**OUT OF AREA**

**SHARED CARE GUIDELINE**

**for**

**Azathioprine or 6-Mercaptopurine**

**for the management of**

**rheumatic diseases, inflammatory bowel disease, autoimmune hepatitis and pulmonary fibrosis**

 **Implementation date: March 2019**

 **Review Date: January 2021**

**This guidance has been prepared by clinicians from Gateshead Health NHS Foundation trust and the clinical content has been approved by Newcastle Gateshead CCG. GPs working with the team from Sunderland and Washington have been involved in the development. The Guideline applies only to patients registered with a GP outwith Gateshead who are under the care of adult Rheumatology, Gastroenterology or Respiratory specialist services at Gateshead Health Foundation Trust.**

**It sets out the details of the transfer of prescribing and respective responsibilities of GPs and specialist services within shared care prescribing arrangements. It is intended to provide sufficient information to allow GPs to prescribe these treatments within a shared care setting.**

 **This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.**

 **Full up-to-date medicines information for individual drugs are available in the BNF (www.medicinescomplete.com) or in the Summary of Product Characteristics (www.medicines.org.uk)**

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| **Committee** | **Date** |
|  |  |

**Approved by:**

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| SHARED CARE GUIDELINE |
| **Non-proprietary name** | Azathioprine or 6-Mercaptopurine  | **Brand name** |  |
| **Dosage form and strength** |  50mg tablets | **BNF Chapter** | Immune system disorders and transplantation |
| **Indication** | The management of rheumatic diseases, inflammatory bowel disease, autoimmune hepatitis  |
| **Licence** | Licensed indications covered by this guideline: Rheumatoid Arthritis and other auto-immune disorders including psoriatic arthritis |
|  **Excluded patients** | Those patients living inside the catchment area of Gateshead Health NHS Foundation Trust  |
| **Eligibility criteria for shared care** | All patients residing outside the catchment area of Gateshead Health NHS Foundation Trust who are under the care of adult Rheumatology, Gastroenterology or Respiratory specialist services  |
| **Dosage information**  | **Adult dosage and administration:** Initially 25-50mg daily with or after food and then gradually increased to a maximum of 200mg daily |
|  **Specialist Responsibilities** | * Initiate treatment with azathioprine, including baseline or pre-treatment monitoring on initiation:
	+ FBC
	+ ESR
	+ CRP
	+ U &E, eGFR and LFTs
	+ TPMT
	+ Baseline hepatitis serology and HIV screen if not previously completed
* Give the patient a 28 day prescription
* Request the participation of the patients GP in a shared care agreement for monitoring once drug titrated to stable dose (normally around 4 months) but shared care should not commence without explicit agreement of the GP
* Secondary care staff will carry out monitoring until receipt of the shared care acceptance and dose has been titrated
* Review the patient’s condition and monitor clinical response to treatment as appropriate
* Liaise with the patient’s GP throughout treatment around:
* Dose of azathioprine prescribed
* Arrangements for monitoring/reviewing patients and the frequency of this
* Provide other relevant clinical information including informing GP if the patient requires intensive rather than standard monitoring (see Appendix1)
* Instruction and information given to patient
* Monitoring and interpreting FBC, ESR. CRP, U&E, eGFR LFT and TPMT results and amending treatment where appropriate
* BSR guidelines state that if dose is increased following stabilisation monitoring frequency should be increased to 2 weekly for 6 weeks. Specialist will advise if this is needed
* If the patient is heterozygous for TMPT then continue monthly monitoring as a minimum
* Communicate promptly with the GP when treatment is changed or, any results of the monitoring undertaken shows an abnormality requiring further investigation or suspension of treatment
* Communicate promptly with the GP if there is any change in the patient’s medical condition or blood tests which may affect the intensity of monitoring
* Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition
* Advise GPs on when to stop treatment (if appropriate)
* Report adverse events to the MHRA via Yellow Card Scheme
* Ensure that clear arrangements exist for GPs to obtain advice and support
 |
| **GP Responsibilities** | * Prescribers are responsible for the prescriptions they sign and they must be prepared to explain and justify their decisions and actions
* GPs should consider the implications of each shared care agreement as proposed by the specialist service
* Contact specialist team to confirm he/she is happy to accept the shared care arrangement, and return the completed agreement form within 14 days
* If GP declines shared care responsibilities it is still the GPs responsibility to record on the primary care record that the drug is being prescribed by secondary care (please refer to local guidance on how to record on the GP clinical system drugs prescribed by the hospital)
* All blood tests, monitoring and prescribing to be carried out by GP with support from secondary care specialist as required
* GPs should contact the patient subject to the shared care agreement to inform them of future monitoring and prescribing arrangements
* GPs may be able to claim a fee for shared care through the direct enhanced service for near patient testing or other local enhanced service. Please check local arrangements
* Standard monitoring protocol is:
* 2 weekly bloods for 4 months (unless alerted otherwise by specialist),
* Monthly for 3 months and then
* 3 monthly
* All patients should be on monthly monitoring at the time shared care is requested
* The GP will be advised at that point whether standard or high-intensity monitoring is required (see below)
* Patients with certain comorbidities require high intensity monitoring (see Appendix 1) which is:
* 2 weekly for 4 months and then
* Monthly
* The hospital will inform the patient and the practice when to drop the monitoring frequency
* Once discharged to shared care it is the GPs responsibility to contact the specialist service for advice if their medical condition changes and it is felt that patient should be moved from standard to intensive monitoring
* If the specialist service increase the dose the GP will be advised in writing of whether to increase the frequency of monitoring to 2 weekly until stable for 6 weeks
* The GP should not prescribe unless:
* The appropriate routine monitoring (as detailed above has been informed)
* The results are available
* No adverse communication from the specialist service has been received
* See Appendix 1 for list of conditions requiring high-intensity monitoring
* The specialist team retain full responsibility for checking the results and initiating any action necessary
* Have a mechanism in place
* To identify when a patient has not attended for monitoring
* To notify specialist team of any relevant adverse reaction or any other relevant laboratory results or other information relevant to patient’s care especially if it could mean the more intensive monitoring schedule is required
* To seek medical advice from Rheumatology team if there are any serious adverse reactions or other concerns
* To ensure rapid review of the patient at the direction of the specialist which may be required – if the patient develops signs or symptoms of infection, requires additional blood tests due to monitoring abnormalities, develops blood abnormalities or other symptoms thought to be unrelated to the underlying rheumatic disease or it’s treatment
* To complete regular monitoring at intervals advised by the specialist team and ensure patient has access to blood test in line with monitoring schedule (see Monitoring section below)
* Azathioprine should be suspended in the event of an infection requiring antibiotics
* Live vaccinations: please refer to green book and local guidelines for management and prevention of infection for advice. The latest green book advice is that almost all individual can be safely vaccinated with all vaccines. In very few individuals vaccination is contraindicated or should be deferred. Where there is doubt advice should be sought from the appropriate specialist. Please refer to Gateshead’s local guidelines for management and prevention of infection in patients with rheumatic disease. For Mycophenolate there is a lack of consistent data therefore advice should be sought from the supervising consultant.
* Pneumococcal and annual flu vaccinations are recommended.
* Shingles vaccination (Varicella Zoster vaccine) contains live, attenuated virus. No specific advice in relation to Azathioprine has been issued at national level. Please refer to the most up to date BSR immunisation guidelines and the Green Book for advice. Whether to immunise or not could be discussed with the supervising consultant on a case by case basis.The Green Book advises it should be safe provided the patient is on ≤3mg/kg/day of azathioprine and ≤1.5mg/kg/day of mercaptopurine.

Please refer to the latest Green Book for current advice. |
| **Common Adverse Effects** | **Adverse event** | **Action to be taken by GP** |
| Fever/Flu like illness – usually abnormal blood indices | Withold until FBC available and discuss with specialist team |
| Abnormal bruising or severe sore throat | Check FBC immediately |
| Abdominal pain | Pancreatitis can occur in the first weeks of treatment  |
| Nausea, vomiting, diarrhoea | * Add anti-emetic e.g. prochlorperazine 5mg three times a day
* Reduce dose
* Stop and refer if severe or if no improvement with above
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| Mouth ulcers | Reduce dose – stop if severe (Stomatitis protocol available from QE) |
| Skin rash | Reduce dose – stop if severe |
| Infection requiring treatment with antibiotics | Suspend azathioprine /mercaptopurine for the duration of the antibiotic course. Patients should be seen by GP on the same day they present with infective symptoms |
| If herpes zoster occurs | Stop azathioprine/mercaptopurine and prescribe aciclovir |
| If patient is in contact with chickenpox or shingles | Contact the specialist team (may need Varicella zoster Immunoglobulin) |
| **Side effects**  | Include: * Hypersensitivity reactions, haematological, gastro-intestinal and hepatic reactions, including cholestasis
* Other reactions include reversible pneumonitis, alopecia and increased risk of infection
* An unusual hypersensitivity reaction may occur early in treatment which presents as fever/ flu like illness usually accompanied by blood abnormalities. **Stop and refer**
* There is an increased risk of developing malignancy with long-term use. This will have been discussed with the patient by the specialist team. The patient should participate in national screening programs
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| **Common Drug Interactions** | * Allopurinol – avoid if possible, risk of severe myelosuppression. If it is initiated the dose of azathioprine must be reduced to 25% and increase monitoring frequency to weekly. Seek further advice from rheumatology department.
* Aminosalicylates – may contribute towards bone marrow toxicity.
* Dabigatran – use with caution as azathioprine can affect platelets.
* Aminosalicylic acid derivatives e.g. sulphasalazine, mesalazine- increased risk of myelosuppressive effects
* Ribavirin – possible enhancement of myelosuppressive effects
* Febuxostat – avoid concomitant use
* ACE inhibitors – may cause anaemia
* Rifampicin
* Warfarin – inhibits anticoagulation effect
* Co-trimoxazole and trimethoprim – increased haematotoxicity

**For a full list of interactions, please consult the latest BNF or SPC** |
| **Cautions and** **Contra-indications** | * TPMT deficiency - may be associated with delayed haematotoxicity including bone marrow toxicity. Can be fatal
* Known hypersensitivity to azathioprine
* Immunisation with live vaccines: Inactivated polio is available, although suboptimal results may be seen
* Individuals with Lesch-Nyhan Syndrome due to congential hypoxanthine-guanine phosphoribosyltransferase (HGPRT) deficiency
* **Renal impairment - stage IV (EGFR <30) – reduce dose or avoid**
* **Liver disease**
* Known haematological problems including recurrent leucopenia
* Active malignancy continuing on DMARDs
* **Pregnancy and breastfeeding**: Seek specialist advice
* **Alcohol**: alcohol may be consumed in moderation, on average one unit per day but avoid binge drinking
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| **Monitoring** | * Disease monitoring – clinical response to therapy will be assessed by the hospital physician in all cases and communicated to the GP
* Routine monitoring:
* FBC, U &Es, CRP,ESR and LFTs (taken every two weeks for the first 4 months, then monthly for three months, then 3 monthly
* The speciality teams use the following blood parameters to determine action where a blood abnormality is detected:
* WBC <3.5 x 109/L: withhold until discussed with the specialist team
* Neutrophils <2 x 109/L: withhold until discussed with specialist. If <1 x 109/L please contact the on-call medical team as patient needs assessed for GCSF which may be administered on the advice of haematology
* Sequential falls in WBC or neutrophils >10% on 3 occasions: withhold until discussed with specialist
* Platelets <150 x 109/L: withhold until discussed with the specialist team
* Sequential falls in platelets: withhold until discussed with specialist unless falls are from high level
* Lymphocytes <0.5 x 109/L: withhold until discussed with specialist Repeat LFTs
* Mild transaminitis is common and normally settles
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| **Communication/Contact Details** | **Rheumatology Contact Details:**Rheumatology Helpline (09:00 -12:00) 0191 445 5240For urgent queries outwith those hours please contact the relevant Consultants secretary.Dr Hamilton 0191 445 2198Dr Saravanan 0191 445 6055Dr Heycock 0191 445 3505Dr Peterson 0191 445 2193Dr Rynne 0191 445 8359Dr Laverick 0191 445 8359TAM clerk 0191 445 2857**Gastroenterology Contact Details:**Lisa Anderson / Andrea Feeley IBD nurses 0191 445 3148Dr Reddy and Dr Niegowski 0191 445 2183Dr Quershi 0191 445 2626Dr Barbour and Dr Johns 0191 445 2611Dr Singh 0191 445 2855Dr Saeed and Dr Mansour 0191 445 2866**Respiratory Contact Details:**Drs Sharrock and Allcock 0191 445 2435Dr Killen 0191 445 6030Dr Thirugnanasothy 0191 445 2182Dr Curtis 0191 445 2389Dr Stiller 0191 445 8023 |

**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to full prescribing data in the SPC or the BNF**

**Appendix 1: Patients who require High-Intensity Monitoring and Action required by GP**

**◼ Known liver disease**

Normally methotrexate would be contraindicated in this situation unless liver disease is mild and advice has been sought from a Gastroenterologist

 ***Action required by GP:***

* Monthly monitoring
* If new diagnosis, seek advice from specialist to set parameters for monitoring and decide if alternative DMARD is needed

**◼ Kidney disease (eGFR <60)**

Dose reduction needed see common adverse effects above. If eGFR < 30 withold until discussed with Specialist team if new

 ***Action required by GP:***

* Monthly monitoring
* If new diagnosis, seek advice from Specialist team as dose adjustment may be needed

**◼ Active malignancy continuing on DMARDs**

 ***Action required by GP***

* Monthly monitoring
* If new malignancy develops seek advice from Specialist team so that clear plan for monitoring / continuation of drug can be made with oncology or other specialist team
* If Oncology decide to commence chemotherapy for known malignancy, alert Specialist Team and Oncology if no instructions have been given to stop DMARD

**◼ Known haematological problems including recurrent leucopenia**

 ***Action required by GP***

* Monthly monitoring
* Specialist will normally set patient specific parameters for action

**◼ BMI< 18 or >30**

 ***Action required by GP***

* Monthly monitoring

Weight management or dietetics input may be needed

**Appendix 2: Shared Care Request Form**

**Please return to Gail Lumsley, Rheumatology Department, Queen Elizabeth Hospital on ghnt.rheumsharedcare@nhs.net**

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| **PRIMARY / SECONDARY CARE SPECIALIST PRESCRIBER TO COMPLETE** |

|  |  |
| --- | --- |
| Name of Specialist |  |
| Address of Specialist | Queen Elizabeth Hospital  |
| Contact phone no |  |

|  |  |
| --- | --- |
| Patient’s name |  |
| Patient’s address |  |
| Patient’s DOB |  |
| Patient’s NHS No |  |
| This patient has been initiated on: | **DRUG** | **DOSE** |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Pharmacy |  | Compliance Aid | 🞎 YES | 🞎 NO |

|  |  |
| --- | --- |
| Administration by:(if appropriate) | e.g. community nurse |
| Monitored by: |  |

|  |  |
| --- | --- |
| Prescription for 28 days given on: |  |
| **This treatment has been explained to the patient and a review arranged for:** |
| Appointments to continue every **………..** months |

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| --- |
| **GP TO COMPLETE ONE SECTION THEN RETURN FORM WITHIN 14 DAYS TO ACCEPT OR DECLINE TRANSFER OF PRESCRIBING** |

|  |
| --- |
| I **ACCEPT** the proposed Shared-Care Agreement for this patient |
| Name of GP |  | DATE |
| Signature |  |  |

|  |
| --- |
| I **DECLINE** the proposed Shared-Care Agreement for this patient |
| Name of GP |  | DATE |
| Signature |  |  |
| My reasons for declining are: |
| **NB: Participation in this shared care arrangement implies that prescribing responsibility is shared between the hospital consultant and the patient’s GP.**  |