

## Shared Care Guideline

### *Rifaximin (Targaxan®) 550mg tablets*

### Treatment of hepatic encephalopathy

Dear GP

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of rifaximin for patients with hepatic encephalopathy can be shared between the specialist (i.e., hepatologist), the patient and yourselves as the patient's general practitioner (GP).

You have been invited to participate but if you are not confident to undertake these roles, then you are under no obligation to do so. We would be grateful if you would reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP, patient, and their carers. The intention to 'share care' should be explained to the patient and/or their carers by the doctor initiating treatment. It is important that patients and/or their carers are consulted about this treatment and agree with it.

When patients are referred into a specialist service outside of their Integrated Care System (ICS), the referring Integrated Care Boards (ICB) become an associate to the contract held between the Provider Trust and their host commissioner. This includes the arrangements it has regarding access to medicines (i.e., treatments for continuation in primary care on the local Formulary, including any associated documentation to support the transfer of prescribing responsibility e.g., shared care agreements). Therefore, there is an expectation that GP practices/Primary Care Networks who refer patients into a Provider Trust follow the Formulary prescribing status and practice relevant to the Trust, including the use of local interface documents associated role and responsibilities.

#### Shared Care criteria

Patients will have been stabilised, receiving a therapeutic dose of rifaximin with time allowed for common adverse events and side effects to have occurred before referral to the GP. A minimum period of one month's stabilisation is required before shared care arrangements are requested.

#### Shared care responsibilities

##### Consultant and Specialist Nurse

1. Send a letter/electronic request to the GP requesting shared care for this patient.
2. Advise the GP of any other co-morbidities via the letter/electronic request.
3. Initiate treatment as per local Trust guideline and prescribe rifaximin until the GP formally agrees to shared care (as a minimum, supply the first 1 month's treatment or until patient is stabilised).
4. Clinical and laboratory supervision of patient by routine clinic follow-up every 3-6 months as per local Trust guideline.
5. Advise GP on review, duration, and discontinuation of treatment where necessary as per local Trust guideline.

6. Review each patient at 6 months to assess the need for continuation/cessation of rifaximin.
7. Stop rifaximin if there is a failure of therapy (i.e., no change in frequency of admissions after 6 months of therapy) or occurrence of super-infections.
8. If rifaximin is required after 6 months, risks and benefits of treatment should be considered and discussed with the patient.
9. Monitoring the progression of disease
10. Evaluation of any adverse effects reported by GP or patient.
11. Ensure that back-up advice is available at all times. See contact details below for further information.

### General Practitioner

1. Monitor patient's overall health and well-being.
2. Report any adverse events reported by the patient to consultant (hepatology / gastroenterology registrar if out of hours) and MHRA (via the Yellow Card scheme) where appropriate.
3. Prescribe the drug treatment as described.
4. To return a copy (this can be electronically) of the standard letter to the consultant accepting or declining shared care.

### Patient

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2. Take rifaximin as prescribed (if unavailable at your local pharmacy, start taking as soon as available).
3. Request prescriptions in advance to ensure continuation of supply.
4. Share any concerns in relation to treatment with rifaximin with the consultant hepatologist.
5. Inform specialist or GP of any other medication being taken, including over-the-counter products.
6. Report any adverse effects or warning symptoms (dizziness, diarrhoea, abdominal pain) to the specialist or GP whilst taking rifaximin.

### Integrated Care System

1. To support GPs in making the decision whether to accept clinical responsibility for prescribing.
2. To support Trusts in resolving issues that may arise because of shared care.

## Indication for Rifaximin (Targaxan®) 550mg tablets

Rifaximin (Targaxan®) 550mg tablet is indicated for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients  $\geq 18$  years of age.

Rifaximin (Targaxan®) 550mg tablet will be started for patients with a clear history of recurrent hepatic encephalopathy (> 2 episodes, equivalent to a Conn score of 2 or more) despite adequate lactulose therapy.

## Dose and Administration

Oral dosing: 550 mg twice daily with a glass of water.  
Available as 550 mg tablets (Targaxan®).

## Adverse Effects

Commonly reported side effects include:

- Depression
- Dizziness, headache
- Dyspnoea
- Rash, pruritis
- Muscle spasms, arthralgia
- Peripheral oedema

- Abdominal pain, distension, diarrhoea, nausea, vomiting, ascites

As the listed adverse effects may also be due to the underlying condition, it is important that all other non-drug related causes are excluded in the first instance.

In case of moderate or severe adverse effects not thought to be due to other causes, please contact the referring consultant for further advice.

In the case of confirmed *C. Difficile*, please stop Rifaximin and treat the *C. Difficile* infection before restarting rifaximin.

Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA (via the Yellow Card scheme).

For a full list of adverse effects, refer to the Targaxan® 550mg tablets Summary of Product Characteristics.

## 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. If CDAD positive, contact the consultant.

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.

Rifaximin may cause a reddish discolouration of the urine.

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

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.

All females of childbearing age should use reliable contraception e.g. barrier methods. The low dose contraceptive pill may have reduced efficacy.

For a full list of cautions, refer to the Targaxan® 550mg tablets Summary of Product Characteristics.

## Contraindications

- Hypersensitivity to rifaximin, rifamycin-derivatives or to excipients as listed in the Targaxan® 550mg tablets Summary of Product Characteristics<sup>2</sup>.
- Cases of intestinal obstruction.

For a full list of contraindications, refer to the Targaxan® 550mg tablets Summary of Product Characteristics.

## Drug Interactions

- In hepatic impaired patients 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. However, the significance of this is unknown.
- 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.
- Caution should be exercised when concomitant use of rifaximin and a P-glycoprotein such as ciclosporin is needed. Concentrations of rifaximin may be markedly raised; however the clinical significance of this is unknown.

For a full list of interactions, refer to the Targaxan® 550mg tablets Summary of Product Characteristics.

## References

1. Nathan M. Bass, Kevin D. Mullen, Arun Sanyal, et al. Rifaximin Treatment in Hepatic Encephalopathy. N Engl J Med [Internet]. 2010 [cited November 2023]; 362:1071-1081. Available from: DOI: 10.1056/NEJMoa0907893
2. National Institute for Health and Care Excellence. Rifaximin for preventing episodes of overt hepatic encephalopathy [Internet]. [London]: NICE; 2015 [cited November 2023]. (NICE technology appraisal [TA337]). Available from: <https://www.nice.org.uk/guidance/ta337>
3. Norgine. TARGAXAN 550 mg film-coated tablets – Summary of Product Characteristics (SmPC). [Internet]. 2022 [cited November 2023]. Available from: <https://www.medicines.org.uk/emc/product/2976/smpc>

## Contact Details

<b>Royal Free Hospital - Liver Unit</b>			
Switchboard Number:		0207 794 0500	
Hepatology Consultants:			
Dr L China	Ext 38097	Dr R Nathwani	Ext 38097
Dr A Dhar	Ext 38325	Prof A O'Brien	Ext 36167
Dr B Hogan	Ext 35056	Dr D Patch	Ext 38097
Prof R Jalan	Ext 36167	Dr J Potts	Ext 38325
Dr Y Kallis	Ext 38325	Dr J Ryan	Ext 36167
Dr B Kok	Ext 38325	Dr B Smith	Ext 35056
Dr N Kumar	Ext 35056	Prof D Thorburn	Ext 38325
Dr D Macdonald	Ext 35056	Dr P Trembling	Ext 35056
Dr A Marshall	Ext 31142	Prof E Tsochatzis	Ext 33575
Dr R Mookerjee	Ext 36167	Dr R Warburton	Ext 38325
Prof K Moore	Ext 34357	Dr R Westbrook	Ext 38325
Specialist Hepatology Pharmacist:		Bleeps 1961/1353 or Ext 31261	
Hepatology CNS:		Mobile: 07960 860 995 (Mon – Fri 09:00-17:00) <a href="mailto:rf-tr.hepatologycns@nhs.net">rf-tr.hepatologycns@nhs.net</a>	
Hepatology Registrar on-call:		Bleep 2530 (available 24 hrs per day)	

Pharmacy Medicines Information:	0207 830 2983 (Mon- Fri 11:00-17:00) <a href="mailto:Rf.medicinesadvice@nhs.net">Rf.medicinesadvice@nhs.net</a>
<b>Barnet Hospital – Liver Unit</b>	
Switchboard Number:	0208 216 4600
Hepatology Consultants:	
Dr L China	Ext 32335/07929789148
Dr R Nathwani	Ext 32335/07929789148
Dr N Kumar	Ext 32335/07929789148
<b>The North Middlesex Hospital</b>	
Switchboard Number:	0208 887 2000
Gastroenterology Consultants:	
Dr I Barnova	Dr P Maxwell
Dr R Bhattacharyya	Dr A Millar
Dr D Chowdhury	Dr C Somasundaram
Dr D Corrigan	Dr Z Thamer
Dr T Mangala	Dr J Wright
Dr D Majumdar	
Hepatology CNS:	
Katie Portou	
Laila Indiongco	

Document Control		
Date	Version	Action
April 2016	V1	New document
November 2020	V2	Updated to include further information on adverse events.
November 2023	V3	Updated to include further information on GP/PCN expectations within introduction. Updates include adding details on rifaximin brand, electronic communication and added interaction with p-glycoproteins such as ciclosporin. Contact details at RFH, Barnet and NMUH updated.

Groups / Individuals who have overseen the development of this guidance:	Dr A Marshall (Hepatology Consultant, RFL) Ms F Jessa (Hepatology Pharmacist, RFL) NCL ICB
Groups which were consulted and have given approval:	NCL Shared Care Group NCL ICB NCL Provider Trusts
File name:	Shared Care Guideline: Rifaximin for the treatment of hepatic encephalopathy
Version number:	3.0
Available on:	<a href="https://nclhealthandcare.org.uk/our-working-areas/medicines-optimisation/shared-care-guidelines-and-factsheets/">https://nclhealthandcare.org.uk/our-working-areas/medicines-optimisation/shared-care-guidelines-and-factsheets/</a>
Disseminated to:	Formulary Pharmacists and Commissioners
Equality impact assessment:	Nil identified
NCL Shared Care Group Approval date:	14 <sup>th</sup> May 2024
Review date:	14 <sup>th</sup> May 2027

**Rifaximin transfer form:** from [Trust] to GP practice - This may be sent electronically

**Section A: to be completed by secondary care** *Send to practice*

*This document is to request the shared care pathway of your patient and comprises an agreement between the GP and named consultant. The patient will continue to be seen by the named consultant as regular follow up.*

<i>Patient details (Name, DOB, address, NHS number)</i>	Clinic details
---	----------------

Department	<input type="text" value="Hepatology"/>		
Clinic phone	<input type="text"/>		
Consultant	<input type="text"/>	Email	<input type="text"/>
Indication for prescription	<input type="text" value="Hepatic encephalopathy"/>		
Drug prescribed	<input type="text" value="Rifaximin (Targaxan®) 550mg tablets"/>		
Date	Drug started <input type="text"/>	Current dose	<input type="text"/>
Relevant conditions	<input type="text"/>		
Monitoring variations	<input type="text"/>		
Date next blood test	<input type="text"/>	Next disease review due in	<input type="text"/> months' time.

**Section B: [Accept Shared Care] to be completed by practice** *Send back **FAO referring consultant** above*

The above patient has been accepted into our monitoring service.

Practice date for next blood test

Signed /  
Designation

Date

Practice details

**Section B: [Reject Shared Care] to be completed by practice** *Send back **FAO referring consultant** above*

The above patient has not been accepted into our monitoring service.

Reason

Signed /  
Designation

Date

Practice details