Rifaximin *(Targaxan®)*

Shared Care Guidelines: For the prescribing of Rifaximin for the reduction in recurrence of episodes of overt hepatic encephalopathy in adult patients

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines how responsibility for prescribing rifaximin for reduction in recurrence of episodes of overt hepatic encephalopthy in patients ≥ 18 years of age might be shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or 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 is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with hepatic encephalopathy are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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

RESPONSIBILITIES and ROLES

Specialist (Consultant Gastroenterologist) responsibilities	
1	Assess the patient as a candidate for treatment with rifaximin in line with NICE guidance and local pathways for management of overt hepatic encephalopathy.
2	Consider any potential drug interactions of the intended treatment regimen with drugs that the patient may already be taking. See drug interactions section below for more details.
3	Initiate treatment and provide at least 28 days supply and until GP agrees to shared care.
4	Discuss the benefits and side effects of treatment with the patient and ensure the patient understands the nature and complications of drug therapy and their role in adhering to therapy.
5	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.
6	Inform the GP in writing of the patient's diagnosis, the treatment regimen to be used, start date of treatment, intended duration of treatment and management advice. Where appropriate the GP can be asked to take over the future prescribing of repeat treatment within this guidance.
7	Review the patient's condition and monitor response to treatment regularly as part of routine clinic follow-up. Changes to therapy as a result of these reviews (or at any other time) and missed clinic appointments should be reported to the GP promptly.
8	Give advice to the GP on when to stop treatment.
9	Report adverse events to the MHRA (yellow card scheme) and share this information with the GP.
10	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner responsibilities	
1	Reply to the request from the specialist to take on prescribing of this medication as soon as practicable.
2	Continue to prescribe the therapy requested, under the guidance of the specialist.
3	Continue to prescribe lactulose throughout treatment with rifaximin
4	Monitor the patient at regular intervals in conjunction with specialist. 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.
5	Consider any potential drug interactions of the intended treatment regimen with drugs that the patient may already be taking, or any newly-initiated drugs. See drug interactions section below for more details.
6	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.

7	Stop treatment on the advice of the specialist.
8	Report adverse events to the specialist and MHRA (yellow card scheme).

Patient's role (or that of their carer)	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.
4	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.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist: Dr Terry Farrant via secretary	01225 824547			Terence.farrant@nhs.net
Specialist: Dr Julia Maltby via secretary	01225 821783			Julia.maltby@nhs.net
Hospital pharmacy department medicines information:	01225 825361	7548		ruh-tr.medicines-information@nhs.net

SUPPORTING INFORMATION

Summary of condition and licensed indications.

- 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.
- Rifaximin is indicated as an option to reduce episodes of overt hepatic encephalopathy

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

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

Contra-indications and precautions for use

- Concomitant administration of rifaximin with other rifamycins not recommended due to potential for severe disruption of gut flora.
- Contra-indicated if there is a known hypersensitivity to rifaximin, other rifamycin antibiotics or any ingredient in the formulation. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic oedema, and anaphylaxis.
- Contra-indicated in intestinal obstruction.
- As <1% is absorbed systemically rifaximin is unlikely to present a significant clinical risk in
- breastfeeding. Decisions about whether to continue treatment during breastfeeding should be made on a case by case basis.
- Rifaximin is not recommended in pregnancy.
- No dosage adjustments are necessary in the elderly or those with hepatic impairment although caution is advised in those patients with severe hepatic impairment (Child-Pugh C or MELD score >25).
- Caution is also advised in patients with impaired renal function

Side-effects

Refer to the SPC for a full list of adverse effects (http://www.medicines.org.uk/emc/medicine/27427)

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, 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.

Refer back to specialist if patient develops overt HE or reports intolerable side effects.

Rifaximin was launched in October 2013 and no longer has black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Monitoring

- 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. Refer back to specialist if there are signs of overt HE.

Drug Interactions

- Concomitant administration of rifaximin with other rifamycins is not recommended.
- The effectiveness of oral contraceptives may be reduced with concomitant use of rifaximin due to effects on the gut flora. Additional contraceptive precautions are recommended particularly if the oestrogen content of oral contraceptives is less than 50 micrograms.
- Caution should be exercised when concomitant use of rifaximin and a P-glycoprotein such as ciclosporin.
- In hepatic impaired patients it cannot be excluded that rifaximin may decrease the exposure of concomitant CYP3A4 substrates administered (e.g. warfarin, antiepileptics, antiarrhythmics[1, 4]

Advice to the patient

- Rifaximin may cause colouration of urine to a red/orange colour, but this is not harmful.
- Lactulose should be continued whilst taking rifaximin

Cost

At current prices (BNF 72, September 2016), one year's treatment with medicine at the standard dose of 550mg twice daily is £3110.76

References

NICE technology appraisal guidance [TA337]. Rifaximin for preventing episodes of overt hepatic encephalopathy. March 2015.

Summary of Product Characteristics for Targaxan (Norgine Limited, accessed online 19/7/2016).

British National Formulary (BNF72) September 2016

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Document details

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