City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

SHARED CARE GUIDELINE

SULFASALAZINE
Treatment of Inflammatory Conditions in Adult Gastroenterology and Rheumatology Patients

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AND FILED IN NOTES

INTRODUCTION – Indication and Licensing

Sulfasalazine is an aminosalicylate compound and is cleaved by bacteria in the gut into 5-aminosalicylic acid (5-ASA or mesalazine) and sulfapyridine. The drug and its metabolites exert immunomodulatory effects, antibacterial effects, effects on the arachidonic acid cascade and alteration of activity of certain enzymes. The mesalazine component is absorbed locally by colonic cells and exerts therapeutic effect in inflammatory bowel disease, but is not responsible for the anti-inflammatory effect in rheumatic conditions. Therapeutic effect in rheumatoid arthritis is usually evident after 1 to 3 months of treatment.

Licensed indications: Crohn's disease (acute), ulcerative colitis and rheumatoid arthritis.

Unlicensed indications: ankylosing spondylitis, psoriatic arthritis and enteropathic arthritis.

PATIENT PATHWAY

Clinical Speciality / Indication	Prescribing Initiated by	Prescribing Continued by	Monitored by	Duration of treatment
Gastroenterology Rheumatology	Gastroenterologist Rheumatologist	Hospital to prescribe until patient is on a stable dose then GP to take over prescribing.	Hospital or GP as per shared care agreement letter.	Ongoing if efficacious.

Reviews & dose adjustments
The patient will be reviewed periodically by the hospital specialist team in clinic. Dosing adjustments are to be done by the hospital and this information communicated to the GP in writing within 14 days.

Patients outside of City and Hackney area
It may be more appropriate for blood test monitoring to be done locally if this is more convenient for the patient. The patient should be given a copy of their latest blood results to bring to their clinic appointment (if the hospital specialist team is not able to access this information electronically).

ORAL DOSE AND ADMINISTRATION

Crohn's disease and ulcerative colitis

- *Acute attack (oral):* 1 to 2g four times daily in conjunction with corticosteroids (if necessary) until remission occurs.
- *Maintenance (oral):* 500mg four times daily (maintenance therapy not used in Crohn's disease).

Rheumatological conditions (use enteric-coated tablets)

- Start at 500mg daily and increase in 500mg increments at intervals of one week until maintenance dose of 2 to 3g daily (in divided doses).
- Enteric-coated tablets should be swallowed whole (not chewed or crushed) and should not be taken at the same time as indigestion remedies.

Dosing in pregnancy

- Doses should not exceed 2g/day for rheumatological conditions and 4g/day for inflammatory bowel disease.
- Prescribe Folic Acid 5mg daily throughout pregnancy.

Vaccinations

- Sulfasalazine is not an immunosuppressant. In patients who have risk factors for flu and pneumonia, offer vaccination against influenza (annually) and pneumococcal (single dose and can be repeated every 5 years).
- Individuals requiring vaccination with live vaccines should have this discussed with their specialist team. These vaccines include: shingles, oral polio, MMR, BCG and yellow fever vaccines.

CAUTIONS

- History of allergy or asthma.
- G6PD deficiency.
- Slow acetylator status (risk of toxicity).

CONTRAINDICATIONS

- Acute porphyria.
- Severe renal impairment.
- Known hypersensitivity to mesalazine (and other aminosalicyclates), sulphonamides and salicylates.

INTERACTIONS

- **Digoxin and folic acid** – absorption possibly reduced by Sulfasalazine

MONITORING STANDARDS FOR MEDICATION AT THE ACUTE NHS TRUST

Pre-treatment monitoring to be done by the specialist team
FBC, LFTs, U&Es (including eGFR), urinalysis, CRP, ESR, B12, folate
Ongoing monitoring
U&Es (including eGFR) and urinalysis at 3 months of treatment then annually (more frequently in renal impairment). **FBC and LFTs** monthly for 3 months, then every 3 months until been on treatment for 12 months, then no routine monitoring needed.

KEY ADVERSE EFFECTS & ACTIONS

- Gastrointestinal disturbances (diarrhoea, nausea, vomiting, loss of appetite, abdominal pain, exacerbation of symptoms of colitis).
- Hypersensitivity reactions (including rash and urticaria).
- Headache, dizziness, tinnitus and fever.
- Blood disorders (including leucopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia).
- Renal dysfunction (crystalluria, interstitial nephritis, nephrotic syndrome). **Ensure adequate fluid intake.**
- **Yellow-orange discolouration of skin, urine, and other body fluids; some soft contact lenses may be stained.**

Laboratory events	**Values**	**Actions (*what action should the GP take if identified in primary care)***
↓ WBC	<3.5 x 10^9/l	Reduction in WBC alone is not usually considered clinically significant. If this is accompanied by a reduction in neutrophil count then **stop drug and seek advice** from the specialist team.
↓ Neutrophil count	<1.6 x 10^9/l	**Stop drug and seek advice** from the specialist team.
↓ Platelet count	<100 x 10^9/l	
↑ MCV	>105fl	Check alcohol intake, B12, folate and TSH and treat any underlying abnormality. If normal, **seek advice** from the specialist team.
↑ ALT/AST	>2 times upper limit of normal	**Stop drug and seek advice** from the specialist team.
↓ eGFR	30 – 60ml/min/1.73	Use with caution and ensure adequate fluid intake.
	<30ml/min/1.73	**Seek advice** from the 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 team will advise.

Adverse effects	**Actions (*what action should the GP take if identified in primary care)***
Dyspepsia, nausea and vomiting	Advise patient to take drug with food and/or try enteric coated tablets if on plain tablets. **Seek advice** from the specialist team if symptoms not improved as dose may need to be reduced.
Abnormal bruising, bleeding or severe sore throat	**Stop drug** and check FBC immediately. **Seek advice** from the specialist team.
Skin rash, oral ulceration	**Stop drug and seek advice** from the specialist team.

Patient should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment. A blood count should be performed and the drug stopped immediately if there is suspicion of a blood dyscrasia.

The SCG lists only the key information. Please refer to the current British National Formulary and Summary of Product Characteristics for comprehensive information on cautions, contraindications, interactions and adverse effects.

PREGNANCY AND BREAST FEEDING

- Sulfasalazine is **compatible with pregnancy**, but there is theoretical risk of neonatal haemolysis in the 3rd trimester. Folic acid supplementation (5mg/day) is recommended throughout pregnancy.
- Sulfasalazine is **compatible with breastfeeding** in healthy full-term infants. Sulfasalazine and sulfapyridine are found in low levels in breast milk. There is a theoretical risk of neonatal haemolysis especially in G6PD-deficient infants. Breastfeeding should be stopped if the infant develops bloody stools or diarrhoea.
- **Oligospermia and infertility** may occur in men treated with Sulfasalazine. Discontinuation of the drug appears to reverse these effects within 2 to 3 months.

Please refer to the current British National Formulary and Summary of Product Characteristics for comprehensive information.

SHARED CARE

Shared care guideline*:* is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use**.**

Consultant

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that the patient understands their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
3. Ensure baseline investigations are normal before commencing treatment.
4. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised).
5. Send a letter to the GP requesting shared care for this patient.
6. Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis.
7. Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated (unless otherwise covered by letter e.g. from Rheumatology Clinical Nurse Specialist).

8. Where the GP is out of area and is not performing the phlebotomy, the blood test form/EPR request MUST specify that blood results are also copied to the GP. Specialist team to check with pathology IT if unsure on how to do this.
9. Evaluation of any reported adverse effects by GP or patient.
10. Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
11. Inform GP of patients who do not attend clinic appointments.

General Practitioner

1. Ensure that the patient understands the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA / CHM, where appropriate.
5. Help in monitoring the progression of disease.
6. Prescribe the drug treatment as described.

City and Hackney Medicines Management Team

1. To provide feedback to acute trusts via the Joint Prescribing and Medicines Management Group.
2. To support GPs to make the decision whether to accept clinical responsibility for prescribing.
3. To support acute trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist.
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist.
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
5. Take/ administer the medication as prescribed.
6. Undertake any monitoring as requested by the GP and/or specialist.

Costs

Drug Product	Cost in primary care
Sulfasalazine 500 mg tablets	112-tab pack = £5.79
Sulfasalazine 500 mg e/c tablets	112-tab pack = £12.78
Salazopyrin® 500mg suppositories	10-suppos pack = £3.30

Based on BNF edition 73 (March – September 2017)

RESOURCES AVAILABLE

- Arthritis Research UK website, accessible *via* http://www.arthritisresearchuk.org
- Crohn's & Colitis UK website accessible *via* https://www.crohnsandcolitis.org.uk

Relevant contact details	
Consultant or Registrar on-call *via* switchboard	020 8510 5555
Clinical Nurse Specialist (helpline)	**Gastroenterology** 07920 546260 **Rheumatology** 07917 521 117
Generic email	**Gastroenterology** huh-tr.gastro@nhs.net **Rheumatology** huh-tr.rheumliaison@nhs.net (clinical queries) huh-tr.rheumatologyadmin@nhs.net (admin queries)
Trust Homerton University Hospital NHS Foundation Medicines Information	020 8510 7000
City and Hackney Medicines Management Team	0203 816 3224

References

- SCG template adopted from NELMMN and Barts Health NHS Trust
- BNF edition 73, accessible *via* https://ebnf.homerton.nhs.uk (last accessed 21 April 2017).
- Summary of product characteristics. Accessible *via* www.medicines.org.uk (last accessed 21 April 2017).
    1. Salazopyrin En-Tabs.
    2. Salazopyrin tablets.
    3. Salazopyrin Suppositories.
- The British Society for Rheumatology, accessible *via*: http://www.rheumatology.org.uk (last accessed 7 April 2017).
    1. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease modifying anti-rheumatic drugs (2017).
    2. BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists (2008).
    3. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding – Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids (2016).

Date SCG approved by Joint Prescribing Group (JPG): 06/2017 Review date: 06/2020