

Shared Care Guideline *Rifaximin (Targaxan®)* 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 are in agreement with it.

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

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 where appropriate.
3. Prescribe the drug treatment as described.
4. To return a copy 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.

CCG

1. To support GPs in making the decision whether or not to accept clinical responsibility for prescribing.
2. To support trusts in resolving issues that may arise as a result of shared care.

Indication

Rifaximin is indicated for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients ≥ 18 years of age.

Rifaximin 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.

Adverse Effects

- Depression
- Dizziness
- Dyspnoea
- Abdominal pain, vomiting
- Rash, pruritis
- Muscle spasms, arthralgia
- Peripheral oedema
- C. Difficile
- Pyrexia
- Insomnia

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 CHM. For a full list of adverse effects, refer to the 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 Summary of Product Characteristics.

Contraindications

- Hypersensitivity to rifaximin, rifamycin-derivatives.
- Cases of intestinal obstruction.

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.

References

1. Nathan M. Bass, Kevin D. Mullen, Arun Sanyal, et al - *Rifaximin Treatment in Hepatic Encephalopathy* - N Engl J Med 2010; 362:1071-1081 March 25, 2010 DOI: 10.1056/NEJMoa0907893
2. NICE TA 337 Rifaximin for preventing episodes of overt hepatic encephalopathy – March 2015 <https://www.nice.org.uk/guidance/ta337>
3. TARGAXAN 550 mg film-coated tablets SPC - Last Updated on eMC 21-Oct-2016 <http://www.medicines.org.uk/emc/medicine/27427>

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Document Control		
Date	Version	Action
April 2016	V1	Share Care produced Sheetal Shah - Principal Pharmacist, Hepatology& Gastroenterology, Royal Free London NHS Foundation Trust – November 2015. Agreed by Camden Clinical Commissioning Group MMC: 25 November 2015 Agreed by NCL Medicines Optimisation Network: 28 June 16 Ratified by NCL Joint Formulary Committee: 28 July 2016 Review date: October 2018
November 2020	V2	Shared care updated: Fatema Jessa, Specialist Hepatology Pharmacist, Royal Free London NHS Foundation Trust – November 2020 Update Approved: Sheetal Shah – Principal pharmacist, Hepatology and Gastroenterology, Royal Free London NHS Foundation Trust – November 2020 Aileen Marshall, Hepatology Consultant, Royal Free London NHS Foundation Trust - November 2020 Ratified by NCL Joint Formulary Committee: November 2020

Rifaximin transfer form: from [Trust] to GP practice

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>Fix address label here (ensure NHS no.on)</i>		<i>Clinic stamp or give details below</i>	
Department	<input type="text"/>		
Clinic phone (remove)	<input type="text"/>	Fax	<input type="text"/>
Consultant	<input type="text"/>	Email	<input type="text"/>
Indication for prescription	<input type="text"/>		
Drug prescribed	<input type="text"/>		
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

Practice stamp *Add fax no. below*

Signed /
Designation

Date

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

Practice stamp *Add fax no. below*

Signed /
Designation

Date