine

Section 2: Treatment schedule

For the management of Renal Autoimmune disease

Azathioprine is often used in combination with corticosteroids when response to steroids alone is insufficient or to allow a reduction in steroid dose, as azathioprine has steroid sparing effects. Occasionally it may be used alone if there is a contraindication to corticosteroids.

When azathioprine is used for its autoimmune properties the usual dose is 1-3 mg/kg/day orally, depending on the clinical condition being treated and the individuals response. The dose can be given as a single daily dose or split as the dose increases. When the patient is clinically stable it is appropriate for the GP to take over the prescribing and monitoring of azathioprine.

PATIENTS WITH RENAL IMPAIRMENT
It has been suggested that toxicity may be enhanced in the presence of renal impairment. Therefore it is recommended that the dosages used should be at the lower end of the normal range and the haematological response monitored carefully. If haematological toxicity occurs the dosage should be further reduced.

PATIENTS WITH HEPATIC IMPAIRMENT
The metabolism of azathioprine may be impaired in patients with hepatic impairment. Regular full blood counts and liver function tests should be carried out and the dose reduced if either haematological or hepatic toxicity occurs.

USE IN THE ELDERLY
There is limited experience using azathioprine in the elderly. Data available do not suggest that the incidence of side effects is greater in this population group; however, it is recommended that the dosages used should be at the lower end of the range.

Section 3: Monitoring see also Link to Blood monitoring card

Baseline U&Es, FBC, LFTs and TPMT (thiopurine methyltransferase) levels will have been checked at the renal unit prior to initiation of therapy. TPMT is the enzyme responsible for the metabolism of azathioprine and its activity is inversely related to the risk of developing acute leucopenia.

The BNF states that during the first four weeks of treatment FBC, LFTs and U&Es should be monitored weekly. (The commentary in the BNF justifies its deviation from the eight weeks recommended in the product literature.) Later on in treatment the blood counts should be checked at the very least every 3 months. Patients will be given a shared care blood test monitoring card and asked to maintain records with the GP/renal unit.

Azathioprine should be WITHHELD (and their nephrologist contacted) if any of the following occur:

WBC	$<4x10^9$/L (or higher, if WBC falling rapidly)
Neutrophils	$<2x10^9$/L

Platelets < $150x10^9$/L
AST/ALT >2 x normal range
Unexplained bruising or sore throat
Severe rash or oral ulceration

The patient will be reviewed regularly in the renal clinic where any dose adjustments will be made and advised promptly to the GP. If at any point the GP has concerns over side effects, ineffectiveness of the drug or any other concerns about azathioprine treatment the patient may be referred back to the clinic or they may telephone the renal Specialist Registrar or supervising Consultant at Southmead Hospital to discuss the issues

Section 4: Side-effects

Azathioprine is associated with a wide range of potential adverse effects. The following is a brief overview. For further information please consult the SPC.

Haematological – dose dependent, generally reversible bone marrow suppression. Usually seen as leucopoenia, sometimes as anaemia and thrombocytopaenia and rarely as agranulocytosis, pancytopaenia and aplastic anaemia.

Gastro-intestinal – nausea (often relieved by administering tablets after meals). Rarely reported diarrhoea and pancreatitis.

Hepatic – cholestasis and degeneration of LFT's.

Hypersensitivity reactions – general malaise, dizziness, nausea and vomiting, diarrhoea, fever, rigors, rash, myalgia, arthralgia and hypotension.

Immunological - greater susceptibility to infectious diseases.

Chicken pox/shingles infection - stop and commence aciclovir.

Section 5: Drug interactions

Allopurinol – this inhibits the enzyme xanthine oxidase, which is responsible for the metabolism of azathioprine to its inactive metabolite. Increased levels of azathioprine can occur therefore, it is recommended that the dose of azathioprine should be reduced to one quarter of the original dose.

There are individuals with an inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) who may be unusually sensitive to the myelosuppressive effect of azathioprine and prone to developing rapid bone marrow depression following the initiation of treatment with azathioprine. This problem could be exacerbated by co-administration with drugs that inhibit TPMT, such as olsalazine, mesalazine or sulfasalazine and patients receiving such drugs may require more frequent monitoring.

Warfarin – Azathioprine may inhibit the anticoagulant effect of warfarin.

Co-trimoxazole, captopril, penicillamine – Haematological abnormalities may develop if given concomitantly with azathioprine.

Live vaccines – Administration of live vaccines to patients is contra-indicated on theoretical grounds.

Section 6: Cautions and special recommendations

Adequate contraception should be advised when either partner is receiving azathioprine. Azathioprine should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit.
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

Patients should be instructed to report immediately any evidence of infection, unexplained bruising or bleeding or other manifestation of bone marrow depression. Patients are given a shared care blood test monitoring card and asked to maintain records with GP/renal unit.

Exposure to sunlight and UV light should be limited by wearing protective clothing and using sunscreen with a high protection factor.

Azathioprine should be taken with or after food.

Section 8: Responsibilities for Secondary Care

To initiate and stabilise treatment, taking responsibility for the monitoring of blood results and the adjustment of doses until monitoring has been formally handed over to primary care.

Section 9: Responsibilities for Primary Care

To provide blood test monitoring, if requested, in primary care while responsibility is still with secondary care, informing secondary care when blood samples have been taken in primary care so that secondary care are aware and can review.
To remain vigilant for development of adverse events and/or toxicity.
When responsibility has been formally handed over to primary care, primary care will be responsible for blood test monitoring and dose adjustment according to the guidance above.

Section 10: Contact details

Name	Organisation	Telephone number	Fax number	E-mail address	Availability
Renal Consultants	Richard Bright Renal Unit	0117 323 5433	0117 950 8677	Charlie.tomson@nbt.nhs.uk	
				Chris.dudley@nbt.nhs.uk	
				Alison.armitage@nbt.nhs.uk	
				Karen.anderson@nbt.nhs.uk	
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				Richard.smith@bristol.ac.uk	
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Section 11: Document details

Date prepared:	June 2011
Prepared by:	Sara Perkins Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.
Date for review:	June 2013
Document identification:	v2.1

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the BNSSG health community in preparing shared care guidance. Please give details.

Section 13: References

1. Summary of product characteristics, Imuran. Accessed via www.emc.medicines.org.uk
2. British National Formulary 61st Edition (March 2011)