

Effect of Other Drugs on Rifampin

Concomitant antacid administration may reduce the absorption of rifampin. Daily doses of rifampin should be given at least 1 hour before the ingestion of antacids.

Concomitant use with probenecid and cotrimoxazole increases the concentration of rifampin which may increase the risk of Rifampin toxicities. Monitor for adverse reactions associated with Rifampin during coadministration.

Other Interactions

Atovaquone: Concomitant use of rifampin with atovaquone decrease concentrations of atovaquone and increase concentrations of rifampin which may increase the risk of Rifampin toxicities. Coadministration of rifampin with atovaquone is not recommended.

Drug/Laboratory Interactions

Cross-reactivity and false-positive urine screening tests for opiates have been reported in patients receiving rifampin when using the KIMS (Kinetic Interaction of Microparticles in Solution) method (e.g., Abuscreen OnLine opiates assay; Roche Diagnostic Systems).

Confirmatory tests, such as gas chromatography/mass spectrometry, will distinguish rifampin from opiates.

Therapeutic levels of rifampin have been shown to inhibit standard microbiological assays for serum folate and vitamin B₁₂. Thus, alternate assay methods should be considered. Transient abnormalities in liver function tests (e.g., elevation in serum bilirubin, alkaline phosphatase, and serum transaminases) and reduced biliary excretion of contrast media used for visualization of the gallbladder have also been observed.

Therefore, these tests should be performed before the morning dose of rifampin.

Carcinogenesis, Mutagenesis, Impairment of Fertility

A few cases of accelerated growth of lung carcinoma have been reported in man, but a causal relationship with the drug has not been established. Hepatomas were increased in female (C3Hf/DP) mice dosed for 60 weeks with rifampin followed by an observation period of 46 weeks, at 20 to 120 mg/kg (equivalent to 0.1 to 0.5 times the maximum dosage used clinically, based on body surface area comparisons). There was no evidence of tumorigenicity in male C3Hf/DP mice or in similar studies in BALB/c mice, or in two-year studies in Wistar rats.

There was no evidence of mutagenicity in both prokaryotic (*Salmonella typhi*, *Escherichia coli*) and eukaryotic (*Saccharomyces cerevisiae*) bacteria, *Drosophila melanogaster*, or ICR/Ha Swiss mice. An increase in chromatid breaks was noted when whole blood cell cultures were treated with rifampin. Increased frequency of chromosomal aberrations was observed *in vitro* in lymphocytes obtained from patients treated with combinations of rifampin, isoniazid, and pyrazinamide and combinations of streptomycin, rifampin, isoniazid, and pyrazinamide.

Pregnancy-Teratogenic Effects

Rifampin has been shown to be teratogenic in rodents. Congenital malformations, primarily spina bifida, were increased in the offspring of pregnant rats given rifampin during organogenesis at oral doses of 150 to 250 mg/kg/day (about 1 to 2 times the maximum recommended human dose based on body surface area comparisons). Cleft palate was increased in a dose-dependent fashion in fetuses of pregnant mice treated at oral doses of 50 to 200 mg/kg (about 0.2 to 0.8 times the maximum recommended human dose based on body surface area comparisons). Imperfect osteogenesis and embryotoxicity were also reported in pregnant rabbits given rifampin at oral doses up to 200 mg/kg/day (about 3 times the maximum recommended human dose based on body surface area comparisons). There are no adequate and well-controlled studies of Rifampin in pregnant women. Rifampin has been reported to cross the placental barrier and appear in cord blood. Rifampin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pregnancy-Non-Teratogenic Effects

When administered during the last few weeks of pregnancy, rifampin can cause postnatal hemorrhages in the mother and infant for which treatment with vitamin K may be indicated.

Nursing Mothers

Because of the potential for tumorigenicity shown for rifampin in animal studies, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

See CLINICAL PHARMACOLOGY-Pediatrics; see also DOSAGE AND ADMINISTRATION.

Geriatric Use

Clinical studies of Rifampin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Caution should therefore be observed in using rifampin in elderly patients. (See WARNINGS.)

ADVERSE REACTIONS

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Gastrointestinal

Heartburn, epigastric distress, anorexia, nausea, vomiting, jaundice, flatulence, cramps, and diarrhea have been noted in some patients. Although *Clostridium difficile* has been shown *in vitro* to be sensitive to rifampin, pseudomembranous colitis has been reported with the use of rifampin (and other broad-spectrum

antibiotics). Therefore, it is important to discuss this diagnosis in patients who develop diarrhea in association with antibiotic use. Tooth discoloration (which may be permanent) may occur.

Hepatic

Hepatotoxicity including transient abnormalities in liver function tests (e.g., elevations in serum bilirubin, alkaline phosphatase, serum transaminases, gamma-glutamyl transferase), hepatitis, a shock-like syndrome with hepatic involvement and abnormal liver function tests, and cholestasis have been reported (see WARNINGS).

Hematologic

Thrombocytopenia has occurred primarily with high dose intermittent therapy but has also been noted after resumption of interrupted treatment. It rarely occurs during well-supervised daily therapy. This effect is reversible if the drug is discontinued as soon as purpura occurs. Cerebral hemorrhage and fatalities have been reported when rifampin administration has been continued or resumed after the appearance of purpura.

Rare reports of disseminated intravascular coagulation have been observed.

Leukopenia, hemolytic anemia, decreased hemoglobin, bleeding, and vitamin K-dependent coagulation disorders (abnormal prolongation of prothrombin time or low vitamin K-dependent coagulation factors) have been observed.

Agranulocytosis has been reported very rarely.

Central Nervous System

Headache, fever, drowsiness, fatigue, ataxia, dizziness, inability to concentrate, mental confusion, behavioral changes, muscular weakness, pains in extremities, and generalized numbness have been observed.

Psychoses have been rarely reported.

Rare reports of myopathy have also been observed.

Ocular

Visual disturbances have been observed.

Endocrine

Menstrual disturbances have been observed.

Rare reports of adrenal insufficiency in patients with compromised adrenal function have been observed.

Renal

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

Dermatologic

Cutaneous reactions are mild and self-limiting and do not appear to be hypersensitivity reactions. Typically, they consist of flushing and itching with or without a rash. More serious cutaneous reactions which may be due to hypersensitivity occur but are uncommon.

Hypersensitivity Reactions

Occasionally, pruritus, urticaria, rash, pemphigoid reaction, erythema multiforme, acute generalized exanthematous pustulosis, Stevens-Johnson syndrome, toxic epidermal necrolysis, Drug Reaction with Eosinophilia and Systemic Symptoms syndrome (see WARNINGS), vasculitis, eosinophilia, sore mouth, sore tongue, and conjunctivitis have been observed.

Anaphylaxis has been reported rarely.

Respiratory, Thoracic and Mediastinal Disorders

Pulmonary toxicity (including, but not limited to, interstitial lung disease, pneumonitis, hypersensitivity pneumonitis, eosinophilic pneumonia, pulmonary infiltrates, organizing pneumonia, respiratory failure, pulmonary fibrosis, and acute respiratory distress syndrome) has been observed (see WARNINGS).

Miscellaneous

Paradoxical drug reaction has been reported with rifampin (see WARNINGS). Edema of the face and extremities has been reported. Other reactions which have occurred with intermittent dosage regimens include "flu syndrome" (such as episodes of fever, chills, headache, dizziness, and bone pain), shortness of breath, wheezing, decrease in blood pressure and shock. The "flu syndrome" may also appear if rifampin is taken irregularly by the patient or if daily administration is resumed after a drug-free interval.

OVERDOSAGE

Signs and Symptoms

Nausea, vomiting, abdominal pain, pruritus, headache, and increasing lethargy will probably occur within a short time after ingestion; unconsciousness may occur when there is severe hepatic disease. Transient increases in liver enzymes and/or bilirubin may occur. Brownish-red or orange discoloration of the skin, urine, sweat, saliva, tears, and feces will occur, and its intensity is proportional to the amount ingested.

Liver enlargement, possibly with tenderness, can develop within a few hours after severe overdosage; bilirubin levels may increase 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. A direct effect upon the hematopoietic system, electrolyte levels, or acid-base balance is unlikely.

Facial or periorbital edema has also been reported in pediatric patients. Hypotension, sinus tachycardia, ventricular arrhythmias, seizures, and cardiac arrest were reported in some fatal cases.

Acute Toxicity

The minimum acute lethal or toxic dose is not well established. However, nonfatal acute overdoses in adults have been reported with doses ranging from 9 to 12 gm rifampin. Fatal acute overdoses in adults have been reported with doses ranging from 14 to 60 gm. Alcohol or a history of alcohol abuse was involved in some of the fatal and nonfatal reports. Nonfatal overdoses in pediatric patients ages 1 to 4 years old of 100 mg/kg for one to two doses has been reported.

Treatment

Intensive support measures should be instituted and individual symptoms treated as they arise. The airway should be secured and adequate respiratory exchange established. Since nausea and vomiting are likely to be present, gastric lavage within the first 2 to 3 hours after ingestion is probably preferable to induction of emesis. Following evacuation of the gastric contents, the instillation of activated charcoal slurry into the stomach may help absorb any remaining drug from the gastrointestinal tract. Antiemetic medication may be required to control severe nausea and vomiting.

Active diuresis (with measured intake and output) will help promote excretion of the drug.

For severe cases, extracorporeal hemodialysis may be required. If this is not available, peritoneal dialysis can be used along with forced diuresis.

DOSAGE AND ADMINISTRATION

Rifampin for Injection, USP can be administered by IV infusion (see INDICATIONS AND USAGE).

See CLINICAL PHARMACOLOGY for dosing information in patients with renal failure.

Tuberculosis

Adults: 10 mg/kg, in a single daily administration, not to exceed 600 mg/day, IV

Pediatric Patients: 10-20 mg/kg, not to exceed 600 mg/day, IV
Rifampin is indicated in the treatment of all forms of tuberculosis. A three-drug regimen consisting of rifampin, isoniazid, and pyrazinamide is recommended in the initial phase of short-course therapy which is usually continued for 2 months. The Advisory Council for the Elimination of Tuberculosis, the American Thoracic Society, and the Centers for Disease Control and Prevention recommend that either streptomycin or ethambutol be added as a fourth drug in a regimen containing isoniazid (INH), rifampin, and pyrazinamide for initial treatment of tuberculosis unless the likelihood of INH resistance is very low. The need for a fourth drug should be reassessed when the results of susceptibility testing are known. If community rates of INH resistance are currently less than 4%, an initial treatment regimen with less than four drugs may be considered.

Following the initial phase, treatment should be continued with rifampin and isoniazid for at least 4 months. Treatment should be continued for longer if the patient is still sputum or culture positive, if resistant organisms are present, or if the patient is HIV positive.

Preparation of Solution for IV Infusion

Reconstitute the lyophilized powder by transferring 10 mL of sterile water for injection to a vial containing 600 mg of Rifampin for Injection. Swirl vial gently to completely dissolve the antibiotic. The reconstituted solution contains 60 mg rifampin per mL and is stable at room temperature for 24 hours. Prior to administration, withdraw from the reconstituted solution a volume equivalent to the amount of rifampin calculated to be administered and add to 500 mL of infusion medium. Mix well and infuse at a rate allowing for complete infusion within 3 hours. Alternatively, the amount of rifampin calculated to be administered may be added to 100 mL of infusion medium and infused in 30 minutes.

Dilutions in dextrose 5% for injection (D5W) are stable at room temperature for up to 4 hours and should be prepared and used within this time. Precipitation of rifampin from the infusion solution may occur beyond this time. Dilutions in normal saline are stable at room temperature for up to 24 hours and should be prepared and used within this time. Other infusion solutions are not recommended.

Incompatibilities

Physical incompatibility (precipitate) was observed with undiluted (5 mg/mL) and diluted (1 mg/mL in normal saline) diltiazem hydrochloride and rifampin (6 mg/mL in normal saline) during simulated Y-site administration.

Meningococcal Carriers

Adults: For adults, it is recommended that 600 mg rifampin be administered twice daily for two days.

Pediatric Patients: Pediatric patients 1 month of age or older: 10 mg/kg (not to exceed 600 mg per dose) every 12 hours for two days.

Pediatric patients under 1 month of age: 5 mg/kg every 12 hours for two days.

HOW SUPPLIED:

Rifampin for Injection, USP is supplied as:

Product Code	Unit of Sale	Strength
305120	NDC 63323-351-20 Individually packaged	600 mg per vial

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Avoid excessive heat (temperatures above 40°C or 104°F).

Protect from light.

The container closure is not made with natural rubber latex.



Lake Zurich, IL 60047

www.fresenius-kabi.com/us

4 5 1 1 5 7 C

Revised: July 2022