Frimley Health NHS Foundation Trust
North East Hampshire and Farnham CCG
East Berkshire CCG
Surrey Heath CCG

SHARED CARE Guideline – Amber Traffic Light Classification	
Name of medicine	Rifaximin 550mg tablets
Indication (including whether for adults and/or children)	Rifaximin 550 mg tablets are indicated for the reduction in recurrence of episodes of overt hepatic encephalopathy in patient's ≥ 18 years of age.
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Date ratified by Frimley Health APC (FH APC):	December 2017

The Shared Care Guideline (SCG) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface.
This **AMBER** shared care sets out the patient pathway relating to this medicine and any information not available in the British National Formulary and manufacturer's Summary of Product Characteristics. Prescribing must be carried out with reference to those publications whenever appropriate.
The SCG must be used in conjunction with the agreed core roles and responsibilities stated below.
An agreement notification form is included in annex A for communication of request for shared care from provider and agreement to taken on prescribing by primary care.

Roles and Responsibilities

Listed below are specific medicine/indication related responsibilities that are additional to those core roles and responsibilities.

Consultant / 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
- Ensure the treatment is being prescribed for reduction in recurrence of episodes of overt hepatic encephalopathy in patients ≥ 18 years. All other indications have not been agreed for shared care.
- Consideration of any contra-indications, special warnings and potential drug interactions of the intended treatment regimen. See section below for more details.
- A minimum of one month's treatment should be dispensed by the hospital. Arrange regular follow up via gastroenterology clinic. 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.

TEMPLATE VERSION CONTROL **Template**		**Adapted from the Prescribing Clinical Network**
Reason for Update or New: New		Author: PCN
Valid from: Jan 2018	Review date: Jan 2021	Approved by: FH APC Dec 2017
Version: 1	Supersedes version: N/A	

- 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. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition. Changes to therapy as a result of these reviews (or at any other time) should be reported to the GP promptly and if treatment is to be discontinued and the reason for this.
- Ensuring that clear arrangements are in place for GP to obtain back up, advice and support.
- This medicinal product is subject to additional monitoring under the MHRA black triangle scheme. The specialist should report known or suspected adverse events to the MHRA via the Yellow Card scheme and share this information with the GP.

Primary Care Prescriber

- Responding to the request from the specialist to take on prescribing as soon as is practicable.
- Prescribe rifaximin at the licensed dose for this indication and continue to prescribe the therapy requested, under the guidance of specialist.
- Support patient in avoiding factors which could precipitate hepatic encephalopathy, for example dehydration and some medicines including sedatives.
- Ensure patient compliant with recommended laxatives to produce two soft stools daily.
- Refer queries to the specialist, e.g. regarding treatment/side effects, and concerns about compliance with treatment.
- Due to the effects on the gut flora, the effectiveness of oral oestrogenic contraceptives could decrease after rifaximin administration. However, such interactions have not been commonly reported. It is recommended to take additional contraceptive precautions, in particular if the oestrogen content of oral contraceptives is less than 50 micrograms
- If patients develop diarrhoea for which there is no other reasonable explanation a stool sample should be sent for *Clostridium difficile* culture and toxin detection.
- Refer patient to the specialist if his or her condition deteriorates.
- Stopping treatment on instruction of the specialist.
- Report adverse events to the specialist and MHRA.

Patient Relatives & Carers

- 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 with rifaximin.
- Seek help urgently from the GP or specialist service if suffering with suspected side effects, or otherwise feeling unwell during treatment.
- Seek urgent medical help if severe diarrhoea occurs
- 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.

Key information on the medicine

Please refer to the current edition of the British National Formulary (BNF), available at https://bnf.nice.org.uk/ and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

Background to disease and use of medicine for the given indication

Rifaximin needs to be initiated by Consultant Gastroenterologists or Hepatologists because of the complexity of the underlying disease, and not due to complex monitoring of the treatment.
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.
Hepatic encephalopathy (HE) is a reversible neuropsychiatric disorder caused by accumulation of toxins in the bloodstream that are normally removed by the liver. HE encompasses a spectrum of neuropsychiatric abnormalities seen in patients with established liver disease, and is most commonly associated with liver cirrhosis. Patients with HE may experience symptoms ranging from subtle neurological abnormalities (e.g., mood alterations, changes in reaction times in daily activities such as driving), to severe neurological impairment (e.g., difficulty in moving and communicating) and in extreme cases, coma.

First line treatment in the pharmacological management of HE involves using synthetic disaccharides osmotic laxatives (such as lactulose) to inhibit ammonia-generating bacteria.

Traffic light status for indication Amber.

Indication

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.

Dosage and Administration

Recommended dose: 550 mg twice a day. Rifaximin should be taken orally with a glass of water, with or without food.

Monitoring

- Gastroenterology team will exclude and/or treat other causes of encephalopathy before rifaximin initiation and review response 4 weeks after initiation of rifaximin.
- Gastroenterology team will stop after 4 weeks if there is no improvement in level of encephalopathy or if intolerable adverse reactions occur.
- 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 of requesting shared care of prescribing.
- At month 3 of therapy a consensus should be reached as to who will take responsibility for repeat prescribing.
- Patients will continue to be followed up by a Gastroenterologist,. 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

Dose change when on maintenance:

- There is no dose adjustment required in elderly and patients with hepatic impairment.
- No clinical data are available on the use of rifaximin in patients with impaired renal function

Contraindications to rifaximin treatment:

Hypersensitivity to rifaximin, rifamycin-derivatives or to any of the excipients listed in the summary of product characteristics.

- Cases of intestinal obstruction.
- Patient aged <18 years.
- Patient is pregnant or breastfeeding

Side effects listed in the BNF (in order of frequency): nausea, vomiting, abdominal pain, flatulence, diarrhoea, dyspnoea, headache, depression, dizziness, muscle spasm, rash, pruritus; *less commonly:* anorexia, taste disturbances, dry mouth, peripheral oedema, sleep disturbances, anxiety, memory impairment, convulsions, hypoaesthesia, paraesthesia, antibiotic-associated colitis, influenza-like symptoms, dysuria, polyuria, glycosuria, polymenorrhoea, blood disorders, hyperkalaemia; rarely blood pressure changes, constipation; *also reported:* syncope.

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.

Interactions

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.

Due to the effects on the gut flora, the effectiveness of oral oestrogenic contraceptives could decrease after rifaximin administration. However, such interactions have not been commonly reported. It is recommended to take additional contraceptive precautions, in particular if the oestrogen content of oral contraceptives is less than 50 µg.

Support and Advice Contact Details for Primary Care Prescribers:

Name	Speciality	Telephone No.	Email address
Hepatology Team	Hepatology	01276 604 239	Fhft.liver.nurse@nhs.net
Hospital Pharmacy		01276 604 604	
Out of Hours			

Annex A: Shared care agreement notification form for medicines and indications approved as amber on the Frimley Health Foundation Trust Formulary

For the attention of the Practice Manager

FAX – Confirm you have the correct Safe Haven Fax Number before sending
E-mail – Confirm both sender and recipient e-mail addresses are nhs.net before sending

To:	[Recipient Name]	Fax:	[fax number]
From:	[Your Name]	Date:	[Click to select date]
Re:	[Subject]	Pages:	[number of pages]
cc:	[Name]		

[Notes]

Name of medicine	XXXXXX
Indication	XXXXXX

Person removing form from fax machine	
Relevant patients GP available to action within 5 days (if not Trust needs to be informed on day of receipt of request)	Yes/ No
If GP is NOT available within 5 days, please communicate to the requesting specialist the date when the GP will be available	

Hospital/ Patient information		**Practice information**	
Consultant Making Request		GP Name:	
Consultant Speciality Details:		Practice:	
Patient Name:		I agree to undertake shared care:	
Patient NHS Number:		I do not agree to undertake shared care:	
Patient Hospital Number:		If NOT please give reasons:	
Patient DOB:		Signed:	
Drug Name/ Dose:		Date:	
Next Prescription Due:		Please return form to:	Specialist safe haven fax number
Discharge letter written and sent:			
Please refer to the Frimley Health Foundation Trust Formulary for relevant shared care documents.			

Primary Care Prescriber should reply within 5 days of receipt of this form indicating participation (or not) in shared care of the patient