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Royal Cornwall Hospitals NHS Trust

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

V2.0

April 2019

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 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.

1.4. **Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation**

The Trust has a duty under the DPA18 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 can't rely on Opt out, it must be Opt in.

The DPA18 covers how the Trust obtains, hold, record, use and store all personal and special category (e.g. Health) information in a secure and confidential manner. This Act covers all data and information whether held electronically or on paper and extends to databases, videos and other automated media about living individuals including but not limited to Human Resources and payroll records, medical records, other manual files, microfilm/fiche, pathology results, images and other sensitive data.

DPA18 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the DPA18 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.
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 3-4 bowel motions per day and this may be increased up to a maximum of 150ml per day in divided doses if needed.

2.3 **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 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.

2.4 **Contraindications and Precautions**
Hypersensitivity to rifaximin, rifamycin-derivatives or to any of the product’s excipients.
Cases of intestinal obstruction.
Rifaximin is not recommended in pregnancy.

2.4.1. Rifaximin should be used with caution as follows:

2.4.1.1. The potential association of rifaximin treatment with Clostridium difficile-associated disease and pseudomembranous colitis cannot be ruled out.

2.4.1.2. Concomitant administration of rifaximin with other rifamycins is not recommended.

2.4.1.3. Patients should be informed that despite the negligible absorption, in common with other rifamycins, rifaximin may cause a reddish discolouration of the urine.

2.4.1.4. 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.

2.4.1.5. 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.

2.5 **Monitoring - Specialist Team**

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

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

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

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

2.5.5. Patients will continue to be followed up by a Hepatologist, Nurse Consultant, specialist nurse or SpR 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.

2.6 **Monitoring - General Practice**

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

2.7 **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.

2.8 **Significant Drug Interactions**

2.8.1. 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.

2.8.2. 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.

2.8.3. 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.

2.8.4. 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.

2.9. Areas of Responsibility for the Sharing of Care

2.9.1. 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.

2.9.2. 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.

2.9.3. Specialist:

2.9.3.1. 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.

2.9.3.2. Consideration of any contra-indications, special warnings and potential drug interactions of the intended treatment regimen.

2.9.3.3. Counselling of the patient with regard to potential side effects of treatment.

2.9.3.4. Ask the GP whether they are willing to participate in shared care using the shared care agreement letter.

2.9.3.5. 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.

2.9.3.6. 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.

2.9.3.7. Notifying the patient's GP if treatment is to be discontinued and the reason for this.

2.9.3.8. 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.

2.9.3.9. Reporting adverse events to the MHRA.

2.9.4. General Practitioner:

2.9.4.1. If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter.

2.9.4.2. Continue to prescribe the therapy requested, under the guidance of specialist.

2.9.4.3. Prescribe one month of rifaximin at a time.

2.9.4.4. Monitor patient at regular intervals in conjunction with specialist.

2.9.4.5. Refer queries to the specialist, e.g. regarding treatment/side effects, and concerns about compliance with treatment.

2.9.4.6. Reporting adverse events to the specialist and MHRA.

2.9.4.7. Stopping treatment in the case of a severe adverse event or on instruction from the specialist

2.9.5. Patient / parent / guardian / carer:

2.9.5.1. Sign the shared care agreement letter

2.9.5.2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.

2.9.5.3. Attend appropriate consultant and GP appointments.

2.9.5.4. Share any concerns in relation to treatment.

2.9.5.5. 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

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	No specific tool
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

Document Title	Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients Shared Care Guideline V2.0		
Date Issued/Approved:	March 2019		
Date Valid From:	April 2019		
Date Valid To:	April 2022		
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	CFT	KCCG
	✓		✓
Executive Director responsible for Policy:	Medical Director		
Date revised:	March 2019		
This document replaces (exact title of previous version):	Rifaximin for preventing episodes of overt hepatic encephalopathy in adult patients V1.12		
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee		
Divisional Manager confirming approval processes	Karen Jarvill		
Name and Post Title of additional signatories	Not required		
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}		
	Name: Kevin Wright		
Signature of Executive Director giving approval	{Original Copy Signed}		

Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only	
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards	None indicated.			
Related Documents:	Summaries of Product Characteristics NICE TA 337 (March 2015). Rifaximin for preventing episodes of overt hepatic encephalopathy			
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
Mar 16	1.0	Initial issue	M Wilcock, Head of Prescribing Support Unit, Pharmacy
Nov16	1.1	Minor amendment to text (including interactions)	M Wilcock, Head of Prescribing Support Unit, Pharmacy
Mar19	2.0	New format	M Wilcock, Head of Prescribing Support Unit, Pharmacy

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document

This document has been created following the Royal Cornwall Hospitals NHS Trust Policy for the Development and Management of Knowledge, Procedural and Web Documents (The Policy on Policies). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Initial Equality Impact Assessment Form

This assessment will need to be completed in stages to allow for adequate consultation with the relevant groups.

<table>
<tr><td colspan="7">Rifaximin for Preventing Episodes of Overt Hepatic Encephalopathy in Adult Patients
Shared Care Guideline V2.0</td></tr>
<tr><td colspan="3">Directorate and service area: Pharmacy</td><td colspan="4">Is this a new or existing Policy?
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="4">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="6">To provide information on prescribing of rifaximin to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="6">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="6">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="6">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="6">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.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td colspan="2">Other</td></tr>
<tr><td>X</td><td></td><td></td><td>X</td><td colspan="2"></td></tr>
<tr><td colspan="6">Please record specific names of groups
Cornwall Area Prescribing Committee</td></tr>
<tr><td>What was the outcome of the consultation?</td><td colspan="6">Agreed</td></tr>
</table>

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:

Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No X**	

9. If you are **not** recommending a Full Impact assessment please explain why.

Not indicated.

Signature of policy developer / lead manager / director		Date of completion and submission
M Wilcock		March 2019
Names and signatures of members carrying out the Screening Assessment	1. M Wilcock 2. Policy Review Group (PRG)	**PRG APPROVED**

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead
c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

This EIA will not be uploaded to the Trust website without the signature of the Human Rights, Equality & Inclusion Lead.

A summary of the results will be published on the Trust's web site.

Signed __ M Wilcock

Date ____March 2019