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:	
Contact number:	Contact number:	

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	1x500 mg	1x500mg	2x500mg	2x500mg
Evening		1x500mg	1x500mg	2x500mg

Available as:

Sulfasalazine 500mg tablets, 500mg enteric coated tablets, suspension 250mg/5ml, 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.

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 patient/carer with relevant (preferably written) information on use, side effects and need for monitoring of medication.
- Arrange pre-treatment baseline investigations.
- Baseline tests:
  - **FBC**
  - **LFT**
  - **U&E and creatinine + urinalysis**
  - **ESR or CRP**

- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, 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.
- Arrange and record ongoing monitoring of :-
    - **FBC** and **LFT** every 2 weeks for the first 3 months, then monthly for the second three months then every 3 months or as clinically indicated.
    - **U+E + urinalysis** – check monthly for first three months and as clinically indicated thereafter
    - **ESR or CRP** may be required
- Repeat FBC, LFT one month after dose increases.
- Repeat prescriptions should be removed from the surgery repeats pile and retained separately for prescribers to review prior to signing. Maximum 28 days supply.
- If co-prescribed with another immunosuppressant or potentially hepatotoxic agent check **FBC** and **LFT** monthly as appropriate
- Report any adverse drug reactions to the initiating specialist and the usual bodies (e.g. MHRA)
- Ensure no drug interactions with other medicines.
- Ask about oral ulceration/sore throat, unexplained rash or unusual bruising.
- Ensure a clinician updates the patient's record following specialist review

Withhold sulfasalazine and contact specialist if:

• WBC	< 3.5 x 10^9/L
• Neutrophils	< 2 x 10^9/L
• Platelets	< 150 x 10^9/L
• MCV	>105 fl Check B_{12}, folate and TSH. If abnormal, treat any underlying abnormality. If normal, discuss with the specialist team.
• AST / ALT	> 2 times the upper limit of normal
• Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results available. Discuss with the specialist team, if necessary.
• Unexplained acute widespread rash	Withhold seek urgent specialist (preferably dermatological) advice.
• Nausea/dizziness/headache	If possible continue, may have to reduce dose or stop if symptoms severe. Discuss with specialist team.
• Oral ulceration	Withhold until discussed with specialist team.

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

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 should be used with caution in pregnancy and breast feeding. Discuss with initiating specialist. In males sulfasalazine can cause a reversible reduction in sperm count. Folic acid should be prescribed to those trying to conceive and during pregnancy.

Adverse effects, Precautions and Contra-indications continued

Breastfeeding: discuss with specialist.
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

GMC: Prescribing guidance: Shared care www.gmc-uk.org/guidance/ethical_guidance/14321.asp(accessed 20/10/2014)

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)

SPC Salazopyrin-EN : http://www.medicines.org.uk/emc/medicine/10722

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.

NICE: Clinical Knowledge summaries for DMARDs http://cks.nice.org.uk/dmards#!scenario:11 (accessed 31/07/2015)

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