BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Azathioprine
Amber *three months*	
Indication	Neurological conditions such as Myasthenia Gravis or CIDP
Speciality / Department	Neurosciences
Trust(s)	North Bristol NHS Trust
	Click here to enter details
	Click here to enter details

Section 2: Treatment Schedule

Usual dose and frequency of administration	When azathioprine is used for its immunosuppressant properties the usual dose is 1-3 mg/kg/day orally, adjusted according to the clinical response and haematological tolerance. The dose can be given as a single daily dose or split as the dose increases. It can be started at the estimated maintenance dose, however it may be also started at a lower dose and increased gradually depending on how the clinician feels the patient will tolerate the drug. A clinical response may not be evident for several months.
Route and formulation	Oral. Film-coated tablets.
Duration of treatment	The maintenance dose may be continued for approximately 1 year before considering a reduction in maintenance dose to the lowest effective level to maintain that response. The reduction in dose should be done gradually reducing by 25-50mg every 3 months or may be reduced more quickly at the discretion of the consultant. If no improvement in the patients condition is seen within 3-6 months, consideration should be given to stopping the drug. Withdrawal of azathioprine should be undertaken gradually with close monitoring.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
Baseline U+E, FBC, LFT's should be carried out prior to initiation of therapy. Thiopurine methyltransferase (TPMT) levels are also checked prior to initiation. This enzyme is responsible for the metabolism of azathioprine and its activity is inversely related to the risk of developing acute severe leucopenia.
Subsequent tests - where appropriate
1. The SPC states that during the first eight weeks of treatment FBC, LFT and U+E should be monitored weekly (more frequently with higher doses or in severe hepatic or renal impairment). Later on in treatment the blood tests should be checked monthly or at intervals no greater than 3 monthly. 2. Azathioprine works by suppressing bone marrow activity, and in immunosuppressant doses causes a rise in MCV (secondary to reticulocytosis) and an absolute lymphopenia. These changes are sometimes used to determine the effective dose. 3. The full list of monitoring on the SPC for azathioprine should also be consulted.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	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 leucopenia, sometimes as anaemia and thrombocytopenia and rarely as agranulocytosis, pancytopenia and aplastic anaemia. Gastro-intestinal – nausea (often relieved by administering tablets after meals / giving azathioprine in divided doses). Rarely reported diarrhoea and pancreatitis. Hepatic – cholestasis and degradation of LFTs. These are usually reversible on withdrawal of therapy. Hypersensitivity reactions – general malaise, dizziness, nausea and vomiting, diarrhoea, fever, rigors, rash, myalgia, arthralgia and hypotension. In the case of a hypersensitivity reaction, the patient should not continue therapy. Chicken pox/shingles infection - stop and commence aciclovir.
Referral back to specialist	Below are giuides at which point the patient should be referred back to the consultant: WBC < 4x10*9/L Neutrophils <2 x 10*9/L Platelets <150 x 10*9/L AST/ALT >2 x normal range If at any point the GP has concerns over side effects, ineffectiveness of the drug or any other concerns about azathioprine treatment they should contact the Neurology Consultant or their Specialist Registrar for further advice.

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	Some important interactions are listed below but please refer to the BNF appendix 1 / SPC for a full and up-to-date list of 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. Warfarin – azathioprine may inhibit the anticoagulant effect of warfarin. Live vaccines – administration of live vaccines to patients is contraindicated on theoretical grounds.
Reminder to ask patient about specific problems	Click here to enter details

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

1. 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.
2. HEPATIC IMPAIRMENT. The metabolism of azathioprine may be impaired in patients with hepatic impairment. Regular full blood count and LFT should be carried out and the dose reduced if either haematological or hepatic toxicity occurs. Azathioprine is contra-indicated in severe hepatic impairment.
3. USE IN THE ELDERLY. There is limited experience using azathioprine in the elderly. Data available dose not suggest that the incidence of side effects is greater in this population group, however, it is recommended that the dosage used should be at the lower end of range.
4. Adequate contraception should be advised when either partner is receiving azathioprine and for at least 3 months after stopping treatment. Azathioprine should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risk versus benefit.
5. CONTRAINDICATIONS – severe, infections, seriously impaired hepatic or bone marrow function, pancreatitis, any live vaccine, pregnancy, lactation.
6. 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

Advice for prescribing clinician to inform patient

1. Patients should be instructed to report immediately any evidence of infection, unexplained bruising or bleeding or other manifestation of bone marrow depression.
2. Exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with high protection factor.
3. Azathioprine should be taken with or after food, with at least a glass of liquid (200ml).

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing for the first three months
2. Undertaking the clinical assessment and monitoring for the first three months.
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood

test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Azathioprine.
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Secondary care will check recommended baseline blood tests and TPMT levels, initiate treatment and prescribing remains with specialist for 3 months. Monitoring will be carried out during the initial treatment phase.
2. Secondary care will provide the patient with necessary counselling on initiating treatment to inform them about risks and benefits of the agent and particular precautions relevant to those of childbearing age.

Section 9: Responsibilities for Primary Care

Core responsibilities

2. Responsible for taking over prescribing after the first three months
3. Responsible for the clinical assessment and monitoring after the first three months
4. Review of any new concurrent medications for potential interactions.
5. Reporting adverse events to the MHRA.
6. Refer for advice to specialist where appropriate.
7. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. The GP should continue blood test monitoring at recommended frequency and where toxicity is suspected, reduce or stop treatment and refer back to secondary care for treatment review.
2. If the GP has particular concerns about therapy or side effects refer back to secondary care. GP to take on prescribing responsibility after initiation and 3 months prescription from secondary care.

Section 10: Contact Details

Name	Organisation	Telephone Number	E mail address
Consultant Neurologist	North Bristol NHS Trust	Access via switchboard 0117 9505050	Click here to enter details
Speciality Neurology Registrar	North Bristol NHS Trust	Access via switchboard 0117 9505050	Click here to enter details
Click here to enter details	Click here to enter details	Click here to enter details	Click here to enter details
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Section 11: Document Details

Date prepared	April 2016 Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.
Prepared by	Victoria Wiggins
Date approved by JFG	Click here to enter details
Date of review	Click here to enter details
Document Identification: Version	Azathioprine SCP updated Dec 15v3

Section 12: Collaboration

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

1. Click here to enter details

Section 13: References

Please list references

Joint Formular Committee. British National Formulary. 70 ed. London: BMJ Group and Pharmaceutical Press; 2015

Actavis UK Ltd. Summary of Product Characteristics for Azathioprine 50mg tablets. Last updated on the eMC 22.09.15. Accessed via www.medicines.org.uk/emc/ on 08.12.15.