Shared Care Guideline for Sulfasalazine (GP Summary)

It is essential that a transfer of care only takes place with agreement of the GP and when sufficient information has been received. If the GP does not agree to share care they will inform the Consultant responsible for the patient's care.

Basingstoke, Southampton & Winchester District Prescribing Committee

Indications	**Licensed:** Rheumatoid arthritis (enteric coated preparation only), induction and maintenance of remission in ulcerative colitis and treatment of Crohn's disease. **Unlicensed:** sero-negative spondylo-arthropathy including psoriatic arthritis and psoriasis. https://www.nice.org.uk/guidance/ng100 https://www.nice.org.uk/guidance/ng130/chapter/Recommendations-for-research From the 2013 guideline - What is the clinical and cost effectiveness of sulphasalazine compared to high-dose branded mesalazine for induction of remission for people with mild moderate ulcerative colitis? This guideline is for adults only
Dose & response	**Dose** is variable depending on indication. Clinical response may take up to 3 months. **Rheumatology**: usually initiated at 500mg/day increasing by 500mg weekly to 2-3g/day (40mg/kg) in divided doses. Dose titration on initiation will be carried out by the Specialist. Enteric coated preparations (Salazopyrin-EN) are preferred as better tolerated. Concomitant NSAIDs and analgesics should be continued at least until response noted by patient. **Gastroenterology**: Rarely used, mesalazine is preferred. Induction dose may be up to 1-2g four times a day until remission, reducing to maintenance dose, typically 2g per day, continued indefinitely as discontinuation, even several years after an acute attack, is associated with a four-fold increase in risk of relapse. **Preparations available:** Sulfasalazine 500mg enteric coated tablets, plain tablets, suspension 250mg in 5ml.
Specialist responsibilities	• Prescribe the initial treatment until dose is stable (usually 2-3 months). • Request blood tests and monitor results until dose stable – usually 2-3 months. • Counsel patients about side effects. Ensure the patient understands their treatment and which warning signs to report. Advise patients to report symptoms of bone marrow suppression, such as inexplicable bruising, bleeding or severe sore throat/oral ulceration, immediately. • Advice and support to GPs should problems occur (e.g. adverse effects, abnormal blood tests) • Review the patient at regular intervals depending on individual need
GP Responsibilities	• Prescribing maintenance dose of sulfasalazine according to the dose regimen suggested by the Rheumatologist. • Request blood test results once dose is stable (usually 2-3 months) and requested by hospital to take over shared care. • Review blood test results before prescribing. • Identify & report any adverse events to the specialist & MHRA and take appropriate action. Report any worsening of control of the condition to the specialist. **Recommended monitoring for new DMARDs** • **FBC, Cr (or eGFR), ALT, albumin every 2 weeks until stable dose for 6 weeks.** • **Then monthly FBC, Cr or eGFR, ALT, albumin for 3 months.** • **Then FBC, Cr or eGFR, ALT, albumin at least every 12 weeks.** • **For dose increases -FBC, Cr or eGFR, ALT, albumin every 2 weeks until stable dose for 6 weeks then back to previous schedule.** **After 12 months, if blood results are stable, no need for routine monitoring.**

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	• Pneumococcal vaccination every 10 years and annual influenza vaccinations are recommended for patients with inflammatory arthritis • Although the shingles (Zostavax) vaccine is a live attenuated vaccine, treatment with sulfasalazine is not considered sufficiently immunosuppressive and is not a contraindication to administering the vaccine.
Patient Responsibilities	• Report to the specialist or GP if they do not have a clear understanding of their treatment • Communicate with the GP any side-effects or problems encountered which may have an impact on taking the medicines • Ensure blood monitoring is undertaken at the requested time intervals • Read the Patient Information leaflet which accompanies the medicine • Inform specialist team where bloods are taken to facilitate access where necessary
Actions to be taken in response to monitoring	**Thresholds at which to discontinue treatment and contact Rheumatology treatment for urgent review:** • **WCC<3.5 x10^9/L** • **Neutrophils<1.6 x10^9/L** • **Unexplained eosinophilia>0.5 x10^9/L** • **Platelets<140 x10^9/L** • **MCV>105** • **ALT>100 units/L** • **Unexplained fall in albumin** • **Creatinine>30% above baseline +/- GFR<60**
Contra-indications	• **Hypersensitivity to sulfonamides or salicylates (e.g. aspirin)** • **Acute intermittent porphyria** • **Severe renal impairment.**
Cautions	• **Hepatic impairment** • **Renal impairment** – risk of toxicity including crystalluria in moderate impairment. Ensure high fluid intake. Avoid use in severe renal impairment. • **Glucose-6-phosphate dehydrogenase** (G6PD) - observe closely for signs of haemolytic anaemia. • **Patients with known anti-nuclear antibody** (ANA) as can induce lupus like illness. • **Pregnancy** – theoretical risk of neonatal haemolysis, no evidence to confirm this association. Folic acid supplements of 5mg/day is recommended to be given to mother and dose of sulfasalazine should not exceed 2 gram/day. Sulfasalazine is generally considered safe in pregnancy https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-SULFASALAZINE-IN-PREGNANCY/ and https://www.nras.org.uk/rheumatoid-arthritis-pregnancy • **Breastfeeding** – small amounts in milk – theoretical risk of neonatal haemolysis, although is generally considered safe during breastfeeding if a child is born full term and is healthy. https://www.ncbi.nlm.nih.gov/books/NBK501317/ Contact Medicines Advice, see below, for queries on Pregnancy and Breastfeeding. • Sulfasalazine can be prescribed to men of childbearing potential although there may be transient reversible oligospermia. • **Contact lens wearers** - may stain lens due to discolouration of body fluids (yellow/orange).
Important adverse effects & management	**About 75% of adverse effects occur within 3 months of initiating therapy and over 90% by 6 months.** **A rapid fall or consistent downtrend in any parameter should prompt caution & extra vigilance.** • **Acute unexplained widespread rash**- withhold and seek urgent specialist (preferably dermatological) advice • **Rash, photosensitivity, sore throat with oral / pharyngeal ulceration -** withhold drug until discussed with specialist. • **Abnormal bruising, severe sore throat -** Request urgent FBC and withhold treatment until results are known and discussed with specialist. • **Significant infection or patient is systemically unwell -** Withhold treatment and discuss with specialist. • **Nausea, loss of appetite** - continue treatment if possible. Advise patients to take tablets with or after meals. Introduce dose increases slowly. Anti-emetics may help resolve symptoms. Discuss with specialist if severe or persistent.

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	• **Vertigo, tinnitus –** symptoms may resolve on reduction of dose. • **Oligospermia -** reversible within 2-3 months of discontinuing treatment.
Important Drug Interactions	• **Azathioprine/mercaptopurine** - Increased risk of haematological toxicity. • **Digoxin - Caution.** May reduce absorption of digoxin. • **Sulfonamides - Caution**. May cause hypoglycaemia. Monitor closely.

This guidance should be read in conjunction with the BNF and SmPC (www.medicines.org.uk)

Contact numbers for urgent GP advice

Southampton - Nurse specialist advice line 023 8120 5352 or bleep SpR 1801 (Mon-Fri 9-5). Out of hours – on-call consultant via hospital switchboard.

Basingstoke - Administration team 01256 312768, advice line (answerphone) 01256 313117 or on-call consultant via switchboard.

Winchester – Administration team 01964 824150, Advice line 01962 824256, on-call SpR bleep 3425 via switchboard.

Southampton Medicines Advice Service (Mon-Fri 9am – 6.30pm) 023 8120 6908/9 or medicinesadvice@uhs.nhs.uk

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