ROYCE®

Rifampicin Capsule

(Rifampicin-Antibiotic)

Presentation :

Royce Rifampicin Capsule 150mg :

Size 2 capsule with opaque blue coloured cap and opaque green coloured body.

Royce Rifampicin Capsule 300mg :

Size 0 capsule with opaque brown coloured cap and opaque pink coloured body.

Content

Royce Rifampicin Capsule 300mg :

Each capsule contains :

Rifampicin 300 mg, Corn Starch, Magnesium Steareate

Each capsule shells contains :

Deionized Water, Sodium Lauryl Sulphate, Povidone, Propyl Paraben, Methyl Paraben.

Capsule Cap

Brilliant Blue FCF (E133), Quinone Yellow (E104), Carmoisine, Titanium Dioxide (E171) and Gelatin.

Capsule Body

Carmoisine (E122), Titanium Dioxide (E171) and Gelatin.

Royce Rifampicin Capsule 150mg :

Each capsule contains :

Rifampicin 150 mg, Corn Starch, Magnesium Steareate

Each capsule shells contains :

Deionized Water, Sodium Lauryl Sulphate, Povidone, Propyl Paraben, Methyl Paraben.

Capsule Cap

Erythrosine (E127), Sunset Yellow FCF, (E110), Brilliant Blue FCF (E133), and Titanium Dioxide (E171) and Gelatin.

Capsule Body

Quinoline Yellow (E104), Sunset Yellow FCF (E110), Brilliant Yellow FCF (E133), Titanium Dioxide (E171) and Gelatin.

Pharmacological Information

Rifampicin inhibits DNA-dependant RNA polymerize of mycobacteria and other microorganisms, leading to suppression of initiation of chain formation (but not chain elongation) in RNA synthesis. More specifically, the B subunit of this complex enzymes in the site of action of the drug. RNA polymerase from mammalian cells does not bind Rifampicin, and RNA synthesis is correspondingly unaffected.

It inhibits the growth of most gram-positive bacteria as well as gram-negative microorganisms as Escherichia coli, Pseudomonas, indole, positive and negative against Neisseria miningitidis. Minimal inhibitory concentrations range from 0.1 to 0.8µg/ml. It also inhibits the growth of certain types of viruses. Rifampicin is readily absorbed from the gastrointestinal tract and peak serum concentrations of about 8µg/ml have been reported 2 hours after a dose of 450mg and 27µg/ml after a dose of 900mg. About 75% to 80% of Rifampicin in the circulation is bound to serum proteins. Rifampicin, but not its main metabolite, undergoes enterohepatic circulation. It is widely distributed in body tissues; it crosses the placenta and diffuses into milk and into the CSF when the meninges are inflame. Food may reduce and delay absorption. Rifampicin is mainly metabolized
to active desecetylrifampicin and it is excreted in the bile and to a lesser extent in the urine. Up to 30% of a dose of 900mg may be excreted in the urine; about ½ of it in 24 hours. It has a biological ½ life about 3 hours.

Indication :

Royce Rifampicin Capsule used in combination with other active antituberculosis drugs is indicated in the treatment of all forms of tuberculosis. It is also effective against many atypical strains of mycobacteria.

Dosage and Administration :
Royce Rifampicin should be given as a single dose before meals to ensure rapid and complete absorption. Dosage should be adjusted according to body weight of patients.
Adults : 450 - 600mg daily as a single dose (based on approximately 10mg per kg body weight). Those patients 50 kg and over should take 600mg daily, whilst patients under 50 kg should take 450mg.
Children: Up to 20mg per kg body weight daily to a maximum of 600mg as a single dose.
Premature and newborn infants : 10mg/kg once daily.

Royce Rifampicin should be given with other effective antituberculosis drugs to prevent the possible emergence of rifampicin-resistant strains of mycobacteria.

Contraindication :
Jaundice; hypersensitivity to Rifampicin antibiotics; first trimester of pregnancy; premature and newborn infants; are concurrently receiving saquinavir/ritonavir therapy.

Warning and Precautions :
Rifampicin should be given under the supervision of a respiratory or other suitably qualified physician. Cautions should be taken in case of renal impairment if dose > 600 mg/day. All tuberculosis patients should have pre-treatment measurements of liver function. Adults treated for tuberculosis with Rifampicin should have baseline measurements of hepatic enzymes, bilirubin, serum creatinine, a complete blood count, and a platelet count (or estimate).
Baseline tests are unnecessary in children unless a complicating condition is known or clinically suspected. Patients with impaired liver function should only be given Rifampicin in cases of necessity, and then with caution and under close medical supervision. In these patients, lower doses of Rifampicin are recommended and careful monitoring of liver function, especially serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) should initially be carried out prior to therapy, weekly for two weeks, then every two weeks for the next six weeks. If signs of hepatocellular damage occur, Rifampicin should be withdrawn.
Rifampicin should also be withdrawn if clinically significant changes in hepatic function occur. The need for other forms of antituberculosis therapy and a different regimen should be considered. Urgent advice should be obtained from a specialist in the management of tuberculosis. If Rifampicin is re-introduced after liver function has returned to normal, liver function should be monitored daily.
In patients with impaired liver function, elderly patients, malnourished patients, and possibly, children under two years of age, caution is particularly recommended when instituting therapeutic regimens in which isoniazid is to be used concurrently with Rifampicin. If the patient has no evidence of pre-existing liver disease and normal pre-treatment liver function, liver function tests need only be repeated if fever, vomiting, jaundice or other deterioration in the patient's condition occur.

Patients should be seen at least monthly during therapy and should be specifically questioned concerning symptoms associated with adverse reactions.
In some patients hyperbilirubinaemia can occur in the early days of treatment. This results from competition between Rifampicin and bilirubin for hepatic excretion.

An isolated report showing a moderate rise in bilirubin and/or transaminase level is not in itself an indication for interrupting treatment; rather the decision should be made after repeating the tests, noting trends in the levels and considering them in conjunction with the patient's clinical condition.

Because of the possibility of immunological reaction including anaphylaxis (See section Side Effect) occurring with intermittent therapy (less than 2 to 3 times per week) patients should be closely monitored. Patients should be cautioned against interrupting treatment.

Rifampicin has enzyme induction properties that can enhance the metabolism of endogenous substrates including adrenal hormones, thyroid hormones and vitamin D. Isolated reports have associated porphyria exacerbation with Rifampicin administration.

Severe, systemic hypersensitivity reactions, including fatal cases, such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome have been observed during treatment with anti-tuberculosis therapy (See

section Side Effect). Rifampicin should be discontinued if an alternative etiology for the signs and symptoms cannot be established.

Severe cutaneous adverse reactions (SCARs) including Steven-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported with a not known frequency in association with Rifampicin treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions.

It is important to note that early manifestations of hypersensitivity, such as fever, lymphadenopathy or biological abnormalities (including eosinophilia, liver abnormalities) may be present even though rash is not evident. If such signs or symptoms are present, the patient should be advised to consult immediately their physician.

If signs and symptoms suggestive of these reactions appear, Rifampicin capsules should be withdrawn immediately and an alternative treatment considered (as appropriate).

Most of these reactions occurred within 2 days to 2 months after treatment initiation; the time to onset can vary depending on the conditions.

Rifampicin capsules may produce a discoloration (yellow, orange, red, brown) of the teeth, urine, sweat, sputum and tears, and the patient should be forewarned of this. Soft contact lenses have been permanently stained (See section Side Effect).

Rifampicin capsules are a well characterized and potent inducer of drug metabolizing enzymes and transporters and might therefore decrease concomitant drug exposure and efficacy (See section Interaction With Other Medicaments). Therefore, potential drug interactions should be considered whenever beginning or discontinuing Rifampicin treatment.

Rifampicin may cause vitamin K dependent coagulopathy and severe bleeding (See section Side Effect). Monitoring of occurrence of coagulopathy is recommended for patients at particular bleeding risk. Supplemental vitamin K administration should be considered when appropriate (vitamin K deficiency, hypoprothrombinemia).

All patients with abnormalities should have follow up examinations, including laboratory testing, if necessary.

Pregnancy and Lactation :
At very high doses in animals Rifampicin has been shown to have teratogenic effects. There are no well controlled studies with Rifampicin in pregnant women. Although Rifampicin has been reported to cross the placental barrier and appear in cord blood, the effect of Rifampicin, alone or in combination with other antituberculosis drugs, on the human foetus is not known. Therefore, Rifampicin should be used in pregnant women or in women of child bearing potential only if the potential benefit justifies the potential risk to the foetus. When Rifampicin is administered during the last few weeks of pregnancy it may cause post-natal haemorrhages in the mother and infant for which treatment with Vitamin K1 may be indicated.

Side Effect :
The following CIOMS frequency rating is used, when applicable:
Very common ≥ 10 %; Common ≥ 1 and <10 %; Uncommon ≥ 0.1 and <1%; Rare ≥ 0.01 and <0.1 %; Very rare <0.01 % ; Unknown (cannot be estimated from available data).

Reactions occurring with either daily or intermittent dosage regimens include:

System Organ Class	Frequency	Preferred Term
Infections and infestations	Unknown	Pseudomembranous colitis Influenza.
Blood and lymphatic system disorders	Common	Thrombocytopenia with or without purpura, usually associated with intermittent therapy, but is reversible if drug is discontinued as soon as purpura occurs.
	Uncommon	Leukopenia.
	Unknown	Disseminated intravascular coagulation, Eosinophilia, Agronulocytosis, Hemolytic anemia, Vitamin K dependent coagulation disorders.
Immune system disorder	Unknown	Anaphylactic reaction.
Endocrine disorder	Unknown	Adrenal insufficiency in patients with compromised adrenal function have been observed.
Metabolism and nutritional disorder	Unknown	Decreased appetite.
Psychiatric disorder	Unknown	Psychotic disorder.
Nervous system disorder	Common	Headache, Dizziness.
	Unknown	Cerebral haemorrhage and fatalities have been reported when rifampicin administration has been continued or resumed after appearance of purpura.
Eye disorders	Unknown	Tear discolouration.
Vascular disorders	Unknown	Shock, Flushing, Vasculitis, Bleeding.
Respiratory, thoracic and mediastinal disorders	Unknown	Dysponea, Wheezing, Sputum discoloured.
Gastrointestinal disorders	Common	Nausea, Vomiting.
	Uncommon	Diarrhea.
	Unknown	Gastrointestinal disorder, Abdominal discomfort, Tooth discolouration (which may be permanent).
Hepatobiliary disorders	Unknown	Hepatitis, Hyperbilirubinaemia.
Skin and subcutaneous tissue disorders	Unknown	Erythema multiforme Stevens-Johnson syndrome (SJS) , Toxic epidermal necrolysis (TEN) , Drug reaction with eosinophilia and systemic symptoms (DRESS) , Acute generalized exanthematous pustulosis (AGEP) (See section Warning and Precautions), Skin reaction , Pruritus, Rash pruritic, Urticaria , Dermatitis allergic, Pemphigoid , Sweat discoloration.
Musculoskeletal and connective tissue disorders	Unknown	Muscle weakness, Myopathy, Bone pain.
Renal and urinary disorders	Unknown	Acute kidney injury usually due to renal tubular necrosis or tubulointerstitial nephritis Chromaturia.
Pregnancy, Puerperium and perinatal conditions	Unknown	Post-partum haemorrhage, Fetal-maternal haemorrhage.
Reproductive system and breast disorders	Unknown	Menstrual disorder.
Congenital, familial and genetic disorders	Unknown	Porphyria.
General disorders and administration site conditions	Very common	Pyrexia, Chills.
	Unknown	Edema.
Investigations	Common	Blood bilirubin increased.
		Aspartate aminotransferase increased.
		Alanine aminotransferase increased.
	Unknown	Blood pressure decreased.
		Blood creatinine increased.
		Hepatic enzyme increased.

Interaction With Other Medicaments :

Pharmacodynamic Interactions

When Rifampicin is given concomitantly with the combination saquinavir/ritonavir, the potential for hepatotoxicity is increased. Therefore, concomitant use of Rifampicin with saquinvir/ritonavir is contraindicated (See section Contraindications).

When Rifampicin is given concomitantly with either halothane or isoniazid, the potential for hepatotoxicity is increased. The concomitant use of Rifampicin and halothane should be avoided. Patients receiving both Rifampicin and isoniazid should be monitored closely for hepatotoxicity.

The concomitant use of Rifampicin with other antibiotics causing vitamin K dependent coagulopathy such as cefazolin (or other cephalosporins with N-methylthiotetrazole side chain) should be avoided as it may lead to severe coagulation disorders, which may result in fatal outcome (especially in high doses).

Effect of Rifampicin on other medicinal products

Induction of Drug Metabolizing Enzymes and Transporters

Rifampicin are a well characterized and potent inducer of drug metabolizing enzymes and transporters. Enzymes and transporters reported to be affected by rifampicin include cytochromes P450 (CYP) 1A2, 2B6, 2C8, 2C9, 2C19, and 3A4, UDP-glucuronyltransferases (UGT), sulfotransferases, carboxylesterases, and transporters including P-glycoprotein (P-gp) and multidrug resistance-associated protein 2 (MRP2). Most drugs are substrates for one or more of these enzyme or transporter pathways, and these pathways may be induced by Rifampicin simultaneously. Therefore, Rifampicin may accelerate the metabolism and reduce the activity of certain co-administered drugs, and has the potential to perpetuate clinically important drug-drug interactions against many drugs and across many drug classes. To maintain optimum therapeutic blood levels, dosages of drugs may require adjustment when starting or stopping concomitantly administered Rifampicin capsules.

Examples of drugs or drug classes affected by Rifampicin:

- Antiarrhythmics (e.g. disopyramide, mexiletine, quinidine, propafenone,tocainide)
- Antiepileptics (e.g. phenytoin)
- Hormone antagonist (antiestrogens e.g. tamoxifen, toremifene, gestinone)
- Antipsychotics (eg. haloperidol, aripiprazole)
- Anticoagulants (e.g. coumarins)
- Antifungals (e.g. fluconazole, itraconazole, ketoconazole,voriconazole)
- Antivirals (e.g. saquinavir, indinavir, efavirenz, amprenavir, nelfinavir, atazanavir, lopinavir, nevirapine)
- Barbiturates
- Beta-blockers (e.g. bisoprolol, propranolol)
- Anxiolytics and hypnotics (e.g. diazepam, benzodiazepines, zolpicolone, zolpidem)
- Calcium channel blockers (e.g. diltiazem, nifedipine, verapamil, nimodipine, isradipine, nicardipine, nisoldipine)
- Antibacterials (e.g. chloramphenicol, clarithromycin, dapsone, doxycycline, fluoroquinolones, telithromycin)
- Corticosteroids
- Cardiac glycosides (e.g digitoxin, digoxin)
- Clofibrate
- Systematic hormonal contraceptives including estrogens and progestogens
- Antidiabetic (e.g. chlorpropamide, tolbutamide, sulfonylureas, rosiglitazone)
- Immunosuppressive agents (e.g. ciclosporin, sirolimus, tacrolimus)
- Irinotecan
- Thyroid hormone (e.g. levothyroxine)
- Losartan
- Analgestics (e.g. methadone, narcotic analgesics)
- Praziquantel
- Quinine
- Riluzole
- Selective 5-HT3 receptor antagonists (e.g. ondansetron)
- Statins metabolised by CYP 3A4 (e.g. simvastatin)
- Theophylline

- Tricyclic antidepressants (e.g. amitriptyline, nortriptyline)
- Cytotoxics (e.g. imatinib)
- Diuretics (e.g. eplerenone)
- Enalapril (decreased enalapril active metabolite exposure. Dosage adjustments should be made if indicated by the patient's clinical condition)
- Hepatitis-C antiviral drugs (eg, daclatasvir, simeprevir, sofosbuvir, telaprevir), (Concurrent use of treatment of hepatitis-C antiviral drugs and rifampicin should be avoided).
- Morphine (Plasma concentrations of morphine may be reduced by rifampicin. The analgesic effect of morphine should be monitored and doses of morphine adjusted during and after treatment of rifampicin)

Rifampicin treatment reduces the systemic exposure of oral contraceptives. Patients on oral contraceptives should be advised to use alternative, non-hormonal methods of birth control during Rifampicin therapy. Also, diabetes may become more difficult to control.

Concurrent use of ketoconazole and Rifampicin has resulted in decreased serum concentrations of both drugs.

If p-aminosalicylic acid and Rifampicin are both included in the treatment regimen, they should be given not less than eight hours apart to ensure satisfactory blood levels.

Effect of other medicinal products on Rifampicin capsules
Concomitant antacid administration may reduce the absorption of Rifampicin. Daily doses of Rifampicin should be given at least 1 hour before the ingestion of antacids.

Other drug interactions with Rifampicin
When the two drugs were taken concomitantly, decreased concentrations of atovaquone and increased concentrations of Rifampicin were observed.

Interference with laboratory and diagnostic tests
Therapeutic levels of Rifampicin have been shown to inhibit standard microbiological assays for serum folate and Vitamin B12. Thus alternative assay methods should be considered. Transient elevation of BSP and serum bilirubin has been reported. Rifampicin may impair biliary excretion of contrast media used for visualization of the gallbladder, due to competition for biliary excretion. Therefore, these tests should be performed before the morning dose of Rifampicin.

Symptoms and Treatment of Overdose :
In cases of overdosage, gastric lavage should be performed. Intensive supportive measures should be instituted and individual symptoms treated as they arise.

Storage Condition :
Keep container tightly closed. Store in a dry place below 30°C. Protect from light.

Pack Size :
Royce Rifampicin Capsule 150mg :
Blister pack of 1x10's, 10x10's,50x10's and 100x10's.
Royce Rifampicin Capsule 300mg :
Blister pack of 1x10's, 10x10's,50x10's and 100x10's.

** Not all presentations may be available locally.*

Registration Numbers :
Royce Rifampicin Capsule 150 mg : MAL19860793AZ
Royce Rifampicin Capsule 300 mg : MAL19860827AZ

Further information can be obtained from your doctor or pharmacist.

ROYCE®

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