PAN MERSEY AREA PRESCRIBING COMMITTEE
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NHS Pan Mersey Area Prescribing Committee

RIFAXIMIN 550mg tablets (Targaxan®)

AMBER

The Pan Mersey Area Prescribing Committee recommends RIFAXIMIN 550mg tablets (Targaxan®), following specialist initiation, as an option for reducing the recurrence of overt hepatic encephalopathy in people aged 18 years or older in accordance with NICE TA 337.

PATIENT RETAINED BY SPECIALIST

NICE TA337 recommends rifaximin, within its marketing authorisation, as an option for reducing the recurrence of episodes of overt hepatic encephalopathy in people aged 18 years or older.

The majority of patients (91%) in the pivotal trial also received lactulose and this is stated in the Summary of Product Characteristics. There are fewer data available to support the use of rifaximin alone. The Pan Mersey APC recommends that lactulose should be continued in all patients unless there is intolerance. In these patients, local expert opinion recommends alternative laxatives (e.g. macrogols) may be used to ensure adequate bowel movements.

The clinical benefit was established from a multicentre randomised double-blind controlled trial in which subjects were treated for 6 months. Treatment beyond 6 months should take into consideration the individual balance between benefits and risks, including those associated with the progression of hepatic dysfunction.

Local expert opinion recommends that patients receiving treatment with rifaximin should be regularly reviewed and treatment should be discontinued if there is one or more of the following:

- a lack of efficacy after a 6 week trial of rifaximin
- a lack of efficacy identified at any follow-up appointment
- transplantation occurs
- continued alcohol intake by a patient with a diagnosis of alcoholic liver disease (case-by-case decision to be made by specialist).

Failure to respond will be according to clinical assessment of the patient at an outpatient review, with input from the patient's family/carers where possible.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

RIFAXIMIN 550mg tablets (Targaxan®)

EFFECTIVENESS

Rifaximin is a minimally absorbed antibiotic agent that has activity against ammonia-producing bacteria found in the gastrointestinal tract.[1] It reduces the production of ammonia, the substance which is responsible for the symptoms of hepatic encephalopathy.

In the pivotal phase III randomised, double-blind, placebo controlled trial, rifaximin was shown to significantly reduce the frequency of breakthrough episodes of hepatic encephalopathy (hazard ratio, HR 0.42; 95% confidence interval, CI 0.28-0.64, p<0.001, relative risk reduction, RRR 58%).[2] Hospitalisation rate for hepatic encephalopathy was 13.6% in the rifaximin group compared to 22.6% in the placebo group (*NB – this was a secondary outcome and the study was not powered to assess this*).

In the open-label extension study, rifaximin was shown to reduce the rate of breakthrough episodes of hepatic encephalopathy and rate of hospitalisation for episodes of hepatic encephalopathy, although NICE consider this to be exploratory effectiveness data only.[2]

SAFETY

Rifaximin is contraindicated in patients with known hypersensitivity to rifaximin or rifamycin derivatives and patients with intestinal obstruction.[1]

Rifaximin is cautioned in patients with risk factors for developing Clostridium difficile infection, and patients with severe hepatic impairment (Child Pugh C or MELD [Model for End-Stage Liver Disease] score > 25).[1] Rifaximin should not be used in combination with any other rifamycin-derivatives.[1]

Many of the listed adverse effects of rifaximin may be related to the underlying condition, as opposed to rifaximin. Consult the Summary of Product Characteristics for a full list of adverse drug reactions and potential drug-drug interactions.

COST[2,3]

Rifaximin 550mg BD - £259 (56 tabs)

Estimated drug cost per annum - £3,380

The NICE Costing Template estimates that 20 patients per 100,000 population per annum will be treated for hepatic encephalopathy. NICE estimates additional drug costs from implementing this NICE TA, compared to baseline spend (2014/15), as £15,496 for 2017/18 (year 3). NICE assumes steady state achieved after year 3.

These additional drug costs will be attributable to increased use of rifaximin.

PATIENT FACTORS

The SPC does not advise specific dosage adjustments in patients with renal impairment or severe hepatic impairment, but rifaximin should be used with caution in these patients due to a lack of data.[1]

Dose adjustments are not required in the elderly. There is no data to support the use of rifaximin in paediatric populations for this indication. Rifaximin is not recommended for use in pregnancy or lactation by the manufacturer. Patients should be warned rifaximin may cause reddish discolouration to the urine.[1]

PRESCRIBING INFORMATION

The recommended dose of rifaximin for reducing the recurrence of episodes of overt hepatic encephalopathy is 550mg twice daily. Patients should continue on concomitant lactulose for this indication wherever possible. No additional monitoring is required in patients receiving rifaximin for this indication.

- Treatment should be initiated by a gastroenterology or hepatology specialist.
- Prescribing should be retained in secondary care until after the first follow-up appointment.
- All patients receiving rifaximin should be reviewed by the specialist and there should be clear documentation of efficacy and on-going need for treatment documented in communication to the patient's GP. Once treatment has been assessed as efficacious, prescribing may be transferred to primary care, but the patient should remain under specialist review.

REFERENCES

1. SPC for Targaxan 550mg film-coated tablets (last updated: 21/10/16) [online]. Accessed 14/03/2017 http://www.medicines.org.uk/emc/
2. NICE technology appraisal guidance 337: Rifaximin for preventing episodes of overt hepatic encephalopathy, March 2015. Accessed 14/03/17 http://www.nice.org.uk/guidance/ta337
3. NICE Costing Template: Implementing the NICE guidance on rifaximin for preventing episodes of overt hepatic encephalopathy (TA337). Accessed 14/03/17 http://www.nice.org.uk/guidance/ta337/resources