Rationale for Initiation, Continuation and Discontinuation (RICaD)

Rifaximin

For preventing episodes of overt hepatic encephalopathy

This document supports the use and transfer of an agent which is classified as **AMBER**.

*It is intended for completion by a Consultant Hepatologist or (if the trust does not have a dedicated liver service) a Consultant Gastroenterologist with a recognised interest in Liver Disease, in order to give Primary Care prescribers a clear indication of the reason for recommending an **AMBER** medication together with suggested criteria for its subsequent continuation or discontinuation. This RICaD should be provided as a supplement to the specialist's clinical letter.

Patient details		**GP details**		**Specialist details**	
Name		**GP Name**	**Dr**	**Specialist Name**	
PID		**GP address**		**I confirm that this patient is eligible to receive rifaximin under the restrictions listed below**	
DOB				**Signature**	
Patient address				**Date**	
				Contact details	

Rationale for Choice

Relevant Diagnosis:	Hepatic Encephalopathy in patients over the age of 18 years. Guidance - NICE TA337
Agreed Indication(s) for inclusion in the BSSE APC Formulary:	Clinically overt Hepatic Encephalopathy refractory to first line therapies as defined by West Haven Criteria Grade 1–4 or the Organisation Mondiale de Gastroentérologie Working Party (see Ferenci P, et al. Hepatology 2002; 35:716–21) as assessed by a Consultant Hepatologist or (if the trust does not have a dedicated liver service) a Consultant Gastroenterologist with a recognised interest in Liver Disease.
Reason why rifaximin has been chosen in preference to drugs without Formulary restrictions:	At present there is no suitable alternative to rifaximin that has an equivalent evidence base or safety profile. It should be noted that **rifaximin is to be used in combination with aperients such as lactulose** (or polyethylene glycol 3350-electrolyte solution), which have been shown to reduce the symptoms of encephalopathy.
Special precautions:	**Contraindications**:- a) Pregnancy. b) Documented drug allergy, rash and/or hypersensitivity to rifaximin, rifampicin –containing products or to any of the excipients. c) Intestinal obstruction. d) Prior non-response to therapy.

Based on HeFT RICaD template
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	Cautions:- a) Patients with a history of *Clostridium difficile* infection. b) The lack of safety data in Child-Pugh C cirrhosis (or MELD >25) means that the drug should be used with caution in advanced liver disease. c) Rifaximin is not recommended to be administered concomitantly with other rifampicin-containing products. d) The effectiveness of oral oestrogenic contraceptives could decrease after rifaximin administration and it is therefore recommended that patients take additional contraceptive precautions. e) Fertility, pregnancy and lactation: the use of rifaximin during pregnancy is not recommended. It is unknown whether rifaximin/metabolites are excreted in human milk. Therefore, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rifaximin therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.
Pre-treatment test results:	Baseline renal function and liver function tests.

Guidance on initiation

Initiation dose:	550 mg twice daily.
Additional information:	The first prescription will be for one month's supply. The published data used this as a regular daily prescription, but intermittent supervised trials of therapy withdrawal to assess the need for continuation are to be encouraged as long as the patient will not come to harm.
Monitoring:	Clinical assessment at one month by the initiating consultant. Blood monitoring including renal and liver function tests and full blood counts at one month. Routine clinical blood monitoring every 3 to 6 months thereafter. There are no specific monitoring requirements. However, it is worth monitoring the patient's clinical condition such as temperature, blood in stools and change in symptoms.

Suggested Criteria for Continuation or Discontinuation

Assessment of Efficacy	
Frequency:	Evidence of overt HE. The drug should only be initiated by a Consultant Hepatologist or a Consultant Gastroenterologist with a recognised interest in Liver Disease once a full assessment of the patient has been completed and other causes for encephalopathy (electrolyte abnormalities, sepsis, anaemia, constipation, dehydration, drugs e.g. diuretics and analgesics etc.) excluded. The patient should be using regular aperients correctly and have documented episodes of validated breakthrough/refractory HE. In subclinical HE corroborative evidence of encephalopathy should be supplied e.g. EEG studies supportive of HE and/or evidence of cirrhosis/porto-systemic shunting. The role of psychomotor testing/evaluation in the initiation of rifaximin for minimal-HE needs further investigation. Initiation of rifaximin cannot be recommended purely on grounds of low grade

	psychomotor impairment/behavioural change at present. These patients should be enrolled in clinical trials.
Location :	Outpatients clinic/GP practice
Method (what tests are required):	The patient should be reviewed by the initiating Consultant Hepatologist or a Consultant Gastroenterologist with a recognised interest in Liver Disease in outpatients one month after starting rifaximin therapy to assess side effects and efficacy. **If, in the Specialist's opinion, the patient is deriving benefits from the drug's continued use, a further month's supply will be issued by the initiating Consultant Hepatologist or a Consultant Gastroenterologist with a recognised interest in Liver Disease.** This will allow sufficient time for the responsibility for continuing the prescription to be passed to Primary Care on the understanding that the patient will be seen every 3-6 months in a secondary care liver clinic for ongoing management of their cirrhosis. This review will also adjudge the necessity of continuing the prescription.
Continuation Criteria:	Satisfactory clinical response one month after treatment initiation. Assessed by initiating clinician. Evidence of ongoing benefit at 6 month clinic reviews (or more frequent review depending on clinical need). The clinical benefit of rifaximin was established from a controlled study 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. The role of rifaximin for patients in whom the DVLA has previously withdrawn their driving license due to episodes of clinically overt HE has not been established. Clinicians are still advised to refer patients whose symptoms resolve with regular rifaximin use back to the DVLA for advice.
Discontinuation Criteria:	1) Lack of clinical benefit (as assessed by Consultant Hepatologist or a Consultant Gastroenterologist with a recognised interest in Liver Disease). 2) Adverse side effects and/or new onset *clostridium difficile* infection whilst using rifaximin 3) Adverse drug reactions.
Follow up action:	These patients should be under secondary care follow up – at the minimum this will comprise 6 monthly reviews in clinic for Hepatoma surveillance.
Shared Care Read code:	In the patients notes, using the appropriate Read code listed below, denote that the patient is receiving treatment under a shared care agreement in the absence of a suitable read code for RICaD.

GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing
SystmOne	XaB58	Shared care