Therapeutics Advisory Group

Improving lives together
Norfolk and Waveney Integrated Care System

NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT

Shared care guidelines for use of Sulfasalazine in the treatment of inflammatory arthritis and inflammatory bowel disease
Monitoring level – Amber 3 for year 1, Amber 2 thereafter

Generic and Proprietary/Brand Name	
Sulfasalazine – see Netformulary for options	
Indications for shared care	
Treatment of inflammatory arthritis	
Specialist Prescribing and Monitoring Responsibilities – summary. Full details in main body of document	**GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities – summary. Full details in main body of document**
• Identify patients who will benefit from treatment • Ensure patient tolerating sulfasalazine for first 10 weeks. • Ensure prior dissemination of sufficient information to patient's GP and other carers. • Inform the GP that sulfasalazine has been commenced, and the dose and future plans for dose escalation • Ask for monitoring to be transferred to primary care once the dose has been stable for 6 weeks • Provide education to GPs, nurses, patients and their carers. • Agree any necessary dose changes. • Review the efficacy of the treatment at intervals and confirm these arrangements with the GP. • Provide patients with a patient held record book/ printout of results. • Provide access to back-up and support facilities. • The decision to restart sulfasalazine after a severe infection where the patient has had a break from therapy should be undertaken by the hospital specialist team and the initial subsequent monitoring until the patient is stable • Check FBC, eGFR, ALT and albumin every 2 weeks, until the patient has been on a stable dose for 6 weeks (• The GP can then be approached	• Prescribe sulfasalazine at the dose recommended by the hospital specialist once the patient is stabilised on treatment for 6 weeks (i.e. usually after 10 weeks' treatment) and side effects have been excluded as far as possible by the hospital. • Check for possible drug interactions • Encourage patients to carry an up-to-date monitoring and record booklet and information sheet as provided by the hospital. • Report side effects and any other issues to specialist. • Stop sulfasalazine if serious adverse drug effect/reaction and contact specialist team. • There is no indication to stop sulfasalazine at the time of routine surgery • Sulfasalazine should be stopped in the event of a severe infection e.g. requiring hospitalisation. • Report any suspected adverse drug reactions to the hospital specialist. • After the patient has been on a stable dose for 6 weeks, at the specialist's request, check FBC, eGFR, ALT and albumin every month for the next 3 months • For patients at low risk of toxicity, then monitor FBC, eGFR, ALT and albumin every 3 months, i.e. from 6 months after starting treatment, at 9 months and at 12 months • Where there is still a low risk of toxicity, monitoring can then cease after 12 months' treatment (at the consultant's discretion)
Patient Information	
Sulfasalazine booklet - Sulfasalazine information booklet (versusarthritis.org)	

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they 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.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment

Sulfasalazine is a disease modifying anti-rheumatic drug which reduces the signs, symptoms and progression of inflammatory arthritis.

Sulfasalazine acts both as an anti-inflammatory and an immunomodulant, inhibiting inflammatory cell chemotaxis and cytokine and antibody production. Around 90% of a dose reaches the colon where bacteria split the drug into sulfapyridine (SP) and mesalazine (ME). These are active, and the unsplit sulfasalazine (SASP) is also active on a variety of symptoms. Most SP is absorbed, hydroxylated or glucuronidated and a mix of unchanged and metabolised SP appears in the urine. SASP is excreted unchanged in the bile and urine.

Licensed use and agreed local off-label use

Induction and maintenance of remission of ulcerative colitis and treatment of active Crohn's disease.

Rheumatoid arthritis Salazopyrin EN-Tabs® (Pharmacia) only

See individual manufacturers' SPCs **www.medicines.org.uk/emc/** for current information

Uses approved under Shared Care Agreement (SCA):

- Inflammatory bowel disease
- Inflammatory arthritis

Form and strength of preparation

- Tablets: Sulfasalazine 500 mg
- Suspension: Sulfasalazine 250mg/5ml Oral Suspension
- Suppositories: Sulfasalazine Suppositories 500mg

See Netformulary

Criteria for patient selection

Treatment of inflammatory bowel disease and inflammatory arthritis.

Side Effects and Management

Link to BNF

Link to SPC

Drug Interactions

Link to BNF

Link to SPC

Cautions and Contraindications

Link to BNF

Link to SPC

Vaccines and immunisation:

Annual vaccination against influenza should be routinely offered as should the one off pneumococcal vaccination.

Shingles:

The Green Book Chapter 28a v3_0 regarding the shingles vaccine, states "*Long term stable low dose corticosteroid therapy (defined as <20mg prednisolone per day for more than 14 days), either alone or in combination with low dose non-biological oral immune modulating drugs (e.g. methotrexate less than or taking 25mg/week), are not considered sufficiently immunosuppressive and these patients can receive the vaccine. Patients on higher doses should be discussed with the consultant*".

Initiation of therapy and ongoing dose regimen

Hospital-led initiation of therapy.

Initial dose:

The dose is adjusted according to the severity of the disease and the patient's tolerance to the drug, as detailed below. In elderly patients, no special precautions are necessary.
The dose of sulfasalazine should be increased slowly:

- Week 1: 500mg each morning
- Week 2: 500mg morning and evening
- Week 3: 1g each morning and 500mg each evening
- Week 4: 1g morning and evening

Maintenance dose:

Continue with 1g twice daily.
Occasionally doses up to 3g/day may be prescribed.
It may be between 6 -12 weeks before a marked effect is seen.

Administration Information

- Sulfasalazine should be given with caution to patients with severe allergy or bronchial asthma.
- Since sulfasalazine may cause haemolytic anaemia, it should be used with caution in patients with G-6-PD deficiency.
- Oral sulfasalazine inhibits the absorption and metabolism of folic acid and may cause folic acid deficiency, potentially resulting in serious blood disorders (e.g. macrocytosis and pancytopenia). This can be normalised by administration of folic acid.
- Because sulfasalazine causes crystalluria and kidney stone formation, adequate fluid intake should be ensured during treatment.

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

Long term therapy.

Baseline assessment and ongoing monitoring – by Specialist

Initial assessment:

Undertake pre-treatment monitoring of FBC, LFTs, U&Es, eGFR

Lung disease:

Routine CXR are not undertaken but clinical assessment of co-existing pulmonary disease may result in pulmonary function tests to assess lung reserve and CT assessment being undertaken.

Pre-existing lung disease is not a contraindication to DMARD use but prescription is undertaken with caution

Liver disease:
In patients with deranged liver biochemistry, hepatotoxic DMARDs should be used with caution, with careful attention to trends in test results. In patients with impaired liver synthetic function (e.g. cirrhosis), DMARD therapy should be used with extreme caution. Patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to DMARD initiation.

Occult viral infections:
Screening for occult viral infections such as HIV and hepatitis B and C should be offered and Varicella status recorded.

Specialist monitoring:
Check FBC, eGFR, ALT and albumin every 2 weeks, until the patient has been on a stable dose for 6 weeks (schedule will therefore be: checks at Baseline, 2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks).
The GP can then be approached to check FBC, eGFR, ALT and albumin every month for 3 months, after which monitoring may be reduced to every 3 months in patients at low risk of toxicity. Clinical discretion dictates frequency of monitoring in these circumstances and the consultant must advise the GP accordingly.
Risk factors for toxicity include: a history of adverse drug events, medical comorbidities including renal and liver impairment (e.g. NAFLD) and malignancy, patients at the extremes of weight (BMI <18 or >30 kg/m2) and old age (>80 years).
Patients on concomitant DMARDs, especially leflunomide, should have monthly monitoring.

GP / Community Team or other Primary Care monitoring responsibilities

- Report any suspected adverse drug reactions to the hospital specialist.
- After the patient has been on a stable dose for 6 weeks, at the specialist's request, check FBC, eGFR, ALT and albumin every month for the next 3 months
- For patients at low risk of toxicity, then monitor FBC, eGFR, ALT and albumin every 3 months, i.e. from 6 months after starting treatment, at 9 months and at 12 months
- NB patients on concomitant DMARDs, especially leflunomide, should continue to have monthly monitoring.
- Where there is still a low risk of toxicity, monitoring can then cease after 12 months' treatment (at the consultant's discretion)
- Risk factors for toxicity include: a history of adverse drug events, medical comorbidities including renal and liver impairment (e.g. NAFLD) and malignancy, patients at the extremes of weight (BMI <18 or >30 kg/m2) and old age (>80 years). Clinical discretion dictates frequency of monitoring in these circumstances and the consultant must advise.
- Look for trends in the monitoring e.g. rapidly falling WCC

If the patient's:

- **WBC <3.5 x 109/L**
- **Neutrophils <1.6 x 109/L**
- **Platelets <140 x 109/L**
- **Unexplained eosinophilia >0.5x109/L**
- **ALT > twice upper limit of normal**
- **Unexplained falling albumin <30g/L**
- **MCV >105fL**
- **Creatinine increase >30% over 12 months and/or eGFR <60ml/min/1.73m2**
- **Symptoms of pneumonitis**

STOP SULFASALAZINE and inform the hospital specialist

- In patients developing significant infection, undertake an urgent FBC to check for leucopenia.

Consultant / Specialist prescribing responsibilities

- Identify those patients who will benefit from treatment with sulfasalazine
- FBC, liver function tests (ALT and albumin), and eGFR as described above.
- Ensure patient tolerating sulfasalazine for first 10 weeks.
- Ensure prior dissemination of sufficient information to patient's GP and other carers.
- Inform the GP that sulfasalazine has been commenced, and the dose and future plans for dose escalation
- Ask for monitoring to be transferred to primary care once the dose has been stable for 6 weeks
- Provide education to GPs, nurses, patients and their carers.
- Provide patients with a patient information sheet and education to the patients and carers on sulfasalazine.
- Agree any necessary dose changes.
- Review the efficacy of the treatment at intervals and confirm these arrangements with the GP.
- Provide patients with a patient held record book/ printout of results.
- Provide access to back-up and support facilities.
- The decision to restart sulfasalazine after a severe infection where the patient has had a break from therapy should be undertaken by the hospital specialist team and the initial subsequent monitoring until the patient is stable

GP prescribing responsibilities

- Prescribe sulfasalazine at the dose recommended by the hospital specialist once the patient is stabilised on treatment for 6 weeks (i.e. usually after 10 weeks' treatment) and side effects have been excluded as far as possible by the hospital. Any decision to alter treatment should usually be taken by the hospital specialist, including nurse practitioner.
- Check for possible drug interactions when newly prescribing or stopping concurrent medication.
- Encourage patients to carry an up-to-date monitoring and record booklet and information sheet as provided by the hospital. Alternatively, a printed copy of blood results can be made available.
- Report side effects and any other issues to the hospital specialist.
- Stop sulfasalazine if serious adverse drug effect/reaction and contact specialist team.
- There is no indication to stop sulfasalazine at the time of routine surgery
- Sulfasalazine should be stopped in the event of a severe infection e.g. requiring hospitalisation.
- The decision to restart sulfasalazine after a severe infection where the patient has had a break from therapy e.g. of more than one month, should be undertaken by the hospital specialist team.

Pregnancy, Paternal Exposure and Breastfeeding

Pregnancy, fertility and breastfeeding:

- SSZ with folate supplementation (5 mg/day) is compatible throughout pregnancy
- SSZ is compatible with breastfeeding in healthy, full-term infants
- Men taking SSZ may have reduced fertility. There is no evidence, however, that conception is enhanced by stopping SSZ for 3 months prior to conception unless conception is delayed >12 months when other causes of infertility should also be considered

Indications for referral back to Specialist

- Deterioration of renal function increases the risk of sulfasalazine toxicity although it can still be prescribed with caution. Please inform the hospital specialist of marked changes.
- If the patient develops a sore throat, abnormal bleeding or bruising, check FBC and stop sulfasalazine if abnormal. Please inform hospital specialist.

Contact details

Consultant and medical staff and nurse practitioners are available to give advice and can be contacted either through the main hospital switchboard or direct.

NNUH Department / Specialist	Contact Telephone Number
Hospital switchboard – ask for specialist or On-Call specialist (rheumatology/dermatology) out-of-hours	(01603) 286286
Rheumatology	
Rheumatology Practitioners	(01603) 287801
Dr Chulanie De Silva	Via (01603) 288623
Dr Karl Gaffney	Via (01603) 289670
Professor Alex MacGregor	Via (01603) 288677
Dr Tarnya Marshall	Via (01603) 288677
Dr Peter Merry	Via (01603) 287003
Dr Chetan Mukhtyar	Via (01603) 286766
Dr Louise Hamilton	Via (01603) 288678
Gastroenterology	
Dr Ian Beales	Via (01603) 288366
Dr Simon Chan	Via (01603) 288534
Dr Helen Fellows	Via (01603) 288368
Dr Ian Fellows	Via (01603) 288356
Dr Andrew Hart	Via (01603) 288367
Dr Sathish Mogan	Via (01603) 288607
Dr Alison Prior	Via (01603) 288358
Dr Richard Tighe	Via (01603) 288230
Dr Mark Tremelling	Via (01603) 288612
Prof Alastair Watson	Via (01603) 288366
Paediatrics (Rheumatology)	
Paediatric Rheumatology Nurse Specialist	Via (01603) 287911
Dr Kate Armon	Via (01603) 287534
Dr Mary-Anne Morris	Via (01603) 289936
Pharmacy	
Medicines Information Helpline	(01603) 287139 or Bleep 500 via 01603 286286

JPUH Department / Specialist	Contact Telephone Number
Hospital switchboard	(01493) 452452
Rheumatology	
Dr Joegi Thomas	Via (01493) 452216

Dr Damodar Makkuni Dr Tarnya Marshall (Thursday mornings only) **Specialist Nurse:** June Sunghuttee	Via (01493) 452216
Gastroenterology	
Consultants: Dr Rawya Badreldin Dr Paul Banim Dr Bernard Brett Dr Anupama de Silva Dr Aamir Saleem Dr Matthew Williams **Inflammatory Bowel Disease (IBD) Nurse:** Rowan Shaws	 Via (01493) 452766 Via (01493) 452766 Via (01493) 453406 Via (01493) 453406 Via (01493) 452858 Via (01493) 453572 Via (01493) 452766
Paediatrics (Rheumatology)– Via Tel 01493 452452	
Dr Shiras Thayath	Via (01493) 453342
Specialist Nurse: Jo Ridgers	Via switchboard

QEH Department / Specialist:	**Contact Telephone Number**
Hospital switchboard	(01553) 613613
Rheumatology	
Dr John Pradeep, Consultant Rheumatologist	Via (01553) 613177
Dr I Riaz	Via 01553 613177
Rheumatology Nurse Specialists	(01553) 613393
Gastroenterology	
Dr Andrew Douds	Via (01553) 613989
Dr Shailesh Karanth	Via (01553) 613708
Dr Rory McGouran	Via switchboard (01553) 613613
Dr Alan Wiles	Via (01553) 613004
Paediatrics (Rheumatology)	
Consultant Paediatrician – Dr Glynis Rewitzky	Via (01553) 613678
Community Paediatric Nurses – Mandy Parker & Jennifer Glover	Via (01553) 613214

Further information and supporting documents

British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) have published guidance on Prescribing drugs in pregnancy and breastfeeding – Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids

Author(s) and Organisation	• Dr Tarnya Marshall, Consultant Rheumatologist, NNUH • Heather Hasthorpe. Lead Rheumatology Clinical Nurse Specialist, NNUH
Date of Approval	March 2024
Reviewed by	Therapeutics Advisory Group
Last review date	August 2021
Date of next review	February 2025

Document history:

Version	Date	Author / Editor	Status	Comment
1.	July 2017	Dr Tarnya Marshall, Consultant Rheumatologist, NNUH Heather Hasthorpe. Lead Rheumatology Clinical Nurse Specialist, NNUH	Draft	Discussed and supported in principle at the July 2017 TAG meeting – amendments under review. Final version approved by the Norfolk & Waveney CCGs' Drugs & Therapeutics Commissioning Group (D&TCG) – August 2017.
2.0	Aug 2021	Jen Carroll, TAG Lead Technician	FINAL	Discussed at August 2021 TAG meeting. Review dates extended for a year from meeting due to covid pressures
3.0	Feb 2024	Jen Carroll, TAG Lead Technician	FINAL	Content not reviewed. Existing SCA transferred to new template in preparation for upload to KNoW