GATESHEAD MEDICINES MANAGEMENT COMMITTEE

Prescribing Guideline for Recommended use of Rifaximin and its place in the management of Persistent hepatic encephalopathy

Rifaximin has been classified as a **GREEN+** drug on the formulary. This means it should be initiated by secondary care but can be safely maintained in primary care without on-going specialist monitoring.

Rifaximin should only be initiated by a consultant gastroenterologist in the management of patients with hepatic encephalopathy that is refractory to standard medical therapy.

Standard medical therapy includes:

1st line = treating the underlying cause.
2nd line = lactulose

It is should not be used as 1st line therapy by GPs in the treatment of hepatic encephalopathy.

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Summary of Prescribing Information

Class: Rifamicin antibiotic
Indication for use: Rifaximin is indicated for the treatment of patients with persistent encephalopathy, which has been refractory to current standard medical therapy (1st line = treat the precipitant, 2nd line = lactulose)
Licensed status: Outside UK product license but licensed in USA by FDA for this indication
Dosage: Recommended daily dosage of rifaximin is 400mg three times a day , taken with or without food.
Dose may be increased on advice of consultant gastroenterologist to 800mg three times a day for a 2 week trial only to assess respone in those patients with refractory encephalopathy who have partially responded to 400mg tds.
No dose adjustment is required in hepatic failure.
Monitoring: No specific monitoring is required in relation to rifaximin
Contraindications:

- Hypersensitivity to active ingredient, rifamicins and any of the excipients.
- Intestinal obstruction
- Serious ulcerous lesions to the intestine.

Drug Interactions: None significant, as not an inhibitor/inducer of cytochrome p450 isoenzymes and less than 0.4% of dose is absorbed orally.
Adverse effects significant:
2% to 10%: Central nervous system: Headache (10%; placebo 9%)
<2%, postmarketing, and/or case reports (limited to important or life-threatening):
Abnormal dreams, allergic dermatitis, angioneurotic edema (includine tongue and facial edema with dysphagia), exfoliative dermatitis, fatigue, flushing, hypersensitivity reactions, insomnia, motion sickness, pruritus, rash, sunburn, tinnitus, urticaria

Cost & Availability:
£15.15 for 9 x Rifaximin (Xifaxanta®) 200mg tablets, available from most wholesalers

The efficacy will be assessed in secondary care 2 to 4 weeks after commencement and will be recommended for long term use if deemed effective in individual patients.

Background Information

There is a sound evidence base for the use of Rifaximin in persistent hepatic encephalopathy. This evidence based has been reviewed and endorsed by the Gateshead Medicines Management Committee, as well as a number of large teaching hospitals nationally.

Some of the references and data are presented below

1. Bucci L, Palmeri GC. Double blind, double-dummy comparison between treatment with Rifaximin and Lactulose in patients with medium to severe degree hepatic encephalopathy. Curr Med Res Opin 1995;13:274-81

Significant differences in clinical and tests for encephalopathy.

- Earlier (day 3) resolution and reduction in ammonia
- Higher tolerability with significantly less side effects.

2. Mas A, Rodes J, Sunyer L, et al. Comparison of rifaximin and lactilol in the treatment of acute hepatic encephalopathy: results of a randomized, double-blind, double-dummy, controlled clinical trial. J Hepatol 2003;38:51-8

3.Paik YH, Lee KS, Han KH, et al. Comparison of Rifaximin and Lactulose for the treatment of hepatic encepahalopathy: a prospective randomised study. Yonsei Med J 2005;46:399-407 Rifaximin a useful and safe alternative therapy in the treatment of acute HE

4. Neff GW, Kremmer N, Zacharis VC, et al. Analaysis of hospitalizations comparing rifaximin versus lactulose in the management of hepatic encephalopathy. Transplant Proc 2006; 38:3552-5

- Drug cost (Lactulose)$50 vs (Rifaximin)$ 620
- Total cost pppy, (Lactulose) $13285 vs (Rifaximin) $7958

5. Leevy CB, Phillips JA. Hospitalisations during the use of rifaximin versus lactulose for the treatment of hepatic encephalopathy. Dig Dis Sci 2007;52:737-41

Rifaxin vs Lactulose

- Fewer days in Hospital 2.5 vs 7.3
- Fewer Hospitalisations 0.5 vs 1.6
- Lower costs $14222 vs $56635
- Significantly less side effects (P<0.001)

6. Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in Hepatic Encephalopathy. N Engl J Med 2010; 362:1071-81.

Randomised, DB, placebo controlled trial

- Standard therapy (90% of patients on both arms were on lactulose)
- Breakthrough Encepahalopathy (Rifaximin)22.1% vs (Placebo) 45.9%(P <0.001)
- Hospitalisations (Rifaximin)13.6% vs (Placebo) 22.6% (P=0.01)
- Adverse events and serious side effects similar in both groups

There have been previous trials comparing Rifaximin vs Neomycin, which have shown that Rifaximin comparable to Neomycin.
Neomycin was an effective therapy in Encephalopathy, but its adverse events have restricted its use and no longer used in treatment of Encephalopathy (Ototoxicity and Nephrotoxicity)