BNSSG Paediatric Shared Care Guidance

Please complete all sections

Section 1: Heading

Drug	Sulfasalazine (or sulphasalazine)
Amber *three months*	
Indication	Treatment of ulcerative colitis and Crohn's disease
Speciality / Department	Paediatric Gastroenterology
Trust(s)	University Hospitals Bristol NHS Foundation Trust

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed for this age group and any relevant dosing information)*

Treatment of an acute attack of mild and moderate and severe ulcerative colitis; Active Crohn's disease

Orally

Age	
2 to 11 years	10 to 15mg/kg (max 1 gram/dose) 4 to 6 times a day; max 70mg/kg/day or 4 grams/day in divided doses**.** The interval between doses should not exceed 8 hours.
12 to 17 years	1 grams four times a day

Rectally

Age	Dose
5 to 7 years	500mg twice a day
8 to 11 years	500mg in the morning and 1 gram at night
12 to 17 years	0.5 to 1 gram twice a day

Maintenance of remission of mild to moderate and severe ulcerative colitis

Orally

Age	Dose
2 to 11 years	5 to 7.5mg/kg 4 times a day (max. per dose 500mg)
12 to 17 years	500mg four times a day

Rectally

Age	Dose
5 to 7 years	500mg twice a day
8 to 11 years	500mg in the morning and 1 gram at night
12 to 17 years	0.5 to 1 gram twice a day

Route and preferred formulation *(Please indicate licensed or unlicensed preparation)*	Oral Suspension 250mg/5ml (*one month expiry when opened*) 500mg gastro-resistant tablets/enteric coated 500mg tablets 500mg suppository Enteric coated/gastro-resistant preparations are the preferred choice of preparation for ulcerative colitis and Crohn's colitis. Gradual dose increase of sulfasalazine over 7 - 14 days may decrease the rate of dose dependent adverse effects such as headaches and gastrointestinal effects.
Duration of treatment	Ongoing

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist)

Baseline tests to be done by secondary care

U&Es, FBC, LFTs

Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results. If the drug is dosed by weight please also indicate intended frequency of weight monitoring/dose adjustment)*

Test	Frequency	Who by	Action/management
U&Es	At 3 months of treatment and then annually thereafter	Primary Care	If creatinine is outside of specific limit for patient given by secondary care, or if no limit is given use generic table given below. If creatinine falls outside of reference range, contact hospital team to discuss. Reference table for children's creatinine levels shown below.
LFTs (ALT, AST, ALP)	Monthly intervals for the first 3 months, then 3 monthly for the first year and 6 monthly thereafter (if dose and bloods are stable).	Secondary care for the first month, then primary care thereafter.	If >2 fold but <4 fold increase, repeat and if still high discuss with hospital team. If > 4 fold, withhold medication, repeat and discuss with hospital team.
FBC	Monthly intervals for the first 3 months, then 3 monthly for the first year and 6 monthly thereafter (if dose and bloods are stable).	Secondary care for the first month, then primary care thereafter.	Full Blood count values: — WBC > 2.5 x 10^9/L (upper limit 4.5 x10^9/L): Repeat and discuss with hospital team. WBC <2.5 x 10^9/L: Stop drug and repeat. Discuss with hospital team. Neutrophils <1.0 x 10^9/L: Repeat and discuss with the

				hospital team.
			Platelets < 150 x 10^9/L	Repeat and discuss with hospital team.

If a mg/kg dose increase is advised by the hospital team, it is advised for the GP to recheck their FBC and LFTs one month after the dose increase then revert back to normal monitoring.

Creatinine reference table for children			
Female		**Male**	
Age range	**Reference interval**	**Age range**	**Reference interval**
0 - 14 days	27 - 77 µmol/L	0 - 14 days	27 - 77 µmol/L
14 days - 1 year	14 - 34 µmol/L	14 days - 1 year	14 - 34 µmol/L
1 year - 3 years	15 - 31 µmol/L	1 year - 3 years	15 - 31 µmol/L
3 years - 5 years	23 - 37 µmol/L	3 years - 5 years	23 - 37 µmol/L
5 years - 7 years	25 - 42 µmol/L	5 years - 7 years	25 - 42 µmol/L
7 years - 9 years	30 - 47 µmol/L	7 years - 9 years	30 - 47 µmol/L
9 years - 11 years	29 - 56 µmol/L	9 years - 11 years	29 - 56 µmol/L
11 years - 12 years	36 - 64 µmol/L	11 years - 12 years	36 - 64 µmol/L
12 years - 13 years	36 - 67 µmol/L	12 years - 13 years	36 - 67 µmol/L
13 years - 14 years	38 - 74 µmol/L	13 years - 14 years	38 - 76 µmol/L
14 years - 15 years	43 - 75 µmol/L	14 years - 15 years	40 - 83 µmol/L
15 years - 16 years	44 - 79 µmol/L	15 years - 16 years	47 - 98 µmol/L
16 years - 17 years	48 - 81 µmol/L	16 years - 17 years	54 - 99 µmol/L
17 years - Adult	45 - 84 µmol/L	17 years - Adult	59 - 104 µmol/L

Frequency of ongoing follow up by secondary care *(Please indicate how often child will continue to be seen by secondary care i.e. at least every 6 months)*	Patients are seen in clinic on a 3 monthly basis so any weight based dose adjustments will be made in clinic.

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNFc or SPC.

Side effects and management

Side effect	Frequency/severity	Action/management
Nausea, vomiting, indigestion and heartburn	very common	Splitting up the dose may help alleviate symptoms. If persists refer back to the hospital team.
Headache	common	Often transient, if persists refer back to the hospital team.
Loss of appetite	not known	If there are concerns with weight loss refer back to the hospital team.
Diarrhoea	common	May be difficult to distinguish from increased inflammatory bowel disease activity. Refer back to hospital team if there are concerns.

	Raised temperature	common	If patient presents with unexplained fever, a FBC is required. Discuss with the hospital team.
	Progressive skin rash often with blisters or mucosal lesions	very rare	Life threatening cutaneous reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) can occur. The highest occurrence is within the first weeks of treatment. Stop drug and urgently refer to the hospital team.
	Abnormal bruising, malaise and severe sore throat	uncommon	Withhold and check FBC. Discuss with hospital team.
	Oral ulceration	common	Withhold and discuss with hospital team.
	Metallic taste in the mouth	common	If troublesome refer back to the hospital team.
	Hepatitis	rare	Monitor LFTs as above.
	Cough and dyspnoea	uncommon	Refer back to hospital team.
	Urine has a frothy appearance	common	Test urine for protein. Refer back to hospital team if proteinuria present.
Referral back to specialist	See above		

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent and the action for GP to take (For full list please see BNFc or SPC)

Issues

Drug Interactions

Drug	Interaction	Management
Digoxin	Reduced absorption of digoxin	Concurrent use need not to be avoided. Cardiac team to monitor digoxin levels if an interaction is suspected.
Azathioprine and mercaptopurine	The haematological toxicity of azathioprine and mercaptopurine may be increased by sulfasalazine	Concurrent use need not be avoided. Monitor bloods as advised in the shared care protocols.
Folic acid	Inhibits the absorption and metabolism of folic	Hospital team to monitor folate levels if there are concerns

		acid	with absorption of folic acid.
	Methotrexate	Nausea may increase	Antiemetic treatment may help alleviate symptoms. Refer to the methotrexate shared care protocol for ondansetron doses. If troublesome, refer back to the hospital team.
	Hypoglycaemia agents	Hypoglycaemia can occur.	Diabetic patients should closely monitor their blood glucose levels.

Suppositories: The literature states that there have been no adverse drug interactions reported due to low absorption levels of the drug when given rectally. However, it is important to be aware that potentially an interaction could occur.

Patients/carers should be asked about the presence of abnormal bruising, rash or mouth ulcers.

Cautions: Acute porphyria; glucose-6-phosphate dehydrogenase (G6PD) deficiency; sulphonamide or salicylate hypersensitivity; risk of haematological toxicity; history of allergy; history of asthma

Allergy & cross-sensitivity: Contraindicated in salicylate or sulfonamide hypersensitivity
Renal & hepatic function: Use with caution in renal and hepatic failure
Oligospermia and infertility may occur in men treated with sulfasalazine. Discontinuation of the drug appears to reverse these effects within 2 to 3 months.
If a dose is missed, the patient should take/administer the next dose as usual. The dose should not be doubled to make up a missed dose.
Annual flu vaccination is recommended

Reminder to ask patient about specific problems	Patients/carers should be asked about the presence of abnormal bruising, rash or mouth ulcers.

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

1. Patients and carers should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever, jaundice or malaise that occurs during treatment as this may indicate myelosuppression, haemolysis or hepatoxicity
2. Soft contact lenses should be avoided as staining can occur.
3. Urine and tears may be stained an orange-yellow colour. Reassure patient that this is normal.
4. Patients should maintain adequate hydration to avoid crystalluria and kidney stone formation

Section 7: Generic principles of shared care for SECONDARY CARE

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and

thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
5. To provide advice to primary care when appropriate.
6. Review in frequency specified in **section 3** and adjust dose for child's age/body weight as appropriate.
7. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
8. Stopping treatment where appropriate or providing advice on when to stop.
9. Reporting adverse events to the MHRA.
10. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

Name	Organisation	Telephone Number	E mail address
Paediatric Pharmacist for Medicine	Bristol Royal Hospital for Children	0117 342 7042	Click here to enter details
Paediatric GI secretary	Bristol Royal Hospital for Children	0117 342 9450	Click here to enter details

Section 10: Document Details

Date prepared	October 2018
Prepared by	Rachel Crampton (Paediatric Pharmacist for Medicine)
Date approved by JFG	February 2019
Date of review	February 2021
Document Identification: Version	V1

Section 11: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

N/A

Section 12: References

Please list references

1. Sulfasalazine suppositories (Pfizer Limited), Summary of Product Characteristics. Accessed via http://emc.medicines.org.uk. Last updated 02/2014 (accessed in October 2018)
2. Sulfasalazine 250mg/5ml Oral suspension (Rosemont), Summary of Product Characteristics. Accessed via http://emc.medicines.org.uk. Last updated 09/2014 (accessed in October 2018)
3. Baxter, K. Stockley's Drug Interactions [online]. London: Pharmaceutical Press. Accessed at http://wwww.medicinescomplete.com (accessed in October 2018)
4. BNF for Children (2017-2018). Accessed at: www.medicinescomplete.com (accessed on October 2018)
5. UK IBD Working Group on behalf of the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN), October 2008. Guidelines for the Management of Inflammatory Bowel Disease (IBD) in Children in the United Kingdom.
6. Royal College of General Practitioners. Inflammatory Bowel Disease Toolkit. Accessed at: http://www.rcgp.org.uk/clinical-and-research/resources/toolkits/inflammatory-bowel-disease-toolkit.aspx
7. Turner D, Ruemmele FM, Orlanksi-Meyer E et al. Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care – an Evidence-Based Guideline from ECCO and ESPGHAN. Journal of Paediatric Gastroenterology Nutrition 2018: 05. Doi 10.1097/MPG.0000000000002035