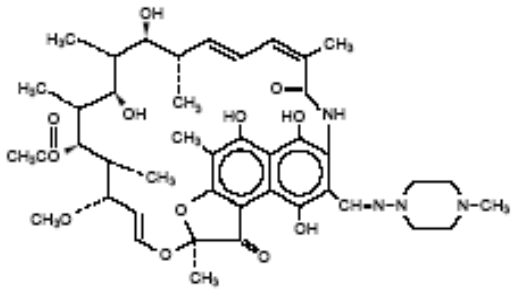
Rifampin Capsules, USP

Rx only

To reduce the development of drug-resistant bacteria and maintain the effectiveness of rifampin capsules and other antibacterial drugs, rifampin capsules should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Rifampin USP, is a semisynthetic antibiotic derivative of rifamycin B, available as 300-mg capsules for oral administration. Rifampin is 3-[[(4- methyl-1-piperazinyl) imino] methyl] rifamycin, and its structural formula is:



Rifampin USP is a red-brown crystalline powder. It is very slightly soluble in water, freely soluble in chloroform, and soluble in ethyl acetate and in methanol. Its molecular weight is 822.95.

Inactive Ingredients. FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, lactose monohydrate, magnesium stearate, methylparaben, propylparaben, silicon dioxide, sodium lauryl sulfate, corn starch, talc, and titanium dioxide.

CLINICAL PHARMACOLOGY

Peak blood levels in normal adults vary widely from individual to individual. Peak levels occur between 2 and 4 hours following the oral administration of a 600-mg dose. The average peak value is 7 mcg/mL; however, the peak level may vary from 4 to 32 mcg/mL.

In normal subjects the biological half-life ($T_{1/2}$) of rifampin in blood is approximately 3 hours. Elimination occurs mainly through the bile and, to a much lesser extent, the urine.

Microbiology

Mechanism of Action

Rifampin inhibits DNA-dependent RNA polymerase activity in susceptible cells. Specifically, it interacts with bacterial RNA polymerase but does not inhibit the mammalian enzyme. This is the mechanism of action by which rifampin exerts its therapeutic effect. Rifampin cross resistance has only been shown with other rifamycins.

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria, and associated test methods and quality control standards recognized by FDA for this drug, please see: http://www.fda.gov/STIC

INDICATIONS and USAGE

Rifampin Capsules, USP are indicated for the treatment of pulmonary tuberculosis and for the treatment of asymptomatic carriers of *N. meningitidis* to eliminate meningococci from the nasopharynx.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of rifampin capsules and other antibacterial drugs, rifampin capsules should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Pulmonary Tuberculosis

In the initial treatment and in the retreatment of pulmonary tuberculosis, rifampin must be used in conjunction with at least one other antituberculous drug.

Frequently used regimens have been the following: isoniazid and
rifampin
ethambutol and rifampin
isoniazid, ethambutol, and rifampin

Neisseria Meningitidis Carriers

Rifampin is indicated for the treatment of asymptomatic carriers of *N. meningitidis* to eliminate meningococci from the nasopharynx.

Rifampin is not indicated for the treatment of meningococcal infection.

To avoid the indiscriminate use of rifampin, diagnostic laboratory procedures, including serotyping and susceptibility testing, should be performed to establish the carrier state and the correct treatment. In order to preserve the usefulness of rifampin in the treatment of asymptomatic meningococcal carriers, it is recommended that the drug be reserved for situations in which the risk of meningococcal meningitis is high.

Both in the treatment of tuberculosis and in the treatment of meningococcal carriers, small numbers of resistant cells, present within large populations of susceptible cells, can rapidly become the predominating type. Since rapid emergence of resistance can occur, culture and susceptibility tests should be performed in the event of persistent positive cultures.

CONTRAINDICATIONS

A history of previous hypersensitivity reaction to any of the rifamycins.

Rifampin is contraindicated in patients receiving lurasidone. Concomitant use of lurasidone with strong CYP3A4 inducers (e.g., rifampin) decreased the exposure of lurasidone compared to the use of lurasidone alone (see **PRECAUTIONS**, Drug Interactions).

WARNINGS

Rifampin has been shown to produce liver dysfunction. There have been fatalities associated with jaundice in patients with liver disease or receiving rifampin concomitantly with other hepatotoxic agents. Since an increased risk may exist for individuals with liver disease, benefits must be weighed carefully against the risk of further liver damage. Periodic liver function monitoring is mandatory.

The possibility of rapid emergence of resistant meningococci restricts the use of rifampin to short-term treatment of the asymptomatic carrier state. Rifampin is not to be used for the treatment of meningococcal disease.

Several studies of tumorigenicity potential have been done in rodents. In one strain of mice known to be particularly susceptible to the spontaneous development of hepatomas, rifampin given at a level 2-10 times the maximum dosage used clinically resulted in a significant increase in the occurrence of hepatomas in female mice of this strain after one year of administration. There was no evidence of tumorigenicity in the males of this strain, in males or females of another mouse strain, or rats.

Usage in Pregnancy

Although rifampin has been reported to cross the placental barrier and appear in cord blood, the effect of rifampin, alone or in combination with other antituberculous drugs, on the human fetus is not known. An increase in congenital malformations, primarily spina bifida and cleft palate, has been reported in the offspring of rodents given oral doses of 150-250 mg/kg/day of rifampin during pregnancy.

The possible teratogenic potential in women capable of bearing children should be carefully weighed against the benefits of therapy.

PRECAUTIONS

General

Prescribing rifampin capsules 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.

Rifampin is not recommended for intermittent therapy; the patient should be cautioned against intentional or accidental interruption of the daily dosage regimen since rare renal hypersensitivity reactions have been reported when therapy was resumed in such cases.

Rifampin has been observed to increase the requirements for anticoagulant drugs of the coumarin type. The cause of this phenomenon is unknown. In patients receiving anticoagulants and rifampin concurrently, it is recommended that the prothrombin time be performed daily or as frequently as necessary to establish and maintain the required dose of anticoagulant.

Urine, feces, saliva, sputum, sweat, and tears may be colored red-orange by rifampin and its metabolites. Soft contact lenses may be permanently stained. Individuals to be treated should be made aware of these possibilities.

It has been reported that the reliability of oral contraceptives may be affected in some patients being treated for tuberculosis with rifampin in combination with at least one other antituberculous drug. In such cases, alternative contraceptive measures may need to be considered.

Rifampin has been reported to diminish the effects of concurrently administered methadone, oral hypoglycemics, corticosteroids, dapsone, digitalis preparations and to reduce the bioavailability and efficacy of verapamil. Appropriate dosage adjustments may be necessary if indicated by the patient's clinical condition.

When rifampin is taken in combination with PAS, decreased rifampin serum levels may result. Therefore, the drugs should be given at least 4 hours apart.

Therapeutic levels of rifampin have been shown to inhibit standard assays for serum folate and vitamin B_{12}. Alternative methods must be considered when determining folate and vitamin B_{12} concentrations in the presence of rifampin.

Since rifampin has been reported to cross the placental barrier and appear in cord blood, neonates of rifampin-treated mothers should be carefully observed for any evidence of adverse effects. Rifampin is excreted in breast milk.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Information for Patients

Patients should be counseled that antibacterial drugs including rifampin capsules should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When rifampin capsules are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment and, (2) increase the likelihood that bacteria will develop resistance and will not be treatable by rifampin capsules or other antibacterial drugs in the future.

Drug Interactions

Table 1: Drug Interactions with Rifampin that Affect Concomitant Drug Concentrations

Drug or Drug Class and Prevention or Management	Clinical Effect
Antipsychotics	
Lurasidone *Prevention or Management:* Concomitant use is contraindicated (See **CONTRAINDICATIONS**)	Decrease exposure

ADVERSE REACTIONS

Gastrointestinal disturbances such as heartburn, epigastric distress, anorexia, nausea, vomiting, gas, cramps, and diarrhea have been noted in some patients. Rarely, pseudomembranous enterocolitis has been reported. Headache, drowsiness, fatigue, ataxia, dizziness, inability to concentrate, mental confusion, visual disturbances, muscular weakness, fever, pains in extremities, generalized numbness, and menstrual disturbances have also been noted.

Hypersensitivity reactions have been reported. Encountered occasionally have been pruritus, urticaria, rash, pemphigoid reaction, eosinophilia, sore mouth, sore tongue, and exudative conjunctivitis.

Rarely, hepatitis or a shock-like syndrome with a hepatic involvement and abnormal liver function tests have been reported. Transient abnormalities in liver function tests (e.g., elevations in serum bilirubin, BSP, alkaline phosphatase, serum transaminases) have also been observed. The BSP test should be performed prior to the morning dose of rifampin to avoid false-positive results.

Thrombocytopenia, transient leukopenia, hemolytic anemia, and decreased hemoglobin have been observed. Thrombocytopenia has occurred when rifampin and ethambutol were administered concomitantly according to an intermittent dose schedule twice weekly and in high doses.

Elevations in BUN and serum uric acid have occurred. Rarely, hemolysis, hemoglobinuria, hematuria, renal insufficiency or acute renal failure have been reported and are generally considered to be hypersensitivity reactions. These have usually occurred during intermittent therapy or when treatment was resumed following intentional or accidental interruption of a daily dosage regimen and were reversible when rifampin was discontinued and appropriate therapy instituted.

Although rifampin has been reported to have an immunosuppressive effect in some animal experiments, available human data indicate that this has no clinical significance.

DOSAGE AND ADMINISTRATION

It is recommended that rifampin be administered once daily, either one hour before or two hours after a meal.

Data are not available for determination of dosage for children under 5.

Pulmonary Tuberculosis

Adults: 600 mg (two 300-mg Capsules) in a single daily administration.

Children: 10 to 20 mg/kg, not to exceed 600 mg/day.

In the treatment of pulmonary tuberculosis, rifampin must be used in conjunction with at least one other antituberculous agent. In general, therapy should be continued until bacterial conversion and maximal improvement have occurred.

Meningococcal Carriers

It is recommended that rifampin be administered once daily for four consecutive days in the following doses:

Adults: 600 mg (two 300-mg Capsules) in a single daily administration.

Children: 10 to 20 mg/kg, not to exceed 600 mg/day.

OVERDOSAGE

Signs and Symptoms

Nausea, vomiting, and increasing lethargy will probably occur within a short time after ingestion; actual unconsciousness may occur with severe hepatic involvement. Brownish-red or orange discoloration of the skin, urine, sweat, saliva, tears and feces is proportional to amount ingested.

Liver enlargement, possibly with tenderness, can develop within a few hours after severe overdosage and jaundice may develop rapidly. Hepatic involvement may be more marked in patients with prior impairment of hepatic function. Other physical findings remain essentially normal.

Direct and total bilirubin levels may increase rapidly with severe overdosage; hepatic enzyme levels may be affected, especially with prior impairment of hepatic function. A direct effect upon hemopoietic system, electrolyte levels, or acid-base balance is unlikely.

Treatment

Since nausea and vomiting are likely to be present, gastric lavage is probably preferable to induction of emesis. Activated charcoal slurry instilled into the stomach following evacuation of gastric contents can help absorb any remaining drug in G.I. tract. Antiemetic medication may be required to control severe nausea/vomiting.

Active diuresis (with measured intake and output) will help promote excretion of the drug. Bile drainage may be indicated in presence of serious impairment of hepatic function lasting more than 24-48 hours; under these circumstances, extracorporeal hemodialysis may be required.

In patients with previously adequate hepatic function, reversal of liver enlargement and impaired hepatic excretory function probably will be noted within 72 hours, with rapid return toward normal thereafter.

Rev. 8-2023

Manufactured for
Oxford Pharmaceuticals, LLC.,
Birmingham, AL 35211