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FOXAMINE™
(RIFAXIMIN)
TABLET

فوکسامن

COMPOSITION:
Foxamine Tablet 200 mg:
Each film coted tablet contains:
Rifaximin ..... 200 mg.

Product Specs.: CCL Pharmaceuticals

Foxamine Tablet 550 mg:
Each film coted tablet contains:
Rifaximin ..... 550 mg.

Product Specs.: CCL Pharmaceuticals

DESCRIPTION:
FOXAMINE tablets contain Rifaximin, a non-aminoglycosides semi-synthetic, nonsystemic antibiotic derived from rifamycin. Rifaximin is a structural analog of Rifampin. Rifaximin is an antibacterial drug. It acts by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase resulting in inhibition of bacterial RNA synthesis.

MICROBIOLOGY:
Rifaximin is a structural analog of Rifampin. Organisms with high Rifaximin minimum inhibitory concentration (MIC) values also have elevated MIC values against Rifampin. Cross-resistance between Rifaximin and other classes of antimicrobials has not been studied.
Rifaximin has been shown to be active against the following pathogen in clinical studies of infectious diarrhea:
Escherichia coli (enterotoxigenic and enteroaggregative strains). For Hepatic Encephalopathy (HE), Rifaximin is thought to have an effect on the gastrointestinal flora.
Pharmacokinetics:
Absorption: Systemic absorption of Rifaximin (200 mg three times daily) was evaluated in 13 subjects challenged with shigellosis on Days 1 and 3 of a three-day course of treatment. Rifaximin plasma concentrations and exposures were low and variable. There was no evidence of accumulation of Rifaximin following repeated administration for 3 days (9 doses). Peak plasma Rifaximin concentrations after 3 and 9 consecutive doses ranged from 0.81 to 3.4 ng/mL on Day 1 and 0.68 to 2.26 ng/mL on Day 3.Similarly, AUC0-last estimates were 6.95 ± 5.15 ngh/mL on Day 1 and 7.83 ± 4.94 ngh/mL on Day 3. After a single dose and multiple doses of Rifaximin 550 mg in healthy subjects, the mean time to reach peak plasma concentrations was about an hour. The pharmacokinetic (PK) parameters were highly variable and the accumulation ratio based on AUC was 1.37. The pharmacokinetics of Rifaximin in patients with a history of HE was evaluated after administration of Rifaximin, 550 mg two times a day. The PK parameters were associated with a high variability and mean Rifaximin exposure (AUC_T) in patients with a history of HE (147 ngh/mL) was approximately 12-fold higher than that observed in healthy subjects following the same dosing regimen (12.3 ngh/mL).When PK parameters were analyzed based on Child-Pugh Class A, B, and C, the mean AUC_T was 10, 13, and 20-fold higher, respectively, compared to that in healthy subjects. A high-fat meal consumed 30 minutes prior to Rifaximin dosing in healthy subjects delayed the mean time to peak plasma concentration from 0.75 to 1.5 hours and increased the systemic exposure (AUC) of Rifaximin by 2-fold.FOXAMINE can be administered with or without food.
Distribution: Rifaximin is moderately bound to human plasma proteins. In vivo, the mean protein binding ratio was 67.5% in healthy subjects and 62% in patients with hepatic impairment when Rifaximin 550 mg was administered.
Metabolism and elimination: The absorbed Rifaximin undergoes metabolism with minimal renal excretion of the unchanged drug. The enzymes responsible for metabolizing Rifaximin are unknown. In a study, Rifaximin was detected in the bile after cholecystectomy in patients with intact gastrointestinal mucosa, suggesting biliary excretion of Rifaximin.
Special Populations:
Patients with renal impairment: The pharmacokinetics of Rifaximin in patients with impaired renal function has not been studied.
Patients with hepatic impairment: The systemic exposure of Rifaximin was markedly elevated in patients with hepatic impairment compared to healthy subjects. The mean AUC in patients with Child-Pugh Class C hepatic impairment was 2-fold higher than in patients with Child-Pugh Class A hepatic impairment.

INDICATIONS :
FOXAMINE 200 mg is indicated for the treatment of patients (≥12 years of age) with Travelers' diarrhea caused by noninvasive strains of Escherichia coli. FOXAMINE should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than Escherichia coli.
FOXAMINE 550 mg is indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients ≥ 18 years of age.

DOSAGE AND ADMINISTRATION :
Traveler's diarrhea: The recommended dose of FOXAMINE is one 200 mg tablet taken orally three times a day for 3 days. FOXAMINE can be administered orally, with or without food.
Hepatic encephalopathy: The recommended dose of FOXAMINE is one 550 mg tablet taken orally two times a day, with or without food.
Hepatic impairment: There is increased systemic exposure in patients with severe hepatic impairment. Therefore, caution should be exercised when administering FOXAMINE to patients with severe hepatic impairment (Child-Pugh C).
Geriatrics: Clinical trial experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
Children and adolescents: The safety and effectiveness of Rifaximin 200 mg in pediatric patients with Travelers' diarrhea less than 12 years of age have not been established. The safety and effectiveness of Rifaximin 550 mg for HE have not been established in patients < 18 years of age.

CONTRAINDICATIONS :
FOXAMINE is contraindicated in patients with a hypersensitivity to Rifaximin, any of the rifamycin antimicrobial agents, or any of the components in FOXAMINE. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic edema, and anaphylaxis.

PRECAUTIONS :
Travelers' Diarrhea Not Caused by Escherichia coli Rifaximin was not found to be effective in patients with diarrhea complicated by fever and/or blood in the stool or diarrhea due to pathogens other than Escherichia coli. Discontinue RIFAXIMIN if diarrhea symptoms get worse or persist more than 24-48 hours and alternative antibiotic therapy should be considered. Rifaximin is not effective in cases of Travelers' diarrhea due to Campylobacter jejuni. The effectiveness of Rifaximin in Travelers' diarrhea caused by Shigella spp. and Salmonella spp. has not been proven. Rifaximin should not be used in patients where Campylobacter jejuni, Shigella spp., or Salmonella spp. may be suspected as causative pathogens.
Clostridium difficile-associated diarrhea:
Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Rifaximin, and may range in severity from mild diarrhea to fatal colitis.

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Development of drug resistant bacteria:
Prescribing FOXAMINE for Travelers' diarrhea in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Severe hepatic impairment: There is increased systemic exposure in patients with severe hepatic impairment. The clinical trials were limited to patients with MELD scores <25. Therefore, caution should be exercised when administering FOXAMINE to patients with severe hepatic impairment (Child-Pugh C).
Pregnancy & lactation:
Pregnancy category C:
There are no adequate and well controlled studies in pregnant women. Rifaximin has been shown to be teratogenic in rats and rabbits at doses that caused maternal toxicity. FOXAMINE tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether Rifaximin is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from FOXAMINE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

DRUG INTERACTIONS:
In vitro drug interaction studies have shown that Rifaximin did not inhibit human hepatic cytochrome P450 isoenzymes 1A2, 2A6, 2B6, 2C9, 2C19, 2D6, 2E1, and 3A4. No clinically significant drug interactions noted in clinical studies.

ADVERSE EFFECTS:
Most common adverse reactions for Rifaximin 200 mg three times daily that occurred at a frequency > 5% in the placebo-controlled trials include flatulence, headache, abdominal pain, rectal tenesmus, defecation urgency and nausea.
The following adverse reactions, presented by body system, have also been reported in <2% of patients taking Rifaximin 200mg three times a day in the placebo-controlled clinical trials.
Blood and Lymphatic System Disorders: Lymphocytosis, monocytosis, neutropenia
Ear and Labyrinth Disorders: Ear pain, motion sickness, tinnitus.
Gastrointestinal Disorders: Abdominal distension, diarrhea, dry throat, gingival disorder, inguinal hernia, dry lips, stomach discomfort.
General Disorders and Administration Site Conditions: Chest pain, fatigue, malaise, pain, weakness.
Infections and Infestations: Dysentery, respiratory tract infection, upper respiratory tract infection
Injury and Poisoning: Sunburn
Investigations: Aspartate aminotransferase increased, blood in stool, blood in urine, weight decreased.
Metabolic and Nutritional Disorders: Anorexia, dehydration.
Musculoskeletal, Connective Tissue, and Bone Disorders: Arthralgia, muscle spasms, myalgia, neck pain.
Nervous System Disorders: Abnormal dreams, dizziness, migraine, syncope, loss of taste.
Psychiatric Disorders: Insomnia
Renal and Urinary Disorders: Choluria, dysuria, hematuria, polyuria, proteinuria, urinary frequency.
Respiratory, Thoracic, and Mediastinal Disorders: Dyspnea, nasal passage irritation, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis, rhinorrhea.
Skin and Subcutaneous Tissue Disorders: Clamminess, rash, sweating increased.
Vascular Disorders: Hot flashes.
Most common adverse reactions in HE (≥ 10%): Peripheral edema, nausea, dizziness, fatigue, ascites, flatulence, and headache. The following adverse reactions, presented by body system, have also been reported in the placebo-controlled clinical trial in greater than 2% but less than 5% of patients taking Rifaximin 550 mg taken orally two times a day for hepatic encephalopathy.
Ear and Labyrinth Disorders: Vertigo
Gastrointestinal Disorders: Abdominal pain lower, abdominal tenderness, dry mouth, esophageal variceal bleed, stomach discomfort.
General Disorders and Administration Site Conditions: Chest pain, generalized edema, influenza like illness, pain
Infections and Infestations: Cellulites, pneumonia, rhinitis, upper respiratory tract infection Injury, Poisoning and Procedural Complications: Contusion, fall, procedural pain.
Investigations: Weight increased.
Metabolic and Nutritional Disorders: Anorexia, dehydration, hyperglycemia, hyperkalemia, hypoglycemia, hyponatraemia Musculoskeletal, Connective Tissue, and Bone Disorders: Myalgia, pain in extremity.
Nervous System Disorders: Amnesia, disturbance in attention, hypoesthesia, memory impairment, tremor.
Psychiatric Disorders: Confusional state.
Respiratory, Thoracic, and Mediastinal Disorders: Epistaxis
Vascular Disorders: Hypotension
Post-Marketing Experience: The following adverse reactions have been identified during post approval use of
Rifaximin: Cases of C. difficile-associated colitis have been reported.
Hypersensitivity reactions, including exfoliative dermatitis, rash, angioneurotic edema (swelling of face and tongue and difficulty swallowing), urticaria, flushing, pruritus and anaphylaxis have been reported. These events occurred as early as within 15 minutes of drug administration.

OVERDOSAGE :
No specific information is available on the treatment of overdosage with Rifaximin. In the case of overdosage, discontinue FOXAMINE, treat symptomatically, and institute supportive measures as required.

INSTRUCTIONS:
- Store below 30ºC.
- Protect from heat, sunlight and moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Foxamine Tablet 200 mg : Pack of 1x10 tablets.
Foxamine Tablet 550 mg : Pack of 1x10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

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