# DMARDs in Adult Rheumatology –Information for GPs

## SULFASALAZINE

**Clinicians should also refer to the overarching DMARD shared care guideline document for details of the individual responsibilities for each group e.g. e.g. GP / Specialist Rheumatology team under this shared care agreement.**

## Information for GPs

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| **Indication** | • Sulfasalazine is recommended by NICE and National Societies for the treatment of numerous rheumatological conditions including Rheumatoid arthritis and Psoriatic arthritis.<br>• Clinicians should refer to the Summary of product characteristics (SPC) for specific licensing information.<br>• Use outside of the licensed indications is regarded as "off label" use. |
| **Drug dose** | • Typically, the Specialist Rheumatology team will initiate sulfasalazine 500mg tablets, **enteric coated**, started at 500mg once a day, increasing by 500mg every week , in divided doses, to 1g twice daily.<br>• Dose can be increased to a maximum dose of 3g per day, in divided doses.<br>• Dosage should be adjusted according to response and tolerance.<br>**Variaton to Sulfasalazine dosing:**<br>• Moderate renal impairment – risk of toxicity, including crystalluria- ensure high fluid intake.<br>• Avoid in severe renal impairment.<br>• Use with caution in hepatic impairment. |
| **Contra-indications / Cautions/ Dose modifications in Special Populations** | • **Clinicians should refer to the Summary of Product Characteristics (SPC's) and current electronic BNF for full details**<br>www.medicines.org.uk/emc<br>www.bnf.org/products/bnf-online<br>• Sulfasalazine should not be prescribed for patients who have an allergy to salicylates (e.g. aspirin) or to sulphonamides (a certain type of antibiotic). |
| **Side effects** | • Clinicians should refer to the Summary of Product Characteristics (SPC's) and current electronic BNF for full details<br>www.medicines.org.uk/emc |

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| | www.bnf.org/products/bnf-online<br><br>• **Blood dyscrasias** (e.g. leucopenia and neutropenia) can occur hence the importance of regular blood tests<br><br>• As sulfasalazine can cause some immunosuppression , clinicians should note to inform patients to contact their doctor immediately if they have any side effects , in particular – breathlessness, dry cough, whites of eyes becoming yellow, severe itching of skin, rash, dark urine, infections (including fever, chills or severe sore throats), new unexplained bleeding or bruising, mouth ulcers, vomiting and diarrhoea (particularly at the start of treatment, or if it is severe, at any stage in treatment).<br><br>• Examples if some common side effects include:<br>○ nausea<br>○ diarrhoea<br>○ abdominal pain<br>○ headache<br>○ dizziness<br><br>• **Clinicians should also refer to table 1 for details of when to contact the Specialist rheumatology team with regards blood test results and development of certain side effects etc.** |
| **Drug Interactions** | • Sulfasalazine can interact with a variety of drugs, some of which can be **significant.**<br><br>Examples include:<br>○ azathioprine<br>○ antacids<br>○ digoxin<br>○ folic acid<br><br>• This is **not an exhaustive list** and **c**linicians should always check the Summary of Product Characteristics (SPC) and the electronic BNF for a **full list** of potential drug interactions before starting any new medication or when stopping any existing medication.<br>www.medicines.org.uk/emc<br>www.bnf.org/products/bnf-online |
| **Pre-treatment Blood Test Monitoring**<br>*(To be done by Specialist Rheumatology team)* | • FBC, U+Es, LFT |

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| **Blood Test Monitoring requirements**<br>*(Typically to be monitored by the GP from week 4 onwards)*<br><br>**(Ref: Based on British Society of Rheumatology Guidelines , 2017 and current clinical practise)** | • FBC, U+E, LFT **fortnightly until dose and monitoring stable for 6 weeks**, then **monthly for 3 months** then **every 12 weeks* thereafter.**<br><br>*More frequent monitoring is appropriate for patients at a higher risk of toxicity.<br><br>• **After 12 months,** the patient should be reviewed. If patient is on a stable dose and blood tests results have been within normal limits, after 12 months, routine blood test monitoring can be discontinued.<br><br>• (**NB: After any dose increase,** blood test monitoring frequency should be carried out every fortnight until on a new stable dose for 6 weeks and then the frequency can revert back to the previous schedule).<br><br>• CRP / ESR should be monitored every 3-6 months as this can help assess disease activity.<br><br>• Ensure a prompt two way communication of blood test results between GP and Specialist team is available. (Paper copies should be sent between parties if electronic access via ICE is not available.) |
| **Time to response** | • 12 weeks |
| **Infections** | • Sulfasalazine can act as an immunosuppressant.<br>• Initiate prompt anti-infective treatment when indicated on the basis that the patient may be immunosuppressed to some degree.<br>• Sulfasalazine need only be stopped during active severe infection (e.g. infection requiring IV antibiotics or hospitalisation), or if infection is associated with neutropenia. It can be restarted after the infection (and neutropenia) has resolved.<br>• <u>If exposed to measles and / or chickenpox</u> : Check immunity to measles and varicella-zoster; if non-immune and exposed to measles or chickenpox contact the Specialist Rheumatology team ASAP for consideration of appropriate immunoglobulin therapy.<br>• <u>If patient develops shingles or chickenpox</u>, stop the drug and treat with aciclovir. |
| **Vaccinations** | • Vaccinations can be administered whilst on Sulfasalazine.<br>• Pneumovax and annual flu vaccination are recommended.<br>• Caution is required to ensure that patients are not receiving additional immuno-suppressants or biologic drugs, as these may not be documented on patient medication lists. If in any doubt please contact the Rheumatology team for further advice. |
| **Alcohol** | • There is no specific interaction between sulfasalazine and alcohol, however, for general health reasons < 14 units / week for women and < 21 units / week for men is recommended. |

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| **Elective surgery** | • Generally, sulfasalazine should not be stopped in the peri-operative period.<br>• Any queries or infection related surgery, should be discussed with Specialist Rheumatology team.<br>• **If in any doubt, contact the Specialist Rheumatology team for advice.** |
| **Contraception** | • The Specialist Rheumatology team should discuss family planning before initiation of treatment.<br>• GPs should refer any female or male patient who is wishing to start a family to the Specialist Rheumatology team.<br>• Oligospermia may occur in men treated with sulfasalazine. Discontinuation of the drug appears to reverse these effects within 2 to 3 months (Ref: SPC) |
| **Pregnancy and breast feeding** | • GP should refer patients who become pregnant to the Specialist Rheumatology team.<br>• It's important that the mother's health is maintained during pregnancy and disease flares are avoided by not stopping sulfasalazine. The lowest effective dose that controls the mother's condition should be used.<br>• Folic acid 5mg daily supplementation is required if patient is trying to conceive **and** during pregnancy. |
| **Photosensitivity** | • Small risk of photosensitivity.<br>• Caution with sun exposure, advise sun protection. |
| **Discolouration of body fluids** | • Can cause an orange/ yellow discolouration of urine and other body fluids.<br>• Some soft, extended wear contact lenses may be stained. |
| **Drug Formulations** | **Oral**<br>• 500mg tablets.<br>• Available as Sulfasalazine (generic) or Salazopyrin EN Tabs ®, enteric coated tablets. **(NB: Specialist Rheumatologists use enteric coated preparation)**<br>• (Liquid suspension 250mg/5ml licensed only for Crohn's disease and Ulcerative Colitis). |
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| **Practical Prescribing Points for GPs to note:** | • Advise patients to attend for a blood test approx. one week before their next prescription is due to ensure that the results can be reviewed before the next prescription is requested for issue.<br>• Check the results of recent blood test **before** issuing a prescription. (Refer to table 1 for actions to take in the event of blood test abnormailities and side effects - page 4 ).<br>• Increase blood test monitoring after a dose increase as detailed above. |

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| | • Prescribers should note that whilst absolute blood test values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance.<br>• Prescribe enteric coated tablets.<br>• Advise patients to swallow the tablets whole, do not crush or chew.<br>• Advise patients that sulfasalazine may cause discoloration of urine and other bodily fluids and contact lenses.<br>• Advise patients to have an adequate fluid intake, as sulfasalazine can cause crystalluria and kidney stone formation.<br>• Advise patients who wish to conceive or who become pregnant to contact their GP and Speciallist Rheumatology team as soon as possible.<br>• Provide a maximum of 4 weeks supply at a time. |
| **Patient Information Leaflets** | • Patients should be advised to read the Arthritis Research UK patient information leaflet and the package insert.<br>• The current Arthritis Research UK leaflet can be downloaded from: http://www.arthritisresearchuk.org/arthritis-information/drugs/sulfasalazine.aspx |

## Table 1:

## Actions to be taken:

**Prescribers should note that whilst absolute values are useful indicators, trends are equally important, and any rapid fall or consistent downward trend in any parameter warrants extra vigilance and urgent discussion with Specialist Rheumatology team.**

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| **WBC <3.5 x $10^9$/L** | **Withold and contact Specialist Rheumatology team urgently if any of the results opposite develop** |
| **Neutrophils <1.6 x $10^9$/L** | |
| **Unexplained eosinophilia >0.5 x $10^9$/L** | |
| **Platelet count <140 x $10^9$/L** | |
| **MCV > 105 f/L** | |
| **Creatinine >30% above baseline and/or calculated GFR <60** | |
| **ALT and/or AST >100 units/L** | |
| **Unexplained fall in serum albumin** | |

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| **Any rapid fall or consistent downward trend in any indices** | |
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| **Acute Widespread Rash or oral ulceration** | Withhold until discussed with Specialist Rheumatology team & consider urgent (preferable dermatological) advice. Investigate alternative cause. |
| **Nausea, vomiting** | Often transient. If possible, continue with use of an anti-emetic or reduce dose by 500mg. If symptoms are severe and persistent, discontinue sulfasalazine and discuss with Specialist Rheumatology team |
| **Diarrhoea** | Withhold until discussed with Specialist Rheumatology team |
| **Dizziness or Headache** | Often transient. If possible, continue. May have to reduce the dose or stop. Discuss with Specialist Rheumatology team if persistent or severe. Look for other causes. |
| **Severe sore throat, abnormal bruising or fever** | Immediate FBC and withhold until result available and contact Specialist Rheumatology team. |

**BACK-UP ADVICE AND SUPPORT**

- **GP queries should be directed to the Rheumatology consultants.**
- **Patient queries should be directed to the Rheumatology Specialist Nurses**

**All urgent requests should be answered within one working day.**

**Contact Details:**

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**References:**


- BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with British Association of Dermatologists. Rheumatology.2008 K Chakravarty et al. www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/diseasemodifying_antirheumatic_drug_dmard_therapy.pdf
- SPC (Summary of product characteristics) www.electronicmedicinescompendium.com
- BSR/BHPR Non-biologic DMARD guidelines ( (2017) https://academic.oup.com/rheumatology/article/56/6/865/3053478
- BNF (electronic) www.bnf.org/products/bnf-online