Nimixa™

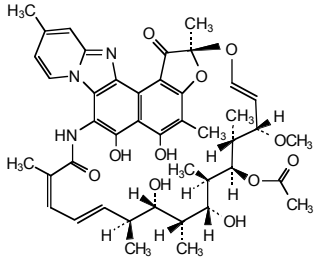
[R i f a x i m i n]

200mg, 550mg Tablets

نِمِکسا

DESCRIPTION

Nimixa (Rifaximin) is a non-aminoglycoside semi-synthetic, nonsystemic antibacterial derived from rifamycin SV. Rifaximin is a structural analog of rifampin. Chemically, rifaximin is (2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E)-5,6,21,23-Tetrahydroxy-27-methoxy-2,4,11,16,20,22,24, 26-octamethyl-1,15-dioxo-1,2-dihydro-2,7- (epoxypentadeca [1,11,13] trienoimino) benzofuro[4,5-e]pyrido[1,2-a]benzimidazol-25-yl acetate. The molecular formula is $C_{43}H_{51}N_3O_{11}$ and the structure formula is:



Rifaximin

QUALITATIVE AND QUANTITATIVE COMPOSITION

Nimixa (Rifaximin) is available for oral administration as:

1. Nimixa Tablets 200mg
   Each film-coated tablet contains:
   Rifaximin BP…200mg

2. Nimixa Tablets 550mg
   Each film-coated tablet contains:
   Rifaximin BP…550mg

CLINICAL PHARMACOLOGY

Mechanism of action

Rifaximin acts by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase resulting in inhibition of bacterial RNA synthesis. Rifaximin has been shown to be active against the non invasive strain of *Escherichia coli* (enterotoxigenic and enteroaggregative strains).

Rifaximin is believed to affect gut bacteria resulting in a decreased production and/or absorption of bacterial derived neurotoxins, including ammonia, responsible for the neurocognitive and neuromuscular dysfunction seen in patients with Hepatic Encephalopathy.

Pharmacokinetics

Absorption

Rifaximin has low intestinal permeability and low aqueous solubility and therefore, it is poorly absorbed from the gastrointestinal tract, having a bioavailability of about only 0.4%.

Distribution

Rifaximin is moderately distributed in adults, rifaximin 800mg/day for 3 days resulted in concentrations of about 8000 µg/g in stools. Plasma protein binding is 68% in healthy individual and 62% in patients with hepatic insufficiency. Rifaximin is moderately bound to human plasma proteins.

Metabolism

Rifaximin undergoes metabolism with minimal renal excretion of the unchanged drug. The enzymes responsible for metabolizing rifaximin are unknown.

Excretion

Rifaximin is excreted primarily in the feces. After administration of 400mg 14C-rifaximin orally to healthy individuals, of the 96.94% total recovery, 96.62% of the administered radioactivity was recovered in feces almost exclusively as the unchanged drug and 0.32% was recovered in urine mostly as metabolites with 0.03% as the unchanged drug.

Special Population

Hepatic Insufficiency

The systemic exposure of rifaximin was markedly elevated in patients with hepatic insufficiency compared to healthy individuals. The mean AUC in patients with Child-Pugh Class C hepatic insufficiency was 2-folds higher than in patients with Child-Pugh Class A hepatic insufficiency. Because of the limited systemic absorption of rifaximin, no specific dosing adjustments are recommended for patients with hepatic insufficiency.

THERAPEUTIC INDICATIONS

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Nimixa (Rifaximin) and other antibacterial drugs, Nimixa (Rifaximin) when used to treat infection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

Traveler's Diarrhea

Nimixa (Rifaximin) Tablets 200mg are indicated for the treatment of patients (≥ 12 years of age) with traveler's diarrhea caused by noninvasive strains of *Escherichia coli.*

Hepatic Encephalopathy

Nimixa (Rifaximin) Tablets 550mg are indicated for reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients 18 years of age.

DOSAGE AND ADMINISTRATION

Nimixa (Rifaximin) tablets can be administered with or without food with the following dosage regimen:

Traveler's Diarrhea

The recommended dose of Nimixa (Rifaximin) is one 200mg tablet taken orally three times a day for 3 days.

Hepatic Encephalopathy

The recommended dose of Nimixa (Rifaximin) is one 550mg tablet taken orally two times a day.

ADVERSE REACTIONS

Traveler's Diarrhea

Common

Flatulence, headache, abdominal pain, rectal tenesmus, defecation urgency, nausea, constipation, pyrexia, vomiting.

Uncommon

Lymphocytosis, monocytosis, neutropenia, ear pain, motion sickness, tinnitus, abdominal distension, diarrhea, dry throat, fecal abnormality, gingival disorder, inguinal hernia, dry lips, stomach discomfort, chest pain, fatigue, malaise, pain, weakness, dysentery, respiratory tract infection, upper respiratory tract infection, sunburn, aspartate aminotransferase increased, blood in stool, blood in urine, weight decreased, anorexia, dehydration, arthralgia, muscle spasms, myalgia, neck pain, abnormal dreams, dizziness, migraine, syncope, loss of taste, insomnia, choluria, dysuria, hematuria, polyuria, proteinuria, urinary frequency, dyspnea, nasal passage irritation, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis, rhinorrhea, clamminess, rash, sweating increased, hot flashes.

Hepatic Encephalopathy

Common

Peripheral edema, nausea, dizziness, fatigue, ascites, muscle spasms, pruritus, abdominal pain, abdominal distension, anemia, cough, depression, insomnia, nasopharyngitis, upper abdominal pain, arthralgia, back pain, constipation, dyspnea, pyrexia, rash.

Uncommon

Vertigo, lower abdominal pain, abdominal tenderness, dry mouth, esophageal variceal bleed, stomach discomfort, chest pain, generalized edema, influenza like illness, pain, cellulitis, pneumonia, rhinitis, upper respiratory tract infection, confusion, fall, procedural pain, weight increased, anorexia, dehydration, hyperglycemia, hyperkalemia, hypoglycemia, hyponatremia, myalgia, pain in extremity, amnesia, disturbance in attention, hypoesthesia, memory impairment, tremor, confusional state, epistaxis, hypotension.

CONTRAINDICATIONS

Rifaximin is contraindicated:

- In patients with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or any of the excipient of product.

- During pregnancy and in women of childbearing potential not using contraception.
- In the treatment of traveler's diarrhea caused by invasive enteric pathogens such as Campylobacter, Salmonella and Shighella, which typically produce dysentery-like diarrhea characterized by fever, blood in the stool and high stool frequency.

PRECAUTIONS

Traveler's Diarrhea Not Caused by Escherichia coli

Upon administration of rifaximin, discontinue rifaximin if diarrhea symptoms due to pathogens other than *Escherichia coli* get worse or persist more than 24-48 hours and alternative antibiotic therapy should be considered.

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. CDAD must be considered in all patients w ho present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued.

Severe (Child-Pugh C) Hepatic Insufficiency

There is increased systemic exposure in patients with severe hepatic insufficiency. Therefore, caution should be exercised when administering rifaximin to patients with severe hepatic insufficiency (Child-Pugh C).

Nursing mother

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 rifaximin, 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

- The systemic drug interaction potential of rifaximin is low as it does not inhibit cytochrome P450 isoenzymes. In patients with normal liver function, rifaximin at the recommended dosing regimen is not expected to induce CYP3A4. It is unknown whether rifaximin can have a significant effect on the pharmacokinetics of concomitant CYP3A4 substrates in patients with reduced liver function.
- Due to the potential for severe disruption of gut flora with unknown consequences rifaximin should not be administered concomitantly with other rifamycins.
- Rifaximin is a substrate of P-glycoprotein, it is unknown whether concomitant drugs that inhibit P-glycoprotein can increase the systemic exposure of rifaximin.

OVERDOSAGE

At doses higher than the recommended dose (> 600 mg/day for traveler's diarrhea or > 1100 mg/day for hepatic encephalopathy), adverse reactions were similar in subjects who received the recommended doses. In the case of overdosage, discontinue rifaximin, treat symptomatically and institute supportive measures as required.

STORAGE

Store at 25^{o}C (Excursions permitted between 15^{o}C - 30^{o}C). Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Nimixa (Rifaximin) Tablets 200mg are available in blister packs of 10's.
Nimixa (Rifaximin) Tablets 550mg are available in blister packs of 10's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:

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