INTERNATIONAL ABBREVIATED PRESCRIBING INFORMATION: XIFAXAN® / TARGAXAN® 550 mg (rifaximin-α)

Presentation: Blister pack with film-coated, pink tablets containing 550 mg rifaximin-α for oral administration.
Indication: Reduction in recurrence of episodes of overt hepatic encephalopathy in patients ≥ 18 years of age.
Dosage and administration: 550 mg twice a day as long term treatment, taken orally with a glass of water, with or without food. No specific dosing adjustment is necessary for patients with hepatic insufficiency or for the elderly. The safety and efficacy of rifaximin-α have not been established in paediatric patients under 18 years of age.
Contraindications: Hypersensitivity to rifaximin, rifamycin derivatives or any of the excipients. Cases of intestinal obstruction.
Warnings and precautions: *Clostridium difficile*-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including rifaximin. The potential association of rifaximin treatment with CDAD and pseudomembranous colitis (PMC) cannot be ruled out. Caution should be used in patients with impaired renal function. Concomitant administration of rifaximin with other rifamycins is not recommended. Rifaximin may cause a reddish discolouration of the urine. Use with caution in patients with severe hepatic impairment (Child-Pugh C) and in patients with MELD (Model for End-Stage Liver Disease) score >25. Caution should be exercised when concomitant use of rifaximin and a P-glycoprotein such as ciclosporin is needed.
Interactions: No experience administering rifaximin to subjects taking another rifamycin antibacterial agent to treat a systemic bacterial infection. *In vitro* data show rifaximin did not inhibit major cytochrome P450 (CYP) drug metabolizing enzymes. Rifaximin did not induce CYP1A2 and CYP2B6 but was a weak inducer of CYP3A4. In healthy subjects studies demonstrated rifaximin did not significantly affect the pharmacokinetics of CYP3A4 substrates, however in hepatic impaired patients rifaximin may decrease exposure of CYP3A4 substrates administered concomitantly (e.g. warfarin, antiepileptics, antiarrhythmics, oral contraceptives) due to higher systemic exposure. Increases and decreases in international normalised ratio have been reported in patients on warfarin and rifaximin. Carefully monitor international normalised ratio if co-administration is necessary. Dose adjustments of anticoagulants may be necessary. *In vitro* work suggests rifaximin is a moderate substrate of P-glycoprotein (P-gp) and metabolised by CYP3A4. It is unknown if concomitant drugs which inhibit P-gp and/or CYP3A4 increase systemic exposure of rifaximin. Clinical interaction between rifaximin and compounds that undergo efflux via P-gp and other transport proteins is unlikely (MRP2, MRP4, BCRP and BSEP).
Pregnancy and lactation: No or limited data on the use of rifaximin in pregnant women. Animal studies showed transient effects on ossification and skeletal variations in the foetus. Use of rifaximin during pregnancy is not recommended. It is unknown whether rifaximin/metabolites are excreted in human milk. A risk to the child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rifaximin therapy.
Undesirable effects: Adverse effects observed in the placebo-controlled study RFHE3001 and long-term study RFHE3002: Common (≥1/100 to <1/10): Depression, dizziness, headache, dyspnoea, upper abdominal pain, abdominal distension, diarrhoea, nausea, vomiting, ascites, rashes, pruritus, muscle spasms, arthralgia, oedema peripheral. Prescribers should consult country approved Summary of Product Characteristics for further information in relation to other undesirable effects.
Overdose: No case of overdose has been reported. In patients with normal bacterial flora, rifaximin in dosages of up to 2,400 mg/day for 7 days did not result in any relevant clinical symptoms related to the high dosage. In case of accidental over-dosage, symptomatic treatments and supportive care are suggested.
Price and pack sizes: PVC-PE-PVDC/Aluminium foil blisters in cartons of 14, 28, 42, 56 or 98 tablets. Contact local distributor for price.
Legal category: POM
Prescribing information: Medicinal product subject to medical prescription.
Marketing authorisation holder: Norgine BV, Antonio Vivaldistraat 150, 1083 HP Amsterdam, The Netherlands.
Product licence number: PL20011/0020
ATC code: A07AA11
Date International Prescribing Information prepared: May 2021
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XIFAXAN®/TARGAXAN® has varying availability and licensing internationally. Before prescribing, consult your country approved prescribing information, available from your local distributor or Norgine Ltd.

Adverse events should be reported to your regulatory agency. Adverse events should also be reported to your local distributor or Norgine Limited, Norgine House, Moorhall Road, Harefield, Uxbridge, Middlesex UB9 6NS, United Kingdom. Email: globalmedinfo@norgine.com