

## Sulfasalazine enteric coated for rheumatoid arthritis and other rheumatological diseases (Adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between consultants and general practitioners (GPs).

This guideline reinforces the basic premise that:

When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the “sharing of information with the individual GP and their mutual agreement to the transfer of care.”

These are not rigid guidelines. On occasions, consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

### Indications:

Sulfasalazine enteric coated is used in the management of rheumatoid arthritis and psoriatic arthritis.

### Dosage and administration:

Week one: 500mg orally daily – 500mg twice a day may be given if tolerated. Giving twice a day minimizes the risk of adverse events.

Week two: 1g orally twice daily

Further increase to maximum 1.5g orally twice daily if tolerated.

### Additional Information

- Sulfasalazine can cause crystalluria and kidney stone formation, therefore, adequate fluid intake should be ensured during treatment.
- Oligospermia and infertility may occur in men treated with sulfasalazine. Discontinuation of the drug appears to reverse effects within 2 to 3 months.
- Can cause yellow-orange discoloration of urine and other body fluids. Some soft contact lenses may be stained

### Monitoring requirements:

#### Before treatment:

- Full blood count (FBC) including platelets,
- Urea and electrolytes (U&Es) and creatinine
- Liver function tests (LFTs)

#### During treatment

- FBC and LFTs monthly for the first 3 months then 3 monthly thereafter if stable. If following the first year dose and blood results have been stable, frequency of blood tests can be reduced to 6 monthly. After 2 years monitoring can be discontinued if stable.
- Following any dose changes repeat FBC and LFTs one month after dose increase then revert to usual monitoring regime if stable.
- U&Es, creatinine and urinalysis monthly for the 1<sup>st</sup> 3 months then 6 monthly or clinically indicated thereafter.
- Patients should be asked about the presence of a rash or oral ulceration at each visit.
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)
- ESR monthly for disease monitoring purposes

### Responsibility for monitoring, once stable, rests with the GP

**Action to be taken if abnormal results/adverse effects:**

- WBC < 3.5 x 10<sup>9</sup>/l      Check neutrophil count
- Neutrophils < 2.0 x 10<sup>9</sup>/l      Monitor weekly. If it falls below 1.5 x 10<sup>9</sup>/l STOP DRUG and contact helpline.
- Platelets < 150 x 10<sup>9</sup>/l      Monitor weekly. If drop below 100 x 10<sup>9</sup>/l contact helpline
- 3 fold rise in ALT/AST      Monitor weekly. If continue to rise, contact helpline
- Unexplained, acute widespread rash: STOP DRUG and seek specialist dermatological advice
- Oral ulceration      Repeat FBC and act on results as above  
Mild: salt water mouth wash  
Moderate: Hydrocortisone (Corlan) pellets (1 applied to affected area qds)  
Severe: Hydrocortisone (Corlan) pellets and contact helpline
- MCV > 100fl      Check B12, Folate and TSH and if low, start appropriate supplements
- Abnormal bruising      Repeat FBC and act on results as above.
- Sore throat      Repeat FBC and act on results as above.
- Dizziness / headache      If possible, continue, may have to reduce the dose or stop
- GI side effects / nausea      Symptomatic measures may help. May have to reduce the dose, or stop

**Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.**

**Contraindications:**

- Patients with a known hypersensitivity to sulfasalazine, its metabolites or any of the excipients as well as sulfonamides or salicylates.
- Patients with porphyria.

**Cautions:**

- Sulfasalazine should be used during pregnancy only if clearly needed – risk of harm cannot be ruled out. If prescribed, ensure folic acid supplementation given
- Sulfasalazine and sulfapyridine are found in low levels in breast milk. Caution should be used, particularly if breastfeeding premature infants or those deficient in G-6-PD
- Sulfasalazine should not be given to patients with impaired hepatic or renal function or with blood dyscrasias, unless the potential benefit outweighs the risk.
- Sulfasalazine may cause haemolytic anaemia - use with caution in patients with G-6-PD deficiency.
- Sulfasalazine should be given with caution to patients with severe allergy or bronchial asthma
- Sulfasalazine can cause crystalluria and kidney stone formation, adequate fluid intake should be ensured during treatment.

**Drug Interactions: see appendix 1 of current BNF before co-prescribing any drug**

- Azathioprine and mercaptopurine: possible increased risk of leucopenia when given with sulfasalazine
- Sulfasalazine possibly reduces absorption of digoxin
- Sulfasalazine possibly reduces absorption of folic acid
- Sulfonamides bear certain chemical similarities to some oral hypoglycemic agents. Patients receiving sulfasalazine and hypoglycemic agents should be closely monitored

**Adverse Effects:**

Diarrhoea, nausea, vomiting, abdominal pain, exacerbation of symptoms of colitis, headache, hypersensitivity reactions (including rash and urticaria); rarely acute pancreatitis, hepatitis, myocarditis, pericarditis, lung disorders (including eosinophilia and fibrosing alveolitis), peripheral neuropathy, blood disorders (including agranulocytosis, aplastic anaemia, leucopenia, methaemoglobinaemia, neutropenia, and thrombocytopenia), renal dysfunction (interstitial nephritis,

nephrotic syndrome), myalgia, arthralgia, skin reactions (including lupus erythematosus-like syndrome, Stevens-Johnson syndrome), alopecia. also cough, insomnia, dizziness, fever, blood disorders (including Heinz body anaemia, megaloblastic anaemia), proteinuria, tinnitus, stomatitis, taste disturbances, and pruritus; *less commonly* dyspnoea, depression, convulsions, vasculitis, and alopecia; also reported loss of appetite, hypersensitivity reactions (including exfoliative dermatitis, epidermal necrolysis, photosensitivity, anaphylaxis, serum sickness), ataxia, hallucinations, aseptic meningitis, oligospermia, crystalluria, disturbances of smell, and parotitis; yellow-orange discoloration of skin, urine, and other body fluids; some soft contact lenses may be stained.

### **Specialist responsibilities:**

- Confirm the diagnosis of rheumatoid arthritis or psoriatic arthritis
- Discuss with the patient the benefits and side effects of treatment with sulfasalazine
- If the patient is a woman of child bearing potential – ensure that they are aware of the importance of effective contraception and the need to discuss with their consultant if they wish to become pregnant
- Ensure that the patient understands and accepts their responsibilities (see section below)
- Seek consent for treatment and document in the patient's notes.
- Ensure baseline monitoring of full blood count and biochemical profile.
- Discuss how the patient/carer can be aware of possible signs sulfasalazine toxicity or intolerance
- Provide written instruction to the GP for initiation and escalation of sulfasalazine.
- Provide the patient with a monitoring booklet and enter the blood results into the booklet.
- Review the patient at the intervals specified below to monitor the patient's disease activity, the efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
- Discontinue if no response or patient has a significant adverse effect.
- Promptly communicate with the GP via a clinic letter any changes in treatment, results of monitoring undertaken, and assessment of adverse events. The clinic letter should clearly state if the dose has remained the same or if a dose adjustment had been made – specifically highlighting the new dose in comparison with the preceding one.
- Advise GPs when to stop treatment.
- Provide clear arrangements for back-up, advice and support.
- Report serious adverse events at <https://yellowcard.mhra.gov.uk/>

### **GP's responsibilities:**

- Initial referral to Consultant Rheumatologist raising the possibility of rheumatological disease
- Provide the patient with monthly repeat prescriptions of medication following written instructions for initiation and escalation by the specialist. The patient should allow at least 48 hours for the prescription from the GP to be generated.
- Continue monitoring as outlined on the first page and document the results in the shared care booklet.
- Ensure patient's monitoring booklet and practice computer system are updated with any dose changes.
- Refer promptly to the specialist if there is a change in the patient's status or concerns regarding compliance. In most cases, do not stop treatment without discussion with the Rheumatology Helpline.
- If patient fails to attend more than 2 monitoring visits it is not safe to continue treatment – contact the Rheumatology Helpline for advice.
- Report serious adverse events to the specialist and at <https://yellowcard.mhra.gov.uk/>
- Administer Pneumococcal Vaccine/ Pneumovax® II and annual influenza vaccines.

<ul style="list-style-type: none"> <li>Consider passive immunisation with Varicella zoster immunoglobulin in non-immune patients exposed to chicken pox or shingles.</li> </ul>		
<p><b>Patient responsibilities:</b></p> <ul style="list-style-type: none"> <li>Read the written patient information provided about the drug and have a clear understanding of the risks / benefits of oral sulfasalazine treatment.</li> <li>Attend for blood tests.</li> <li>Limit intake of alcohol to the national safe weekly limits.</li> <li>Report any adverse effects to their GP and/or specialist whilst treated with sulfasalazine.</li> <li>Take monitoring booklet every time the patient sees the GP, has a hospital appointment or visits the pharmacist.</li> </ul>		
<p><b>Secondary care review: During initiation:</b> 4 – 6 weekly until controlled  <b>Once disease controlled:</b> Annual review by consultant</p>		
<p>Availability: Salazopyrin EN-Tabs 500mg tablet: 112 = £8.43 or  generic sulfasalazine e/c: 500mg tablet: 112 = £11.26 (if Salazopyrin EN unavailable)</p> <p><i>Prices from online MIMS February 2016</i></p>		
<p><b>Back up advice and support:</b>  Rheumatology Helpline</p>		<p><b>Telephone:</b> 0151 604 7505</p>
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