SULFASALAZINE
RHEUMATOLOGY LOCAL SAFETY MONITORING SCHEDULE

This local safety-monitoring schedule supports clinicians under the Local Enhanced Service for High Risk Drug Monitoring (formerly Near Patient Testing). Aligning clinical and prescribing responsibility enhances patient safety because the individual signing the prescription will also be responsible for ensuring that any necessary monitoring has been undertaken and will have access to the results of this.

The prescriber and specialist assume joint clinical responsibility for the drug and the consequences of its use.

Specialist details	**GP details**	**Patient details**
Name:	Name:	Name:
Address:	Address:	Contact number:
Email:	Email:	NHS
Contact number:	Contact number:	DOB
Signature		Signature

INTRODUCTION

Sulfasalazine is an aminosalicylate anti-inflammatory, and is structurally related to both salicylates (e.g. aspirin) and sulphonamides. Sulfasalazine is metabolised to mesalazine and sulfapyridine, the latter of which acts as a carrier to the site of action but is also responsible for the majority of adverse effects of sulfasalazine. The drug is unlikely to be effective after a total colectomy.

Licensed indication: rheumatoid arthritis;

Unlicensed indications: sero-negative spondylo-arthropathy including psoriatic arthritis.

ADULT DOSAGE AND ADMINISTRATION

A typical dose regimen in **Rheumatology** may be 500mg/day increasing by 500mg weekly to 2g-3g/day given in 2 -3 divided doses with or after food. Do not crunch or chew the tablets.

	WEEK 1	**WEEK 2**	**WEEK 3**	**WEEK 4**
MORNING	1 X 500MG	1 X 500MG	2 X 500MG	2 X 500MG
LUNCHTIME				
EVENING		1 X 500MG	1 X 500MG	2 X 500MG

Available as:

Sulfasalazine 500mg tablets, 500mg enteric-coated tablets, suspension 250mg/5ml, and 500mg suppositories. **Only the 500mg enteric-coated tablets are licensed for use in rheumatoid arthritis**, and this form should be prescribed unless agreed otherwise with the specialist. The suspension can be useful in patients who have difficulty swallowing the tablets.

It may take up to 3 months for significant response to be achieved.

MONITORING

Arrange and record on-going monitoring as agreed with the specialist

- Check FBC, U&E's, LFT's every 2 weeks until on stable dose for 6 weeks, Once on stable dose repeat monthly for 3 months and thereafter at least every 12 weeks for 12 months after which if stable no routine monitoring is required
- More frequent monitoring is appropriate in patients at higher risk of toxicity.
- Dose increases should be monitored by FBC, U&E's, and LFT's every 2 weeks until on a stable dose for 6 weeks then revert back to previous schedule.
- CRP & ESR may be done every 3 months

SPECIALIST RESPONSIBILITIES

- Provide GP with clear written advice on required dosage and frequency of Sulfasalazine, written monitoring guidelines and drug information.
- Check for interactions with other medicines.
- Provide the patient/carer with relevant (written) information on use side effects and need for monitoring of infection.
- Provide shared care monitoring record booklet if required.

In patients with a clinical suspicion of parenchymal lung disease, formal lung function testing and appropriate imaging (chest radiograph with or without high resolution CT imaging) should be performed and referral to a respiratory specialist be considered. Background lung disease should not be considered an absolute contraindication to sulfasalazine use, although in patients with poor respiratory reserve (in whom an acute pneumonitis would be more hazardous), caution is advised.

- For any patient currently smoking access to smoking cessation services should be offered.
- Arrange pre-treatment baseline investigations
    - Height, weight and blood pressure.
    - FBC
    - U&E's
    - LFT's
    - ESR &CRP
    - Varicella Zoster IgG in suspected non-immune patients and notify general practitioner as appropriate.
    - Hepatitis B & C and HIV serology
- Review results of safety monitoring and request additional tests as required
- Review in clinic as appropriate to assess response to treatment and the need to continue therapy sending a written summary to the GP whenever the patient is reviewed.
- Identify and report adverse events to the GP and the MHRA (via yellow card).
- Provide any other advice or information for the GP if required

PRIMARY CARE RESPONSIBILITIES

- Prescribe enteric coated sulfasalazine (see above) at the dose recommended provided patient is having appropriate regular blood monitoring and monitoring results are within acceptable range.
- Ensure no drug interactions with other medicines.
- Repeat prescriptions should be removed from the surgery repeats pile and retained separately for prescribers to review prior to signing. Maximum 28 days supply.
- Monitoring of the drug as outlined on page 2 as per the BSR (British Society of Rheumatologists) guidelines and in conjunction with the Specialist Rheumatologist.
- These guidelines set out to provide a standard monitoring template. It is essential that each patient is considered on an individual basis and monitoring frequency is appropriately reviewed, for example in elderly patients, those with a history of drug-related toxicity, co-morbidity and polypharmacy more frequent monitoring may be appropriate.
- Patients on combination DMARD therapy may need more frequent monitoring. Please check the local Safety Monitoring Schedule for each drug.
- Report any adverse drug reactions to the initiating specialist and the usual bodies (e.g. MHRA) yellow form.
  - Administer Influenza vaccine annually unless otherwise advised by the initiating specialist
  - Check the patient has had one dose of Pneumococcal vaccine administered as a single dose of the polysaccharide PPV-23 (Pneumovax) ideally this should be administered prior to the initiation of DMARD's however, if this is not possible it should be administered irrespective.
  - **Varicella Zoster**
    - Non immune patients should avoid contact with people with chicken pox or shingles; consider passive immunisation using varicella immunoglobulin (VSIG) if exposure is suspected (contact Public Health England /Blood Transfusion Service for advice) consider active immunisation of non-immune subjects before starting immunosuppression (after discussion with specialist)
    - Varicella infection can be severe in immunosuppressed patients and early systemic anti- viral and supportive therapy may be required. Suspend methotrexate if possible until recovered
  - **Shingles**
    - Consider active immunisation before starting immunosuppression inpatients over the age of 69 years.
- Ask about oral ulceration / sore throat, unexplained rash or unusual bruising at every consultation.
- If a patient develops symptoms/signs of systemic infection, this should be treated promptly and methotrexate withheld until the infection has cleared.
- Ensure a clinician updates the patients record following specialist review

Withhold Sulphasalazine and contact specialist if:

- White cell Count <3.5 x10^9/l
- Neutrophils <1.6 x 10^9/l
- Unexplained eosinophilia >0.5 x 10^9/l
- Platelet count < 140 x 10^9/l
- Mean cell volume >105 f/l
- Creatinine Increase by > 30% over 12 months and /or calculated GFR<60ml/min/1.73m^2
- ALT and / or AST >100 U/l
- Unexplained reduction in albumin <30 g/l

Please note: A rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance. Some patients may have abnormal baseline values, specialist will advise. Results should be recorded in the patient's shared care-monitoring booklet if issued.

ADVERSE EFFECTS, PRECAUTIONS AND CONTRA-INDICATIONS

- **Rash/stomatitis:** withhold and discuss with specialist if severe or persistent. Minor rashes affecting a small skin area can be tolerated, but more severe reactions (which can include Stevens-Johnson syndrome) require immediate and permanent withdrawal of sulfasalazine
- **Nausea/loss of appetite**: continue if possible. Slow increase in dose (new patients) and/or anti-emetic medication may resolve symptoms. If persistent, reduce maintenance dose. If symptoms are severe and persistent, discontinue sulfasalazine.
- **Vertigo/ tinnitus**: symptoms may resolve on reduction of the dose.
- **Yellow discolouration**: may colour urine, soft contact lenses or skin, orange/yellow.
- **Pregnancy / Contraception**: Sulfasalazine with folate supplementation (5mg daily) is compatible throughout pregnancy
- **Men taking sulfasalazine may have reduced fertility**

- **Breastfeeding:** sulfasalazine is compatible in healthy full term infants
- **Renal impairment** (moderate) may cause significant crystalluria and patients must have high fluid intake. Avoid in severe renal impairment (eGFR under 30 ml/min).
- **G6PD**: patients with glucose-6-phosphate dehydrogenase deficiency should be closely observed for signs of haemolytic anaemia.
- **Serious blood dyscrasias** have been reported, and so haematological investigations should be performed in the event of unexplained bleeding, bruising, purpura, anaemia, fever or sore throat.

CONTRAINDICATIONS INCLUDE

- Hypersensitivity to sulfasalazine, sulphonamides, or salicylates
- Acute intermittent porphyria
- Severe renal impairment (see above)

COMMON DRUG INTERACTIONS

- Concomitant use of nephrotoxic agents such as **NSAIDs** and **azathioprine** may increase the risk of renal reactions.
- **Azathioprine** given with sulfasalazine may contribute to bone marrow toxicity.
- Absorption of **digoxin** and folate may be reduced. Review dosage requirement after sulfasalazine introduction.

COMMUNICATION

For any queries relating to this patient's treatment with Sulfasalazine please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions Please refer to full prescribing data in the SPC or the BNF

REFERENCES

1. GMC: Prescribing guidance: Shared care www.gmc-uk.org/guidance/ethical_guidance/14321.asp(accessed 20/10/2014)
2. NMC: Standards of proficiency for nurse and midwife prescribers http://www.nmc-uk.org/Documents/NMC-Publications/NMC-Standards-proficiency-nurse-and-midwife-prescribers.pdf (accessed 3/11/2014)
3. SPC Salazopyrin-EN : http://www.medicines.org.uk/emc/medicine/10722
4. Chakravarty, K., McDonald, H., Pullar, T. et al. (2008) BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. *Rheumatology* **47**(6), 924-925.
5. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. *Ledingham J, Gullick N, Irving K, Gorodkin R, Aris M, Burke J, Gordon P, Christidis D, Galloway S, Hayes E, et al. Rheumatology (Oxford). 2017 Jun 1; 56(6):865-868.*
6. BSR AND BHPR guideline on prescribing drugs in pregnancy and breastfeeding – Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. . *Flint J, Panchal S, et al. Rheumatology (Oxford). 2016; 55: 1693 – 1697*
7. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding – part II: analgesics and other drugs used in rheumatology practice. *Flint J, Panchal S, et al. Rheumatology (Oxford). 2016:55:1968-1702*