Royal Cornwall Hospitals NHS Trust

Policy Under Review

Please note that this policy is under review. It does, however, remain current Trust policy subject to any recent legislative changes, national policy instruction (NHS or Department of Health), or Trust Board decision. For guidance, please contact the Author/Owner.

Information Category	Detailed Information
Document Title:	Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients Shared Care Guideline V3.0
This document replaces (exact title of previous version):	Rifaximin for preventing episodes of overt hepatic encephalopathy in adult patients V2.2
Date Issued / Approved:	May 2022
Date Valid From:	June 2022
Date Valid To:	June 2026
Author / Owner:	Hepatology Team / Pharmacy - Head of Prescribing Support Unit
Contact details:	01872 253548
Brief summary of contents:	Some clinical issues and details of prescribing responsibilities for GP and specialists.
Suggested Keywords:	Rifaximin.
Target Audience:	**RCHT:** Yes **CFT:** No **CIOS ICB:** No
Executive Director responsible for Policy:	Chief Medical Officer
Approval route for consultation and ratification:	Cornwall Area Prescribing Committee
Manager confirming approval processes:	Richard Andrzejuk
Name of Governance Lead confirming consultation and ratification:	Kevin Wright

Information Category	Detailed Information
Links to key external standards:	None
Related Documents:	Summaries of Product Characteristics. NICE TA 337 (March 2015). Rifaximin for preventing episodes of overt hepatic encephalopathy.
Training Need Identified:	No
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet
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Royal Cornwall Hospitals NHS Trust

Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients Shared Care Guideline

V3.0

June 2022

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of rifaximin when used for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients ≥ 18 years of age.

1.2. This shared care guideline sets out details for the sharing of care of adult patients prescribed rifaximin. These guidelines provide additional limited information necessary to aid in the treatment of these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, ABPI summary of product characteristics, and do not replace them.

1.3. This version supersedes any previous versions of this document.

Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 please see the *Information Use Framework Policy* or contact the Information Governance Team rch-tr.infogov@nhs.net

2. The Guidance

2.1. Rifaximin has a broad spectrum of activity against gram positive and gram negative, aerobic and anaerobic bacteria. In inhibiting the division of urea-deaminating bacteria, rifaximin reduces the production of ammonia and other compounds which are believed to be important in the pathogenesis of hepatic encephalopathy.

2.2. Rifaximin 550 mg tablets are indicated for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients ≥ 18 years of age.

2.3. The Summary of Product Characteristics (SPC) advises that in the pivotal study, 91% of the patients were using concomitant lactulose. Lactulose dose: 15-30ml BD orally aiming for 2-3 bowel motions per day but not diarrhoea - aiming for soft stools rather than loose.

2.4. Preparations and Dosage

The recommended dose is one 550 mg tablet (Targaxan), twice a day. The clinical benefit was established from a controlled study in which subjects were treated for 6 months. The SPC states that “Treatment beyond 6 months should take into consideration the individual balance between benefits and risks, including those associated with the progression of hepatic dysfunction.” It also notes: “Treatment with rifaximin for periods up to 24 months (OLE study RFHE3002) did not result in any loss of effect regarding the protection from breakthrough overt HE episodes, and the reduction of the burden of hospitalization. Time to first breakthrough of overt HE episode analysis showed long-term maintenance of remission in both groups of patients, new and continuing rifaximin.”

Rifaximin can be administered with or without food, and should be given with a glass of water.

2.5. Contraindications and Precautions

2.5.1. Hypersensitivity to rifaximin, rifamycin-derivatives or to any of the product’s excipients.

2.5.2. Cases of intestinal obstruction.

2.5.3. Rifaximin is not recommended in pregnancy.

2.5.4. Rifaximin should be used with caution as follows:

- The potential association of rifaximin treatment with Clostridium difficile-associated disease and pseudomembranous colitis cannot be ruled out.
- Concomitant administration of rifaximin with other rifamycins is not recommended.
- Patients should be informed that despite the negligible absorption, in common with other rifamycins, rifaximin may cause a reddish discolouration of the urine.
- Hepatic Impairment: use with caution in patients with severe (Child-Pugh C) hepatic impairment and in patients with MELD (Model for End-Stage Liver Disease) score > 25.
- Whilst interactions have not been commonly reported, the use of additional contraceptive precautions is recommended, in particular if the oral contraceptive oestrogen content is below 50 micrograms.

2.6. Monitoring - Specialist Team

2.6.1. Hepatology team will exclude and/or treat other causes of encephalopathy before rifaximin initiation and review response 4 weeks after initiation of rifaximin.

2.6.2. Hepatology team will stop after 4 weeks if there is no improvement in level of encephalopathy or if intolerable adverse reactions occur.

2.6.3. If patients are responsive to rifaximin and it is well tolerated a further 2 month supply of rifaximin will be prescribed via the hospital team and a letter sent to GP at this point requesting shared care of prescribing.

2.6.4. At month 3 of therapy a consensus should be reached as to who will take responsibility for prescribing.

2.6.5. Patients will continue to be followed up by the Hepatology team at a liver clinic. The frequency of review will depend on the clinical status of the patient (at the discretion of the liver team) but will be no less frequent than every 6 months. Patients active on transplant list will be reviewed at monthly intervals until time of transplant.

2.7. Monitoring - General Practice

No specific requirements. Any deterioration in clinical state suggesting encephalopathy should be referred back to the hospital team.

2.8. Side Effects

Common adverse events (occurring in ≥1/100 to <1/10 of patients) as listed in the SPC: depression; dizziness; headache; dyspnoea; abdominal pain and distension; diarrhoea, nausea, vomiting, ascites, rashes, pruritus, mucle spasms, arthralgia, peripheral oedema. See SPC for full details of adverse events.

2.9. Significant Drug Interactions

2.9.1. Due to the lack of data and the potential for severe disruption of gut flora with unknown consequences, concomitant administration of rifaximin with other rifamycins is not recommended.

2.9.2. Whilst interactions have not been commonly reported, the use of additional contraceptive precautions is recommended, in particular if the oral contraceptive oestrogen content is below 50 micrograms.

2.9.3. The SPC states that in healthy subjects, clinical drug interaction studies demonstrated that rifaximin did not significantly affect the pharmacokinetics of CYP3A4 substrates, however, in hepatic impaired patients it cannot be excluded that rifaximin may decrease the exposure of concomitant CYP3A4 substrates administered (e.g. warfarin, antiepileptics, antiarrhythmics, oral contraceptives), due to the higher systemic exposure with respect to healthy subjects.

2.9.4. Both decreases and increases in international normalized ratio have been reported in patients maintained on warfarin and prescribed rifaximin. If co-administration is necessary, the international normalized ratio should be carefully monitored with the addition or withdrawal of rifaximin. Adjustments in the dose of oral anticoagulants may be necessary.

2.10. Areas of Responsibility for the Sharing of Care

2.10.1. These are suggested ways in which the responsibilities for the management of adult patients with who are prescribed **rifaximin** can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

2.10.2. In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.10.3. Specialist:

- Assessment of the patient as a candidate for treatment with rifaximin in line with NICE TA337 and local pathways for management of overt hepatic encephalopathy.
- Consideration of any contra-indications, special warnings and potential drug interactions of the intended treatment regimen.
- Counselling of the patient with regard to potential side effects of treatment.
- Ask the GP whether they are willing to participate in shared care using the suggested wording template (Appendix 3).
- A minimum of three month's treatment should be prescribed by the hospital e.g. initial one month (possibly as inpatient) and further two months after first clinic review. The GP must be informed in writing of the patient's diagnosis, the treatment regimen to be used (in particular whether rifaximin is to be prescribed concomitantly with lactulose), start date of treatment, review information and management advice. Where appropriate, the GP can be asked to take over the future prescribing of repeat treatment within this guidance.
- Review of the patient's treatment in regular outpatient appointments. Where treatment continues beyond six months the specialist should ensure a regular risk-benefit analysis is undertaken as part of ongoing review. Changes to therapy as a result of these reviews (or at any other time) should be reported to the GP promptly.
- Notifying the patient's GP if treatment is to be discontinued and the

reason for this.

- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.
- Reporting adverse events to the MHRA.

2.9.4. General Practitioner:

- To respond to the shared care request from the consultant in writing without undue delay
- Continue to prescribe the therapy requested, under the guidance of specialist.
- Prescribe one month of rifaximin at a time.
- Monitor patient at regular intervals in conjunction with specialist.
- Refer queries to the specialist, e.g. regarding treatment/side effects, and concerns about compliance with treatment.
- Reporting adverse events to the specialist and MHRA.
- Stopping treatment in the case of a severe adverse event or on instruction from the specialist

2.9.5. Patient / parent / guardian / carer:

- Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
- Attend appropriate consultant and GP appointments.
- Share any concerns in relation to treatment.
- Seek help urgently from the GP or specialist service if suffering with suspected side effects, or otherwise feeling unwell during treatment.

2.9.6. Back-up advice and support is available from the relevant clinical team

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	Audit and review tool using patient documentation.
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Inclusion & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients Shared Care Guideline V3.0
This document replaces (exact title of previous version):	Rifaximin for preventing episodes of overt hepatic encephalopathy in adult patients V2.2
Date Issued/Approved:	May 2022
Date Valid From:	June 2022
Date Valid To:	June 2025
Directorate / Department responsible (author/owner):	Hepatology Team / Pharmacy - Head of Prescribing Support Unit
Contact details:	01872 253548
Brief summary of contents:	Some clinical issues and details of prescribing responsibilities for GP and specialists
Suggested Keywords:	Rifaximin
Target Audience:	RCHT: Yes CFT: No KCCG: No
Executive Director responsible for Policy:	Medical Director
Approval route for consultation and ratification:	Cornwall Area Prescribing Committee
General Manager confirming approval processes:	Richard Andrzejuk
Name of Governance Lead confirming approval by specialty and care group management meetings:	Kevin Wright
Links to key external standards:	None
Related Documents:	Summaries of Product Characteristics NICE TA 337 (March 2015). Rifaximin for preventing episodes of overt hepatic encephalopathy
Training Need Identified?	No

Information Category	Detailed Information
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet
Document Library Folder/Sub Folder:	Clinical / Pharmacy

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
Mar 16	1.0	Initial issue	M Wilcock, Head of Prescribing Support Unit, Pharmacy
Nov 16	1.1	Minor amendment to text (including interactions)	M Wilcock, Head of Prescribing Support Unit, Pharmacy Department, RCHT
Mar 19	2.0	New format	M Wilcock, Head of Prescribing Support Unit, Pharmacy
March 2020	2.1	Appendix 3 added following FRG approval - CHA4215 Shared Care Agreement Letter Consultant Request	Demi Louise Kent, Corporate records Manager
Sept 2021	2.2	Replacement of shared care agreement letter with suggested template wording	M Wilcock, Head of Prescribing Support Unit, Pharmacy
May 2022	3.0	Lactulose dose at 2.3 altered Amendment of text at 2.6.5 to just Hepatology team rather than list of HCPs. Minor typographical errors corrected	M Wilcock, Head of Prescribing Support Unit, Pharmacy

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This document is only valid on the day of printing

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Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity & Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy / policy / proposal / service function to be assessed:	Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients Shared Care Guideline V3.0
Directorate and service area:	Pharmacy
Is this a new or existing Policy?	Existing
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow
Contact details:	01726 627953

Information Category	Detailed Information
1. **Policy Aim - Who is the Policy aimed at?** (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	To provide information on prescribing of rifaximin to enable General Practitioners to take over prescribing responsibility from secondary care.
2. **Policy Objectives**	To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)
3. **Policy Intended Outcomes**	Confident and competent prescribers, enabling medicines to be access in a primary care setting.
4. **How will you measure each outcome?**	Six monthly review
5. **Who is intended to benefit from the policy?**	General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.

Information Category	Detailed Information
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/ visitors: No • Local groups/ system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/ groups:** Cornwall Area Prescribing Committee
6c. What was the outcome of the consultation?	Agreed
6d. Have you used any of the following to assist your assessment?	**National or local statistics, audits, activity reports, process maps, complaints, staff or patient surveys:**

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	
Sex (male or female)	No	
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	
Religion or belief	No	
Marriage and civil partnership	No	

Protected Characteristic	(Yes or No)	Rationale
Pregnancy and maternity	No	
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis

Appendix 3. Suggested wording for Specialist communication re commencement of shared care

This patient is suitable for treatment with (insert drug name) for the treatment of (insert indication) which has been accepted for Shared Care. I am therefore requesting your agreement to share the care of this patient, as they are now stable on the treatment. Where baseline investigations are set out in the shared care protocol, I have carried these out.

Treatment was started on (insert date started) (insert dose).

If you are in agreement, please undertake monitoring and treatment from (insert date). (please note: date must be at least 1 month from stabilisation of treatment.)

Baseline tests: (insert information)

Next review with this department: (insert date)

You will be sent a written summary within (XX) days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking (insert drug name).

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.