Name: Attach Banda Label here Address: Date of Birth: NHS number:

Coventry & Warwickshire Area Prescribing Committee

Shared Care Agreement

RIFAXIMIN: : Maintenance of Remission from Hepatic Encephalopathy

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of rifaximin can be shared between the specialist and general practitioner (GP). **GPs are invited to participate**. If the GP isn't confident to undertake these roles, then he/she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist**. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Specialist responsibilities

1. Identify and initiate rifaximin treatment in the outpatient clinic or during inpatient stay.
2. Discuss the risk/benefit of treatment with the patient.
3. Ask the GP whether he or she is willing to participate in shared care by faxing the template letter (Continue to prescribe until GP has agreed to take over prescribing).
4. Review clinical condition at regular intervals – minimum 6 monthly to determine need for ongoing treatment.
5. Keep GP informed on progress of the patient.
6. Advise when treatment should be discontinued.
7. Have a mechanism in place to receive rapid referral of a patient from the GP if required.
8. Report adverse events to the MHRA on a Yellow Card form and to the GP (if in CWPT via the Clinical Governance Pharmacist – see Medicines Policy Section 20).
9. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner responsibilities

1. Reply to the request for shared care as soon as practicable by faxing back signed form.
2. Continue the maintenance prescribing.
3. Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
4. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises

Patient/carer's role

1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2. To ensure medication is taken as prescribed.
3. Report any adverse effects or warning symptoms to the specialist or GP whilst taking rifaximin. The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card form, avail. at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours). The form can also be downloaded from http://yellowcard.mhra.gov.uk/

BACK-UP ADVICE AND SUPPORT: See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care.

SUPPORTING INFORMATION (see SPC for complete details/specific guidance http://emc.medicines.org.uk)

Licensed indications:
Prevention of recurrent episodes of overt hepatic encephalopathy in patients >18 years

Dosage and administration:
550mg twice daily PO.

Monitoring:
No specific drug monitoring required

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.
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.

Contra-indications:
Hypersensitivity to rifaximin or rifamycin derivatives.
Intestinal obstruction.

Side effects:
The most common side effects reported in the trials were peripheral oedema, nausea, dizziness, fatigue, and ascites.

Drug interactions (see also above under cautions):
There is no experience regarding administration of rifaximin to subjects who are taking another rifamycin antibacterial agent to treat a systemic bacterial infection.
In vitro data show that rifaximin did not inhibit the major cytochrome P-450 (CYP) drug metabolizing enzymes (CYPs1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, and 3A4). In *in vitro* induction studies, rifaximin did not induce CYP1A2 and CYP 2B6 but was a weak inducer of CYP3A4.

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), due to the higher systemic exposure with respect to healthy subjects.
An *in vitro* study suggested that rifaximin is a moderate substrate of P-glycoprotein (P-gp) and metabolized by CYP3A4. It is unknown whether concomitant drugs which inhibit P-gp and/or CYP3A4 can increase the systemic exposure of rifaximin.
The potential for drug-drug interactions to occur at the level of transporter systems has been evaluated *in vitro* and these studies suggest that a clinical interaction between rifaximin and other compounds that undergo efflux via P-gp and other transport proteins is unlikely (MDR1, MRP2, MRP4, BCRP and BSEP).

Annual Cost:
£259.23 per person (Drug Tariff Dec 2019)

References:
[1]Bass N, Mullen K, Sanyal A et al. Rifaximin treatment in hepatic encephalopathy. *N Eng J Med* 2010; 362:1071-81.
[2]Mullen K, Sanyal A, Bass N *et al*. Rifaximin is safe and well tolerated for long-term maintenance of remission from overt hepatic encephalopathy. *Clin Gastroenterol Hepatol 2014 Aug;12(8):1390-7*
NICE guidance (TA337) Rifaximin for preventing episodes of overt hepatic encephalopathy
SPC Targaxan (accessed eMC 9th June 2015)
BNF 69 (March 2015)