RIFADIN® (rifampin capsules USP) and
RIFADIN IV (rifampin for injection USP)

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

**DESCRIPTION**

RIFADIN (rifampin capsules USP) for oral administration contain 150 mg or 300 mg rifampin per capsule. The 150 mg and 300 mg capsules also contain, as inactive ingredients: corn starch, D&C Red No. 28, FD&C Blue No. 1, FD&C Red No. 40, gelatin, magnesium stearate, and titanium dioxide.

RIFADIN IV (rifampin for injection USP) contains rifampin 600 mg, sodium formaldehyde sulfoxylate 10 mg, and sodium hydroxide to adjust pH.

Rifampin is a semisynthetic antibiotic derivative of rifamycin SV. Rifampin is a red-brown crystalline powder very slightly soluble in water at neutral pH, freely soluble in chloroform, soluble in ethyl acetate and in methanol. Its molecular weight is 822.05 and its chemical formula is C_{34}H_{48}N_{4}O_{6}. The chemical name for rifampin is 3-[[4-(4-Methyl-1-piperazinyl)-2-imino]methyl]rifamycin S. Rifampin is a red-brown crystalline powder very slightly soluble in water at neutral pH, freely soluble in chloroform, soluble in ethyl acetate and in methanol.

**CLINICAL PHARMACOLOGY**

**Oral Administration**

Rifampin is readily absorbed from the gastrointestinal tract. Peak serum concentrations in healthy adults and pediatric populations vary widely from individual to individual. Following a single 600 mg oral dose of rifampin in healthy adults, the peak serum concentration averages 7 mcg/mL but may vary from 4 to 32 mcg/mL. Absorption of rifampin is reduced by about 30% when the drug is ingested with food.

Rifampin is widely distributed throughout the body. It is present in effective concentrations in many organs and body fluids, including cerebrospinal fluid. Rifampin is about 80% protein bound. Most of the unbound fraction is not ionized and, therefore, diffuses freely into tissues.

In healthy adults, the mean biological half-life of rifampin in serum averages 3.35±0.66 hours after a 600 mg oral dose, with increases up to 5.9±2.45 hours reported after a 900 mg dose. With repeated administration, the half-life decreases and reaches average values of approximately 2 to 3 hours.

**Intravenous Administration**

After intravenous administration of a 300 or 600 mg dose of rifampin infused over 30 minutes to 1 hour, peak plasma concentrations were 9.0±3.0 and 17.5±5.0 mcg/mL, respectively. Total body clearances after the 300 and 600 mg IV doses were 0.19±0.06 and 0.14±0.03 L/hr/kg, respectively. Volumes of distribution at steady state were 0.65±0.14 and 0.64±0.11 L/kg for the 300 and 600 mg IV doses, respectively. After intravenous administration of 300 or 600 mg doses, rifampin plasma concentrations in these volunteers remained detectable for 8 and 12 hours, respectively (see Table). Plasma concentrations (mean ± standard deviation, mcg/mL)

<table>
<thead>
<tr>
<th>Rifampin Dosage IV</th>
<th>30 min</th>
<th>1 hr</th>
<th>2 hr</th>
<th>4 hr</th>
<th>8 hr</th>
<th>12 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg</td>
<td>8.9±2.9</td>
<td>4.9±1.3</td>
<td>4.0±1.3</td>
<td>2.5±1.0</td>
<td>1.1±0.6</td>
<td>&lt;0.4</td>
</tr>
<tr>
<td>600 mg</td>
<td>17.4±5.1</td>
<td>11.7±2.8</td>
<td>9.4±2.3</td>
<td>6.4±1.7</td>
<td>3.5±1.4</td>
<td>1.2±0.6</td>
</tr>
</tbody>
</table>

Plasma concentrations after the 600 mg dose, which were disproportionately higher (up to 30% greater than expected) than those found after the 300 mg dose, indicated that the elimination of larger doses was not as rapid. After repeated once-a-day infusions (3-hr duration) of 600 mg in patients (n=5) for 7 days, concentrations of IV rifampin decreased from 5.8±1.38 mcg/mL 8 hours after the infusion of 300 mg to 2.6±1.98 mcg/mL 8 hours after the infusion on day 7.

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Rifampin is rapidly eliminated in the bile and undergoes progressive enterohepatic circulation and deacetylation to the primary metabolite, 25-desacetyl-rifampin. This metabolite is microbiologically active. Less than 30% of the dose is excreted in the urine as rifampin or metabolites. Serum concentrations do not differ in patients with renal failure at a studied dose of 300 mg and, consequently, no dosage adjustment is required.

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**Mechanism of Action**

Rifampin inhibits DNA-dependent RNA polymerase activity in susceptible Mycobacterium tuberculosis organisms. Specifically, it interacts with bacterial RNA polymerase but does not inhibit the mammalian enzyme.

**Resistance**

Organisms resistant to rifampin are likely to be resistant to other rifamycins.

In the treatment of both tuberculosis and the meningococcal carrier state (see INDICATIONS AND USAGE), the small number of resistant cells present within large populations of susceptible cells can rapidly become predominant. In addition, resistance to rifampin has been determined to occur in strains of the drug-resistant DNA-dependent RNA polymerase. Since resistance can emerge rapidly, appropriate susceptibility tests should be performed in the event of persistent positive cultures.

**Activity in vitro and in vivo**

Rifampin has bactericidal activity in vitro against slow and intermittently growing M. tuberculosis organisms.

Rifampin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section:

- **Aerobic Gram-Negative Microorganisms:** Neisseria meningitidis
- “Other” Microorganisms: Mycobacterium tuberculosis

The following in vitro data are available, but their clinical significance is unknown:

- Rifampin exhibits in vitro activity against most strains of the following microorganisms; however, the safety and effectiveness of rifampin in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled trials:
  - Aerobic Gram-Positive Microorganisms: Staphylococcus aureus (including Methicillin-Resistant S. aureus/MRSA), Staphylococcus epidermidis
  - Aerobic Gram-Negative Microorganisms: Haemophilus influenzae
  - “Other” Microorganisms: Mycobacterium leprae
  - B-lactamase production should have no effect on rifampin activity.

**Susceptibility Testing**

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

**INDICATIONS AND USAGE**

In the treatment of both tuberculosis and the meningococcal carrier state, the small number of resistant cells present within large populations of susceptible cells can rapidly become the predominant type. Bacteriologic cultures should be obtained before the start of therapy to confirm the susceptibility of the organism to rifampin and they should be repeated throughout therapy to monitor the response to treatment. Since resistance can emerge rapidly, susceptibility tests should be performed in the event of persistent positive cultures during the course of treatment. If test results show resistance to rifampin and the patient is not responding to therapy, the drug regimen should be modified.

**Tuberculosis**

Rifampin is indicated in the treatment of all forms of tuberculosis. A three-drug regimen consisting of rifampin, isoniazid, and pyrazinamide (e.g., RIFATER®) 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 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
Rifampin is indicated for the treatment of asymptomatic carriers of Neisseria meningitidis to eliminate meningococci from the nasopharynx. Rifampin is not indicated for the treatment of meningococcal infection because of the possibility of the rapid emergence of resistance to rifamycins. (See CONTRAINDICATIONS.) Rifampin should not be used indiscriminately, and, therefore, diagnostic laboratory procedures, including serotyping and susceptibility testing, should be performed for establishment of the carrier state and the correct treatment. So that the usefulness of rifampin in the treatment of asymptomatic meningococcal carriers is preserved, the drug should be used only when the risk of meningococcal disease is high.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of rifampin and other antibacterial drugs, rifampin 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.

CONTRAINDICATIONS

RIFADIN is contraindicated in patients with a history of hypersensitivity to rifampin or any of the components, or to any of the rifamycins. (See WARNINGS.) Rifampin is contraindicated in patients who are also receiving ritonavir-boosted saquinavir due to an increased risk of severe hepatocellular toxicity. (See PRECAUTIONS, Drug Interactions.) Rifampin is contraindicated in patients who are also receiving atazanavir, darunavir, fosamprenavir, saquinavir, or tipranavir due to the potential of rifampin to substantially decrease plasma concentrations of these antiviral drugs, which may result in loss of antiviral efficacy and/or development of viral resistance.

WARNINGS

Rifampin has been shown to produce liver dysfunction. Fatalities associated with jaundice have occurred in patients with liver disease and in patients taking rifampin with other hepatotoxic drugs. Patients should be given the choice of a proven to treat infections while the drug is being given. In cases of necessity and then with caution and under strict medical supervision. In these patients, careful monitoring of liver function, especially SGPT/ALT and SGOT/AST should be carried out prior to therapy and then every 2 to 4 weeks during therapy. If signs of hepatocellular dysfunction should be observed. In some cases, hyperbilirubinemia resulting from competition between rifampin and bilirubin for excretory pathways of the liver can occur, and the early days of treatment. 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.

Rifampin has enzyme-inducing properties, including induction of delta amino levulinic acid synthetase. Isolated reports have associated porphyria exacerbation with rifampin administration. The possibility of rapid emergence of resistant meningococci restricts the use of RIFADIN to short-term treatment of the asymptomatic carrier state. RIFADIN is not to be used for the treatment of meningococcal disease. Systemic hypersensitivity reactions, including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, may occur in patients receiving rifampin (see ADVERSE REACTIONS). Signs and symptoms of hypersensitivity reactions may include fever, rash, urticaria, angioedema, hypoproteinemia, acute bronchospasm, conjunctivitis, thrombocytopenia, neutrophilic leukocytosis, and elevated liver enzymes or fulminant liver failure (syndrome (weakness, fatigue, muscle pain, nausea, vomiting, headache, chills, aches, tetching, dizziness, shortness of breath, chest pain, cough, syncope, palpitations). These reactions may be severe and DRESS may be fatal. Manifestations of hypersensitivity, such as fever, lymphadenopathy or laboratory abnormalities (including eosinophilia, liver abnormalities), may be present even though rash is not evident. Monitor patients receiving RIFADIN for signs and/or symptoms of hypersensitivity reactions. If these signs or symptoms occur, discontinue RIFADIN and administer supportive measures.

PRECAUTIONS

General

RIFADIN should be used with caution in patients with a history of diabetes mellitus, as diabetes management may be more difficult.

Concurrent use of ketoconazole and rifampin has resulted in decreased serum concentrations of rifampin and increased concentrations of rifampin were observed. Other Interactions

Rifampin has been reported to increase the requirements for anticoagulant drugs of the coumarin type. 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.

Other Interactions

When the two drugs were taken concomitantly, decreased concentrations of atovaquone and increased concentrations of rifampin were observed. Concomitant use of ketoconazole and rifampin has resulted in decreased serum concentrations of atovaquone. When rifampin was combined with atovaquone, atovaquone was reduced to a greater extent than with either drug alone. It will be necessary to adjust the dosages of these drugs if they are given concurrently with rifampin. Patients using oral or other systemic hormonal contraceptives may be affected; consideration should be given to using alternative contraceptive measures.

Rifampin has been reported to accelerate the metabolism of the following drugs: anticonvulsants (e.g., phenytoin, digoxin, antiarrhythmics (e.g., disopyramide, mexiletine, quinidine, tocainide), oral anticoagulants, antifungals (e.g., fluconazole, itraconazole, ketoconazole), barbiturates, beta-blockers, calcium channel blockers (e.g., diltiazem, nifedipine, verapamil), clofibrate, oral or other systemic hormonal contraceptives, dapsone, diazepam, doxycycline, fluoroquinolones (e.g., ciprofloxacin, enoxacin, norfloxacin, ofloxacin), haloperidol, oral hypoglycemic agents (sulfonylureas), levethromycin, methadone, narco analgesics, progestins, quinine, tacrolimus, theophylline, tricyclic antidepressants (e.g., amitriptyline, nortriptyline) and tocainide. These antiviral drugs must not be coadministered with rifampin. (See CONTRAINDICATIONS.)

Rifampin is contraindicated in patients who are also receiving ritonavir-boosted saquinavir due to an increased risk of severe hepatocellular toxicity. Therefore, concomitant use of these medications is contraindicated.

Enzyme Induction

Rifampin is known to induce certain cytochrome P-450 enzymes. Administration of rifampin with drugs that undergo biotransformation through these metabolic pathways may result in increased elimination of concomitantly administered drugs. To obtain optimum therapeutic blood levels, dosages of drugs metabolized by these enzymes may require adjustment when starting or stopping concomitantly administered rifampin. Rifampin has been reported to substantially decrease the plasma concentrations of the following antiviral drugs: atazanavir, darunavir, fosamprenavir, saquinavir, and tipranavir. These antiviral drugs must not be coadministered with rifampin. (See CONTRAINDICATIONS.)

Rifampin has been reported to accelerate the metabolism of the following drugs: anticonvulsants (e.g., phenytoin, digoxin, antiarrhythmics (e.g., disopyramide, mexiletine, quinidine, tocainide), oral anticoagulants, antifungals (e.g., fluconazole, itraconazole, ketoconazole), barbiturates, beta-blockers, calcium channel blockers (e.g., diltiazem, nifedipine, verapamil), clofibrate, oral or other systemic hormonal contraceptives, dapsone, diazepam, doxycycline, fluoroquinolones (e.g., ciprofloxacin), haloperidol, oral hypoglycemic agents (sulfonylureas), levethromycin, methadone, narco analgesics, progestins, quinine, tacrolimus, theophylline, tricyclic antidepressants (e.g., amitriptyline, nortriptyline) and tocainide. These antiviral drugs must not be coadministered with rifampin. (See CONTRAINDICATIONS.)

Rifampin may cause vitamin K–dependent coagulopathy and severe bleeding (see ADVERSE REACTIONS). 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).

RIFADIN IV

For intravenous infusion only. Must not be administered by intramuscular or subcutaneous route. Avoid extravasation during injection: local irritation and inflammation may occur. (See PRECAUTIONS, Drug Interactions.)
Probenecid and cotrimoxazole have been reported to increase the blood level of rifampin. When rifampin is given concomitantly with either probenecid or cotrimoxazole, the potential for hepatotoxicity is increased. The concomitant use of rifampin and probenecid should be avoided. Patients receiving both rifampin and probenecid should be monitored closely for hepatotoxicity.

Plasma concentrations of sulfapyridine may be reduced following the concomitant administration of sulfasalazine and rifampin. This finding may be the result of alteration in the colonic bacteria responsible for the reduction of sulfasalazine to sulfapyridine and mesalamine.

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.

Transient abnormalities in liver function tests (e.g., elevation in serum bilirubin, alkaline phosphatase, and serum transaminases) and reduced bilirubin 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 C3H/HeN mice dosed for 78 weeks with rifampin followed by an observation period of 9 months. There was no evidence of tumorigenicity in male C3Hf/DP mice or in similar studies in BALB/c mice, or in two year 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 Salmonella typhimurium) and eukaryotic (Saccharomyces cerevisiae) bacteria, Drosophila melanogaster or ICR/Hi Swiss mice. An increase in chromatin 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

Category C

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 Phase II trials, 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/Hi Swiss mice. An increase in chromatin 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.

Rifampin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pediatric Use

Clinical studies of RIFADIN 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 used in using rifampin in elderly patients. (See WARNINGS.)

ADVERSE REACTIONS

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 consider this diagnosis in patients who develop diarrhea in association with antibiotic use. Tooth discoloration (which may be permanent) may occur.

Hepatic

Transient abnormalities in liver function tests (e.g., elevations in serum bilirubin, alkaline phosphatase, serum transaminases) have been observed. Rarely, hepatitis or a shock-like syndrome with hepatic involvement and abnormal liver function tests has been reported.

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 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, hemo-globunuria, 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 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, nephropathy, erythema multiforme including Stevens-Johnson syndrome, toxic epidermal necrolysis, Drug Reaction with Eosinophilia and Systemic Symptoms syndrome (see WARNINGS), vasculitis, esosipholia, sore mouth, sore tongue, and conjunctivitis have been observed.

Anaphylaxis has been reported rarely.

Miscellaneous

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.

Psychotic episodes, possibly with delirium, 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. 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

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

DOSAGE AND ADMINISTRATION

Rifampin can be administered by the oral route or by IV infusion (see INDICATIONS AND USAGE). IV doses are the same as those for oral use.

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, oral or IV

Pediatric Patients: 10–20 mg/kg, not to exceed 600 mg/day, oral or IV

It is recommended that oral rifampin be administered once daily, either 1 hour before or 2 hours after a meal with a full glass of water.

Rifampin is indicated in the treatment of all forms 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 (e.g., RIFAMATE®) 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 up to 30 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 8 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 6 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.

Preparation of Extemporaneous Oral Suspension
For pediatric and adult patients in whom capsule swallowing is difficult or where lower doses are needed, a liquid suspension may be prepared as follows:
RIFADIN 1% w/v suspension (10 mg/mL) can be compounded using one of four syrups—Simple Syrup (Syrup NF), Simple Syrup (Humco Laboratories), SyrPalta® Syrup (Emerson Laboratories), or Raspberry Syrup (Humco Laboratories).
1. Empty the contents of four RIFADIN 300 mg capsules or eight RIFADIN 150 mg capsules onto a piece of weighing paper.
2. If necessary, gently crush the capsule contents with a spatula to produce a fine powder.
3. Transfer the rifampin powder blend to a 4-ounce amber glass or plastic (high density polyethylene [HDPE], polypropylene, or polycarbonate) prescription bottle.
4. Rinse the paper and spatula with 20 mL of one of the above-mentioned syrups, and add the rinse to the bottle. Shake vigorously.
5. Add 100 mL of syrup to the bottle and shake vigorously.

This compounding procedure results in a 1% w/v suspension containing 10 mg rifampin/mL. Stability studies indicate that the suspension is stable when stored at room temperature (25±3°C) or in a refrigerator (2–8°C) for four weeks. This extemporaneously prepared suspension must be shaken well prior to administration.

HOW SUPPLIED
150 mg maroon and scarlet capsules imprinted “RIFADIN 150.”
Bottles of 30 (NDC 0068-0510-30)
300 mg maroon and scarlet capsules imprinted “RIFADIN 300.”
Bottles of 60 (NDC 0068-0508-60)
Storage: Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature]. Keep tightly closed. Store in a dry place. Avoid excessive heat.
RIFADIN IV (rifampin for injection USP) is available in sterile glass vials containing 600 mg rifampin (NDC 0068-0597-01).
Storage: Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature]. Avoid excessive heat (temperatures above 40°C or 104°F). Protect from light.

REFERENCES

Rifadin capsules are manufactured for:
sanofi-aventis U.S. LLC
Bridgewater, NJ 08807
A SÃOFRÉN COMPANY

Rifadin IV (rifampin for injection USP) is manufactured by:
sanofi-aventis U.S. LLC
Bridgewater, NJ 08807
A SÃOFRÉN COMPANY

Revised August 2018
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RIF-FSPL-SL-AUG18