LINCOLNSHIRE CLINICAL COMMISSIONING GROUPS in association with UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE: SULFASALAZINE for the treatment of active Rheumatoid Arthritis.

General Principles

Shared Care Responsibilities:

In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (BNF 74, September 2017 – March 2018, pg.5)

Aims:

(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.

(2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.

(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.

(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further copies

Further copies of any guidelines in this series are available from members of the Optum Medicines Management and Optimisation Team.

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Principles of shared care

NHS England published Guidance - Responsibility for Prescribing between primary, secondary and tertiary care – January 2018.
Key recommendations from guidance:

1.0 Introduction

1.1 Shared Care Prescribing guidelines are local policies to enable General Practitioners to accept responsibility for the prescribing and monitoring of medicines/ treatments in primary care in agreement with the initiating service.
1.4 Where possible shared acre should be disease specific rather than medicine specific and link into complement local integrated care pathways and shared acre policies. Medicines and conditions suitable for shared care will be identified by local medicines committees and will be classified as AMBER (AMBER 1 for Lincolnshire) through the traffic light system. … However it should be remembered that the provision of shared care prescribing guidelines does not necessarily mean that the GP has to agree to accept clinical and legal responsibility for prescribing; that they should only do so if they feel clinically confident in managing that condition.

2.3 reasonable predictable clinical situation

2.3.1 Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stale or predictable.

2.4 Agreement of shared care between consultant and GP

2.4.1 Referral to the GP should only take place once the GP has agreed in each individual case and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that the supply arrangements have been finalised. The secondary/ tertiary provider must supply an adequate amount of the medication to cover the transition period. The patiet should then be informed to obtain further prescriptions from the GP.

2.7 Clear definition of responsibility

2.7.1 The areas of care for which each clinician has responsibility should be clearly defined.

2.8 Clinical responsibility

2.8.1 Clinical responsibility for prescribing is held by the person signing the prescription who must also ensure adequate monitoring.

2.9 Communication network & emergency support

2.9.1.Telephone details and (if appropriate) secure email addresses of both parties should be exchanged and recorded. This will enable the practice to access timely advice, guidance and information if problems arise, and will also enable secondary care clinicians to easily contact the GP if necessary. This should include out of hours contact numbers, how to access the on-call duty doctor. Patients and their carers should also be provided with contact details for support and help if required both in and out of hours.
2.9.2 People who are being treated on the advice of a secondary acre team, but are no longer being seen in that setting , may still need a review should problems arise. The appropriate level of care or advice should be available from the secondary care team in a timely manner without necessarily requiring a new referral.

6.0 Monitoring

6.0.1 All appropriate monitoring arrangements must be fulfilled. The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered.

Drug Details

Approved Name: **Sulfasalazine**
Brand Name: Generic, Salazopyrin®
Form and Strength: 500mg tablets, enteric coated tablets 500mg,suspension 250mg/5ml.
Only the Sulfasalazine E.C is licensed for treatment of Rheumatoid Arthritis and is the product which should be used first-line. The suspension should be reserved for use for those with proven swallowing difficulties when a liquid formulation is clinically indicated.

Specialist Responsibilities

The specialist secondary/tertiary care service will:
1. Send a letter to the GP requesting that the GP participates in shared care. As part of the communication the GP should be signposted to where they can find a copy of the shared care protocol e.g. the PACEF website http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef
2. Ensure that, where prescribing has been initiated by the specialist, the patient will receive supplies of sulfasalazine from the hospital or prescribed from the hospital on FP10 until the GP formally agrees to shared care.
3. Conduct initial tests of complete and differential blood counts, LFTs and renal Function, ESR and CRP.
4. Initiate and stabilise patient on sulfasalazine therapy.
5. Assess the patient's response to sulfasazine.
6. Liaise with the GP regarding conducting and interpreting future monitoring tests.
7. Undertake monitoring at appropriate intervals until dose stabilised and GP has agreed to undertake routine monitoring.
8. Provide the patient with a leaflet specifically advising patients on blood dyscrasias.
9. Periodically review the patient's clinical condition and communicate promptly to the GP any changes in dose or monitoring requirements.
10. Advise the GP on when to adjust dose, stop treatment or consult with specialist. dosage alterations where appropriate.
11. Be available to give advice to the GP and ensure that clear backup arrangements exist for GPs to obtain advice and support. (See contact details)

GP Responsibilities

The GP will:
1. Notify the consultant in writing that s/he agrees to participate in shared care.
2. Monitor the patient's overall health and wellbeing.
3. Monitor for adverse effects and drug interactions.
4. Prescribe the medication once shared care has been agreed.
5. Carry out monitoring tests according to guidelines specified in the monitoring section.
6. Act promptly on the results of the blood tests and adjust or stop the dose if appropriate.

If in doubt STOP the treatment and contact the Specialist – within 7 days.

Referral Criteria

1. Patients will have received at least 3 months of sulfasalazine therapy on hospital prescription.
2. Patients will have been stabilised on a suitable dose of sulfasalazine. During this time it may be more convenient for the patient to have blood tests conducted at the GP surgery, but the responsibility for ensuring that the monitoring is done and the interpretation of the results remains with the specialist until the GP has agreed to shared care.
3. The specialist will have carried out an assessment of efficacy.

Licensed Indications

Rheumatology

Treatment of active rheumatoid arthritis.

Recommended Dosage and Administration

Rheumatoid Arthritis

Treatment is commenced at a dose of 500mg daily for one week and increased by 500mg daily each week to a maximum of 2-3g daily in divided doses according to the schedule shown below:
First week: one tablet each evening;
Second week: one tablet each morning and each evening;
Third week: one tablet each morning and two tablets each evening;
Fourth week: two tablets each morning and two tablets each evening.

Dose escalation above 2g is only rarely encountered.
Alternatively, the total daily dose may be divided and taken three or four times a day.
Should a patient experience nausea, the dose should be reduced to a previously tolerated dose for one week and then increased.
It is recognised that the licensing restrictions of EC and non-coated preparations result from commercial considerations and that some specialists are happy to use non-coated tablets for the treatment of RA.

Background Pharmacology

Rheumatoid arthritis is common and affects over 1% of the population. The disease runs a variable and unpredictable course. Research has shown that early intervention with disease specific disease-modifying antirheumatic drugs (DMARDS) is the cornerstone of treatment. Used in the early stages they may curb or arrest the progressive synovitis and joint destruction and therefore limit joint disability.
Sulfasalazine acts by suppressing the inflammatory activity of RA. It is composed of sulphapyridine (a sulphonamide) and 5-aminosalicylic acid joined together by an azo bond. When taken orally, the majority of the dose reaches the colon where the azo bond is cleaved to release the separate components. In RA, sulfasalazine is thought to act as a disease modifying agent. Clinical and haematological response may be seen after one month of treatment, but may be delayed for up to 12 weeks.

Preparations Available

Sulfasalazine is available as both enteric coated and uncoated tablets containing 500mg of sulfasalazine.
N.B. Only enteric coated sulphasalazine tablets are licensed for use in patients with RA. This is due to commercial reasons rather than any absolute contraindication to the use of standard release sulfasalazine in RA patients.

Adverse Effects

For further information on adverse effects please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk

About 75% of adverse effects occur within 3 months of initiating therapy and over 90% by 6 months. Some undesirable effects are dose-dependent and symptoms can often be alleviated by reduction of the dose. Side effects due to both sulphapyridine and 5-ASA can occur. Patients with slow acetylator status are more likely to experience adverse effects related to sulphapyridine.

Common adverse effects (as listed in BNF)
Arthralgia, cough,diarrhoea ,dizziness, fever, gastrointestinal discomfort, headache, insomnia,leucopenia, nausea, skin reactions, stomatitis, taste altered,tinnitus, urine abnormalities.vomiting.

Uncommon adverse effects
Alopecia, depression, dyspnoea, face oedema,myalgia, photosensitivity reaction, seizure,thrombocytopenia, vasculitis, vertigo.

Rare or very rare adverse effects
Agranulocytosis. Bone marrow disorders, cardiac inflammation, hepatitis, neutropenia, pancreatitis, peripheral neuropathy, renal impairment, respiratory disorders.

Frequency not known
Anaemia, angioedema,appetite decreased, ataxia, cyanosis, encephalopathy, eosinophilia, haemolytic anaemia,hallucination, hepatic failure, hyperthrombinaemia, lymphadenopathy, macrocytosis, meningitis aseptic, methaemoglobinaemia, nephrotic syndrome, nephritis tubulointersititial, oligozoospermia (reversible), parotitis, periorbital oedema, pseudomembraneous enterocolitis, serum sickness, severe cutaneous adverse reactions (SCARs), smell disorders, systemic lupus erythematosus (SLE) yellow discolouration of body fluids. ulcerative colitis aggravated.

Drug Interactions

For detailed information on drug interactions, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk
Below is a summary of some of the key interactions.

Azathioprine
Possible increased risk of leucopenia when given with sulfasalazine

Digoxin
Sulfasalazine possibly reduces absorption of digoxin

Folic acid
Sulfasalazine possibly reduces absorption of folic acid.

Folinic acid
Sulfasalazine possibly reduces the absorption of folinic acid

Precautions and Contraindications

For further information on contraindications and cautions in use, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk

Contraindications
Sulfasalazine is contraindicated in patients with a history of sensitivity to sulfasalazine,sulphonamides or salicylates,
Acute Porphyrias
Severe renal failure
Pregnancy and breast feeding
Suspected serious infection - Stop sulfasalazine in all cases of active or suspected infection.
Patients with poor respiratory reserve

Cautions in use
Patients with a history of allergy or asthma.
Hepatic impairment use with caution.
Renal impairment – Renal function should be monitored more frequently if used in renal impairment. Risk of toxicity including crystalluria in moderate impairment-ensure high fluid intake. Avoid use in severe renal impairment.
Limit alcohol content to within national recommendations.
Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency should be closely observed for signs of haemolytic anaemia.
Patients with known anti-nuclear antibody (ANA) as can induce lupus like illness.
Patients with blood dyscrasias. Close monitoring of full blood counts including differential white cell count and platelet count is considered essential,
Pregnancy – theoretical risk of neonatal haemolysis; adequate folate supplements should be given to mother and dose of sulfasalazine should not exceed 2gram/day.Caution is advised in the third trimester as other sulphonamides have caused jaundice in the new-born when given near term.
Breastfeeding – small amounts in milk – theoretical risk of neonatal haemolysis.
Sulfasalazine can be prescribed to men of childbearing potential although there may be transient reversible oligospermia.
Folic acid supplement should be prescribed to those trying to conceive and during pregnancy.
Caution in use if a contact lens wearer, may stain lens due to discolouration of body fluids (yellow/orange)

Monitoring

FBC, U&E, LFT, Creatinine Clearance prior to commencing treatment
FBC, U & E, LFT – fortnightly for 6 weeks and then monthly for 3 months and then every 3 months.
If stable after first year frequency of blood tests can be reduced to every 6 months. (FBC, LFT and U&E's..
BSR/BHPR guidelines state that after 1 year of therapy blood monitoring can be discontinued this will be at the discretion of the consultant rheumatologist.
Locally monitoring is sometimes decreased to once yearly.
Following dose changes repeat FBC, LFT one month after dose increases. If stable revert to usual monitoring regime.
Urgent FBC if patient complains of illness during initiation of treatment.

Patients should be asked about the presence of rash or oral ulceration at each visit.

Treatment should be stopped and specialist advice sought if:

WBC below 3.5 x 10^9/l
Neutrophils below 2.0 x 10^9/l
Platelets below 150 x 10^9/l
AST, ALT or Alk. Phos show greater than 2 fold increase
Rash or oral ulceration

Withhold until the FBC result is available if the patient shows abnormal bruising or complains of a sore throat.

If MCV>105fl investigate and if B12 or folate, low start appropriate supplementation.

Nausea/headache/dizziness – if possible continue. May have to reduce dose or stop if severe.
Abnormal bruising or severe sore throat: Check FBC immediately and withhold until results available. Discuss with the specialist team, if necessary.

Remember: if in doubt STOP the sulfasalzine and contact the specialist (within 7 days).

Indication of Likely Cost of Therapy in Primary Care

Sulfasalazine 500mg enteric coated tablets £8.43 (112)
Sulfasalazine 500mg tablets £6.94 (112)
Sulfasalazine 250mg/5ml oral sugar free suspension 500ml £44.51

Information Given to the Patient

ARC leaflet.
Warn patient that medicine may colour urine orange/yellow.
May stain soft contact lenses.
For EC tablets, swallow whole, not chewed, do not take indigestion remedies at the same time of day.

Contact Details

ULHT Rheumatology Team:
First contact the nurse's helpline
Rheumatology Nurses Lincoln (01522) 573828 (Helpline)
Rheumatology Nurses Pilgrim (01205) 445730

Dr Joshi's secretary (01522) 573036
Dr Obaid's secretary (01522) 573413
Dr Chikura's secretary (01522) 573413
Dr Palkonyai's secretary (01522) 573036

Note:
ULHT do not provide care for all patients on sulfasalazine for arthritis in Lincolnshire. The ULHT rheumatology team cannot provide advice and guidance for patients under the care of other units.

References

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4. Quick reference guideline for monitoring of disease modifying anti-rheumatic drug (DMARD) therapy. Updated November 2009.
5. South West Yorkshire Area Prescribing Committee Shared Care Guidelines Sulfasalazine Monitoring Protocol . last revised July 2012.
6. Drug Tariff January 2015
7. Lancashire Medicines Management Group Shared Care Guideline Sulfasalazine. September 2014.
8. Interface Pharmacist network Sulfasalazine gastroenterology/rheumatology shared care guideline. Accessed January 2015 – review date October 2011.
Additional references October update
9.Derbyshire Joint Area Prescribing Committee Shared Care Agreement. Sufasalazine for patients 16 years +. Reviewed August 2017.

Author(s)

Dr S. Obaid – Consultant Rheumatologist
Dr A Abhishek – Registrar Rheumatology
C.M Johnson – Interface Lead Pharmacist NHS Lincolnshire
Reviewed
C.M Johnson – Support Service Pharmacist, Optum MMO.
and Dr S. Obaid – Consultant Rheumatologist ULHT.
Charlotte Wright – Specialist Nurse, ULHT
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