THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Guideline

For

Sulfasalazine in Adults

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Based on the previous SCG for Sulfasalazine in Adults

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Shared Care Guideline for Sulfasalazine in Adults

Statement of Purpose

This shared care guideline has been written to enable the continuation of care by primary care clinicians of adult patients initiated on sulfasalazine by the rheumatology or gastroenterology departments at Sheffield Teaching Hospitals. Primary care will only be requested to take over prescribing of sulfasalazine within its licensed indication.

Responsibilities of consultant clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent;
- To undertake pre-treatment tests;
- To initiate sulfasalazine in appropriate patients and issue patient with patient information leaflet;
- To prescribe sulfasalazine until the patient is stable;
- To contact patient's GP to request prescribing under shared care using the shared care transfer form. Send a link to or copy of the shared care guideline to the patient's GP;
- To advise the GP regarding continuation of treatment, including the length of treatment;
- To review patients after 12 months of treatment and communicate with GPs as to whether blood monitoring should be stopped or identify patients who may require longer periods of monitoring even if they have had stable bloods for a year;
- To discuss any concerns with the GP regarding the patient's therapy;
- To monitor disease appropriately whilst the patient is under shared care,

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment;
- To agree to prescribe for patients in line with the shared care guidelines;
- To report any adverse reaction to the CHM and the referring consultant;
- To continue to prescribe for the patient as advised by the consultant;
- To undertake monitoring as stated above and transcribe results clearly into the patients individual management plan (a 'blue book' which the patient will have been given from STH);
- To inform the consultant if the patient discontinues treatment for any reason;
- To seek the advice of the consultant if any concerns with the patient's therapy;
- To conduct an annual face to face medication review or more frequent if required;
- In the event that the GP is not able to prescribe, or where the shared care guideline is agreed but the consultant is still prescribing certain items e.g. hospital only product, the GP will provide the consultant with full details of existing therapy promptly by fax on request;
- Check for possible drug interactions when newly prescribing or stopping concurrent medication;
- For medication supplied from another provider, GPs are advised to follow the recommendations for recording on the clinical practice system:
  Recording Specialist Issued Drugs on Clinical Practice Systems
  http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Practice%20resources%20and%20PGDs/Recording_SIDs_on_practice_clinical_systems%20.pdf

Responsibilities of patients/carers

- To attend hospital and GP clinic appointments and to bring monitoring booklet (if required); failure to attend may potentially result in the medication being stopped;

- Present rapidly to the GP or specialist should their clinical condition significantly worsen;
- Report any suspected adverse effects to their specialist or GP whilst taking sulfasalazine;
- To read the drug information given to them;
- To take sulfasalazine as prescribed;
- Inform the specialist, GP or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication;
- Take responsibility for appropriate contraceptive precautions.

Indication

Sulfasalazine is indicated for the treatment of adult patients for:

- Induction and maintenance of remission of ulcerative colitis; treatment of active Crohn's Disease.
- Treatment of rheumatoid arthritis

Selection of patients

All adult patients will be treated and stabilised on sulfasalazine by a secondary care specialist. Once stabilised, patients are suitable for referral to a primary care service – this will usually take 3 months.

The following patients are excluded from this shared care guideline:

- Hepatic impairment;
- Sensitivity to salicylates or sulphonamides;
- Children under 16 years;
- Patients who prefer to attend hospital.

Dosage

Oral

EN-Tablets should be used across all Rheumatology indications. They should not be crushed or broken. Only the enteric coated tablets: Salazopryin EN ® are licensed for rheumatoid arthritis.

The dose is adjusted according to the severity of the disease and the patient's tolerance to the drug, as detailed below.

Elderly Patients: No special precautions are necessary.

a) <u>Ulcerative colitis</u>

<u>Adults</u>

<u>Severe Attack</u>: sulfasalazine 500mg: 2-4 tablets four times a day may be given in conjunction with steroids as part of an intensive management regime. Rapid passage of the tablets may reduce effect of the drug.

Night-time interval between doses should not exceed 8 hours.

<u>Moderate Attack</u>: sulfasalazine 500mg: 2-4 tablets four times a day may be given in conjunction with steroids.

<u>Mild Attack</u>: sulfasalazine 500mg: 2 tablets four times a day with or without steroids.

Maintenance Therapy: With induction of remission reduce the dose gradually to 4 tablets per day. This dosage should be continued indefinitely, since discontinuance even several years after an acute attack is associated with a four fold increase in risk of relapse.

Tablets should be taken after food; antacids reduce absorption.

b) Crohn 's Disease

In active Crohn's Disease, sulfasalazine should be administered as in attacks of ulcerative colitis (see above).

c) Rheumatoid Arthritis

Patients with rheumatoid arthritis, and those treated over a long period with NSAIDs, may have sensitive stomachs and for this reason enteric-coated sulfasalazine (Salazopyrin® EN-Tabs) are recommended for this disease, as follows:

The patient should start with one tablet daily, increasing the dosage by a tablet a day each week until one tablet four times a day, or two three times a day is reached, according to tolerance and response. Onset of effect is slow and a marked effect may not be seen for six weeks. A reduction in ESR and C-reactive protein should accompany an improvement in joint mobility.

NSAIDs may be taken concurrently with sulfasalazine. Continue NSAIDs or analgesics at least until treatment response.

Contra-indications

- Hypersensitivity to sulfasalazine or its metabolites, salicylates, sulphonamides or to any of the excipients
- Impairment of liver or renal function or with blood dyscrasias, unless potential benefit outweighs the risk
- Patients with porphyria

Pregnancy and Breast feeding

Sulfasalazine can cause a fall in sperm count, leading to a temporary decrease in fertility, but must not be relied upon for contraception but patients are counselled about this on initiation of treatment. It is considered safe for a woman to continue to use sulfasalazine when trying to conceive, and she should take folic acid 400micrograms daily.
Sometimes sulfasalazine is continued through pregnancy (dose should not exceed 2g/day) to prevent a flare of disease if the benefit outweighs the risk. Therefore it is important to consult the specialist if the patient is trying to conceive or becomes pregnant whilst taking sulfasalazine.

Sulfasalazine is found in low levels in breast milk. The Salazopyrin SPC recommends that patients should avoid breast feeding whilst taking sulfasalazine as there have been reports of bloody stools and diarrhoea in infants who were breast feeding from mothers on sulfasalazine. BSR guidelines however state that sulfalsazine is compatible with breast feeding healthy full term infants. Therefore please consult with the specialist in mothers wanting to breast feed.

Side –effects

The details below are not a complete list and the BNF and the SPC remain authoritative.

Overall, about 75% of adverse drug reactions occur within 3 months of starting therapy, and over 90% by 6 months. Some undesirable effects are dose-dependent and symptoms can often be alleviated by reduction of the dose.
The most commonly encountered side effects reported are: nausea, headache, rash, loss of appetite and raised temperature.
Urine may change colour to orange.
Certain types of extended wear soft contact lenses may be permanently stained during therapy.

Monitoring

NB Sulfasalazine itself can interfere with ALT and AST assays, such that the levels of these liver enzymes can be falsely reduced thus masking hepatotoxicity. Hence need for extended LFTs to include GGT.

Secondary care –
Baseline: FBC; extended LFTs (including GGT); U&Es; and CRP (rheumatology patients).
Monitoring in initial period: FBC and extended LFTs (including GGT) every two weeks for 6 weeks, then monthly for 3 months or until stable; U&Es every month for 3 months then as clinically needed.

Primary Care –Once shared care: Extended LFTs (including GGT), FBC and CRP (rheumatology patients) should be performed every 3 months; U&Es should be monitored as clinically indicated. An ICE test profile is available for monitoring purposes to ensure all recommended blood tests are done.

Monitoring is not routinely required once a patient has had stable blood levels for a year. Selected patients who are deemed to be at higher risk may require longer periods of monitoring but those patients will be clearly identified by the responsible consultant.

The patient should also be counselled to report immediately with any sore throat, fever, malaise, pallor, purpura, bleeding, bruising, jaundice or unexpected non-specific illness as this may indicate myelosuppression, haemolysis or hepatoxicity. Treatment should be stopped immediately while awaiting the results of blood tests.

If MCV> 105 fL check vitamin B12, folate and TSH. If abnormal, treat any underlying abnormality. If normal, discuss with specialist team.

Check full blood count if significant infection present

If any increase in dose: re-check bloods within one month and if tests normal can then return to previous monitoring schedule.

<u>Stop sulfasalazine and contact helpline if:</u>

WBC $<3.5 \times 10^9$/L

Neutrophils $<1.6 \times 10^9$/L
Creatinine increase >30% over 12 months and/or eGFR <60 ml/min/1.73m^2

Unexplained eosinophilia $>0.5 \times 10^9$/L
ALT and/or AST >100 U/L
Platelet count $<140 \times 10^9$/L

Unexplained reduction in albumin <30 g/L

New rash, sore throat with oral and pharyngeal ulceration, unexplained bruising/bleeding, fever, jaundice, pallor, purpura, malaise, or any unexpected non-specific illness as this may indicate myelosuppression, haemolysis or hepatoxicity. Treatment should be stopped immediately while awaiting the results of blood tests.

Interactions

The details below are not a complete list and the current BNF and the SPC remain authoritative.

Reduced absorption of digoxin, resulting in non-therapeutic serum levels, has been reported when used concomitantly with oral sulfasalazine.

Sulfonamides bear certain chemical similarities to some oral hypoglycemic agents. Hypoglycemia has occurred in patients receiving sulfonamides. Patients receiving sulfasalazine and hypoglycemic agents should be closely monitored.

Bone marrow suppression and leucopenia have been reported when the thiopurine 6-mercaptopurine or its prodrug, azathioprine, and oral sulfasalazine were used concomitantly.

Additional information

Sulfasalazine should be given with caution to patients with severe allergy or bronchial asthma.

Since sulfasalazine may cause haemolytic anaemia, it should be used with caution in patients with G-6-PD deficiency.

Oral sulfasalazine inhibits the absorption and metabolism of folic acid and may cause folic acid deficiency potentially resulting in serious blood disorders (e.g. macrocytosis and pancytopenia), this can be normalised by administration of folic acid or folinic acid.

Because sulfasalazine causes crystalluria and kidney stone formation, 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 these effects within 2 to 3 months

Pneumococcal polysaccharide vaccine & annual inactivated flu vaccine should be given.

It is a recommendation by NICE, that patients with RA have an annual review by their Rheumatology Consultant. Patients are also encouraged to have a yearly review with their GP in Primary care

Re-Referral guidelines

See under monitoring section above
Pregnancy
Deterioration of disease

Financial implications

Prescribing of sulfasalazine will move from secondary to primary care. Prescribing in primary care will be on FP10 prescriptions. Out patient appointments at STH will be reduced.

Support, education and information

A drug information sheet and shared care booklet has been issued to your patient.

If any problems occur or you have any concerns please contact relevant specialist:

Rheumatology help line (Mon-Fri 0900-1600)	(0114) 2713086 (option 3)
Inflammatory Bowel Disease Helpline (Mon-Fri 0900- 1600)	(0114) 2712209
On call specialist via STH NHS Foundation Trust switchboard:	(0114) 2711900

Secondary care assumes responsibility for the monitoring and re-prescription of sulfasalazine until stable dosage has been successfully achieved.

Patient information leaflets:
These are provided to rheumatology patients by secondary care, but can also be downloaded here http://www.arthritisresearchuk.org/~/media/Files/Arthritis-information/Drugs/Sulfasalazine%202252%2015-1.ashx

References

Full prescribing information is in the sulfasalazine summary of product characteristics (SPC), available from www.emc.medicines.org.uk

BNF www.medicinescomplete.com/mc/bnf/current/

BSR/BHPR Non-biologic DMARD Guidelines (2017)
https://academic.oup.com/rheumatology/article/56/6/865/3053478/BSR-and-BHPR-guideline-for-the-prescription-and

Yorkshire Rheumatology Regional Guidelines for the monitoring of adult patients on DMARDs including biologic therapy. Sixth edition revised May 2014
http://www.leedsformulary.nhs.uk/docs/10.01YorkshireRheumGuidelinesforptsonDMARDs.pdf

BSR and BHPR guideline on prescribing drugs in pregnancy and breast feeding – part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids
https://academic.oup.com/rheumatology/article/55/9/1693/1744535#supplementary-data