Clinical use:

In the trials of ZAXINE for HE, 91% of the patients were using lactulose concomitantly. Differences in the treatment effect of those patients not using lactulose concomitantly could not be assessed.

ZAXINE has not been studied in patients with MELD (Model for End-Stage Liver Disease) scores >25. There is increased systemic exposure to rifaximin in patients with hepatic dysfunction.

Studies specifically designed to determine the dose in elderly patients (>65 years of age) have not been performed. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Safety and effectiveness has not been investigated in children and adolescents <18 years of age.

Contraindications:

- Hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents

Relevant warnings and precautions:

- Should not be used for the treatment of systemic bacterial infections
- Potential for increased systemic exposure to rifaximin in disease states in which intestinal barrier function or gut motility is altered
- Possible relationship between treatment and carcinogenicity cannot be ruled out
- *Clostridium difficile*-associated disease (CDAD) has been reported with use of nearly all antibacterial agents, including ZAXINE, and may range in severity from mild diarrhea to fatal colitis. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality. Careful medical history is necessary. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued
- Not recommended in patients with intestinal obstruction
- Discontinue if a severe hypersensitivity reaction occurs
- Pharmacokinetics not studied in impaired renal function
- Not for use during pregnancy
- Unknown if ZAXINE is excreted in human milk; a decision should be made whether to discontinue nursing or to discontinue the drug

For more information:

Please consult the Product Monograph at https://health-products.canada.ca/dpd-bdpp/index-eng.jsp for important information relating to adverse reactions, drug interactions and dosing which have not been discussed in this piece. The Product Monograph is also available by calling 1-844-587-4623.

References:

1. ZAXINE Product Monograph. Salix Pharmaceuticals, Inc., February 11, 2019.
2. Bass NM *et al.* Rifaximin treatment in hepatic encephalopathy. *N Eng J Med* 2010;362:1071-81.
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Pr Zaxine 550®
rifaximin 550 mg tablets

LUPIN PHARMA CANADA

PAAB

LUP19-144 EN

IN THE FACE OF OVERT HEPATIC ENCEPHALOPATHY RECURRENCE, CONSIDER ZAXINE.

ZAXINE is indicated for the reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients ≥18 years of age.

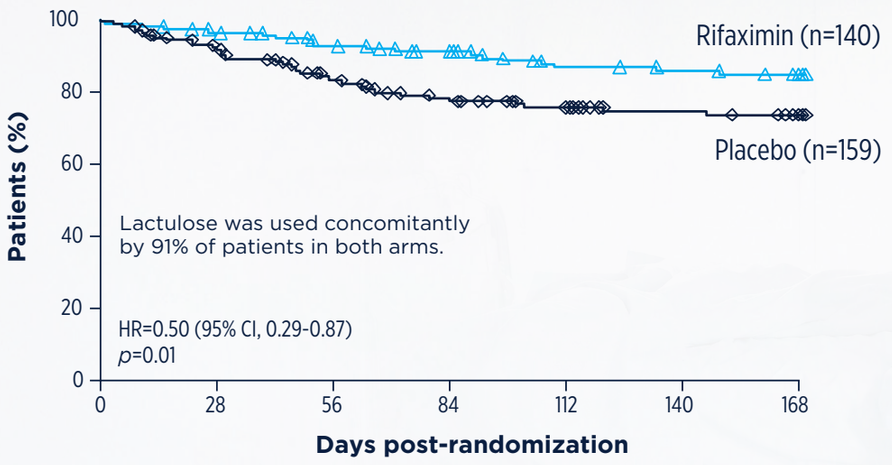
Pr Zaxine 550®
rifaximin 550 mg tablets

ZAXINE: Demonstrated efficacy in adults in remission from overt HE

1 tablet twice per day, with or without food

Significantly reduced the risk of HE-related hospitalizations (secondary endpoint)[1,2*]

Time to first HE-related hospitalization



Adapted from Bass *et al.*[2]

50% risk reduction in time to first HE-related hospitalization

- 14% of ZAXINE patients had an HE-related hospitalization vs. 23% with placebo at 6 months, p=0.01[1*†]

NNT: 9[2‡]

Pr Zaxine 550® rifaximin 550 mg tablets **is covered with special authorization on most provincial formularies[3-11§]**

Treatment duration beyond 6 months should take into consideration the individual balance between benefits and risks, including those associated with the progression of hepatic dysfunction and increasing systemic exposure to rifaximin.[1]

* Double-blind, placebo-controlled, trial of 299 adults with ≥2 episodes of overt HE associated with hepatic cirrhosis (Conn score ≥2) during the previous 6 months, remission at enrollment (Conn score 0, 1) and a score of ≤25 on the MELD scale. Patients were randomized to ZAXINE 550 mg BID or placebo for 6 months.

† HE-related hospitalization was defined as hospitalization directly caused by HE or a hospitalization during which an HE event occurred.[2]

‡ Number of patients needed to treat with ZAXINE for 6 months to reduce the risk of 1 HE-related hospitalization.

§ Covered in AB, BC, MB, NB, NFLD, NS, ON, SK and in QC. In QC, the coverage criteria are as follows: for the prevention of recurrences of HE in cirrhotic persons for whom lactulose taken optimally did not adequately prevent the occurrence of overt episodes; unless there is serious intolerance or a contraindication, lactulose must be administered concomitantly. Please refer to the respective formularies for complete details.