NHS
Basildon and Brentwood
Clinical Commissioning Group

Azathioprine in various conditions

MONITORING	RESPONSIBILITY	CONDITIONS	TESTS
Ongoing	GP	All	• FBC, LFT, U&Es **3 monthly**

Criteria for managing events & symptoms occurring during Azathioprine therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
MCV	Increased > 105 f/l	**Seek specialist advice**. Check TFT, B12 and folate, Monitor LFTs as could be dose-related.
WBC	< 3.0 x 109/L	**Seek specialist advice**, repeat FBC in 1 or 2 weeks.
Neutrophils	< 1.6 x 10^9/l – consider stopping drug 1.6-2 x 10^9/l – check trend	
Platelets	< 100x 10^9/l - consider stopping drug 100-140 x 10^9/l – check trend	
Haemoglobin	<80g/dL - consider stopping drug 80-100g/dL – check trend	
Significant deterioration in renal function	Creatinine increase >30% over 12 months or calculated GFR <60ml/min	**Seek specialist advice.** Caution dose reduction advised in renal impairment
Elevation in liver enzymes (AST, ALT) or falling albumin	>2x upper limit of normal (ULN) - consider dose adjustment; >3x ULN - consider stopping drug Albumin <30 g/l - please review patient for other medical problems	**Seek specialist advice.**

SYMPTOMS	MANAGEMENT
Rash , oral ulceration, stomatitis	**Stop azathioprine** , repeat FBC immediately and discuss with specialist
Cough, dyspnoea infection, fever, rigors	
Abnormal bruising or bleeding or severe or persistent sore throat	
Abdominal pain suggestive of pancreatitis, jaundice,	
Nausea, vomiting and diarrhoea	Withdrawal of drug may be necessary if persistent
Hair loss, pneumonitis	Rare but stop and discuss with specialist

Hydroxychloroquine Monitoring

MONITORING	TESTS
GP: Ongoing	No routine monitoring required (annual blood tests FBC, LFTs,U&Es recommended) **Ophthalmologic examination**, the Royal College of Ophthalmologists (RCO) recommend an **annual** eye assessment (ideally including optical coherence tomography) if continued for >5 years. **Stop** if there are any abnormalities and refer to specialist team **Ask patient about visual symptoms at every clinic appointment** **Patients should be advised to stop taking the drug immediately and report any:** • **visual disturbance or change of colour vision to their GP or hospital specialist**

Criteria for managing events & symptoms occurring during Hydroxychloroquine therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
MCV	Increased > 105 f/l	**Seek specialist advice**. Check TFT, B12 and folate, Monitor LFTs as could be dose-related.
WBC	< 3.0 x 109/L	**Seek specialist advice**, repeat FBC in 1 or 2 weeks.
Neutrophils	< 1.6 x 10^9/l – consider stopping drug 1.6-2 x 10^9/l – check trend	
Platelets	< 100x 10^9/l - consider stopping drug 100-140 x 10^9/l – check trend	
Haemoglobin	<80g/dL - consider stopping drug 80-100g/dL – check trend	
Significant deterioration in renal function	Creatinine increase >30% over 12 months or calculated GFR <60ml/min	**Seek specialist advice.** Caution dose reduction advised in renal impairment
Elevation in liver enzymes (AST, ALT) or falling albumin	>2x upper limit of normal (ULN) - consider dose adjustment; >3x ULN - consider stopping drug Albumin <30 g/l - please review patient for other medical problems	**Seek specialist advice.**

SYMPTOMS	MANAGEMENT
Skin rash, pruritus	**Stop** drug and discuss with rheumatologist
Visual changes, retinal damage	**Stop** and seek advice; In its early form it appears reversible on discontinuation of hydroxychloroquine
Abnormal bruising or bleeding or sore throat.	**Stop**, repeat FBC immediately.
Any other unexplainable symptoms	**Stop** drug and discuss with specialist

Leflunomide in Rheumatoid arthritis

MONITORING	TESTS
Ongoing	**After six months:** FBC, LFTs, BP and weight **every two months**. If co-prescribed with another immunosuppressant or potentially hepatotoxic drug, continue monitoring at least **once a month**

Criteria for managing events & symptoms occurring during Leflunomide therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
WBC	Decrease to < 3.5 x 109/L	**Withhold** until discussed with specialist team.
Neutrophils	Decrease to < 2.0 x 109/L	
Platelets	< 150 x 109/L	
AST and ALT	2 - 3x upper limit of reference range	If current dose >10mg daily, reduce to 10mg daily and re-check weekly until normalised. If AST and ALT returning to normal leave on 10mg daily. **If LFTs remain elevated, withdraw and discuss with specialist team**
	> 3x upper limit of reference range	**Re-check LFTs within 72h**, if remain more than three times the reference range, **stop drug** and discuss with specialist team
Fall in albumin	< 150 x 109/L	Repeat LFTs as early sign of liver toxicity. **Stop and discuss** with specialist team if continue to deteriorate.
BP >140/90		Treat in line with National Institute For Clinical Excellence (NICE) guidance. If patient develops severe hypertension which remains uncontrolled despite optimal antihypertensive treatment, stop leflunomide and consider washout

SYMPTOMS	MANAGEMENT
Rash/Itch, Hair Loss, Headache	Consider dose reduction; if severe, stop, consider washout*.
Gastrointestinal disturbances (diarrhoea, nausea)	Symptomatic treatment and consider dose reduction; if severe or persistent, stop and consider washout*.
Hypertension	If blood pressure >140/90 treat in line with NICE guidance. If remains uncontrolled stop and consider washout*.
Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results available. Follow relevant course of action from table above. Discuss with specialist team if necessary
Weight loss	Monitor carefully. If >10% weight loss with no other cause identified, reduce dosage or stop and consider washout*.
Dry cough, breathlessness	**Stop** if increasing shortness of breath occurs. **Seek urgent** advice from specialist team.

Washout Procedure

Leflunomide has a **long half-life of up to 6 weeks**. Adverse effects may be seen for a long time after the drug is stopped. A washout procedure can be considered in patients having severe side effects or in men or women considering conception. (If a waiting period of up to approximately 2 years under reliable contraception is considered impractical, prophylactic institution of a washout procedure is advisable).

It is usually recommended to give Colestryramine 8g TDS or activated powdered charcoal 50g QDS for 11 days then measure metabolite A771 726 twice at intervals of at least 14 days. This should fall to less than 0.02 mg/I. It is recommended to wait at least 3 months before considering conception.

Mercaptopurine in inflammatory bowel disease

MONITORING	RESPONSIBILITY	CONDITIONS	TESTS
Ongoing	GP	All	• FBC, LFT, U&Es **3 monthly**

Criteria for managing events & symptoms occurring during mercaptopurine therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
MCV	Increased > 105 fL	**Seek specialist advice**. Check TFT, B12 and folate, Monitor LFTs as could be dose-related.
WBC	< 3.5 x 10^9/L	**Seek specialist advice**, repeat FBC in 1 or 2 weeks.
Neutrophils	< 1.6 x 10^9/l – consider stopping drug 1.6-2 x 10^9/l – check trend	
Platelets	< 140x 10^9/l - consider stopping drug	
Haemoglobin	<80g/dL - consider stopping drug 80-100g/dL – check trend	
Significant deterioration in renal function	Creatinine increase >30% over 12 months or calculated GFR <60ml/min	**Seek specialist advice.** Caution dose reduction advised in renal impairment
Elevation in liver enzymes (AST, ALT) or falling albumin	>2x upper limit of normal (ULN) - consider dose adjustment; >3x ULN - consider stopping drug Albumin <30 g/l - please review patient for other medical problems	**Seek specialist advice.**

SYMPTOMS	MANAGEMENT
Rash , oral ulceration, stomatitis	**Stop mercaptopurine** , repeat FBC immediately and discuss with specialist
Cough, dyspnoea infection, fever, rigors	
Abnormal bruising or bleeding or severe or persistent sore throat	
Abdominal pain suggestive of pancreatitis, jaundice,	
Nausea, vomiting and diarrhoea	Withdrawal of drug may be necessary if persistent
Hair loss, pneumonitis	Rare but stop and discuss with specialist

Methotrexate in Rheumatoid arthritis (oral, sub cutaneously or intramuscularly)

MONITORING	RESPONSIBILITY	TESTS
		• Thereafter, FBC, U&Es creatinine/calculated GFR, ALT and/or AST

Recommendations from British Society of Rheumatologists for managing abnormal results

LABORATORY EVENTS	VALUES	ACTION
Elevation in liver enzymes AST, ALT, GGT or falling	Serial rise over 3 visits	**Stop treatment and seek advice from**
Mild-to-moderate renal	Mild: GFR 20 to 50 mL/min	
	< 3.5 x 10^9/L	
	< 2.0 x 10^9/L	
	< 140 x 10^9/L	
	> 0.5 x 10^9/L	
	>10% on 3 occasions	
		Seek advice from specialist team • check serum B12, folate and TFTs and • May require folinic acid rescue for bone marrow toxicity

Criteria for managing side effects occurring during Methotrexate therapy in primary care

SYMPTOMS	MANAGEMENT
Rash	**Stop drug** and discuss with specialist team. ***(See relevant telephone number(s) on page 5)***
Severe sore throat, abnormal bruising or bleeding	**Stop drug** and repeat FBC immediately. Follow relevant course of action from table above.
Unexplained or prolonged cough, dyspnoea or fever	**Stop drug** and seek advice from specialist team.
Oral ulceration and stomatitis	May be overcome by low-dose folate (e.g. increase from 5mg to 10mg per week). If persistent, seek advice.
Unexplained or prolonged dyspepsia, diarrhoea, nausea, vomiting	May be overcome by low-dose folate and/or taking tablets with evening meal or eating a banana with the dose or increasing the fluid intake over 24 hours prior to taking methotrexate. If persistent, seek advice.

Sufasalazine in Ulcerative Colitis, Crohn's disease and Rheumatoid arthritis

MONITORING	TESTS
Ongoing	• FBC, LFT, U&Es **3 monthly** If dose and monitoring is **stable after one year**, then no routine monitoring needed (annual blood tests recommended) Ask about rash and oral ulceration at each visit.

Criteria for managing events & symptoms occurring during Sulfasalazine therapy in primary care

LABORATORY EVENTS	VALUES	ACTION
MCV	Increased > 105 fL	**Seek specialist advice**. Check TFT, B12 and folate, Monitor LFTs as could be dose-related.
WBC	< 3.5 x 10^9/L	**Seek specialist advice**, repeat FBC in 1 or 2 weeks.
Neutrophils	< 1.6 x 10^9/l – consider stopping drug 1.6-2 x 10^9/l – check trend	
Platelets	< 140x 10^9/l - consider stopping drug	
Haemoglobin	<80g/dL - consider stopping drug 80-100g/dL – check trend	
Significant deterioration in renal function	Creatinine increase >30% over 12 months or calculated GFR <60ml/min	**Seek specialist advice.** Caution dose reduction advised in renal impairment
Elevation in liver enzymes (AST, ALT) or falling albumin	>2x upper limit of normal (ULN) - consider dose adjustment; >3x ULN - consider stopping drug Albumin <30 g/l - please review patient for other medical problems	**Seek specialist advice.**

SYMPTOMS	MANAGEMENT
Abnormal bruising/ bleeding or severe sore throat	**Check FBC** immediately and withhold sulfasalazine until results available. Follow relevant course of action from table above Discuss with specialist team if necessary.
Dyspepsia, nausea, dizziness, headache	**Reduce dose**. Take with food; try anti emetic Stop if persistent or unacceptable. Enteric coated tablets may be tried if patient is taking plain tablets
Unexplained acute widespread rash	Often non-specific erythematous, dry and itchy. **Stop drug** and Seek for advice (dermatology) if severe. Consider using 1% hydrocortisone and /or antihistamines. Consider other causes of rash
Oral ulceration, stomatitis	**Stop** if severe and discuss with rheumatologist. Consider carbenoxolone or benzydamine mouthwashes
Fever / Flu like illness	**Stop drug**. Unusual hypersensitivity reaction.
Discoloration of urine and/ or soft contact lenses	Reassure patient