THE SHEFFIELD AREA PRESCRIBING GROUP

Guidance

For

Rifaximin 550 mg (Targaxan®) in Adults with Hepatic Encephalopathy

Guidance developed by:

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Guidance for Rifaximin 550mg (Targaxan®)

Summary

1. Rifaximin initiated in hospital by specialist
2. Supplied by hospital; a minimum of 14 days to be provided by STH
3. GP to continue supply until outpatient review, without putting rifaximin on repeats
4. Outpatient clinic review 4-8 weeks from initiation of rifaximin, where decision made whether to continue or stop rifaximin, and GP informed, promptly
5. After outpatient appointment and decision is made to continue with rifaximin; put on repeat with review date or maximum number of issues to tie in with the next specialist review (note this is a high-cost drug)
6. Specialist to review patient after 6 months and make decision to continue or stop
7. Specialist to review patient after 12 months and consider discontinuing

Statement of Purpose

This guidance has been written to support primary care clinicians in the management of patients initiated on rifaximin in hospital for the reduction of recurrent episodes of overt hepatic encephalopathy (HE).

Introduction

Rifaximin (Targaxan®) is a semi-synthetic derivative of the antibiotic rifamycin. Rifaximin decreases intestinal production and absorption of ammonia, which is thought to be responsible for the neurocognitive symptoms of hepatic encephalopathy, thereby delaying the recurrence of acute episodes. Targaxan® has a marketing authorisation in the UK 'for the reduction in recurrence of episodes of overt hepatic encephalopathy in patients aged 18 years or older'. The summary of product characteristics highlights that 91% of people in the pivotal study were using concomitant lactulose.

Indication / patient group

HE not responsive to lactulose alone, or if appropriate, metronidazole or neomycin

Excluded Patients – see also section on contraindications / precautions

Patients with small intestinal bacterial overgrowth (SIBO) and any other unlicensed indications are excluded from this guideline

Management of condition

Initiated by specialist in hospital

Medication / Dosage / Duration of treatments

Targaxan® (rifaximin) 550mg BD. For duration see below. Rifaximin can be administered with or without food and should be given with a glass of water.

See SPC for more details: https://www.medicines.org.uk/emc/medicine/27427#gref

The NICE appraisal committee noted that the long-term benefits associated with rifaximin were uncertain, but that the greatest benefits would be expected in the early stages of treatment.

Monitoring requirements

Routine disease monitoring to continue but no additional monitoring specific to the drug is required to be undertaken by GP. The specialist will decide on how often each patient will be reviewed to decide whether treatment should be continued but generally this will be every 6 months. The specialist will write to GP after each review with decision whether to continue or stop treatment.

Follow up

- Outpatient clinic appointment 4-8 weeks from discharge to review condition. Rifaximin will be stopped if there is deterioration in the level of encephalopathy or failure to reduce hospital admissions. Rifaximin will be continued if an improvement is seen. GP to be informed of outcome.
- Specialist to review patient after 6 months. If patient having repeat episodes of HE, then consider value of continuing treatment. If patient has improved/no recurrence of HE then continue rifaximin
- Longer term, continue to monitor at least annually. If patient has continued to be free from, HE recurrence, then consider discontinuing.

The details below are not a complete list and the BNF and the SPC remain authoritative.

Side effects / Contraindications / Interactions

Full list of side-effects / contraindications and interactions is given in the Targaxan® summary of product characteristics (SPC), available from www.emc.medicines.org.uk .

Contraindications:

- Hypersensitivity to rifaximin, rifamycin-derivatives or to any of the product's excipients.
- Cases of intestinal obstruction
- Pregnancy and breast feeding

Special warnings/precautions:

- The potential association of rifaximin treatment with *Clostridium difficile*-associated disease and pseudomembranous colitis cannot be ruled out.
- Concomitant administration of rifaximin with other rifamycins is not recommended.
- Patients should be informed that despite the negligible absorption, in common with other rifamycins, 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.
- Whilst interactions have not been commonly reported, the use of additional contraceptive precautions is recommended, in particular if the oral contraceptive oestrogen content is below 50 micrograms.

Adverse effects

The summary of product characteristics lists the following common adverse reactions for rifaximin: depression, dizziness, headache, dyspnoea, upper abdominal pain, abdominal distension, diarrhoea, nausea, vomiting, ascites, rashes, pruritus, muscle spasms, arthralgia, and peripheral oedema.

Interactions

SPC states that whilst studies in healthy subjects have shown no significant interaction, 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.

Both decreases and increases in INR have been reported in patients on warfarin and rifaximin. If co-administration is necessary, the INR should be carefully monitored with addition or withdrawal of rifaximin

Information for patients

Continue taking rifaximin until reviewed by your consultant or GP

The hospital will provide the initial supply on the TTO (minimum 14 days as per hospital contract). Further supplies should be sought via your GP –see above.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist: Dr Amer Al-Joudeh	2714642			amer.al-joudeh@nhs.net

Cost

At current prices, the cost of one year's treatment with rifaximin 550 mg tablets (one tablet, twice daily) is approximately £3,000 (*Drug Tariff, Feb 2022*).

References

- European Association for the Study of the Liver via www.easl.eu http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/hepatic-encephalopathy-in-chronic-liver-disease-2014
- Online BNF via https://bnf.nice.org.uk/medicinal-forms/rifaximin.html
- Targaxan® SPC via https://www.medicines.org.uk/emc/product/2976
- NICE TA337 Rifaximin for preventing episodes of overt hepatic encephalopathy http://www.nice.org.uk/guidance/ta337

Amendment January 2022

Added in: After outpatient appointment and decision is made to continue with rifaximin; put on repeat with review date or maximum number of issues to tie in with next specialist review (note this is a high-cost drug)

Amendment November 2021

Added use in adults to title, removed section under medication/ dose relating to treatment beyond 6 months, replaced e mail address with secure nhs.net e mail address and extended expiry by 2 years to January 2024.