Northern Lincolnshire
Area Prescribing Committee

Guidelines for the Prescribing of Rifaximin for Hepatic Encephalopathy

APPROVAL PROCESS

Written by:	Osman Ali
Reference:	https://www.nice.org.uk/guidance/ta337
Approved by:	HERPC
Ratified by:	Northern Lincolnshire APC
Review Date:	July 2023
Acknowledgements:	Adopted from HERPC https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/rifaximin.pdf

1. Background	Rifaximin is a non-absorbed semi-synthetic derivative of rifamycin with a wide spectrum of antibacterial activity against aerobic and anaerobic gram-positive and gram-negative organisms. It acts by binding to the β-subunit of bacterial DNA-dependent RNA polymerase resulting in inhibition of bacterial RNA synthesis. In hepatic encephalopathy (HE) it is thought to reduce the colony count of ammonia producing gut flora and to decrease the systemic absorption of ammonia from the intestinal lumen. Rifaximin should only be initiated by a Consultant Hepatologist or Consultant Gastroenterologist **Note** Rifaximin is also licensed for traveller's diarrhoea (at a different dose to that mentioned below) - not routinely commissioned within Northern Lincolnshire and Goole Rifaximin is also approved for treatment of bacterial colonisation of small bowel in immunodefficient patients– (at a different dose to that mentioned below). This is an unlicensed indication for prescribing by Consultant Immunologist only (**Red indication**)
2. Indications	Reducing recurrence of episodes of overt hepatic encephalopathy in adults (NICE TA337)
3. Locally agreed off-label use	None
4. Initiation and ongoing dose regime Note - •Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results for at least 4 weeks •The duration of treatment will be determined by the specialist based on clinical response and tolerability.	550mg twice daily. Initial 6 week treatment to be prescribed by the specialist (at least 6 weeks). It is anticipated that the GP will prescribe prescription following the one month specialist review. The specialist will continue to review the patient at 3 – 6 monthly intervals.

•All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician •Termination of treatment will be the responsibility of the specialist.	
5. Baseline investigations, initial monitoring and dose titration to be undertaken by specialist	**Baseline:** • LFT, month one and 3 monthly thereafter. • FBC • U&Es **Monitoring:** Consultant Hepatologist or Consultant Gastroenterologist. Practitioner will inform patient about expected response to treatment and side effects of medication. Written information to be given and discussed with patient. If there is no improvement in the level of encephalopathy or failure to prevent hospital admissions with hepatic encephalopathy then the Rifaximin will be stopped. The onset of encephalopathy is an indication for liver transplant so patients who are considered suitable candidates will be assessed. At transplantation Rifaximin will be stopped. In those patients who are not suitable for transplant but have responded to Rifaximin, the drug will be continued and it's use reviewed at clinic visits.

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<tr><td>6. Ongoing monitoring requirements to be undertaken by primary care.</td><td>The need for continuation of rifaximin will have been assessed by the consultant in clinics at one month post initiation of rifaximin. It is anticipated that GPs will continue the prescription of rifaximin following this month of treatment review. Rifaximin is licensed for HE in the UK and has few side effects, there being no on-going monitoring required by the GP. The patient will continue to be reviewed regularly in the Hepatology and Gastroenterology clinics, being followed up at least every 3 - 6 months after commencing rifaximin depending on individual patient condition.

GPs will be advised to ensure that if patients develop diarrhoea, that a stool sample is sent for culture and clostridium difficile toxin.</td></tr>
<tr><td>7. Responsibilities of clinicians involved</td><td>
<table>
<tr><th>Stage of treatment</th><th>Specialist</th><th>GP</th></tr>
<tr><td>Initiation</td><td>• Assess the patient following referral by GP.

• Prescribe initial 6 week supply

• Recommend appropriate treatment to GP.

• Carry out full baseline full blood count and biochemistry profile</td><td></td></tr>
<tr><td>Maintenance</td><td>• Assess clinical response to treatment
• Provide adequate advice and support for the GP</td><td>Prescribe on FP10
Monitor for adverse effects.

Refer back to consultant where necessary</td></tr>
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</td></tr>
<tr><td rowspan="2">8. Pharmaceutical aspects</td><td>Route of administration :</td><td>Oral</td></tr>
<tr><td>Formulation :</td><td>550mg Tablet</td></tr>
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<tr><td rowspan="2"></td><td>Administration details :</td><td>Take TWICE DAILY</td></tr>
<tr><td>Other important information:</td><td></td></tr>
<tr><td>9. Contraindications
Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.</td><td colspan="2">• Rifaximin may cause allergic reactions, rashes, and itching or more general side effects such as nausea, abdominal pain, dizziness, fatigue, headaches, muscle cramps and joint pain
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• Rifaximin can alter the normal bacteria in the colon and encourage overgrowth of certain bacteria such as Clostridium difficile, which can cause inflammation of the colon (pseudomembranous colitis). Patients who develop signs of pseudomembranous colitis after starting Rifaximin (diarrhoea, fever and abdominal pain) will be advised to contact their physician immediately.

• Contraindicated in patients with Rifamycin hypersensitivity</td></tr>
<tr><td>10. Significant interactions
For a comprehensive list consult the BNF or Summary of Product Characteristics (SPC)</td><td colspan="2">Due to the negligible gastrointestinal absorption of orally administered Rifaximin (less than 1%), the systemic drug interaction potential is low.

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).</td></tr>
<tr><td rowspan="7">11. Adverse Effects and management</td><td>Result</td><td>Action</td></tr>
<tr><td>Gastro-intestinal: Abdominal pain, Diarrhoea, Nausea.</td><td>Discuss with specialist immediately.</td></tr>
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<tr><td>12. Advice to patients and carers
The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient</td><td colspan="2">Consultant practitioner will inform patient about expected response to treatment and side effects of medication.

Written information to be given and discussed with patient.</td></tr>
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with any relevant information and advice, including patient information leaflets on individual medicines.	
13. Preconception care, Pregnancy and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	**Pregnancy** – discuss with specialist if patient is pregnant or planning pregnancy **Breast feeding** — present in milk in small amounts. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rifaximin therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.
14. Specialist contact information	Gastroenterologist Secretaries Dr Sarwar Secretary 03033 305192 Dr Mysore Secretary 03033 302754
15. Additional information	Advice will be given to the GP on duration of treatment and dose changes for each individual patient.
16. References	• BNF Monograph: https://bnf.nice.org.uk/drug/rifaximin.html • Summary of Product Characteristics: https://www.medicines.org.uk/emc/product/2976#gref
17. To be read in conjunction with the following documents	https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf