BSW APC: BaNES, Swindon & Wiltshire (BSW) CCG, Avon & Wiltshire Mental Health Partnership NHS Trust (AWP), Royal United Hospitals Bath NHS Foundation Trust, Great Western Hospitals NHS Foundation Trust, Salisbury NHS Foundation Trust, Virgin Care, Swindon Community Health Services, Wiltshire Health & Care

SHARED CARE AGREEMENT

Rifaximin (Targaxan®) for the reduction in recurrence of episodes of overt hepatic encephalopathy (HE) – Adults

Amber TLS – 1 Month

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and in the patient's best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) concerned and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

Responsibilities of Secondary Care Specialist

- Assess the patient as a candidate for treatment with rifaximin in line with NICE guidance and local pathways for management of overt hepatic encephalopathy (HE).
- Initiate treatment and prescribe for the length of time agreed (1 month) – this should be enough time to allow optimisation of treatment and demonstrate that the patient's response is consistent.
- Discuss the benefits and side effects of treatment with the patient.
- Review concurrent medications for potential interactions prior to initiation.
- Undertake the clinical assessment and relevant monitoring at baseline and during the initiation period.
- Communicate details of treatment to GP (in writing or via secure email) within the first month of treatment and ask the GP whether he or she is willing to participate in shared care.
- Discuss shared care arrangements with the patient/carer, obtain their consent and explain their responsibilities.
- Review the patient's condition and monitor response to treatment regularly where indicated.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Supply GP with clinic letter or discharge summary within 14 days of an outpatient review or inpatient admission, and inform GP if patient does not attend scheduled clinic appointments.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Report adverse events to the MHRA.
- Stop treatment where appropriate or provide GP with advice on when to stop.

Responsibilities of GP/Primary Care Prescriber

- Reply to the request for shared care as soon as practicable using the forms linked here (in writing or via secure email).
- Prescribe medicine at the dose recommended after the initiation period.
- Continue to prescribe lactulose throughout treatment with rifaximin.
- Undertake ongoing clinical assessment and relevant monitoring following initiation period.
- Review any new concurrent medications for potential interactions.
- Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Report adverse events to the specialist and MHRA (yellow card scheme).
- Stop treatment on the advice of the specialist.

Responsibilities of Patient/Carer

- Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
- Share any concerns in relation to treatment with medicine.
- Report any adverse effects to the specialist or GP whilst taking the medicine.
- Attend appointments for clinical review and monitoring.
- If the patient is seen by another service, clinic, or hospital, they should advise the healthcare professionals offering treatment about their treatment, particularly if new medicines are administered or prescribed.

1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	**Summary of condition.** • Rifaximin is a minimally absorbed derivative of the antibiotic rifamycin, which decreases the intestinal production and absorption of ammonia, a key player in the pathogenesis of HE. • Rifaximin is considered as an addition to lactulose and after potential precipitating factors for HE have been investigated, identified and addressed. **Treatment Aims (Therapeutic plan)** To reduce "the recurrence of episodes of overt hepatic encephalopathy in people aged 18 years or older". Additional aims include: • Reduction in hospital admissions • Reduction in hospital length of stay • Improvement in quality of life
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	• Rifaximin is indicated as an option to reduce episodes of overt hepatic encephalopathy. • Rifaximin is a non-absorbed antibacterial agent. Rifaximin has a broad antimicrobial spectrum against most of the Gram-positive and negative, aerobic and anaerobic bacteria, including ammonia producing species. Rifaximin may inhibit the division of urea-deaminating bacteria, thereby reducing the production of ammonia and other compounds that are believed to be important to the pathogenesis of hepatic encephalopathy.
3. Pharmaceutical aspects	Route of administration: — Orally with a glass of water Formulation: — 550 mg film-coated tablets Administration details: — Can be administered with or without food Other important information: — Click or tap here to enter text.
4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results. 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. The duration of treatment will be determined by the specialist, based on clinical response and tolerability. Termination of treatment will be the responsibility of the specialist.	**Treatment Schedule (including dosage and administration)** • Rifaximin 550mg, orally, twice daily. The dose should be taken with a glass of water and can be administered with or without food Duration of treatment with rifaximin will be frequently reviewed by the specialist, but may be expected to continue: • Until liver transplantation or death Rifaximin may be stopped by the specialist if: • There is evidence of lack of efficacy (e.g. further recurrent episodes with other precipitants, such as infections or GI bleeding or electrolyte disturbance). • There is a significant improvement or deterioration in liver function (e.g. with antiviral therapy, or in context of liver failure, respectively) • The patient does not tolerate therapy

5. Ongoing monitoring requirements to be undertaken by primary care	• Regular review in Gastro/Hepatology Outpatients (e.g., 4–12-week intervals, as appropriate) • There are no monitoring specific tests required however monitoring for signs of HE is prudent.
6. Action(s) to be taken by primary care if abnormal result(s)	• Refer to specialist if there are signs of overt HE.
7. Cautions and contraindications Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	**Contraindications:** • Hypersensitivity to rifaximin, rifamycin-derivatives or to any of the excipients. • Cases of intestinal obstruction **Cautions:** • Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including rifaximin. The potential association of rifaximin treatment with CDAD and pseudomembranous colitis (PMC) cannot be ruled out. • 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. • Patients should be informed that despite the negligible absorption of the drug (less than 1%), like all rifamycin derivatives, 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. • Caution should be exercised when concomitant use of rifaximin and a P-glycoprotein such as ciclosporin is needed. • Both decreases and increases in international normalized ratio (in some cases with bleeding events) 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 treatment with rifaximin. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5). • This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.
8. Significant medicine and food interactions and management For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)	• There is no experience regarding administration of rifaximin to subjects who are taking another rifamycin antibacterial agent to treat a systemic bacterial infection. • 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. • 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.

<table>
<tr><td></td><td colspan="2">• In healthy subjects, co-administration of a single dose of ciclosporin (600 mg), a potent P-glycoprotein inhibitor, with a single dose of rifaximin (550 mg) resulted in 83-fold and 124-fold increases in rifaximin mean Cmax and AUC∞. The clinical significance of this increase in systemic exposure is unknown.</td></tr>
<tr><td rowspan="2">9. Adverse effects and management
Include details of incidence, identification, importance and management. For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)</td><td>Adverse Effect</td><td>Action to be taken if detected</td></tr>
<tr><td>• The side effect profile is very good as the drug is minimally absorbed. Side effects are usually mild or moderate and include nausea, vomiting, abdominal pain, flatulence, diarrhoea, dyspnoea, headache, depression, dizziness, muscle spasm, peripheral oedema, rash, pruritus; Uncommonly: anorexia, dry mouth, anxiety, confusional state, convulsions, hypoaesthesia, dysuria, anaemia, hyperkalaemia; rarely blood pressure changes, constipation.</td><td>• Refer to specialist if patient develops overt HE or reports intolerable side effects.</td></tr>
<tr><td>10. 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 with any relevant information and advice, including patient information leaflets on individual medicines.</td><td colspan="2">• Rifaximin may cause colouration of urine to a red/orange colour, but this is not harmful.
• Lactulose should be continued whilst taking rifaximin.</td></tr>
<tr><td>11. 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.</td><td colspan="2">• It is unknown whether rifaximin/metabolites are excreted in human milk. A risk to the breast-fed child cannot be excluded.
• A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rifaximin therapy considering the benefit of breast feeding for the child and the benefit of therapy for the woman
• Rifaximin is not recommended in pregnancy. There is no or limited data from the use of rifaximin in pregnant women.</td></tr>
<tr><td rowspan="13">12. Specialist contact information</td><td colspan="2">RUH</td></tr>
<tr><td>E-mail: ruh-tr.gasreosecs@nhs.net</td><td></td></tr>
<tr><td>Dr Julia Maltby- Secretary:</td><td>01225 821569</td></tr>
<tr><td>Dr Sakitha Paranahewa- Secretary:</td><td>01225 821569</td></tr>
<tr><td>Dr Terry Farrant- Secretary:</td><td>01225 826675</td></tr>
<tr><td>GWH:</td><td></td></tr>
<tr><td>E-mail: gwh.hepatologyteam@nhs.net</td><td></td></tr>
<tr><td>Dr Moby Joseph</td><td>mobyjoseph@nhs.net</td></tr>
<tr><td>Dr Manish Hegde</td><td>manish.hegde@nhs.net</td></tr>
<tr><td>SFT:</td><td></td></tr>
<tr><td>E-mail: sft.admin.gastro@nhs.net</td><td>01722 336262 Ext 5590 (Medical secretary)</td></tr>
<tr><td colspan="2">Other Specialist Contact Information</td></tr>
<tr><td colspan="2">• Cynapsis app can be used to contact gastroenterology for advice & guidance at RUH and in the next couple of months for SFT enquiries.</td></tr>
<tr><td>13. Additional information</td><td colspan="2">• Click or tap here to enter text.</td></tr>
</table>

For example, process for when Specialist or GP changes roles; specific issues related to patient age/ capacity/ specific monitoring.	
14. References	• Summary of Product Characteristics for Rifaximin (Targaxan) via https://www.medicines.org.uk/emc/product/2976/smpc • BNF online via https://bnf.nice.org.uk/ (Accessed 30/12/21) • NICE technology appraisal guidance [TA337]. Rifaximin for preventing episodes of overt hepatic encephalopathy. March 2015. https://www.nice.org.uk/guidance/ta337 (Accessed 30/12/21)
15. To be read in conjunction with the following documents	• NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/

Shared Care Response Templates:
Shared Care Agreements - Medicines

Written by (Author Name, Organisation & Role):	Adapted from version by SFT and BCAP by Nicola Young by Rachel Hobson
Contributors:	Click or tap here to enter text.
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