

Shared Care Guideline Stepping Hill Hospital and North Derbyshire CCG

Shared Care Guideline for Azathioprine in Rheumatological Conditions in Adults		Reference Number
Version: 1	Replaces:	Issue date: November 2017
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Date noted by JAPC: June 2018		Review Date: October 2019

Please complete all sections

1. Name of Drug, Brand Name, Form and Strength	Azathioprine 25mg and 50mg tablets
2. Licensed Indications (state if this is an unlicensed indication)	Azathioprine is indicated either alone or in combination with corticosteroids and/or other drugs and procedures in severe cases of the following diseases, in patients who are intolerant to steroids or who are dependent on steroids and in whom the therapeutic response is inadequate despite treatment with high doses of steroids: <ul style="list-style-type: none"> • Severe active rheumatoid arthritis that cannot be kept under control by less toxic agents (disease modifying anti-rheumatic drugs, DMARDs) or when other DMARDs are contra-indicated • Systemic lupus erythematosus • Dermatomyositis • Polyarteritis nodosa

	<ul style="list-style-type: none"> Other connective tissue disease e.g. polymyositis, vasculitis 		
3. Criteria for shared care	<p>Prescribing responsibility will only be transferred when</p> <ul style="list-style-type: none"> Treatment is for a specified indication. Patient has completed three months treatment (prescribed and monitored by Rheumatology Team), has reached the target dose and blood test results are stable The GP has agreed in writing in each individual case that shared care is appropriate. The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements 		
4. Patients excluded from shared care	<ul style="list-style-type: none"> Patient does not consent to shared care. Patient does not meet criteria for shared care. 		
5. Therapeutic use & background	<p>Azathioprine tablets are used as an immunosuppressant anti-metabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) and procedures which influence the immune response. Therapeutic effect may be evident only after weeks or months and can include a steroid-sparing effect, thereby reducing the toxicity associated with high dosage and prolonged usage of corticosteroids.</p>		
6. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	<p><u>Contraindications:</u> Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever) should be avoided in patients taking azathioprine. Azathioprine is contra-indicated in patients known to be hypersensitive to azathioprine. Hypersensitivity to 6-mercaptopurine (6-MP) should alert the prescriber to probable hypersensitivity to azathioprine. TPMT (thiopurine methyl transferase) deficiency (homozygous state)- avoid can be fatal. Contraindicated in patients with severe infection. Severely impaired hepatic or bone marrow function.</p> <p><u>Cautions:</u> Treatment may need to be monitored more frequently in the following if high doses are used:</p> <ul style="list-style-type: none"> In elderly patients If renal function is impaired If hepatic function is mild/moderately impaired If bone marrow function is mildly to moderately impaired <p>Caution in patients with poor respiratory reserve as azathioprine associated with pneumonitis. Caution in patients with active/history of pancreatitis. TPMT deficiency (heterozygous state), may be associated with delayed haematotoxicity including bone marrow toxicity. Localised or systemic infection including hepatitis B or C and history of tuberculosis.</p>		
7. Prescribing in pregnancy and lactation	<p>Prescribing during pregnancy and lactation should be agreed with and is responsibility of the Specialist.</p> <p>Azathioprine is compatible throughout pregnancy with doses that are less than 2mg/kg/day. It is also compatible with breastfeeding and paternal exposure in doses less than 2mg/kg/day.</p> <p>Prescribing during pregnancy and lactation with doses above 2mg/kg/day should be responsibility of the consultant rheumatologist.</p>		
8. Dosage regimen for continuing care	<table border="1"> <tr> <td>Route of administration:</td> <td>Oral</td> </tr> </table> <p>Preparations available: Azathioprine 25mg tablets Azathioprine 50mg tablets</p> <p>A "specials" suspension is available; however this is expensive and should only be used in exceptional circumstances. Caution: azathioprine is a cytotoxic agent and as such if the tablets are crushed or halved and the film coating is broken it should be then handled</p>	Route of administration:	Oral
Route of administration:	Oral		

	in accordance with handling of cytotoxic agents according to local guidelines.
	Please prescribe: 1mg/kg/day increasing after 4-6 weeks to 2-3mg/kg/day rounded up or down to the nearest whole tablet.
	Is titration required Yes
	Titrate dosage according to response. Maintenance dosage up to a maximum 2-3mg/kg/day
	Adjunctive treatment regime: Annual flu vaccinations are safe and recommended. Pneumococcal vaccination is safe and recommended. Shingles vaccine (varicella-zoster) – currently recommended in people over the age of 69 years. To date the JCVI recommendations have not been extended to younger age groups in the rheumatic disease population. Low levels of immunosuppression are not considered an absolute contraindication, and the JCVI Green Book addresses this, recommending that low-dose CSs (prednisolone<20mg daily) and oral DMARD therapy at standard doses are not a contraindication in most patients, although clinician discretion is advised. In non-immune patients exposed to chickenpox or shingles, passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG). It is the specialist's responsibility to make the recommendation for vaccination at the appropriate time.
	Conditions requiring dose reduction: Lower doses if there is significant renal or hepatic impairment, in elderly patients, bone marrow mild/moderately impaired and with hypersplenism.
	Usual response time : 6 weeks to 3 months
	Duration of treatment: Ongoing
	Treatment to be terminated by: Treatment to be terminated by healthcare professional in consultation with Rheumatology Team.
	NB. All dose adjustments will be the responsibility of the initiating specialist unless directions have been specified in the medical letter to the GP.
9. Drug Interactions <i>For a comprehensive list consult the BNF or Summary of Product Characteristics</i>	The following drugs must <u>not</u> be prescribed without consultation with the specialist: <ul style="list-style-type: none"> • Immunisation using a live vaccine (eg: oral polio, oral typhoid, MMR, BCG, yellow fever) has the potential to cause infection in immunocompromised patients. • Allopurinol has the potential to cause azathioprine toxicity; and may require a dose reduction. • Coumarins – Azathioprine possibly reduced anticoagulant effects of anticoagulant (e.g. warfarin) • Febuxostat – avoid in combination with Azathioprine. • Sulfamethoxazole (e.g. Trimethoprim or Co-trimoxazole) – increased risk of haematological toxicity when Azathioprine given concurrently and this combination should be avoided. • Avoid use with clozapine, increased risk of agranulocytosis. • Ribavirin - severe myelosuppression has been reported following concomitant administration of azathioprine and ribavirin; therefore co-administration is not advised. • Sulfasalazine - increased risk of haematological toxicity when Azathioprine given

	concurrently. Additional monitoring of FBC may be required.		
10. Adverse drug reactions <i>For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF</i>	<p>The following drugs may be prescribed with caution:</p> <ul style="list-style-type: none"> • ACE inhibitors - co-prescription may cause anaemia • Phenytoin, Sodium Valproate, Carbamazepine - there is reduced absorption of these drugs] • Aminosalicylates may contribute to bone marrow toxicity • Alcohol intake no more than 14 units weekly • Shingles vaccine (varicella-zoster) - Low levels of immunosuppression are not considered an absolute contraindication, and the JCVI Green Book addresses this, recommending that low-dose CSs (prednisolone<20mg daily) and oral DMARD therapy at standard doses are not a contraindication in most patients, although clinician discretion is advised. 		
	<p>Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.</p>		
	<p>Adverse event System – symptom/sign</p>	<p>Action to be taken Include whether drug should be stopped prior to contacting secondary care specialist</p>	<p>By whom</p>
	<p>WCC<3.5 x 10⁹/l Neutrophils <1.6 x 10⁹/l Platelets <140 x 10⁹/l Unexplained eosinophilia >0.5 x 10⁹/L Unexplained fall in serum albumin <30g/l</p>	<p>Withhold until discussion with Rheumatology Team</p>	<p>GP</p>
	<p>ALT and/or AST > 100 units/L OR Any sudden increases (e.g. double of baseline ALT)</p>	<p>Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction</p>	<p>GP</p>
<p>Rash or oral ulceration</p>	<p>Withhold until discussion with Rheumatology Team</p>	<p>GP</p>	
<p>MCV>105 fl</p>	<p>Check serum folate, B12, alcohol history and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team</p>	<p>GP</p>	

Abnormal bruising or severe sore throat	Withhold until urgent FBC results available and discuss with Rheumatology Team as can cause bone marrow suppression.	GP
Creatinine >30% above baseline and/or calculated GFR <60	Use clinical judgement. Repeat in 1 week and if still >30% above baseline withhold until discussed with the Rheumatology Team	GP
<p><i>The patient should be advised to report any of the following signs or symptoms to their GP without delay:</i></p> <ul style="list-style-type: none"> • Signs or symptoms indicating blood dyscrasias e.g. sore throat, infection, unexplained or abnormal bruising or bleeding. • Any signs of bone marrow suppression (ie infection, fever, unexplained bruising or bleeding) • Jaundice • Abdominal pain – may be sign of pancreatitis <p>Please note that, in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.</p> <p>If the patient has not previously had chicken pox and they come into contact with someone who has chicken pox or shingles or the patient develops chicken pox or shingles.</p>		
<p><i>Other important co morbidities (e.g. Chickenpox exposure):</i></p> <ul style="list-style-type: none"> • History of TB – treatment with these drugs should be avoided and infectious diseases specialist advice sought if treatment with Azathioprine deemed necessary. • History of active hepatitis B or C – treatment with these drugs should be avoided (consider vaccination where appropriate). • Live vaccines should not be given concurrently with these treatments. • Annual flu vaccinations are safe and recommended (due to suppressed immune system with these drugs). • Pneumococcal vaccination is safe and recommended (due to suppressed immune system with these drugs). • Shingles vaccine (varicella-zoster) – currently recommended in people over the age of 69 years. To date the JCVI recommendations have not been extended to younger age groups in the rheumatic disease population. Low levels of immunosuppression are not considered an absolute contraindication, and the JCVI Green Book addresses this, recommending that low-dose CSs (prednisolone<20mg daily) and azathioprine <3mg/kg/day is compatible with the shingles vaccine. • In non-immune patients exposed to chickenpox or shingles, passive immunization should be carried out using varicella zoster immunoglobulin (VZIG). • Patients should try to avoid contact with people who have active chickenpox or shingles and should report any such contact urgently to their GP or specialist. • Sunscreens should be encouraged to reduce sunlight exposure. • During infection requiring antibiotics azathioprine should be temporarily discontinued until the patient has recovered from the infection. 		
<p>Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the “Yellow Card” scheme.</p>		

11. Baseline investigations	<i>List of investigations / monitoring undertaken by secondary care</i> FBC U&Es incl GFR LFT (ALT, AST and albumin) Height and weight Blood pressure Pre-viral screen in high risk patients: HIV, HBV (surface antigen, core antibody), HCV (antibody test) and consider herpes zoster status (if appropriate) TPMT assay (normal reference range > 68mu/L) <20mu/l do not give Azathioprine 20-68mu/l Discuss with Consultant and use reduced dosage. Screening for lung disease should be undertaken at clinician discretion on a case by case basis.				
12. Ongoing monitoring requirements to be undertaken by GP (Local commissioning arrangements may vary).	Is monitoring required?		Yes (N.B. Bolton DAWN monitoring based on BSR guidelines 2008/2017 for initiation/dose increases/parenterals; subsequent shared care as per GMMMG)		
	Monitoring	Frequency	Results	Action	By whom
	FBC, U&E, LFTs with albumin, (ESR desirable but not essential)	<p>During dose titration: Every 2 weeks until achieve a stable dose for 6 weeks.</p> <p>Maintenance dose: Monthly for 3 months then at least every 3 months. More frequent monitoring is appropriate in patients at higher risk of toxicity.</p> <p>Dose Increases/Starting an additional DMARD: Every 2 weeks until on stable dose for 6 weeks then revert back to previous schedule.</p>	WCC < 3.5 x 10 ⁹ /l Neutrophils < 1.6 x 10 ⁹ /l Platelets < 140 x 10 ⁹ /l Unexplained eosinophilia > 0.5 x 10 ⁹ /L Unexplained fall in serum albumin < 30g/l	Withhold until discussion with Rheumatology Team	GP
			ALT and/or AST > 100 units/L OR Any sudden increases (e.g. double of baseline ALT)	Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction	GP
		MCV > 105 fl	Check serum folate, B12, alcohol history and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team	GP	

			<p>Creatinine >30% above baseline and/or calculated GFR <60</p>	<p>Use clinical judgement. Repeat in 1 week and if still >30% above baseline withhold until discussed with the Rheumatology Team</p>	<p>GP</p>
<p>13. Pharmaceutical aspects</p>	<p>No special considerations</p>				
<p>14. Responsibilities of initiating specialist (Local commissioning arrangements may vary).</p>	<ul style="list-style-type: none"> • Undertake baseline monitoring. • Supply the first three months of medication (and additional two weeks to cover transition between Secondary to Primary care prescribing responsibility). • Supply blood forms for three months at the time of prescribing (patient to use these at their GP or local phlebotomy service during the initiation period). • Monitor blood test results during the first three months initiation period. • Advise GP on dose adjustments. • Monitor patient's initial reaction to and progress on the drug. • Ensure that the patient has an adequate supply of medication until GP supply can be arranged. • Patients will be considered suitable for transfer to GP prescribing ONLY when they meet the criteria listed in section 3 above. • The initiating specialist prescriber will write formally to the GP to request shared care using the GMMMG agreed process. Failure to supply all the required information will result in the refusal of the request until all information has been supplied • Patients will only be transferred to the GP once the GP has agreed. • Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP. • Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before specialist review. • Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient or inform GP if the patient does not attend appointment. • Provide GP with advice on when to stop this drug. • When and additional anti-rheumatology medication is added (either a biologic or a DMARD) the specialist should inform the GP and confirm if any changes to or additional monitoring is required. If no extra monitoring is needed, this should also be stated. • Act upon communication from the GP in a timely manner. • Provide patient with relevant drug information to enable Informed consent to therapy. • Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action. • Patients should be advised to seek medical attention for the following: <ul style="list-style-type: none"> ○ Patients should report all symptoms and signs suggestive of blood disorders (e.g. sore throat, bruising and mouth ulcers) ○ Patients should report all symptoms and signs suggestive of liver toxicity (e.g. nausea, vomiting, abdominal discomfort, dark urine and jaundice) 				

	<ul style="list-style-type: none"> ○ Patient should report any upper abdominal pain as this is an indicator of development of pancreatitis. ● Provide patient with relevant drug information to enable understanding of the role of monitoring. ● Be available to provide patient specific advice and support to GPs as necessary. ● Provide patient with specialist nurse helpline contact number e.g. rheumatology helpline
<p>15. Responsibilities of the GP</p> <p>(Local commissioning arrangements may vary).</p>	<ul style="list-style-type: none"> ● Facilitate blood tests at surgery during the initial three months of treatment. Blood forms will be provided by the referring consultant and results will therefore be sent back to the appropriate consultant. ● Continue treatment as directed by the specialist. ● Act upon communication from the specialist in a timely manner. ● Ensure no drug interactions with concomitant medicines. ● To monitor and prescribe in collaboration with the specialist according to this protocol. ● To undertake vaccination as directed by the initiating specialist, the BNF or Green Book. ● Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. ● GPs should reply to request for shared care to either accept or decline within 14 days. A form is available on the GMMMMG website to facilitate this, if you so wish. ● If the GP does not feel it is appropriate to take on the prescribing then the prescribing responsibilities will remain with the specialist. The GP should indicate the reason for declining. ● Enter a READ code (e.g. 8BM5.00) on to the patient record to highlight the existence of shared care for the patient. ● Undertake more frequent tests if there is evidence of clinical deterioration, abnormal results, or other risk factors. Contact specialist team for advice on monitoring in these circumstances if required. ● Check all monitoring results prior to issuing a repeat prescription to ensure it is safe to do so. ● If a patient fails to attend for monitoring: <ul style="list-style-type: none"> ○ Only issue a 28 day prescription and send them the next available appointment for a blood test ○ If they fail to attend a second blood test then contact the specialist team for advice and to discuss suitability for continued shared care before supplying further prescriptions ● Monitor the patient's general wellbeing. ● Seek urgent advice from secondary care if: <ul style="list-style-type: none"> ○ Signs or symptoms indicating blood dyscrasias eg sore throat, infection, unexplained or abnormal bruising or bleeding. ○ Any signs of bone marrow suppression (ie infection, fever, unexplained bruising or bleeding) ○ Jaundice ○ The patient becomes pregnant ○ Non compliance is suspected ○ The GP feels a dose change is required ○ There is marked deterioration renal function ○ The GP feels the patient is not benefiting from the treatment ● The shared care agreement will cease to exist, and prescribing responsibility will return to secondary care, where: <ul style="list-style-type: none"> ○ The clinical situation deteriorates such that the shared care criterion of stability is not achieved. ○ The clinical situation requires a major change in therapy.

	<ul style="list-style-type: none"> ○ GP feels it to be in the best stated clinical interest of the patient for prescribing responsibility to transfer back to the specialist team. The specialist team will accept such a transfer within a timeframe appropriate to the clinical circumstances. • There must be discussion between the specialist team and GP on this matter and agreement from the specialist team to take back full prescribing responsibility for the treatment of the patient. The specialist team should be given 14 days' notice in which to take back prescribing responsibilities from primary care. 								
16. Responsibilities of the patient	<ul style="list-style-type: none"> • To take medication as directed by the prescriber, or to contact the GP if not taking medication • To attend hospital and GP clinic appointments, bring monitoring booklet (if issued) • Failure to attend will result in medication being stopped (on specialist advice). • To report adverse effects to their Specialist or GP. 								
17. Additional Responsibilities e.g. Failure of patient to attend for monitoring, Intolerance of drugs, Monitoring parameters outside acceptable range, Treatment failure, Communication failure	<table border="1"> <thead> <tr> <th>List any special considerations</th> <th>Action required</th> <th>By whom</th> <th>Date</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> <td> </td> </tr> </tbody> </table>	List any special considerations	Action required	By whom	Date				
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18. Supporting documentation	The SCG must be accompanied by a patient information leaflet. (Available from http://www.medicines.org.uk/emc OR http://www.mhra.gov.uk/spc-pil/) Arthritis Research UK Patient Information Leaflet Azathioprine								
19. Patient monitoring booklet	Not routinely issued.								
20. Contact details	See Appendix 1								

Appendix 1 – Local Contact Details

Secondary care contact information	If stopping medication or needing advice please contact:
	Dr <i>[insert text here]</i>
	Contact number: <i>[insert text here]</i>
	Hospital: <i>[insert text here]</i>
	To contact Rheumatology Department Stepping Hill Hospital: <i>Consultants:</i> Dr C. Filer Dr A. Ismail Dr L. Mercer Rheumatology Nurse Helpline 0161 419 4250 Rheumatology Medication Helpline 0161 419 5202 Rheumatology Secretaries 0161 419 5069

Shared Care Guideline Summary: Azathioprine for the treatment of *Rheumatological Conditions* in adults

Drug	Azathioprine 25mg and 50mg tablets															
Indication	Rheumatological conditions															
Overview	Azathioprine is indicated either alone or in combination with corticosteroids and/or other DMARDs in the treatment of rheumatological conditions.															
Specialist's Responsibilities (N.B. Bolton DAWN monitoring based on BSR guidelines 2008/2017 for initiation/dose increases/parenterals; subsequent shared care as per GMMMG)	<p>Initial investigations: Assessment and diagnosis. Discuss the benefits and side effects of treatment with the patient. Baseline FBC, U&Es, LFTs, GFR, Height, Weight, Blood pressure, TPMT Assay and Pre-viral screen in high risk patients: HIV, HBV, HCV. Screening for lung disease and Herpes Zoster status should be undertaken at clinician discretion on a case by case basis.</p> <p>Initial regimen: 1mg/kg/day increasing after 4-6 weeks to 2-3mg/kg/day</p> <p>Clinical monitoring: Specialist review to ensure continued benefit</p> <p>Frequency of Monitoring: During dose titration: every 2 weeks until achieve maintenance dose. Maintenance dose: Monthly for 3 months then 3-monthly thereafter. Initial monitoring for the first 3 months will be carried out by the specialist OR as per local commissioning arrangements.</p> <p>Safety monitoring: FBC, U&E and LFTs</p> <p>Prescribing duration: Started by specialist and supplied by specialist for the initial 3 months of treatment, thereafter transferred to GP OR as per local commissioning arrangements.</p> <p>Prescribing details: Initiated by specialist, prescribed and monitored by the specialist for the first 3 months and then care transferred over to the GP OR as per local commissioning arrangements. To stop the drug or provide information to the GP on when to stop the drug.</p> <p>Documentation: The specialist team will write formally to the GP to request shared care using the GMMMG agreed process. Patients will only be transferred to the GP once the GP has agreed. Provide GP with diagnosis, relevant clinical information, treatment plan, duration of treatment with 14 days of seeing the patient or inform GP if the patient does not attend appointment.</p>															
GP's Responsibilities (N.B. Bolton DAWN monitoring based on BSR guidelines 2008/2017 for initiation/dose increases/parenterals; subsequent shared care as per GMMMG)	<p>Maintenance prescription: prescribe and monitor azathioprine 3 months after initiation in accordance with the specialist's recommendations OR as per local commissioning arrangements.</p> <p>Clinical monitoring: To report to and seek advice from the specialist on any aspect of patient care which is of concern to the GP and may affect treatment.</p> <p>Safety monitoring:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td rowspan="4" style="width: 15%; vertical-align: top;">FBC, U&E, LFTs with albumin, (CRP desirable but not essential)</td> <td style="width: 25%;">During dose titration: Every 2 weeks until achieve a stable dose for 6 weeks.</td> <td style="width: 30%;">WCC < 3.5 x 10⁹/l Neutrophils < 1.6 x 10⁹/l Platelets < 140 x 10⁹/l Unexplained eosinophilia > 0.5 x 10⁹/L Unexplained fall in serum albumin < 30g/l</td> <td style="width: 30%; text-align: center;">Withhold until discussion with Rheumatology Team</td> </tr> <tr> <td>Maintenance dose: Monthly for 3 months then at least every 3 months. More frequent monitoring is appropriate in patients at higher risk of toxicity.</td> <td>ALT and/or AST > 100 units/L OR Any sudden increases (e.g. double of baseline ALT)</td> <td style="text-align: center;">Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction</td> </tr> <tr> <td>Dose Increases/Starting an additional DMARD: Every 2 weeks until on stable dose for 6 weeks then revert back to previous schedule.</td> <td style="text-align: center;">MCV > 105 fl</td> <td style="text-align: center;">Check serum folate, B12 and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team</td> </tr> <tr> <td></td> <td style="text-align: center;">Creatinine > 30% above baseline and/or calculated GFR < 60</td> <td style="text-align: center;">Use clinical judgement. Repeat in 1 week and if still > 30% above baseline withhold until discussed with the</td> </tr> </table>			FBC, U&E, LFTs with albumin, (CRP desirable but not essential)	During dose titration: Every 2 weeks until achieve a stable dose for 6 weeks.	WCC < 3.5 x 10 ⁹ /l Neutrophils < 1.6 x 10 ⁹ /l Platelets < 140 x 10 ⁹ /l Unexplained eosinophilia > 0.5 x 10 ⁹ /L Unexplained fall in serum albumin < 30g/l	Withhold until discussion with Rheumatology Team	Maintenance dose: Monthly for 3 months then at least every 3 months. More frequent monitoring is appropriate in patients at higher risk of toxicity.	ALT and/or AST > 100 units/L OR Any sudden increases (e.g. double of baseline ALT)	Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction	Dose Increases/Starting an additional DMARD: Every 2 weeks until on stable dose for 6 weeks then revert back to previous schedule.	MCV > 105 fl	Check serum folate, B12 and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team		Creatinine > 30% above baseline and/or calculated GFR < 60	Use clinical judgement. Repeat in 1 week and if still > 30% above baseline withhold until discussed with the
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		Rheumatology Team
	<p>Duration of treatment: Stop treatment on advice of specialist.</p> <p>Re-referral criteria: Seek urgent advice from secondary care if:</p> <ul style="list-style-type: none"> ➢ Signs or symptoms indicating blood dyscrasias e.g. sore throat, infection, unexplained or abnormal bruising or bleeding. ➢ Any signs of bone marrow suppression (i.e. infection, fever, unexplained bruising or bleeding) ➢ Jaundice ➢ The patient becomes pregnant ➢ Non compliance is suspected ➢ The GP feels a dose change is required ➢ There is marked deterioration renal function ➢ The GP feels the patient is not benefiting from the treatment ➢ Patient fails to attend for monitoring on two consecutive occasions <p>Documentation: GPs should reply to request for shared care to either accept or decline within 14 days. A form is available on the GMMM website to facilitate this, if you so wish.</p>	
Adverse Events	Adverse events	Action
	WCC < 3.5 x 10 ⁹ /l Neutrophils < 1.6 x 10 ⁹ /l Platelets < 140 x 10 ⁹ /l Unexplained eosinophilia > 0.5 x 10 ⁹ /L Unexplained fall in serum albumin < 30g/l	Withhold until discussion with Rheumatology Team
	ALT and/or AST > 100 units/L OR Any sudden increases (e.g. double of baseline ALT)	Withhold until discussed with the Rheumatology Team. Check any other reason such as alcohol, drug interaction including over the counter medication as risk of hepatic dysfunction
	Rash or oral ulceration	Withhold until discussion with Rheumatology Team
	MCV > 105 fl	Check serum folate, B12 and TSH. Treat any underlying abnormality. If results normal discuss with Rheumatology Team
	Abnormal bruising or severe sore throat	Withhold until urgent FBC results available and discuss with Rheumatology Team as can cause bone marrow suppression.
	Creatinine > 30% above baseline and/or calculated GFR < 60	Use clinical judgement. Repeat in 1 week and if still > 30% above baseline withhold until discussed with the Rheumatology Team
Contra-indications Cautions Drug Interactions	<p>Please refer to the BNF and/or SPC for information.</p> <p>In non-immune patients exposed to chickenpox or shingles, passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG). It is the specialist's responsibility to make the recommendation for vaccination at the appropriate time.</p>	
Other Information	<ul style="list-style-type: none"> • Azathioprine – providing the film coating of the tablets remains intact, there is no risk and no additional precautions are required when handling them. These tablets should not be divided/split/crushed. • During infection requiring antibiotics azathioprine should be temporarily discontinued until the patient has recovered from the infection. • Annual flu vaccinations are safe and recommended. • Pneumococcal vaccination is safe and recommended. 	
Contact Details	<p>Name: [insert text here] Address: [insert text here] Telephone: [insert text here]</p>	

Appendix 3 - Shared Care Referral

Sent electronically by Stepping Hill (if available) when appropriate to transfer prescribing and monitoring responsibilities to GP

Dear Dr,

This patient is suitable for treatment with a medication which has been accepted for shared care according to the Derbyshire Joint Area Prescribing Committee and Stockport NHS Foundation Trust shared care protocol.

I am therefore requesting your agreement to share the care of this patient. Please see the corresponding letter (sent on the same date as this agreement request) for details of the medication. Pre-treatment investigations have been undertaken as per the shared care agreement and the patient has received the first three months of medication, is tolerating the treatment well and all blood tests have remained within the acceptable ranges.

Please return the response form within the next 14 days via fax to 0161 419 5548.

For further information please refer to the Shared Care Protocol which can be accessed below:
http://www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/out_of_area_shared_care_guidelines

Thank you

The Rheumatology Team,

Response Form (to be completed by the GP and returned to the fax number above)

Dear Dr _____,

I have received your request for shared care of the above patient who has been receiving treatment for the past 3 months with _____ as prescribed by their rheumatology consultant.

A: I am willing to accept the shared care for this patient, to continue to prescribe and monitor as set out in the protocol

B: I wish to discuss this request with you

C: I am unable to undertake shared care of this patient.

If unable to undertake shared care, please state why:

GP Signature:

Date:

GP address/practice stamp

Yours sincerely