# SY ICB Shared Care Protocol

## For
## Sulfasalazine use in Adults

**Note – This protocol is based on the National Sulfasalazine Shared Care Protocol developed 4 July 2022**

**It is intended for use exclusively within Sheffield & Rotherham places.**

**Authors: Sharron Kebell, Specialised Commissioning Pharmacist, SY ICB & Dr Rachel Tattersall, Consultant Rheumatologist, STH.**

**Version 1**

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## Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Transfer to primary care is normally after the patient has been treated for at least 3 months and the dose has been optimised and with satisfactory investigation results for at least 4 weeks. Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose and formulation, baseline and most recent test results, confirm the monitoring schedule and when the next monitoring is required. Include contact information (section 13).
- Conduct the required annual reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Give advice to primary care on continuing treatment if a woman becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.

## Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being received by the GP practice, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into account any potential drug interactions in section 7.
- Adjust the dose of sulfasalazine prescribed as advised by the specialist.

- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist, as described in section 10
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Stop sulfasalazine and make an urgent referral to the specialist if signs of myelosuppression, hepatic or renal dysfunction develop or a serious skin reaction or oral ulceration is observed.
- Seek advice from the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

### Patient and/or carer responsibilities

- Take sulfasalazine as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of sulfasalazine with their pharmacist before purchasing any OTC medicines.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

## 1. Background

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Sulfasalazine is a disease modifying antirheumatic drug (DMARD) used to treat a number of rheumatological conditions, and to induce and maintain remission in certain inflammatory gastrointestinal diseases.

This shared care protocol does not cover the treatment of people less than 18 years old.

## 2. Indications

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The licensed indications for sulfasalazine are:

- Rheumatoid arthritis (EC tablets only)
- Ulcerative colitis
- Active Crohn’s disease

*N.B.It is anticipated that no new patients suffering from GI indications in isolation will be initiated on sulfasalazine*

Sulfasalazine is also used off-label for other chronic inflammatory disorders including:

- Seronegative spondyloarthropathies such as psoriatic arthritis
- Sarcoidosis

## 3. Locally agreed off-label use

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**To be agreed and completed locally (include supporting information)**

Not applicable as no additional off – label indications.

## 4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC), and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

**Contraindications:**

- Known hypersensitivity to sulfasalazine, its metabolites or any of the excipients as well as sulfonamides or salicylates.
- Porphyria.

**Cautions:**

- Hepatic or renal impairment.
- Pre-existing blood dyscrasias.
- Severe allergy or bronchial asthma.
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency due to risk of haemolytic anaemia.
- Folic acid deficiency.
- Adequate fluid intake should be maintained during treatment to avoid crystalluria and kidney stone formation.
- Slow acetylator status increases the risk of sulfapyridine-related adverse drug reactions (ADRs) which can present as a drug-induced lupus-like syndrome.

## 5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for at least 3 months, and the dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

**Initial stabilisation:**

Rheumatoid arthritis (using enteric coated (EC) tablets or plain tablets)
500mg daily, increasing by 500mg each week until 2-3g per day in divided doses is reached according to response. Only the enteric coated tablets are licensed in rheumatoid arthritis; use of other formulations is off-label.

Treatment of acute attacks of ulcerative colitis and Crohn's disease:
Oral: 1-2g four times daily until remission. The night-time interval between doses should not exceed 8 hours.

For other indications take specialist advice.

**The initial stabilisation period must be prescribed by the initiating specialist.**

**Maintenance dose (following initial stabilisation):**

Rheumatoid arthritis and other indications (using EC tablets or plain tablets,):
2-3g daily in 3-4 divided doses.
Ulcerative colitis and Crohn's disease:
Oral: Usual maintenance dose 500mg four times daily.

**The initial maintenance period must be prescribed by the initiating specialist.**

**Conditions requiring dose adjustment:**

In patients with GFR <10 mL/min, start at very low dose and monitor.

## 6. Pharmaceutical aspects

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| Route of administration: | Oral |
| Formulation: | 500mg tablets<br><br>500mg enteric coated (EC) tablets<br><br>250mg/5mL oral suspension<br><br>Licensed indications vary with formulation. See relevant summary of product characteristics for full details. |
| Administration details: | EC tablets should be swallowed whole and not crushed or broken. |
| Other important information: | Plain tablets are only licensed for use in ulcerative colitis or active Crohn's disease. It should be noted that apart from Sheffield, all of the South Yorkshire rheumatology specialists have supported the off-label use of plain tablets for rheumatological indications. N.B. Sheffield rheumatologists are not prepared to accept risk of prescribing off-label sulfasalazine in absence of strong evidence to support use.<br><br>EC tablets are licensed for use in rheumatoid arthritis as well as ulcerative colitis and active Crohn's disease. Their use in ulcerative colitis and Crohn's disease is usually recommended if the patient experiences gastro-intestinal intolerance with the plain tablets.<br><br>Sulfasalazine may cause a yellow-orange discolouration of body fluids and skin. Certain types of extended wear soft-contact lenses may be permanently stained.<br><br>Sulfasalazine itself can interfere with ALT and AST assays, such that the levels of these liver enzymes can be falsely reduced thus masking hepatotoxicity. Hence need for extended LFTs to include GGT – see section 8 and section 9. |

## 7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF & SPC for comprehensive information and recommended management

- **Digoxin:** Reduced absorption may be seen when used concomitantly with sulfasalazine.
- Sulfonamides are chemically similar to some **oral hypoglycaemic agents** and may cause hypoglycaemia. Patients receiving sulfasalazine and hypoglycaemic drugs should closely monitor blood glucose.
- **Azathioprine and 6-mercaptopurine:** Possible risk of bone marrow suppression and leucopenia
- **Folate** absorption and metabolism may be reduced by sulfasalazine**.**
- **Darolutamide , voxilaprevir and tepotinib** may increase exposure to sulfasalazine, manufacturer advises avoid.
- Sulfasalazine is predicted to affect the efficacy of bulevirtide

## 8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

**Baseline investigations**

- Urea and electrolytes (U&Es) including creatinine and eGFR
- Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), albumin, total protein, bilirubin, alkaline phosphatase and GGT (extended LFTs)
- Full blood count (FBC)
- Weight
- Height and blood pressure
- Assess for co-morbidities which may influence DMARD choice
- Screening for HIV and hepatitis B and C
- Screening for lung disease, including tuberculosis, should be undertaken at clinician discretion on a case by case basis.
- Provide or request appropriate vaccination prior to treatment initiation, according to local arrangements (e.g. pneumococcal, influenza, COVID-19)

**Initial monitoring and at dose change:**

To be repeated every 2 weeks until the dose has been stable for 6 weeks, then monthly for three months. It is anticipated that transfer of prescribing to primary care should be around 12 - 14 weeks after initiation of the medicine.

- BP
- FBC
- U&Es, including creatinine and eGFR
- AST and/or ALT, albumin, total protein, bilirubin, alkaline phosphatase and GGT (extended LFTs)
- Rheumatology patients: C-reactive protein (CRP) &/or erythrocyte sedimentation rate (ESR)

Following a dose change repeat every 2 weeks until the dose has been stable for 6 weeks, then revert to previous schedule.

**Ongoing monitoring:**

The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment, and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually.

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

## 9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

| Monitoring and advice | Frequency |
|---|---|
| • FBC<br>• U&Es including creatinine and eGFR<br>• Alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total protein, bilirubin, alkaline phosphatase and GGT (extended LFTs) | At least every 12 weeks<br><br>N.B. Monitoring is not routinely required once a patient has had stable blood levels for a year. Selected patients who are deemed to be at |

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| • Rheumatology patients: CRP &/or ESR | higher risk may require longer periods of monitoring, but those patients will be clearly identified by the responsible consultant. |
| Vaccines are safe and recommended for this patient group and should be offered in line with the standard schedule. Refer to Green Book Chapter 6 for further details.<br><br>**Annual** influenza (The Green Book, Chapter 19) vaccinations are recommended. | • Shingles vaccination: one course when eligible under the national schedule.<br>• Other vaccinations as per national schedule.<br>• Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list. |

## 10. Adverse effects and other management

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**Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit** www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

| Result | Action for primary care |
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| **As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.** If clinically concerned i.e. if patient is acutely unwell and with abnormal blood results, suspected to be related to sulfasalazine, withhold and **GP** to discuss as per contact details for urgent advice in section 13. For non-urgent queries about abnormal blood results, not answered by advice below: please contact appropriate service, as per details in section 13 | |

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| **Full blood count**<br><br>• WCC less than 3.5 $x10^9$/L<br>• Lymphocytes less than 0.5 $x10^9$/L<br>• Neutrophils less than 1.6 $x10^9$/L<br>• Platelets less than 140 $x10^9$/L<br>• Unexplained eosinophilia; greater than 0.5 $x10^9$/L | Withhold treatment and communicate result with specialist. |
| MCV >105 fL | Consider interruption in treatment.<br><br>Check serum folate, B12, alcohol history and TSH and treat any underlying abnormality. If results of these additional investigations are normal communicate result with specialist team urgently. |
| Signs or symptoms of bone marrow suppression, e.g. unexplained bleeding or bruising with or without sore throat, purpura, mouth ulcers. | Check FBC immediately, withhold treatment while awaiting results, and communicate result with the specialist team. See haematological monitoring above. |
| Acute infection | During serious infections (e.g. requiring intravenous antibiotics or hospitalisation) temporarily withhold sulfasalazine until the patient has recovered. Consider additional investigations (e.g. FBC), if clinically appropriate. |
| **Liver function tests:**<br><br>ALT and/or AST greater than 100units/L<br><br>And/or a sudden increase (e.g. doubling of baseline) | • Withhold and communicate result with specialist team.<br>• Check any other reason for risk of hepatic dysfunction such as alcohol history and |

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| Unexplained fall in albumin; less than 30g/L<br><br>Jaundice | drug interactions, including OTC or complementary medication. |
| **Renal function**<br><br>Creatinine increase of greater than 30% from baseline in the last 12 months | Use clinical judgement and repeat in 1 week<br><br>If still more than 30% from baseline, withhold and communicate result with specialist. |
| **Gastrointestinal disorders**<br><br>Nausea, vomiting, diarrhoea or unintentional weight loss | Review for reversible causes. Advise patient to take with food. If no improvement contact specialist team. |
| **Other symptoms**<br><br>• Skin/mucosal reaction, e.g. serious rash<br>• Diffuse alopecia<br>• Breathlessness or cough<br>• Peripheral neuropathy | Consider withholding treatment and discussing with specialist.<br><br>For widespread rash, discontinue and discuss with specialist urgently. |

## 11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

**The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:**

- Sore throat, mouth ulcers, fever, malaise, swollen lymph nodes, or unexplained bleeding or bruising
- Progressive skin rash with blisters or oral ulcerations – see below
- Nausea, vomiting, diarrhoea, jaundice, dark urine and unintentional weight loss.
- Hair loss

- Breathlessness, infection or cough
- Symptoms of peripheral neuropathy e.g. pins and needles, numbness or burning pain in extremities

**The patient should be advised:**

- Life-threatening skin reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of sulfasalazine. The highest risk for occurrence is within the first weeks of treatment. Patients should be advised to report a progressive skin rash often with blisters or mucosal lesions, or any other sign of hypersensitivity.
- During a serious infection, sulfasalazine should be temporarily discontinued until the patient has recovered from the infection.
- Tell anyone who prescribes them a medicine that they are taking sulfasalazine. Always ask a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.
- That vaccination in line with current national advice (e.g. for COVID-19, influenza) is safe and recommended.
- Sulfasalazine may cause a harmless yellow-orange discolouration of body fluids and skin. Certain types of extended wear soft-contact lenses may be permanently stained.
- To maintain adequate fluid intake during treatment to reduce the risk of crystalluria and kidney stones.

Patient information:

General information: https://www.nhs.uk/medicines/sulfasalazine/

General information: https://patient.info/medicine/sulfasalazine-salazopyrin-sulazine

Rheumatology: https://www.versusarthritis.org/about-arthritis/treatments/drugs/sulfasalazine/

## 12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

**All patients should be informed of the risks and benefits of taking this medicine during pregnancy and breastfeeding. The specialist team should be contacted if a patient becomes pregnant or is planning to become pregnant or breastfeed.**

The BSR guideline on prescribing DMARDs in pregnancy and breast feeding advises the following:

**Pregnancy:**

Sulfasalazine is compatible throughout pregnancy, folic acid supplementation (5 mg/day) is recommended during periconception period (3 months prior to conception per UKTIS) and first trimester (section 7).

Information for healthcare professionals: https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-SULFASALAZINE-IN-PREGNANCY/

Information for patients and carers: https://www.medicinesinpregnancy.org/Medicine--pregnancy/Sulfasalazine/

**Breast feeding:**

Sulfasalazine is compatible with breast feeding in healthy, full-term infants.

There have been reports of bloody stools or diarrhoea in infants who were breastfeeding from mothers on sulfasalazine. In cases where the outcome was reported, bloody stools or diarrhoea resolved in the infant after discontinuation of sulfasalazine in the mother.

**Paternal exposure**:

Men taking sulfasalazine may have reduced fertility, due to oligospermia and impaired mobility, which may take 2-3 months to return to normal following treatment cessation.

## 13. Specialist contact information

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**Sheffield Teaching Hospitals**

**Rheumatology**

Name: Julie Cole

Role and specialty: Rheumatology: Clinical Nurse Specialist,

Rheumatology Daytime telephone number: 0114 2713086

Email addresses:

For routine primary care queries e.g. abnormal blood monitoring results not covered by the SCP please email : sth.rheumatologygpcorrespondence@nhs.net – usual response time is within two working days.

If patient acutely unwell and this is thought related to sulfasalazine, **GP** only, to contact Rheumatology on call, hours 9 am to 5 pm only - via STH switchboard

For patient queries: sth.ropd@nhs.net

**Gastroenterology**

Non – urgent queries relating to sulfasalazine in existing patients with only GI indications should be referred to original gastroenterology consultant or secretary otherwise e mail: sth.ibdnurseadmin@nhs.net

If patient acutely unwell and this is thought related to sulfasalazine, **GP** only, to contact Gastroenterology on call, hours 9 am to 5 pm only - via STH switchboard.

**The Rotherham NHS Foundation Trust**

**Rheumatology**

Nurses telephone helpline: 01709424739

Consultant: Dr. Leticia Garcia (working days Mon-Wed) 01709 425171

Nurse Specialists: Sisters Sue Elsey, Louise Hale, Kerry Hopewell and Mandy Hademan

- Bleep 079 via switchboard (01709 820000)

Specialist Registrar: Bleep 101 via switchboard (01709 820000)

For individual patient enquiries- clinicians are advised to use the Advice & guidance from eReferrals.

For general enquiries (not patient specific)- rgh-tr.rheumatologysecretaries@nhs.net

## 14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

## 15. References

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- Salazopyrin En tabs. Date of revision of the text 29.05.24. Accessed via https://www.medicines.org.uk/emc/product/6686/smpc on 27.11.24
- Salazopyrin tablets. Date of revision of the text 05.06.24. Accessed via https://www.medicines.org.uk/emc/product/3838/smpc on 27.11.24
- Sulfasalazine 250mg/5mL oral suspension. Date of revision of the text 20.02.24. Accessed via https://www.medicines.org.uk/emc/product/413/smpc on 27.11.24
- British Society of Rheumatology and British Health Professionals in Rheumatology. 2017. Guidelines for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Accessed via https://academic.oup.com/rheumatology/article/56/6/865/3053478.
- British Society of Rheumatology. 2023. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Accessed via https://doi.org/10.1093/rheumatology/keac551 on 26.11.24.
- eBNF – accessed via https://bnf.nice.org.uk/on 27.11.24
- UK Teratology Information Service. Use of sulfasalazine in pregnancy. Version 4 November 2024. Accessed via https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-SULFASALAZINE-IN-PREGNANCY/ on 27.11.24
- Best Use of Medicines in Pregnancy. Last updated November 2024, accessed via https://www.medicinesinpregnancy.org/Medicine--pregnancy/Sulfasalazine/ on 27.11.24
- NICE Clinical Knowledge Summaries - DMARD management. Last revised December 23. Accessed via https://cks.nice.org.uk/topics/dmards/management/ on 3.12.24
- Menter, MD et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. JAAD: 2009: 61: 3: 451-485. DOI: https://doi.org/10.1016/j.jaad.2009.03.027
- Briggs G. Drugs in Pregnancy and Lactation, Ninth Edition. Sulfasalazine Monograph.

## 16. Other relevant national guidance

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- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

## 17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

**Each speciality may have different criteria for referral. Seek advice where necessary.**
Each directorate has their own arrangements / paperwork for transferring care to primary care, the National Shared Care Transfer Forms are available here if needed.