

**798FM.2.1 SULFASALAZINE FOR USE IN RHEUMATOLOGY AND GASTROENTEROLOGY  
Shared Care Protocol**

This protocol provides prescribing and monitoring guidance for sulfasalazine therapy. It should be read in conjunction with the [shared care responsibilities](#) document, the Summary of Product Characteristics (SPC) available on [www.medicines.org.uk/emc](http://www.medicines.org.uk/emc) and the [BNF](#).

**BACKGROUND FOR USE**

- Sulfasalazine is a disease modifying antirheumatic drug (DMARD).
- Indications, dose adjustments and monitoring requirements for sulfasalazine (licensed and unlicensed indications) defined in this protocol are in line with national guidance published by the British Society for Rheumatology<sup>1</sup> and the British Society of Gastroenterology<sup>2</sup>.
- Sulfasalazine uses in this protocol are limited to:
  - **Rheumatology**
    - Rheumatoid arthritis (licensed).
    - Seronegative spondylarthropathies, including psoriatic arthritis (unlicensed).
    - It can be used in combination with other DMARDs, such as methotrexate or hydroxychloroquine in patients with more severe disease.
  - **Gastroenterology**
    - Induction and maintenance of remission of ulcerative colitis, treatment of active Crohn's disease (licensed).

In many patients its use has been superseded by mesalazine preparations which have similar efficacy, are often better tolerated and lack the "sulpha" related side effects. It remains useful in some patients with inflammatory bowel disease with related seronegative arthropathy.

**SUPPORTING INFORMATION**

- Sulfasalazine is an established drug with a known side effect profile.

**CONTRAINDICATIONS**

- Glucose-6-phosphate dehydrogenase deficiency (G6PD) deficiency or porphyria - do not use - may cause haemolysis.
- Sulphonamide or salicylate hypersensitivity - do not use.

**PRECAUTIONS**

- Pregnancy and breastfeeding: If there is a high risk of disease flare, sulfasalazine can be continued in a dose not exceeding 2 gram per day. Folic acid 5 mg daily should be prescribed in those trying to conceive and during pregnancy. Sulfasalazine is compatible with breastfeeding in healthy, full-term infants.
- Men taking sulfasalazine may have reduced fertility. This may persist for up to 3 months after stopping therapy. The patient needs to seek advice if struggling to conceive while on sulfasalazine.
- Chronic kidney disease stage IV or V: Use with caution. Stop if glomerular filtration rate (GFR) <10 ml/min.
- Chickenpox/shingles: Stop sulfasalazine if proven infection. For those with exposure to chickenpox or shingles and no history of infection/vaccination, check that immunity to Varicella zoster virus (VZV) infection has been checked. If the patient is susceptible, a course of oral aciclovir or valaciclovir is recommended unless there are significant concerns of renal toxicity or malabsorption. Discuss with a microbiologist.

## DOSAGE <sup>2,3</sup>

Indication	Dose	Ref
<b>Rheumatology indications</b>	Increase slowly. Week 1: 500 mg each morning Week 2: 500 mg bd Week 3: 1 g each morning and 500 mg each evening Week 4: 1 g bd (usual maintenance dose) Occasionally, doses of 3 g per day can be used.	1
<b>Inflammatory bowel disease</b>	<b>Acute attacks:</b> 1 - 2 g qds - dose adjusted to response. Ideally night time interval between doses should not exceed 8 hours. May be given in conjunction with steroids as part of an intensive monitoring regimen for acute attacks. <b>Maintenance dose:</b> Doses may be reduced gradually to 500 mg to 1 g qds, although many patients remain in remission using twice daily dosage.	2

### Prescribing points

- Tablets should be taken with or after food and swallowed whole with a full glass of water.
- Maintain adequate fluid intake to avoid crystalluria.
- The enteric coated sulfasalazine preparation should be used.

### TIME TO RESPONSE

- Rheumatoid arthritis: Minimum of 3 months.
- Inflammatory bowel disease: A few days.

### PRE-TREATMENT ASSESSMENT BY THE SPECIALIST

- Height, weight and blood pressure where relevant to the speciality.
- Full blood count (FBC), liver function tests (LFT), urea and electrolytes (U&E) and estimated GRF (eGRF).
- C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) for rheumatology patients.
- Chest X-ray if there is a history of smoking or lung disease.
- Lung function tests and high-resolution computed tomography (HRCT) should be considered in individual patients where there is clinical suspicion of lung disease. Baseline lung function tests may be indicated in patients with pre-existing lung disease i.e. chronic obstructive pulmonary disease (COPD). Any patient currently smoking should be offered an access to smoking cessation services.
- Offer testing for hepatitis B, C and human immunodeficiency virus (HIV) serology in particular if patient is at risk of occult viral infection.
- Check VZV serology (if no history of varicella). The specialist should give advice about treatment required if there is exposure to or new diagnosis of chickenpox or shingles.

### COMMENCING SULFASALAZINE

- The decision to initiate sulfasalazine should be made in conjunction with the patient/carer and supervised by a specialist. Patients should be provided with written information and education about their treatment. When appropriate they should be advised about the impact of sulfasalazine upon fertility, pregnancy and breastfeeding.

### VACCINATION

- Pneumococcal vaccination should be administered as a single dose polysaccharide PPV-23 (Pneumovax<sup>®</sup>), if possible, prior to initiation of sulfasalazine therapy or as soon as possible after.
- Annual influenza vaccine should be recommended to all patients.
- Live vaccinations are not generally contraindicated on sulfasalazine monotherapy, although specialist discretion is advised.

## ONGOING MONITORING SCHEDULE

<b>Rheumatology Gastroenterology</b>	<b>FBC, alanine aminotransferase (ALT), albumins (ALB), creatinine/ calculated eGFR</b> every 2 weeks until dose remains unchanged for 6 weeks; thereafter every month for 3 months; thereafter every 3 months. Routine monitoring of sulfasalazine <b>monotherapy</b> can be discontinued after 12 months on the advice of the specialist. More frequent monitoring is appropriate for patients at higher risk of toxicity i.e. on combination therapies. The specialist will advise the GP if this is necessary. After dose increase, blood tests should be monitored 2 weekly for 6 weeks followed by return to the previous schedule. This will be initiated by the specialist.
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**In addition to absolute values for haematological indices, a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance. In order to monitor trends, it is recommended that all blood test results are entered in the patient held monitoring booklet.**

### ROLES AND RESPONSIBILITIES

Shared care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Unless otherwise stated in the protocol, the responsibilities are as follows:

#### **Specialist**

- Initiate treatment and prescribe until the dose is stable and/or the GP formally agrees to shared care.
- Ensure the patient understands the nature and complications of drug therapy and their role in reporting adverse effects promptly.
- Provide copy of patient information leaflet and drug monitoring card where appropriate.
- Send a letter to the GP requesting shared care. Outline shared care protocol criteria and how often monitoring should be done.
- Liaise with GP regarding changes in disease management, drug dose and missed clinic appointments.
- Be available to give advice to GP and patient throughout treatment.

#### **GP**

- Prescribe medication once the dose is stable and shared care is agreed.
- Ensure all monitoring is completed in accordance to the specific shared care protocol.
- Check and record results then advise the specialist of any deteriorations or abnormal results.
- Notify the specialist to any changes in patient's condition, any adverse drug reactions or failure to attend tests.

#### **Patient**

- Agree to treatment and monitoring after making an informed decision.
  - Agree to being under the shared care of the GP and specialist.
  - Attend for blood tests and monitoring when required.
  - Ensure monitoring card is kept up to date and is brought to all appointments.
  - Report any side effects to the GP or a member of the specialist team.
- Note: if the patient does not attend blood monitoring, then treatment will be stopped. If the patient is more than 4 weeks late with their monitoring, then treatment should be stopped.

Side Effects	Action
<b>Acute widespread skin rash</b>	<b>Withhold and seek urgent specialist advice. If it presents with unexplained fever, FBC required.</b>
White blood cell (WBC) <math><3.5 \times 10^9/l</math> Neutrophils <math><1.6 \times 10^9/l</math> Platelets <math><140 \times 10^9/l</math>	Withhold and discuss with specialist.
Liver function tests  Up to 2 fold rise 2 - 3 fold rise in ALT >3 fold rise in ALT or unexplained reduction in ALB <math><30 \text{ g/l}</math>	Repeat in 2 weeks. If still raised, discuss with specialist. Reduce the dose by 500 mg - 1000 mg and repeat in 1 - 2 weeks. Withhold until discussed with specialist.
Mean cell volume (MCV) <math>>105 - 110 \text{ fl}</math>	Check folate, B <sub>12</sub> and thyroid function tests (TFT), and treat if appropriate. If WBC normal repeat in 4 weeks. Folic acid should be given at a dose of 5 mg PO once daily and vitamin B <sub>12</sub> is given as hydroxocobalamin injection 1 mg intramuscular (IM) three times a week for 2 weeks , then 1 mg IM every three months.
MCV <math>>110 \text{ fl}</math>	Stop sulfasalazine and seek advice.
Creatinine rise >30% over 12 months or eGFR <math><60</math>	Dose adjustment may be needed. Patients who develop dehydration, pre-renal or acute renal failure while on sulfasalazine should have sulfasalazine withheld and FBC monitored closely. Review any changes in medication particularly angiotensin converting enzyme inhibitors (ACEI) and angiotensin-receptor blockers (ARB). Contact specialist for advice.
Oral ulceration	Withhold, investigate alternative cause. If settles promptly, re-challenge with a lower dose. If symptoms recur stop and contact specialist. If this presents with unexplained fever, FBC required.
Abnormal bruising or severe sore throat	Withhold and check FBC.
Nausea, vomiting, dizziness headache	Often transient. If possible, continue with use of anti-emetic or reduce dose by 500 mg.
Diarrhoea	Rarely occurs other than on initiating treatment. Reduce the dose by 500 mg daily and discuss with the specialist.
Patients wearing soft contact lenses	Can cause staining.
Yellow/brown discolouration of urine	Reassure patient.

- Sulfasalazine can be withheld for a few days without inducing a flare.
- Non-steroidal anti-inflammatory drugs (NSAIDs) may be continued.

#### DRUG INTERACTIONS - see [SPC](#)

Digoxin	Sulfasalazine may reduce digoxin absorption resulting in non-therapeutic serum levels and monitoring of digoxin levels may be required.
Oral hypoglycaemics	Sulfasalazine may cause hypoglycaemia. Patients should be advised to keep an eye on their blood glucose and report to GP if they are having hypos.
Folic acid	Sulfasalazine may impair folate absorption. Check serum folate if symptoms of folate deficiency.
Azathioprine	Sulfasalazine may produce additive toxic effects on bone marrow causing myelosuppression.
Mercaptopurine	Sulfasalazine may increase the risk of hepatotoxicity and myelosuppression.

## SHARED CARE AGREEMENT FORM

Available on DocGen. When not available, use the Word version linked [here](#)

### REFERENCES

1. Flint et al, BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding - Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. *Rheumatology (Oxford)* 2016; 55 (9): 1693-1697. doi.
2. Carter M J, Lobo A J & Travis S P L on behalf of the IBD Section of the British Society of Gastroenterology. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2004; 53 (Suppl V); v1-v16.
3. Ledingham J et al. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. *Rheumatology (Oxford)* 2017 kew479. doi: 10.1093/rheumatology/kew479.
4. Sulfasalazine SPC <https://www.medicines.org.uk/emc/product/6686/smpc>.
5. BNF online <https://bnf.nice.org.uk/drug/sulfasalazine.html>.

### BACK-UP INFORMATION AND ADVICE

Contact Details	Wycombe and Amersham	Stoke Mandeville
Rheumatology	01296 315960 (specialist nurse helpline - may take 48 hours for response; not for urgent queries) In an emergency contact consultant rheumatologist 01494 734079 Secretaries Office: 01494-734079  E-mail: <a href="mailto:bht.rheumatology@nhs.net">bht.rheumatology@nhs.net</a>	01296 315960 (specialist nurse helpline - may take 48 hours for response; not for urgent queries) In an emergency contact consultant rheumatologist of the week 01296 316664 Rheumatology registrar: Bleep 905/907 via switchboard. E-mail: <a href="mailto:bht.rheumatology@nhs.net">bht.rheumatology@nhs.net</a>
Gastroenterology	Registrar bleep 6582, 6583 via switchboard Consultant secretary: Dr Cullen: 01494 425959 Dr Gorard: 01494 425267	Registrar bleep 992 via switchboard Consultant secretary: Dr Blackwell: 01296 316718 Dr Sekhar: 01296 315299 Dr Weldon: 01296 315222
Medicines Resource Centre	01494 425355	

Title of Guideline	Sulfasalazine for Use in Rheumatology and Gastroenterology - Shared Care Protocol
Guideline Number	798FM
Version	2.1
Effective Date	December 2019
Review Date	December 2022
Original Version Produced	April 2011
Amended	September 2020
<i>Approvals:</i>	
Medicines Value Group	26 <sup>th</sup> September 2019
Clinical Guidelines Subgroup	5 <sup>th</sup> November 2019
Author/s	Jackie Hall Rheumatology Lead SPN, Dr M Magliano, Consultant Rheumatologist
SDU(s)/Department(s) responsible for updating the guideline	Rheumatology and Gastroenterology
Uploaded to Intranet	5 <sup>th</sup> December 2019 and 16 <sup>th</sup> September 2020
Buckinghamshire Healthcare NHS Trust/Buckinghamshire Clinical Commissioning Group	