Effective Shared Care Agreement (ESCA)

Azathioprine

ESCA: For the treatment of rheumatoid arthritis or psoriatic arthritis

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of azathioprine for rheumatoid arthritis or psoriatic arthritis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with rheumatoid arthritis or psoriatic arthritis are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of rheumatoid arthritis or psoriatic arthritis.
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made.
4. Do baseline monitoring prior to initiation of azathioprine.
5. Initiate treatment and stabilise dose of azathioprine.
6. Review the patient's condition and monitor response to treatment regularly.
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay.
8. Report serious adverse events to the MHRA.
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below).

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days.						
2. Prescribe azathioprine at the dose recommended.						
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist						
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment.						
6. Refer back to specialist if condition deteriorates.						
7. Report serious adverse events to specialist and MHRA.						
8. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with azathioprine with the specialist, clinical nurse specialist or GP.
3. Report any adverse effects to the specialist or GP whilst taking azathioprine.
4. Attend regular outpatient appointments with the specialist.

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

SUPPORTING INFORMATION

Indication	Azathioprine either alone or more usually in combination with corticosteroids and/or other drugs and procedures, has been used with clinical benefit (which may include reduction of dosage or discontinuation of corticosteroids) in a proportion of patients suffering from the following: severe rheumatoid arthritis;
Dosage and Administration	**Dose and titration (based on how well tolerated by the patient and the current blood picture)** **BSR Recommended:-** Typical dose: 1 mg/kg/day—increasing after 4–6 weeks to 2–3 mg/kg/day. <u>Suggested dose regimen:-</u> 50 mg in the evening for two to four weeks, then 75 mg in the evening for two to four weeks, then 100 mg in the evening (or 50 mg BD) for two to four weeks, then 150 mg in the evenings (or 75 mg BD). Adjust dose according to patient response and weight, Maintenance dose is often determined on clinical grounds ie response and tolerance, so only rarely is a dose of 150 mg exceeded (Available in 25 mg and 50 mg size tablets).
Renal Impairment **Hepatic impairment**	Renal, hepatic impairment or elderly patients should have doses at the lower end of the dosage range initiated and haematological response should be monitored more closely.
Contra-indications / Special precautions	**Contraindications:-** In patients known to be hypersensitive to azathioprine. Hypersensitivity to 6-mercaptopurine (6-MP) In patients who may be pregnant, or who are likely to become pregnant without careful assessment of risk versus benefit **Caution** • Patients receiving azathioprine should be instructed to report immediately any evidence of infection, unexpected bruising or bleeding or other manifestations of bone marrow depression. • 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. Also it has been reported that decreased TPMT activity increases the risk of secondary leukaemias and myelodysplasia in individuals receiving 6-mercaptopurine (the active metabolite of azathioprine) in combination with other cytotoxics • It has been suggested that the toxicity of azathioprine may be enhanced in the presence of renal insufficiency, but controlled studies have not supported this suggestion. Nevertheless, it is recommended that the dosages used should be at the lower end of the normal range and that haematological response should be carefully monitored. Dosage should be further reduced if haematological toxicity occurs. • Caution is necessary during the administration of azathioprine to patients with hepatic dysfunction, and regular complete blood counts and liver function tests should be undertaken. In such patients the metabolism of azathioprine may be impaired, and the dosage of azathioprine should therefore be reduced if hepatic or haematological toxicity occurs. • Patients receiving immunosuppressive therapy are at an increased risk of developing non-Hodgkin's lymphomas and other malignancies, notably skin cancers (melanoma and non-melanoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer *in situ*. Exposure to sunlight and UV light should be limited and patients should wear protective clothing and use a sunscreen with a high protection factor to minimize the risk of skin cancer and photosensitivity, • Infection with varicella zoster virus (VZV; chickenpox and herpes zoster) may become severe during the administration of immunosuppressants. Caution should be exercised especially with respect to the following: • Before starting the administration of immunosuppressants, the prescriber should check to see if the patient has a history of VZV. Serologic testing may be useful in determining previous exposure. Patients who have no history of exposure should avoid contact with individuals with chickenpox or herpes zoster. If the patient is exposed to VZV, special care must be taken to avoid patients developing chickenpox or herpes zoster, and passive immunisation with varicella-zoster immunoglobulin (VZIG) may be considered. If the patient is infected with VZV, appropriate measures should be taken, which may include antiviral therapy and supportive care.

Side Effects	Very common	Depression of bone marrow function; leucopenia.		
	Common	Thrombocytopenia.		
	Rash or mouth ulcers may respond to a dose reduction otherwise treatment should be discontinued			
Monitoring	Treatment should not be initiated unless patients can be adequately monitored for toxic effects throughout the duration of therapy. **PLEASE NOTE:- The monitoring criteria differ from the BSR guidelines**			
		Local	**BSR**	
	Pretreatment Assessment	FBC, U&E, creatinine, LFTs, renal, C-reactive protein. Consider TMPT assay	FBC, U&E, creatinine, LFTs, and TPMT assay	
	After commencing treatment	FBC, LFT every 2 weeks for first 3 months the every month for 4 months and thereafter every 2-3 months for long term use.	FBC and LFTs weekly for 6 weeks and continue every 2 weeks until dose stable for 6 weeks; then monthly. If maintenance dose is achieved and stable for 6 months consider discussing with patient to reduce monitoring to 3 monthly In people heterozygote for TPMT, monitoring should continue at monthly intervals at minimum	
	Following changes in dose		Repeat FBC and LFTs 2 weeks after dose change and then monthly	
	Regular review		U&E and creatinine should be repeated 6 monthly.	
	Disease monitoring	Occasional ESR/CRP helps assessment		
	Actions to be taken BSR Recommendations:	WBC<3.5x10^9/l	Withhold until discussed with specialist team.	
		Neutrophils<2.0x10^9/l	Withhold until discussed with specialist team.	
		Platelets<150x10^9/l	Withhold until discussed with specialist team.	
		AST, ALT>twice upper limit of normal	Withhold until discussed with specialist team.	
		Rash or oral ulceration	Withhold until discussed with specialist team.	
		MCV>105 fl	Check serum folate and B12 & TSH. Treat any underlying abnormality. If results normal discuss with specialist team.	
		Abnormal bruising or severe sore throat	Withhold until FBC results available and discuss with the specialist team.	
	TPMT range	<6 nmol/g Hb/h	Deficient	NO TREATMENT
		6-34 nmol/g Hb/h	Low	NO TREATMENT
		35-79 nmol/g Hb/h	Normal	TREAT & Monitor
		>79 nmol/g Hb/h	High	TREAT & Monitor
	Dose reduction	Side effects:- nausea, diarrhoea rash, recurrent infection		
	Important notes	• Live vaccines should not be administered • Influenza and pneumovax vaccines are recommended • Patients without immunity who are exposed to chickenpox or shingles should be administered varicella zoster immunoglobulin – seek specialist advice • Effective contraception should be recommended during therapy • Patient should be counselled to observe for signs of bone marrow suppression i.e inexplicable bruising, bleeding or infection		

Drug Interactions (highlighted interaction are the significant ones)	As per BNF May 2015 online. For more information please refer to the SmPC

Agent	Notes
Allopurinol	enhanced effects and increased toxicity of azathioprine when given with allopurinol (reduce dose of azathioprine to one quarter of usual dose)
Captopril	increased risk of anaemia or leucopenia when azathioprine given with captopril especially in renal impairment
Coumarins	azathioprine possibly reduces anticoagulant effect of coumarins **Note:** Change in patient's clinical condition, particularly associated with liver disease, intercurrent illness, or drug administration, necessitates more frequent testing. Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may also affect anticoagulant control
Enalapril	increased risk of anaemia when azathioprine given with enalapril especially in renal impairment
Febuxostat	avoidance of azathioprine advised by manufacturer of febuxostat
Ribavirin	myelosuppressive effects of azathioprine possibly enhanced by ribavirin
Sulfamethoxazole	increased risk of haematological toxicity when azathioprine given with sulfamethoxazole (as co-trimoxazole)
Trimethoprim	increased risk of haematological toxicity when azathioprine given with trimethoprim (also with co-trimoxazole)

References

- British Society for Rheumatology (BSR) guidelines
- Imuran Tablets SmPC
- Azathioprine BNF

I agree to participate in this shared care agreement for the treatment of the below named patient with azathioprine for rheumatoid arthritis or psoriatic arthritis

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: