SHARED CARE GUIDELINE

Drug: Sulfasalazine

Introduction	**Indications**: Licensed: Rheumatoid arthritis; ulcerative colitis, Crohn's disease in adults and children Unlicensed: Sero-negative spondyloarthropathy including psoriatic arthritis and psoriasis. **Background:** Following oral administration around 90% of a dose reaches the colon where bacteria split the drug into sulfapyridine and 5-aminosalicylic acid (mesalazine). Overall the drug and its metabolites exert immunomodulatory effects, antibacterial effects, effects on the arachidonic acid cascade and alteration of activity of certain enzymes. The net result clinically is a reduction in activity of the inflammatory bowel disease. The enteric coated Sulfasalazine is licensed for the treatment of rheumatoid arthritis, where the effect resembles penicillamine or gold. Clinical response cannot be expected before 3 months. **Definitions:** Stable dose – the dose will be titrated to achieve efficacy at the lowest dose. Once efficacy achieved and provided the patient can tolerate the dose, this will be termed "stable dose" Stable bloods – results of blood tests remain below the "alert" thresholds as set by national guidelines and have stayed at similar levels for at least two consecutive tests. N.B. The patient can continue to have active disease despite being on a stable dose or having stable bloods, so the "patient" is not referred to as "stable"
Form	Tablets: 500mg[2] Tablets EN: 500mg[3] Suppositories: 0.5g[4] Liquid: 250mg/5ml[5]
Dose & Administration	A typical dose regimen for rheumatoid arthritis is 500mg daily increasing by 500mg daily at weekly intervals to a maximum 2g-3g/day in divided doses. Occasionally doses above 3g/day are prescribed Treatment of acute attacks of ulcerative colitis is 1-2g four times a day until remission achieved. Maintenance falls back to 500mg four times a day. Night time interval between doses should **not** exceed 8 hours
Secondary Care Responsibilities	• Confirm the diagnosis. • Check for absence of pregnancy in women of child-bearing age and ensure the patient understands the importance of contraception. • Discuss the benefits and side effects of treatment with the patient. Ensure that the patient understands which warning signs and symptoms to report. • Advise patient on appropriate fluid intake • Perform pre-treatment screening: FBC, LFT, U&E's and, creatinine/ eGFR • Ensure that the patient understands not to expect improvement from the treatment straight away. • Provide the patient with a monitoring and dosage record booklet and ensure that the patient knows when and where to attend for monitoring. Encourage the patient to take responsibility for ensuring that results of tests are entered in the monitoring booklet. • Make arrangements for shared care with the patient's GP. • Review the patient regularly to monitor the patient's response to therapy. • Advise the GP on frequency of monitoring, management of any dose adjustments and when to stop treatment. • Ensure that clear backup arrangements exist for GPs to obtain advice.
Primary Care Responsibilities	• Provide the patient with prescriptions for Sulfasalazine; ensure EN tablets for rheumatoid arthritis. • Ensure that the patient understands their treatment and which warning symptoms to report (see adverse effects below). • Monitor at the recommended frequencies (see MONITORING below) and ensure that test results are recorded in the monitoring booklet. • Report any adverse events to the consultant or specialist nurse and stop treatment on their advice or immediately if an urgent need arises (see MONITORING below). • Report any worsening of control of the condition to the consultant or the specialist nurse. • Follow recommended immunisation programme
Immunisations	In patients exposed to chicken pox or shingles, if required, passive immunisation should be considered for varicella. Refer to Green book: Varicella: the green book, chapter 34 - Publications - GOV.UK
Common Drug Interactions	• Sulfasalazine possibly reduces absorption of digoxin. • Oral hypoglycemic agents • Bone marrow suppression and leucopenia have been reported when sulfasalazine given with azathioprine or mercaptopurine. This list is not exhaustive, please refer to SPCs and BNF

Cautions	• Glucose-6-phosphate dehydrogenase deficiency: May cause hemolysis. • Renal impairment (moderate): Risk of toxicity including crystalluria, ensure high fluid intake. • Pregnancy and breastfeeding • Severe infections – temporarily stop treatment
Contraindications	• Hypersensitivity to sulfasalazine, sulfonamides or salicylates. • Porphyria. • Severe renal failure

This guidance does not replace the SPC's, which should be read in conjunction with this guidance.

MONITORING AND ADVERSE EFFECTS

Treatment Status	FBC	LFT	U+E	Creatinine/ eGFR	ESR or CRP
Initial monitoring in first two months	Every 2 weeks	Every 2 weeks	Every 2 weeks	Every 2 weeks	Every 3 months (for RA only)
For next three months	Every month	Every month	Every month	Every month	Every 3 months (for RA only)
After five months *	Every 3 months	Every 3 months	N/A	N/A	

***Please note:** If the patient is also being treated with **leflunomide**, increased monthly monitoring is required, as specified in the leflunomide shared care guidance. (Where other biologic/DMARDs are used in combination with sulfasalazine, the standard monitoring requirements, as outlined above, continue to apply).

As per secondary care responsibilities, for clarity the frequency of monitoring should be specified in the initial shared care request.

- Repeat FBC and LFTs one month after a dose increase.
- MCV > 105fL Check thyroid function, B12 and folate. Treat any underlying abnormality. If results normal discuss with specialist team.

In the event of the following adverse laboratory results or patient reported symptoms, withhold sulfasalazine until discussed with specialist team and repeat the test after two weeks:

- WCC < 3.5 x 10^9/L or less than the lower limit of reference range as per lab
- Neutrophils < 2.0 x 10^9/L or less than the lower limit of reference range as per lab
- Platelets < 150 x 10^9/L or less than the lower limit of reference range as per lab
- AST/ALT > 2 times the upper limit of reference range
- Abnormal bruising or **severe** sore throat
- Rash or oral ulceration

Other adverse effects:

- Nausea/dizziness/headache. If possible continue, may have to reduce dose or stop if symptoms severe. Discuss with specialist team.
- Loss of appetite, raised temperature, leucopenia, hypoglycaemia, insomnia, taste distortion, tinnitus, cough, pruritus, arthralgia, proteinuria are all relatively common
- Impaired folate absorption
- Oligospermia (reversible on discontinuing salazopyrin)

This list is not exhaustive, please refer to SPCs and BNF

References

1. http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/diseasemodifying_antirheumatic_drug_dmard_therapy.pdf
2. http://www.medicines.org.uk/emc/medicine/3344/SPC/Salazopyrin+Tablets/
3. http://www.medicines.org.uk/emc/medicine/10722/SPC/Salazopyrin+En-Tabs/
4. http://www.medicines.org.uk/emc/medicine/3345/SPC/Salazopyrin+Suppositories/
5. http://www.medicines.org.uk/emc/medicine/22489/SPC/Sulfasalazine+250mg+5ml+Oral+Suspension/
6. BNF 66 September 2013-March2014
7. http://cks.nice.org.uk/dmards#!scenariorecommendation:12

RELEVANT CONTACT LIST

Speciality	
Name and Title	Tel. No.