induces its own metabolism resulting in a lower area under the curve after 4 weeks of continuous treatment than after the first few doses.

About 53% of a dose is found in the urine, mainly as metabolites and about 30% of a dose is excreted in the faeces. The mean half-life for rifabutin is reported to be about 40 hours, with a range of 16 to 69 hours.

◊ References.

1. Skinner MH, *et al.* Pharmacokinetics of rifabutin. *Antimicrob Agents Chemother* 1989; **33:** 1237–41.

HIV-infected patients. Malabsorption of rifabutin and other antituberculous drugs may occur in patients with HIV infection and tuberculosis, and may contribute to acquired drug resistance and reduced efficacy of tuberculosis treatment. For further information on the absorption of antituberculous drugs in HIV-infected patients see Pharmacokinetics, under Rifampicin, p.328.

The pharmacokinetics of rifabutin were studied in HIV-infected patients with normal renal and hepatic function.[1] A two-compartment open pharmacokinetic model was proposed. Rifabutin was rapidly but incompletely absorbed from the gastrointestinal tract and bioavailability was poor, being 20% on day 1 of the study and 12% on day 28. Mean peak plasma concentrations occurred 2 to 3 hours after oral doses and were about 350, 500, and 900 nanograms/mL after doses of 300, 600, and 900 mg respectively. The peak and trough concentrations after 600 mg twice daily were about 900 and 200 nanograms/mL respectively. Rifabutin was about 70% bound to plasma proteins. The area under the curve showed a decrease on repeated dosage which might be explained by the induction of drug-metabolising liver enzymes. A large volume of distribution of 8 to 9 litres/kg, indicative of extensive tissue distribution, and a mean terminal half-life of 32 to 38 hours were reported.

This study[1] also showed that the peak plasma concentration of the major metabolite, 25-deacetylrifabutin, was 10% of the parent compound. Only 4% of unchanged rifabutin was excreted in the urine after oral use and between 6 to 14% after intravenous use. Total urinary excretion of rifabutin and metabolite 72 hours after intravenous use was 44%; total faecal excretion was between 30 and 49%.

Peak and trough concentrations at steady state were reported as 900 and 200 nanograms/mL respectively in a patient with tuberculosis given rifabutin 450 mg daily.[2] While these figures were the same as those previously reported with 600 mg twice daily,[1] the earlier study showed that there was considerable interpatient variability.

CSF concentrations in 5 patients with AIDS on rifabutin 450 mg daily ranged from 36 to 70% of serum concentrations.[3]

1. Skinner MH, *et al.* Pharmacokinetics of rifabutin. *Antimicrob Agents Chemother* 1989; **33:** 1237–41.
2. Gillespie SH, *et al.* The serum rifabutin concentrations in a patient successfully treated for multi-resistant mycobacterium tuberculosis infection. *J Antimicrob Chemother* 1990; **25:** 490–1. Correction. *ibid.* 1991; **27:** 877.
3. Siegal FP, *et al.* Dose-limiting toxicity of rifabutin in AIDS-related complex: syndrome of arthralgia/arthritis. *AIDS* 1990; **4:** 433–41.

Metabolism. Five metabolites of rifabutin were identified in an *in-vitro* study[1] using human hepatic and enterocyte microsomes. Cytochrome P450 isoenzyme CYP3A4 was involved in the formation of all metabolites except 25-*O*-deacetylrifabutin. Deacetylation of rifabutin was apparently mediated by microsomal cholinesterase,[1] although another study[2] showed that further metabolism of 25-*O*-deacetylrifabutin is dependent on CYP3A4. The results[1] also suggested that metabolism by intestinal CYP3A4 contributes significantly to presystemic metabolism of rifabutin (and consequently its low bioavailability) and to drug interactions with azole antifungals and with macrolides (see above).

1. Iatsimirskaia E, *et al.* Metabolism of rifabutin in human enterocyte and liver microsomes: kinetic parameters, identification of enzyme systems, and drug interactions with macrolides and antifungal agents. *Clin Pharmacol Ther* 1997; **61:** 554–62.
2. Trapnell CB, *et al.* Metabolism of rifabutin and its 25-desacetyl metabolite, LM565, by human liver microsomes and recombinant human cytochrome P-450 3A4: relevance to clinical interaction with fluconazole. *Antimicrob Agents Chemother* 1997; **41:** 924–6.

Uses and Administration

Rifabutin is a rifamycin antibacterial used as an alternative to the macrolides for the prophylaxis of *Mycobacterium avium* complex (MAC) infection in immunocompromised patients. It is also used for the treatment of other nontuberculous mycobacterial infections (including those due to MAC) (p.181) and tuberculosis (p.196). When used for treatment rifabutin, like rifampicin, should be used with other antibacterials to prevent the emergence of resistant organisms.

Rifabutin is given as a single oral daily dose. The dose for the prophylaxis of MAC infection is 300 mg daily. For the treatment of nontuberculous mycobacterial infections the dose is 450 to 600 mg daily in a multidrug regimen for up to 6 months after negative cultures are obtained. For pulmonary tuberculosis the usual dose is 300 mg daily for at least 6 months as part of a multidrug regimen; it can also be given intermittently (usually 3 times each week) as an alternative to daily use.

For details of doses in infants, children, and adolescents, see below.

Doses should be reduced to 300 mg daily in patients also receiving macrolides or azole antifungals (see under Adverse Effects, Effects on the Eyes, above). Dosage alterations may also be necessary in patients receiving HIV-protease inhibitors (see under Tuberculosis, below) and in those with severe renal impairment (see below).

◊ Reviews.

1. Brogden RN, Fitton A. Rifabutin: a review of its antimicrobial activity, pharmacokinetic properties and therapeutic efficacy. *Drugs* 1994; **47:** 983–1009.

Administration in children. For the prophylaxis of MAC in HIV-infected infants and children with low CD4+ counts, the American Academy of Pediatrics (AAP) suggests an oral dose of rifabutin 5 mg/kg daily in those older than 6 years; the *BNFC* suggest the same dose may be given from 1 year of age and those 12 years of age and older may be given the usual adult dose.

For the treatment of nontuberculous mycobacterial disease in children aged 1 month to 12 years the *BNFC* suggests a dose of 5 mg/kg once daily for at least 6 months as part of a multidrug regimen; those 12 years of age and older may be given the usual adult dose.

For the treatment of tuberculosis in those 12 years of age and older the *BNFC* suggests a dose of 150 to 450 mg once daily for at least 6 months as part of a multidrug regimen.

Administration in renal impairment. Dosage of rifabutin should be reduced by 50% in patients with severe renal impairment (creatinine clearance less than 30 mL/minute).

Cryptosporidiosis. Rifabutin may have a potential prophylactic effect against cryptosporidiosis (p.823).

Mycobacterium avium complex infections. Alterations in rifabutin dosage may be necessary in patients receiving antiretrovirals for the management of HIV infection; further details are given under Tuberculosis, below.

Peptic ulcer disease. For mention of the use of rifabutin in eradication regimens for *Helicobacter pylori* see p.1702.

References.

1. Borody TJ, *et al.* Efficacy and safety of rifabutin-containing 'rescue therapy' for resistant Helicobacter pylori infection. *Aliment Pharmacol Ther* 2006; **23:** 481–8. Correction. *ibid.*; **24:** 439.
2. Miehlke S, *et al.* Randomized trial of rifabutin-based triple therapy and high-dose dual therapy for rescue treatment of Helicobacter pylori resistant to both metronidazole and clarithromycin. *Aliment Pharmacol Ther* 2006; **24:** 395–403.
3. González Carro P, *et al.* Efficacy of rifabutin-based triple therapy in Helicobacter pylori infected patients after two standard treatments. *J Gastroenterol Hepatol* 2007; **22:** 60–3.
4. Navarro-Jarabo JM, *et al.* Efficacy of rifabutin-based triple therapy as second-line treatment to eradicate helicobacter pylori infection. *BMC Gastroenterol* 2007; **7:** 31. Available at: http://www.biomedcentral.com/1471-230X/7/31 (accessed 12/11/07).

Toxoplasmosis. A beneficial response to rifabutin used with pyrimethamine was reported in a patient with AIDS-related *Toxoplasma gondii* encephalitis.[1] The patient was allergic to sulfonamides and clindamycin, which are commonly used (see p.826).

1. Schürmann D, *et al.* Rifabutin appears to be a promising agent for combination treatment of AIDS-related toxoplasma encephalitis. *J Infect* 1998; **36:** 352–3.

Tuberculosis and HIV infection. Rifabutin may be used in place of rifampicin in short-course therapy for tuberculosis in patients given antiretroviral drugs for HIV infection and may be preferred for patients unable to take efavirenz.[1,2] However, dose modifications are often necessary; additionally, some combinations, notably rifabutin with delavirdine, or saquinavir alone, should not be used, although rifabutin may be given with saquinavir if ritonavir is also given.

- In patients taking ritonavir-boosted HIV-protease inhibitors the dose of rifabutin should be substantially reduced from 300 mg daily or intermittently to 150 mg every other day or three times each week
- In patients taking unboosted atazanavir the dose of rifabutin should be substantially reduced from 300 mg daily or intermittently to 150 mg every other day or three times each week
- In those taking unboosted amprenavir, fosamprenavir, indinavir, or nelfinavir the daily dose of rifabutin should be decreased from 300 mg to 150 mg, and the dose for intermittent therapy should be 300 mg three times weekly. The dose of indinavir may need to be increased
- In patients taking efavirenz, the dose of rifabutin should be increased from 300 mg daily or intermittently to 450 to 600 mg daily or three times each week
- In patients taking nevirapine or etravirine, the usual dose of rifabutin is given (300 mg daily or 300 mg three times each week); rifabutin should not be used in patients taking etravirine plus ritonavir-boosted darunavir or saquinavir

1. CDC. Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis (issued December 2007). Available at: http://www.cdc.gov/tb/TB_HIV_Drugs/PDF/tbhiv.pdf (accessed 28/07/08)
2. Pozniak AL, *et al.* British HIV Association. BHIVA treatment guidelines for TB/HIV infection, February 2005. Available at: http://www.bhiva.org/files/file1001577.pdf (accessed 28/07/08)

Preparations

USP 31: Rifabutin Capsules.

Proprietary Preparations (details are given in Part 3) ***Austral.:*** Mycobutin; ***Austria:*** Mycobutin; ***Belg.:*** Mycobutin; ***Canad.:*** Mycobutin; ***Cz.:*** Mycobutin; ***Fin.:*** Ansatipin; ***Fr.:*** Ansatipine; ***Ger.:*** Alfacid; Mycobutin†; ***Gr.:*** Ansatipin†; Mycobutin; ***Hong Kong:*** Mycobutin; ***Israel:*** Mycobutin; ***Ital.:*** Mycobutin; ***Neth.:*** Mycobutin; ***NZ:*** Mycobutin; ***Port.:*** Mycobutin; ***Rus.:*** Mycobutin (Микобутин); ***S.Afr.:*** Mycobutin; ***Spain:*** Ansatipin; ***Swed.:*** Ansatipin; ***Switz.:*** Mycobutin; ***Turk.:*** Mycobutin; ***UK:*** Mycobutin; ***USA:*** Mycobutin.

Rifampicin *(BAN, rINN)*

Ba-41166/E; L-5103; NSC-113926; Rifaldazine; Rifampicina; Rifampicinas; Rifampicine; Rifampicinum; Rifampin *(USAN)*; Rifampisiini; Rifampisin; Rifamycin AMP; Ryfampicyna. 3-(4-Methylpiperazin-1-yliminomethyl)rifamycin SV; (12*Z*,14*E*,24*E*)-(2*S*,16*S*,17*S*,18*R*,19*R*,20*R*,21*S*,22*R*,23*S*)-1,2-Dihydro-5,6,9,17,19-pentahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-8-(4-methylpiperazin-1-yliminomethyl)-1,11-dioxo-2,7-(epoxypentadeca-[1,11,13]trienimino)naphtho[2,1-*b*]furan-21-yl acetate.

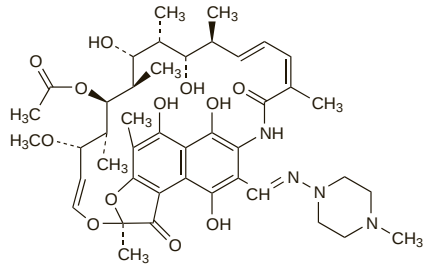
Рифампицин

$C_{43}H_{58}N_4O_{12}$ = 822.9.

CAS — 13292-46-1.

ATC — J04AB02.

ATC Vet — QJ04AB02; QJ54AB02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Rifampicin). A reddish-brown or brownish-red, crystalline powder. Slightly soluble in water, in alcohol, and in acetone; soluble in methyl alcohol. A 1% suspension has a pH of 4.5 to 6.5. Store at a temperature not exceeding 25° in an atmosphere of nitrogen in airtight containers. Protect from light.

USP 31 (Rifampin). A red-brown crystalline powder. Very slightly soluble in water; freely soluble in chloroform; soluble in ethyl acetate and in methyl alcohol. A 1% suspension in water has a pH of 4.5 to 6.5. Store at a temperature not exceeding 40° in airtight containers. Protect from light.

Adverse Effects

Rifampicin is usually well tolerated. Adverse effects are more common during intermittent therapy or after restarting interrupted treatment.

Some patients may experience a cutaneous syndrome that presents 2 to 3 hours after a daily or intermittent dose as facial flushing and itching, with or without a rash, or rarely eye irritation and visual disturbances. A flu-like syndrome characterised by episodes of fever, chills, headache, dizziness, bone pain, shortness of breath, and malaise has been associated with intermittent use. It usually occurs after 3 to 6 months of intermittent treatment and has a higher incidence with doses of 25 mg/kg or more given once weekly than with currently recommended regimens. Anaphylaxis or shock has occurred rarely.

Gastrointestinal adverse effects include nausea, vomiting, anorexia, diarrhoea, and epigastric distress. Taking doses on an empty stomach is recommended for maximal absorption, but dosage after a meal will minimise gastrointestinal intolerance. Pseudomembranous colitis has been reported. Rifampicin produces transient

abnormalities in liver function and hepatitis. Fatalities due to hepatotoxicity have been reported occasionally (see Effects on the Liver, below).

Rifampicin can cause thrombocytopenia and purpura, usually when given as an intermittent regimen, and if this occurs further use of rifampicin is contra-indicated. Other haematological adverse effects include eosinophilia, leucopenia, and haemolytic anaemia.

Alterations in kidney function and renal failure have occurred, particularly during intermittent therapy. Menstrual disturbances have been reported.

Nervous system adverse effects include headache, drowsiness, ataxia, dizziness, and numbness.

Oedema, myopathy, and muscular weakness have been reported.

Thrombophlebitis has occurred after prolonged intravenous infusion. Extravasation during intravenous infusion may cause local irritation and inflammation.

Rifampicin causes a harmless orange-red discoloration of the urine, faeces, sweat, saliva, sputum, tears, and other body fluids. Soft contact lenses may become permanently stained.

Effects on the blood. Thrombocytopenia may occur in patients taking rifampicin, most commonly as intermittent therapy, and probably has an immunological basis. The platelet count may fall within 3 hours of a dose and return to normal within 36 hours, if additional doses are not given.[1] There may also be a risk of thrombocytopenia when re-introducing rifampicin to patients who have interrupted their treatment.[2] Thrombocytopenia has also been reported in a patient taking rifampicin for the first time for meningococcal prophylaxis.[3] Thrombotic thrombocytopenic purpura has been reported in a patient after two weeks of treatment with oral rifampicin and intravenous vancomycin for a meticillin-resistant *Staphylococcus aureus* infection.[4] Fatalities have occurred when rifampicin was not withdrawn once thrombocytopenic purpura had developed or when treatment with rifampicin was resumed in patients who had experienced purpura.[1] However, there is a report of the successful re-introduction of rifampicin in a patient who developed thrombocytopenia without rifampicin-dependent antibodies.[5]

Bleeding from the oral cavity not associated with thrombocytopenia has been reported in a patient taking rifampicin.[6] Leucopenia,[7,8] haemolysis or haemolytic anaemia,[9] and red cell aplasia[10] have occurred. Disseminated intravascular coagulation has been reported in a patient receiving intermittent rifampicin therapy.[11] The incidence of deep-vein thrombosis increased in one group of hospitalised tuberculosis patients when rifampicin was introduced as standard therapy,[12] but data from others have not supported a causal relationship.[13]

1. Girling DJ. Adverse effects of antituberculosis drugs. *Drugs* 1982; **23:** 56–74.
2. Burnette PK, *et al.* Rifampin-associated thrombocytopenia secondary to poor compliance. *Drug Intell Clin Pharm* 1989; **23:** 382–4.
3. Hall AP, *et al.* New hazard of meningococcal chemoprophylaxis. *J Antimicrob Chemother* 1993; **31:** 451.
4. Gupta R, Wargo KA. Rifampin-induced thrombotic thrombocytopenic purpura. *Ann Pharmacother* 2005; **39:** 1761–2.
5. Bhasin DK, *et al.* Can rifampicin be restarted in patients with rifampicin-induced thrombocytopenia? *Tubercle* 1991; **72:** 306–7.
6. Sule RR. An unusual reaction to rifampicin in a once monthly dose. *Lepr Rev* 1996; **67:** 227–33.
7. Van Assendelft AHW. Leucopenia in rifampicin chemotherapy. *J Antimicrob Chemother* 1985; **16:** 407–8.
8. Vijayakumaran P, *et al.* Leucocytopenia after rifampicin and ofloxacin therapy in leprosy. *Lepr Rev* 1997; **68:** 10–15.
9. Lakshminarayan S, *et al.* Massive haemolysis caused by rifampicin. *BMJ* 1973; **2:** 282–3.
10. Mariette X, *et al.* Rifampicin-induced pure red cell aplasia. *Am J Med* 1989; **87:** 459–60.
11. Souza CS, *et al.* Disseminated intravascular coagulopathy as an adverse reaction to intermittent rifampin schedule in the treatment of leprosy. *Int J Lepr* 1997; **65:** 366–71.
12. White NW. Venous thrombosis and rifampicin. *Lancet* 1989; **ii:** 434–5.
13. Cowie RL, *et al.* Deep-vein thrombosis and pulmonary tuberculosis. *Lancet* 1989; **ii:** 1397.

Effects on the gastrointestinal tract. In addition to symptoms of gastrointestinal intolerance, there have been reports of gastrointestinal bleeding and erosive gastritis,[1] ulcerative colitis,[2] and eosinophilic colitis[3] in patients receiving rifampicin.

1. Zargar SA, *et al.* Rifampicin-induced upper gastrointestinal bleeding. *Postgrad Med J* 1990; **66:** 310–11.
2. Tajima A, *et al.* Rifampicin-associated ulcerative colitis. *Ann Intern Med* 1992; **116:** 778–9.
3. Lange P, *et al.* Eosinophilic colitis due to rifampicin. *Lancet* 1994; **344:** 1296–7.

Effects on the liver. Transient abnormalities in liver function are common during the early stages of antituberculous therapy with rifampicin and other first-line antituberculous drugs, but sometimes the hepatotoxicity may be more serious and require a change of treatment. Drug-induced hepatitis usually occurs within the first few weeks of treatment and it may not be possible to identify which drug or drugs are responsible. Rifampicin is thought to have a lower potential for hepatotoxicity than isoniazid or pyrazinamide.[1]

Risk factors for hepatotoxicity include alcoholism, old age, female gender, malnutrition, HIV infection, and chronic hepatitis B and C infections.[1]

The Joint Tuberculosis Committee of the British Thoracic Society has published recommendations[2] for initial measurement of liver function in all patients and regular monitoring in patients with pre-existing liver disease. Details are given concerning the response to deteriorating liver function and guidelines included for prompt re-introduction of appropriate antituberculosis therapy once normal liver function is restored. Similar guidelines have been produced for the USA.[3,4]

The incidence of severe hepatotoxicity was found to be lower in patients receiving isoniazid, rifampicin, and pyrazinamide for initial treatment of active disease, than in those receiving rifampicin and pyrazinamide for 2 months for latent tuberculosis infection. Management of latent tuberculosis with the rifampicin plus pyrazinamide regimen was also associated with a higher incidence of severe hepatotoxicity than was isoniazid monotherapy for 6 months.[5] Severe and sometimes fatal hepatotoxicity has been associated with the combined regimen of rifampicin and pyrazinamide for the treatment of latent tuberculosis in a predominantly HIV-negative study population.[5-9] In the USA, the CDC and the American Thoracic Society[10] now recommend that the combination of rifampicin with pyrazinamide should not generally be offered to persons with latent tuberculosis. However, an evaluation of studies[11] for the prevention of tuberculosis, involving HIV-infected patients, reported very little evidence of hepatotoxicity among patients taking rifampicin plus pyrazinamide and among those taking isoniazid.

For further information on hepatotoxicity caused by antituberculous drugs see Effects on the Liver, under Isoniazid, p.288.

Hepatitis and liver dysfunction have also been reported in patients taking rifampicin, in the absence of other hepatotoxic drugs, for the treatment of pruritus associated with primary biliary cirrhosis.[12]

1. Yew WW, Leung CC. Antituberculosis drugs and hepatotoxicity. *Respirology* 2006; **11:** 699–707.
2. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. *Thorax* 1998; **53:** 536–48. [Although these guidelines were replaced by ones issued by NICE in 2006 the latter do not *"explain tuberculosis or its treatment in detail"* and therefore reference to the earlier guidelines has been retained] Also available at: http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Tuberculosis/Guidelines/Chemotherapy.pdf (accessed 29/07/08)
3. American Thoracic Society, CDC, and the Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; **52** (RR-11): 1–77. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf (accessed 05/10/07) Correction. *ibid.* 2005; **53:** 1203. [dose]
4. Saukkonen JJ, *et al.* American Thoracic Society. An official ATS statement: hepatotoxicity of antituberculosis therapy. *Am J Respir Crit Care Med* 2006; **174:** 935–52. Also available at: http://www.thoracic.org/sections/publications/statements/resources/hepatotoxicity-of-antituberculosis-therapy.pdf (accessed 05/10/07)
5. van Hest R, *et al.* Hepatotoxicity of rifampin-pyrazinamide and isoniazid preventive therapy and tuberculosis treatment. *Clin Infect Dis* 2004; **39:** 488–96.
6. CDC. Update: fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations—United States, 2001. *MMWR* 2001; **50:** 733–5. Also available at http://www.cdc.gov/mmwr/PDF/wk/mm5034.pdf (accessed 05/10/07)
7. CDC. Update: fatal and severe liver injuries associated with rifampin and pyrazinamide treatment for latent tuberculosis infection. *MMWR* 2002; **51:** 998–9. Also available at http://www.cdc.gov/mmwr/PDF/wk/mm5144.pdf (accessed 05/10/07)
8. Jasmer RM, *et al.* Short-course rifampin and pyrazinamide compared with isoniazid for latent tuberculosis infection: a multicenter clinical trial. *Ann Intern Med* 2002; **137:** 640–7.
9. Ijaz K, *et al.* Severe or fatal liver injury in 50 patients in the United States taking rifampin and pyrazinamide for latent tuberculosis infection. *Clin Infect Dis* 2006; **42:** 346–55.
10. CDC. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States, 2003. *MMWR* 2003; **52:** 735–9. Also available at: http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf (accessed 05/10/07)
11. Gordin FM, *et al.* Hepatotoxicity of rifampin and pyrazinamide in the treatment of latent tuberculosis infection in HIV-infected persons: is it different than in HIV-uninfected persons? *Clin Infect Dis* 2004; **39:** 561–5.
12. Prince MI, *et al.* Hepatitis and liver dysfunction with rifampicin therapy for pruritus in primary biliary cirrhosis. *Gut* 2002; **50:** 436–9.

Effects on the lungs. Pulmonary fibrosis[1] in one elderly man and pneumonitis[2] in another were attributed to rifampicin.

1. Umeki S. Rifampicin and pulmonary fibrosis. *Arch Intern Med* 1988; **148:** 1663, 7.
2. Kunichika N, *et al.* Pneumonitis induced by rifampicin. *Thorax* 2002; **57:** 1000–1001.

Effects on the pancreas. Chronic pancreatic insufficiency has been reported in a patient after use of rifampicin, isoniazid, ethambutol, and pyrazinamide.[1]

1. Liu BA, *et al.* Pancreatic insufficiency due to antituberculosis therapy. *Ann Pharmacother* 1997; **31:** 724–6.

Effects on the skin. Skin reactions to rifampicin are usually mild, irrespective of it being given daily or intermittently.[1] However, there have been a few isolated reports of severe reactions such as toxic epidermal necrolysis,[2] exfoliative dermatitis,[3] fixed drug eruptions,[4,5] and acute generalised exanthematous pustulosis.[6] Contact dermatitis has been seen after handling rifampicin powder.[7]

1. Girling DJ. Adverse reactions to rifampicin in antituberculosis regimens. *J Antimicrob Chemother* 1977; **3:** 115–32.
2. Okano M, *et al.* Toxic epidermal necrolysis due to rifampicin. *J Am Acad Dermatol* 1987; **17:** 303–4.
3. Goldin HM, *et al.* Rifampin and exfoliative dermatitis. *Ann Intern Med* 1987; **107:** 789.
4. Mimouni A, *et al.* Fixed drug eruption following rifampin treatment. *DICP Ann Pharmacother* 1990; **24:** 947–8.
5. John SS. Fixed drug eruption due to rifampin. *Lepr Rev* 1998; **69:** 397–9.
6. Azad A, Connelly N. Case of rifampicin-induced acute generalized exanthematous pustulosis. *Intern Med J* 2006; **36:** 619–20.
7. Anker N, Da Gunha Bang F. Long-term intravenous rifampicin treatment: advantages and disadvantages. *Eur J Respir Dis* 1981; **62:** 84–6.

Hypersensitivity. References.

1. Girling DJ. Adverse reactions to rifampicin in antituberculosis regimens. *J Antimicrob Chemother* 1977; **3:** 115–32.
2. Wurtz RM, *et al.* Anaphylactoid drug reactions to ciprofloxacin and rifampicin in HIV-infected patients. *Lancet* 1989; **i:** 955–6.
3. Harland RW, *et al.* Anaphylaxis from rifampin. *Am J Med* 1992; **92:** 581–2.
4. Cnudde F, Leynadier F. The diagnosis of allergy to rifampicin confirmed by skin test. *Am J Med* 1994; **97:** 403–4.
5. Sharma VK, *et al.* Rifampicin-induced urticaria in leprosy. *Lepr Rev* 1997; **68:** 331–2.
6. Martínez E, *et al.* Shock and cerebral infarct after rifampin reexposure in a patient infected with human immunodeficiency virus. *Clin Infect Dis* 1998; **27:** 1329–30.

Lupus. Symptoms including malaise, arthralgia, arthritis, and oedema of the extremities, occurring in 4 patients taking rifampicin and 3 taking rifabutin, were considered to be due to drug-induced lupus syndrome.[1] Cutaneous lupus erythematosus was reported in a patient receiving rifampicin with clarithromycin and ethambutol.[2] All patients had positive anti-nuclear antibody titres.[1,2]

1. Berning SE, Iseman MD. Rifamycin-induced lupus syndrome. *Lancet* 1997; **349:** 1521–2.
2. Patel GK, Anstey AV. Rifampicin-induced lupus erythematosus. *Clin Exp Dermatol* 2001; **26:** 260–2.

Overdosage. Cases of skin pigmentation induced by rifampicin overdose have been reviewed.[1] Reddish-orange discoloration of the skin appeared within a few hours of taking the drug; urine, mucous membranes, and sclera were also discoloured. Periorbital or facial oedema, pruritus, and gastrointestinal intolerance occurred in most patients. Treatment was supportive and clinical symptoms resolved in most patients over 3 to 4 days, although fatalities occurred with doses over 14 g.

1. Holdiness MR. A review of the redman syndrome and rifampicin overdosage. *Med Toxicol Adverse Drug Exp* 1989; **4:** 444–51.

Precautions

Liver function should be checked before treatment with rifampicin and special care should be taken in alcoholic patients or those with pre-existing liver disease who require regular monitoring during therapy. UK licensed product information states that use is contra-indicated in patients with jaundice. A self-limiting hyperbilirubinaemia may occur in the first 2 or 3 weeks of treatment. Alkaline phosphatase values may be raised moderately due to rifampicin's enzyme-inducing capacity. Isolated results showing hyperbilirubinaemia in the first few weeks and/or moderately elevated transaminase values are not indications to withdraw rifampicin. However, dose adjustment is necessary when there is other evidence of hepatic impairment and treatment should be suspended when there is evidence of more serious liver toxicity.

Blood counts should be monitored during prolonged treatment and in patients with hepatic disorders. Should thrombocytopenia or purpura occur then rifampicin should be withdrawn permanently. UK product information also recommends such withdrawal in patients who develop haemolytic anaemia or renal failure.

Use of rifampicin after interruption of treatment has been associated with increased risk of serious adverse effects.

Patients should be advised that rifampicin may colour faeces, saliva, sputum, sweat, tears, urine, and other body-fluids orange-red. Soft contact lenses may become permanently stained.

Rifampicin should not be given by the intramuscular or subcutaneous route. When given by intravenous infusion care should be taken to avoid extravasation.

Adrenocortical insufficiency. Adrenal insufficiency has been associated with tuberculosis and induction of microsomal enzymes by rifampicin may accelerate the metabolism of cortisol and precipitate an acute adrenal crisis in such patients.[1] Induction of microsomal enzymes may be enough to compromise even patients with mildly impaired cortisol production. Critical hypotension has also developed in non-Addisonian patients within a week to 10 days of starting rifampicin therapy. However, it has not been necessary to suspend the use of rifampicin if patients are treated with corticosteroids.[2] The effectiveness of corticosteroid therapy can be reduced by rifampicin.

1. Elansary EH, Earis JE. Rifampicin and adrenal crisis. *BMJ* 1983; **286:** 1861–2.
2. Boss G. Rifampicin and adrenal crisis. *BMJ* 1983; **287:** 62.

Breast feeding. Rifampicin is excreted into breast milk. No adverse effects have been seen in breast-fed infants whose mothers were taking rifampicin, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 05/10/07)

Porphyria. Rifampicin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. Treatment guidelines produced by WHO,[1] by an expert group in the UK,[2] and by the CDC in the USA[3] have recommended treatment of pregnant patients with the same rifampicin-containing multidrug regimens as would be used in non-pregnant patients. While use of rifampicin in pregnant patients is generally considered to be safe, the drug does cross into the fetus[4] and malformations and bleeding tendencies have been reported.[5] A literature review[5] revealed 386 normal term infants and 29 elective terminations out of 446 pregnancies in patients who took rifampicin with other antimycobacterial drugs. A variety of malformations were reported; there were 14 abnormal infants or fetuses, 2 premature births, 9 still-births and 7 spontaneous abortions. It was considered that rifampicin did not increase the overall risk of congenital malformations.

Rifampicin treatment can increase the metabolism of vitamin K, resulting in clotting disorders associated with vitamin K deficiency. Bleeding disorders in 2 mothers shortly after delivery, and scalp haemorrhage, anaemia, and shock in one of the infants have been reported.[6] The authors recommended blood coagulation monitoring and giving prophylactic vitamin K to mothers and neonates when the mother has received rifampicin during pregnancy.

1. WHO. *Treatment of tuberculosis: guidelines for national programmes*. 3rd ed. Geneva: WHO, 2003 (and 2004 revision). Available at: http://whqlibdoc.who.int/hq/2003/WHO_CDS_TB_2003.313_eng.pdf (accessed 05/10/07)
2. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. *Thorax* 1998; **53:** 536–48. [Although these guidelines were replaced by ones issued by NICE in 2006 the latter do not *"explain tuberculosis or its treatment in detail"* and therefore reference to the earlier guidelines has been retained] Also available at: http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Tuberculosis/Guidelines/Chemotherapy.pdf (accessed 29/07/08)
3. American Thoracic Society, CDC, and the Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; **52** (RR-11): 1–77. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf (accessed 05/10/07) Correction. *ibid.* 2005; **53:** 1203. [dose]
4. Holdiness MR. Transplacental pharmacokinetics of the antituberculosis drugs. *Clin Pharmacokinet* 1987; **13:** 125–9.
5. Snider DE, *et al.* Treatment of tuberculosis during pregnancy. *Am Rev Respir Dis* 1980; **122:** 65–79.
6. Chouraqui JP, *et al.* Hémorragie par avitaminose K chez la femme enceinte et le nouveau-né: rôle éventuel de la rifampicine: a propos de 2 observations. *Therapie* 1982; **37:** 447–50.

Interactions

Rifampicin accelerates the metabolism of many drugs by inducing microsomal liver enzymes (in particular the cytochrome P450 isoenzyme CYP3A) or drug transporter proteins (such as p-glycoprotein). Drugs so affected may require an increase in dosage to maintain effectiveness and patients should be monitored closely when starting or stopping concurrent rifampicin treatment. Women taking oral contraceptives should use additional precautions or change to a non-hormonal form of contraception (see Rifamycins, p.2068).

The absorption of rifampicin may be reduced by antacids, but this interaction can be overcome by giving rifampicin 1 hour before any antacids. Similarly, rifampicin and preparations containing bentonite (for example some aminosalicylic acid preparations) should be given 8 hours apart. Isoniazid and halothane may increase the potential for hepatotoxicity when given with rifampicin. Atovaquone may increase the concentration of rifampicin, while rifampicin decreases the concentration of atovaquone. Some other interactions affecting the activity of rifampicin are discussed below.

◊ Reviews.

1. Finch CK, *et al.* Rifampin and rifabutin drug interactions: an update. *Arch Intern Med* 2002; **162:** 985–92.
2. Yew WW. Clinically significant interactions with drugs used in the treatment of tuberculosis. *Drug Safety* 2002; **25:** 111–33.
3. Niemi M, *et al.* Pharmacokinetic interactions with rifampicin: clinical relevance. *Clin Pharmacokinet* 2003; **42:** 819–50.

Antiretroviral drugs. Rifamycins can induce the metabolism of *zidovudine*, the NNRTIs delavirdine, efavirenz, and nevirapine, and *HIV-protease inhibitors*, resulting in potentially subtherapeutic plasma concentrations. In addition HIV-protease inhibitors inhibit the metabolism of rifamycins resulting in elevated plasma-rifamycin concentrations and an increased incidence of adverse effects.[1,2]

Guidelines in the UK[3] and the USA[2] recommend that rifampicin should not be used with the *NNRTIs* delavirdine, and etravirine but opinion varies on whether it should be used with nevirapine. Licensed product information for nevirapine contraindicates the use of rifampicin and nevirapine. Rifampicin decreases the serum concentration of efavirenz and it is recommended that the dose of efavirenz be increased in patients weighing more than 60 kg; no dose modification is needed for rifampicin.

It is also recommended that rifampicin should not be used with unboosted or low-dose ritonavir-boosted *HIV-protease inhibitor* regimens. For reference to suitable antiretroviral regimens for use in patients requiring rifampicin-containing treatment for tuberculosis, see p.196.

Rifampicin significantly decreases the serum concentration of the CCR-5 receptor antagonist, *maraviroc*, and it is recommended that the dose of maraviroc be increased; no dose modification is needed for rifampicin. No clinically significant interactions are expected with the integrase inhibitor *raltegravir*,[2] or the HIV fusion inhibitor *enfuvirtide*.[4] For further information on drug interactions with HIV-protease inhibitors see Table 1, p.917 and with NNRTIs see Table 2, p.944. See also p.324 for comment on the interaction of antiretrovirals with rifabutin.

1. Anonymous. Clinical update: impact of HIV protease inhibitors on the treatment of HIV-infected tuberculosis patients with rifampin. *MMWR* 1996; **45:** 921–5.
2. CDC. Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis (issued December 2007). Available at: http://www.cdc.gov/tb/TB_HIV_Drugs/PDF/tbhiv.pdf (accessed 28/07/08)
3. Pozniak AL, *et al.* British HIV Association. BHIVA treatment guidelines for TB/HIV infection, February 2005. Available at: http://www.bhiva.org/files/file1001577.pdf (accessed 28/07/08)
4. Boyd MA, *et al.* Lack of enzyme-inducing effect of rifampicin on the pharmacokinetics of enfuvirtide. *J Clin Pharmacol* 2003; **43:** 1382–91.

Clofazimine. Use of clofazimine in leprosy patients receiving rifampicin with or without dapsone may decrease the rate of absorption of rifampicin and increase the time to peak plasma concentration.[1] In patients receiving clofazimine, rifampicin, and dapsone, the area under the curve for rifampicin was reduced.[1] However, a multiple dose study[2] showed that the pharmacokinetics of rifampicin were similar after 7 days of treatment with rifampicin and dapsone or rifampicin, dapsone, and clofazimine.

1. Mehta J, *et al.* Effect of clofazimine and dapsone on rifampicin (Lositril) pharmacokinetics in multibacillary and paucibacillary leprosy cases. *Lepr Rev* 1986; **57** (suppl 3): 67–76.
2. Venkatesan K, *et al.* The effect of clofazimine on the pharmacokinetics of rifampicin and dapsone in leprosy. *J Antimicrob Chemother* 1986; **18:** 715–18.

Co-trimoxazole. In 15 patients receiving therapy including rifampicin for tuberculosis, a course of co-trimoxazole resulted in increases in maximum plasma concentrations and in the area under the concentration-time curve for rifampicin.[1] No adverse effects were observed and the clinical implications of this observation remain unclear. In another study,[2] significant reductions in the area under the plasma concentration-time curves for trimethoprim and sulfamethoxazole were observed after therapy including rifampicin was given to 10 HIV-infected patients on co-trimoxazole prophylaxis. Again, the clinical significance of this interaction is unclear.

1. Bhatia RS, *et al.* Drug interaction between rifampicin and cotrimoxazole in patients with tuberculosis. *Hum Exp Toxicol* 1991; **10:** 419–21.
2. Ribera E, *et al.* Rifampin reduces concentrations of trimethoprim and sulfamethoxazole in serum in human immunodeficiency virus-infected patients. *Antimicrob Agents Chemother* 2001; **45:** 3238–41.

Isoniazid. There is little significant pharmacokinetic interaction between rifampicin and isoniazid.[1] Although lower blood concentrations of rifampicin have been reported with isoniazid, the effect is not considered clinically significant.[2] Since both drugs are hepatotoxic, there could be an increased incidence of hepatic damage, although the benefits of using this combination are considered to outweigh any potential risks.

1. Acocella G, *et al.* Kinetics of rifampicin and isoniazid administered alone and in combination to normal subjects and patients with liver disease. *Gut* 1972; **13:** 47–53.
2. Mouton RP, *et al.* Blood levels of rifampicin, desacetylrifampicin and isoniazid during combined therapy. *J Antimicrob Chemother* 1979; **5:** 447–54.

Ketoconazole. Giving rifampicin, ketoconazole, and isoniazid together has produced low serum concentrations of each drug resulting in failure of antifungal treatment.[1] Rifampicin serum concentrations are reduced when rifampicin is given with ketoconazole;[2] separation of the doses by 30 minutes[3] to 12 hours[2] may result in similar rifampicin concentrations to those attained when rifampicin is given alone, although serum concentrations of ketoconazole remain depressed regardless of the timing of doses.

1. Abadie-Kemmerly S, *et al.* Failure of ketoconazole treatment of Blastomyces dermatitidis due to interaction of isoniazid and rifampin. *Ann Intern Med* 1988; **109:** 844–5. Correction. *ibid.* 1989; **111:** 96.
2. Engelhard D, *et al.* Interaction of ketoconazole with rifampin and isoniazid. *N Engl J Med* 1984; **311:** 1681–3.
3. Doble N, *et al.* Pharmacokinetic study of the interaction between rifampicin and ketoconazole. *J Antimicrob Chemother* 1988; **21:** 633–5.

Probenecid. Although a study[1] showed that probenecid could increase serum-rifampicin concentrations, another[2] subsequently found that the effect was uncommon and inconsistent and concluded that probenecid had no place as an adjunct to routine rifampicin therapy.

1. Kenwright S, Levi AJ. Impairment of hepatic uptake of rifamycin antibiotics by probenecid and its therapeutic implications. *Lancet* 1973; **ii:** 1401–5.
2. Fallon RJ, *et al.* Probenecid and rifampicin serum levels. *Lancet* 1975; **ii:** 792–4.

Antimicrobial Action

Rifampicin is bactericidal against a wide range of micro-organisms and interferes with their synthesis of nucleic acids by inhibiting DNA-dependent RNA polymerase. It has the ability to kill intracellular organisms. It is active against mycobacteria, including *Mycobacterium tuberculosis, M. avium,* and *M. leprae* and, having high sterilising activity against these organisms, it possesses the ability to eliminate semi-dormant or persisting organisms. Rifampicin is also active against Gram-positive bacteria, especially staphylococci, but less active against Gram-negative organisms. The most sensitive Gram-negative bacteria include *Neisseria meningitidis, N. gonorrhoeae, Haemophilus influenzae,* and *Legionella* spp. Rifampicin also has activity against *Chlamydia trachomatis* and some anaerobic bacteria. At high concentrations it is active against some viruses.

Strains of *M. tuberculosis, M. leprae,* and other susceptible bacteria (such as *N. meningitidis*) have shown resistance, both initially and during treatment. Acquired resistance to rifampicin develops rapidly if it is used alone in the treatment of clinical infection, and resistance is thought to be due to a single-step mutation of the DNA-dependent RNA polymerase. Thus in tuberculosis and leprosy treatment regimens, rifampicin is used with other antimycobacterials to delay or prevent the development of rifampicin resistance. Resistance does not appear to be a problem when rifampicin is used alone in the management of latent tuberculosis, probably because the bacillary load is low. Cross-resistance has been shown between rifampicin and other rifamycins. Strains of *M. tuberculosis* resistant to both rifampicin and isoniazid (termed multidrug-resistant tuberculosis) are increasingly being reported; some strains are also resistant to second-line antimycobacterials (termed extensively drug-resistant tuberculosis).

Pharmacokinetics

Rifampicin is readily absorbed from the gastrointestinal tract and peak plasma concentrations varying from 4 to 32 micrograms/mL (average 7 micrograms/mL) have been reported after a dose of 600 mg. Food may reduce and delay absorption. Rifampicin is about 80% bound to plasma proteins. It is widely distributed in body tissues and fluids and diffusion into the CSF is increased when the meninges are inflamed. Rifampicin is distributed into breast milk and crosses the placenta (see Breast Feeding and Pregnancy, under Precautions, above). Half-lives for rifampicin have been reported to range initially from 2 to 5 hours, the longest elimination times occurring after the largest doses. However, as rifampicin induces its own metabolism, elimination time may decrease by up to 40% during the first 2 weeks, resulting in half-lives of about 2 to 3 hours. The half-life is prolonged in patients with severe hepatic impairment.

Rifampicin is rapidly metabolised in the liver mainly to active 25-*O*-deacetylrifampicin and excreted in the bile. Deacetylation diminishes intestinal reabsorption and increases faecal excretion, although significant enterohepatic circulation still takes place. About 60% of a dose eventually appears in the faeces. The amount excreted in the urine increases with increasing doses and up to 30% of a dose may be excreted in the urine, about half of it being unchanged drug. The metabolite formylrifampicin is also excreted in the urine. In patients with renal impairment the half-life of rifampicin is not prolonged at doses of 600 mg or less.

Distribution. Rifampicin is widely distributed in most body tissues and fluids after oral or intravenous use.[1] Rifampicin is also able to penetrate into polymorphonuclear leucocytes to kill intracellular pathogens.[2] Rifampicin does not appear to diffuse well through the uninflamed meninges[3] but therapeutic concentrations have been attained in the CSF after daily doses of 600 and 900 mg when the meninges are inflamed;[4] concentrations in the CSF are about 10 to 20% of simultaneous serum concentrations, and approximately represent the fraction unbound to plasma proteins. Corticosteroids do not appear to influence the penetration of rifampicin into the CSF of patients with tuberculous meningitis.[5]

1. Holdiness MR. Clinical pharmacokinetics of the antituberculosis drugs. *Clin Pharmacokinet* 1984; **9:** 511–44.
2. Prokesch RC, Hand WL. Antibiotic entry into human polymorphonuclear leukocytes. *Antimicrob Agents Chemother* 1982; **21:** 373–80.
3. Sippel JE, *et al.* Rifampin concentrations in cerebrospinal fluid of patients with tuberculous meningitis. *Am Rev Respir Dis* 1974; **109:** 579–80.
4. D'Oliveira JJG. Cerebrospinal fluid concentrations of rifampin in meningeal tuberculosis. *Am Rev Respir Dis* 1972; **106:** 432–7.
5. Woo J, *et al.* Cerebrospinal fluid and serum levels of pyrazinamide and rifampicin in patients with tuberculous meningitis. *Curr Ther Res* 1987; **42:** 235–42.

HIV-infected patients. Malabsorption of rifampicin and other antituberculous drugs has been reported in some patients with HIV infection and tuberculosis,[1-6] and may contribute to acquired drug resistance and reduced efficacy of tuberculosis treatment. It is not clear whether this is related to the HIV infection itself or associated diarrhoea. A pilot study[2] in 26 HIV-positive patients undergoing multidrug antituberculosis treatment found that serum concentrations of isoniazid were generally regarded as adequate; serum concentrations of rifampicin and ethambutol were low. A study[3] in patients with HIV infection but not co-infected with tuberculosis reported reduced absorption for rifampicin and pyrazinamide compared to healthy subjects; isoniazid was generally well absorbed. A pharmacokinetic study[4] reported malabsorption of all first-line antituberculous drugs in patients who had advanced HIV infection with diarrhoea and cryptosporidial infection. A further pharmacokinetic study,[5] in a similar subject population, found a significant degree of malabsorption of rifampicin and isoniazid in HIV-infected patients with or without diarrhoea. Low serum concentrations of rifabutin were reported in HIV-infected patients co-infected with tuberculosis treated with an intermittent (twice-weekly) tuberculosis regimen.[6] However, others found that HIV infection either did not affect[7,8] or uncommonly affected[9] the pharmacokinetics of antituberculous drugs.

Some authorities[10,11] consider that HIV-infected patients (including children) with tuberculosis have a similar response to short-course multidrug therapy as HIV-negative tuberculosis patients, and that most can be treated with the standard 6-month regimen. US[11,12] and UK[13] guidelines recommend that highly intermittent (once or twice weekly) tuberculosis regimens should not be used for co-infected patients with CD4+ cell counts less than 100 cells/microlitre.

1. Patel KB, *et al.* Drug malabsorption and resistant tuberculosis in HIV-infected patients. *N Engl J Med* 1995; **332:** 336–7.
2. Peloquin CA, *et al.* Low antituberculosis drug concentrations in patients with AIDS. *Ann Pharmacother* 1996; **30:** 919–25.
3. Sahai J, *et al.* Reduced plasma concentrations of antituberculosis drugs in patients with HIV infection. *Ann Intern Med* 1997; **127:** 289–93.
4. Gurumurthy P, *et al.* Decreased bioavailability of rifampin and other antituberculosis drugs in patients with advanced human immunodeficiency virus disease. *Antimicrob Agents Chemother* 2004; **48:** 4473–5.
5. Gurumurthy P, *et al.* Malabsorption of rifampin and isoniazid in HIV-infected patients with and without tuberculosis. *Clin Infect Dis* 2004; **38:** 280–3.
6. Weiner M, *et al.* Association between acquired rifamycin resistance and the pharmacokinetics of rifabutin and isoniazid among patients with HIV and tuberculosis. *Clin Infect Dis* 2005; **40:** 1481–91.
7. Choudhri SH, *et al.* Pharmacokinetics of antimycobacterial drugs in patients with tuberculosis, AIDS, and diarrhea. *Clin Infect Dis* 1997; **25:** 104–11.
8. Taylor B, Smith PJ. Does AIDS impair the absorption of antituberculosis agents? *Int J Tuberc Lung Dis* 1998; **2:** 670–5.
9. Perlman DC, *et al.* The clinical pharmacokinetics of pyrazinamide in HIV-infected persons with tuberculosis. *Clin Infect Dis* 2004; **38:** 556–64.
10. WHO. *TB/HIV. A clinical manual.* 2nd ed. Geneva: WHO, 2004. Available at: http://whqlibdoc.who.int/publications/2004/9241546344.pdf (accessed 05/10/07)
11. CDC. Treating opportunistic infections among HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America. *MMWR* 2004; **53** (RR-15): 1–112. Also available at: http://www.cdc.gov/mmwr/PDF/RR/RR5315.pdf (accessed 05/10/07)
12. CDC. Treating opportunistic infections among HIV-exposed and infected children: recommendations from CDC, the National Institutes of Health, and the Infectious Diseases Society of America. *MMWR* 2004; **53** (RR-14): 1–92. Also available at: http://www.cdc.gov/mmwr/PDF/RR/RR5314.pdf (accessed 05/10/07)
13. Pozniak AL, *et al.* British HIV Association. BHIVA treatment guidelines for TB/HIV infection, February 2005. Available at: http://www.bhiva.org/files/file1001577.pdf (accessed 05/10/07)

Intravenous administration. Mean peak plasma concentrations of 10 micrograms/mL have been reported after rifampicin 600 mg by intravenous infusion over 3 hours. Peak plasma concentrations declined with repeated doses but to a less marked extent than occurs with oral use.[1] Mean peak plasma concentrations of 27 micrograms/mL have been reported in children after doses of 11.5 mg/kg infused over 30 minutes. Mean concentrations of 1.9 micrograms/mL were reported 8 hours after the dose.[2]

1. Acocella G, *et al.* Serum and urine concentrations of rifampicin administered by intravenous infusion in man. *Arzneimittelforschung* 1977; **27:** 1221–6.
2. Koup JR, *et al.* Pharmacokinetics of rifampin in children I. Multiple dose intravenous infusion. *Ther Drug Monit* 1986; **8:** 11–16.

Oral administration. Gastrointestinal absorption of rifampicin is considered good. However, analysis of serum-rifampicin concentrations in children indicated that only 50 ± 22% of a freshly prepared oral suspension was absorbed.[1] Varying oral bioavailability from capsule formulations has also been reported and could result in ineffective therapy[2] or higher than needed serum concentrations.[3]

The oral bioavailability of rifampicin and isoniazid, but not of pyrazinamide, was decreased by food in a study.[4] Another report[5] also showed reduced peak serum concentrations when rifampicin was given with a high-fat meal, and it was suggested that rifampicin should preferably be given on an empty stomach.

1. Koup JR, *et al.* Pharmacokinetics of rifampin in children II. Oral bioavailability. *Ther Drug Monit* 1986; **8:** 17–22.
2. Holdiness MR. Clinical pharmacokinetics of the antituberculosis drugs. *Clin Pharmacokinet* 1984; **9:** 511–44.
3. Ganiswarna SG, *et al.* Bioavailability of rifampicin caplets (600 mg and 450 mg) in healthy Indonesian subjects. *Int J Clin Pharmacol Ther Toxicol* 1986; **24:** 60–4.
4. Zent C, Smith P. Study of the effect of concomitant food on the bioavailability of rifampicin, isoniazid and pyrazinamide. *Tubercle Lung Dis* 1995; **76:** 109–13.
5. Peloquin CA, *et al.* Pharmacokinetics of rifampin under fasting conditions, with food, and with antacids. *Chest* 1999; **115:** 12–18. Correction. *ibid.*; 1485.

Uses and Administration

Rifampicin belongs to the rifamycin group of antimycobacterials (p.159) and is used in the treatment of various infections due to mycobacteria and other susceptible organisms (see Antimicrobial Action, above). It is usually given with other antibacterials to prevent the emergence of resistant organisms.

Rifampicin is used, mainly with isoniazid and pyrazinamide, as a component of multidrug regimens for the treatment of tuberculosis, and with dapsone and clofazimine in the treatment of leprosy. For the treatment of nontuberculous mycobacterial infections it is usually used with clarithromycin and ethambutol as part of a multidrug regimen.

Other uses include the treatment of brucellosis, Legionnaires' disease, mycetoma, penicillin-resistant pneumococcal meningitis, Q-fever, and various staphylococcal infections, including endocarditis. Rifampicin is used for the prophylaxis of epiglottitis and meningitis due to *Haemophilus influenzae* and for meningococcal meningitis. It is also used for the eradication of pharyngeal streptococcal carriage in pharyngitis, to reduce staphylococcal carriage, and to eliminate the carrier states for meningococcal and *H. influenzae* meningitis. It may be used as part of a multidrug regimen for the treatment of inhalation and gastrointestinal anthrax. For discussions of all these infections and their treatment, see under Choice of Antibacterial, p.162.

The usual oral adult dose of rifampicin is 8 to 12 mg/kg (to a maximum of 600 mg) daily, preferably on an empty stomach, or the same dose by intravenous infusion as the base or the sodium salt; higher doses are sometimes used (see below).

Rifampicin is given in the initial and continuation phases of short-course **tuberculosis** regimens (p.196) with other antimycobacterials. Rifampicin is given orally on an empty stomach in adult doses of 10 mg/kg (maximum 600 mg) daily or two or three times weekly. (WHO does not recommend twice-weekly regimens as there is an increased risk of treatment failure if one of the doses are missed.) Alternatively, doses may be expressed as follows: with daily use, adults weighing less than 50 kg receive 450 mg and those over 50 kg receive 600 mg; with intermittent use, adults receive 600 to 900 mg three times weekly. The maximum recommended dose is considered to be 900 mg because a greater incidence of adverse effects is associated with doses above 900 mg.

For the treatment of latent tuberculosis oral rifampicin 10 mg/kg (to a maximum dose of 600 mg) may be given once daily with isoniazid for 3 months. If the contact is infected with isoniazid-resistant tuberculosis then rifampicin monotherapy may be given daily for 4 to 6 months.

In **leprosy** regimens (p.176), rifampicin is usually given with dapsone for paucibacillary leprosy, and with dapsone and clofazimine for multibacillary leprosy. WHO recommends that rifampicin is given once monthly in a usual oral adult dose of 600 mg. Single-dose treatment with rifampicin, ofloxacin, and minocycline may be an alternative in patients with single-lesion paucibacillary leprosy.

In the treatment of **brucellosis**, **Legionnaires' disease**, and serious **staphylococcal infections** a dose of 600 to 1200 mg daily, orally or by intravenous infusion, in divided doses has been recommended in combination with other antibacterials.

For **prophylaxis** against meningococcal meningitis and the treatment of meningococcal carriers, rifampicin is usually given in an oral dose of 600 mg twice daily for 2 days. For prophylaxis against meningitis due to *Haemophilus influenzae*, an oral dose of 20 mg/kg once daily (to a maximum dose of 600 mg daily) for 4 days is given to adults.

For details of doses in infants, children, and adolescents, see below.

Fixed-dose combination products for antimycobacterial therapy have been developed in order to improve patient compliance and avoid monotherapy, thereby decreasing the risk of acquired drug resistance. Combination products containing rifampicin with isoniazid, isoniazid and pyrazinamide, isoniazid and ethambutol, and isoniazid, ethambutol, and pyrazinamide are available in some countries.

Doses of rifampicin should be reduced in patients with hepatic impairment (see below).

Administration in children. For the treatment of **tuberculosis** in infants, children, and adolescents the American Academy of Pediatrics (AAP) suggests a dose of rifampicin of 10 to 20 mg/kg (to a maximum of 600 mg) daily or twice weekly by mouth, for both the initial and continuation phases. For children 1 month and older the *BNFC* suggests a dose of 10 mg/kg once daily or 15 mg/kg (to a maximum of 900 mg) three times a week by mouth; while WHO recommends 8 to 12 mg/kg (to a maximum of 600 mg) once daily or two or three times a week.

For the treatment of *latent* tuberculosis the *BNFC* suggests that children 1 month and older are given rifampicin 10 mg/kg (to a maximum of 600 mg) once daily by mouth with isoniazid for 3 months. If the contact is infected with isoniazid-resistant tuberculosis then rifampicin monotherapy should be given daily for 6 months. The AAP, however, suggest rifampicin 10 to 20 mg/kg daily by mouth for 6 months.

In the treatment of tuberculosis and latent tuberculosis the *BNFC* suggests a maximum dose of rifampicin of 450 mg daily for children weighing less than 50 kg.

In **leprosy** regimens rifampicin is usually given with dapsone for the treatment of paucibacillary leprosy, and with dapsone and clofazimine for the treatment of multibacillary leprosy. WHO recommends that rifampicin is given once monthly in a dose of 450 mg by mouth to children 10 years of age and older.

In the treatment of **brucellosis, Legionnaires' disease**, and serious **staphylococcal infections** doses recommended by the *BNFC* are 5 to 10 mg/kg twice daily in neonates and infants up to 12 months of age, and 10 mg/kg in those older than one year of age. Doses are given by mouth or intravenous infusion and in combination with other antibacterials.

For prophylaxis against meningococcal **meningitis** the AAP recommends infants less then 1 month old are given 5 mg/kg, while infants and children aged 1 month or more are given 10 mg/kg (to a maximum of 600 mg), both twice daily by mouth for 2 days. The *BNFC* recommends doses of 5 mg/kg for neonates and infants up to 12 months of age and 10 mg/kg for children between 1 and 12 years of age, each twice daily by mouth for 2 days.

For prophylaxis against meningitis due to *Haemophilus influenzae* the AAP recommends infants less then 1 month old are given 10 mg/kg once daily by mouth for 4 days, while the *BNFC* suggests that this dose should be given to infants aged 1 to 3 months. For older infants and children both the AAP and the *BNFC* recommend a dose of 20 mg/kg (to a maximum of 600 mg) once daily by mouth for 4 days.

Administration in hepatic impairment. Reduced doses of rifampicin are recommended for patients with hepatic impairment and a maximum of 8 mg/kg daily has been suggested. See also Precautions, above.

Ehrlichiosis. Beneficial responses to rifampicin have been reported[1] in 2 pregnant women with human granulocytic anaplasmosis (see Ehrlichiosis, p.168), in whom the usual treatment with a tetracycline was contra-indicated.

1. Buitrago MI, *et al*. Human granulocytic ehrlichiosis during pregnancy treated successfully with rifampin. *Clin Infect Dis* 1998; **27:** 213–15.

Meningitis prophylaxis. ***HAEMOPHILUS INFLUENZAE MENINGITIS PROPHYLAXIS.*** Meningeal infection with *Haemophilus influenzae* type b (Hib) in children is associated with substantial morbidity, but the incidence has decreased since the introduction of immunisation with *H. influenzae* type b vaccine. Although a worldwide problem, the disease (p.178) and its prophylaxis has been studied mainly in the USA, where it was shown that children under 4 years of age formed the highest risk group for primary infection while children under 2 years of age formed the highest risk group for secondary infection.[1] The goal of prophylaxis in close contacts is to eliminate carriage of the organism to prevent spread to young children. Risk of infection to young children with recent household contact to the primary case of infection with *H. influenzae* type b is increased 600- to 800-fold,[1,2] but only increased 20-fold[3] from day-care or school contact. The risk may be higher when more than 1 index patient is identified.

Rifampicin in doses of 20 mg/kg once daily for 4 days (maximum dose 600 mg) has been shown to eradicate Hib nasopharyngeal carriage in at least 95% of contacts of the primary case.[4] There is some evidence from a study involving 68 families of patients with Hib infection that rifampicin 20 mg/kg daily for 2 days may be as effective as a 4-day course in eradicating Hib pharyngeal colonisation.[5] Rifampicin prophylaxis appears to be successful in preventing infection in household contacts, but benefit in school settings where there has been a single index case has not been established.[3]

Recommendations have been made for rifampicin prophylaxis.[6,7] The American Academy of Pediatrics (AAP) recommends[6] that all household contacts be given rifampicin prophylaxis where there is at least 1 contact person who is younger than 4 years of age who is not or incompletely immunised against Hib, where there is an unimmunised child younger than 12 months of age, or where there is an immunocompromised child (regardless of vaccine status), in the household. Similar recommendations have been made in the UK.[7] The AAP[6] also recommends rifampicin prophylaxis when 2 or more cases of Hib disease have occurred within 60 days in a day-care or school. In the UK,[7] prophylaxis has been recommended for all room contacts when 2 or more cases of disease have occurred within 120 days. Rifampicin prophylaxis is not recommended for pregnant women.[6]

For recommended *doses* see Uses and Administration and Administration in Children, above.

Rifampicin should also be given to the primary case since treatment of the infection does not eradicate nasopharyngeal carriage.[2,6]

1. Casto DT, Edwards DL. Preventing Haemophilus influenzae type b disease. *Clin Pharm* 1985; **4:** 637–48.
2. Cartwright KAV, *et al*. Chemoprophylaxis for Haemophilus influenzae type b: rifampicin should be given to close contacts. *BMJ* 1991; **302:** 546–7.
3. ASHP Commission on Therapeutics. ASHP therapeutic guidelines on nonsurgical antimicrobial prophylaxis. *Clin Pharm* 1990; **9:** 423–45.
4. Band JD, *et al*. Prevention of Hemophilus influenzae type b disease. *JAMA* 1984; **251:** 2381–6.
5. Green M, *et al*. Duration of rifampin chemoprophylaxis for contacts of patients infected with Haemophilus influenzae type B. *Antimicrob Agents Chemother* 1992; **36:** 545–7.
6. Pickering L, *et al*. eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006.
7. Department of Health. *Immunisation Against Infectious Disease* 2006: "The Green Book" Available at: http://www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Greenbook/DH_4097254 (accessed 05/10/07)

MENINGOCOCCAL MENINGITIS PROPHYLAXIS. *Neisseria meningitidis* is an important cause of bacterial meningitis (p.178); all age groups are at risk during epidemics but children are usually at highest risk during endemic outbreaks. Vaccines are available for meningococci groups A, C, Y, and W135 but not usually for group B, therefore antimicrobial prophylaxis remains important in preventing the spread of the disease. The aim of prophylaxis is to eliminate nasopharyngeal carriage of the organism. Sulfadiazine and minocycline are no longer used because of resistance and adverse effects. The current antibacterial of choice is rifampicin which should be given for 2 days (for doses see Uses and Administration and Administration in Children, above). Alternatives include a single oral dose of ciprofloxacin, ofloxacin, or azithromycin, or a single intramuscular dose of ceftriaxone.[1,2] Antibacterial prophylaxis should be given as soon as possible to close contacts (ideally within 24 hours of diagnosis of the index case). It is also recommended for child care or nursery school contacts in the USA,[2] but is not usually advised for this group in the UK after a single case.[1] The index patient should also receive rifampicin for 2 days before hospital discharge since treatment with penicillin does not eliminate nasopharyngeal carriage.

1. PHLS, Public Health Medicine Environmental Group, Scottish Centre for Infection and Environmental Health. Guidelines for public health management of meningococcal disease in the UK. *Commun Dis Public Health* 2002; **5:** 187–204. Also available at: http://www.hpa.org.uk/cdph/issues/CDPHvol5/no3/Meningococcal_Guidelines.pdf (accessed 05/10/07)
2. CDC. Recommendations of the Advisory Committee on Immunization Practices (ACIP): prevention and control of meningococcal disease. *MMWR* 2005; **54** (RR-7): 1–21. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5407.pdf (accessed 05/10/07)

Naegleria infections. For mention of the use of rifampicin in primary amoebic meningoencephalitis, see p.822.

Preparations

BP 2008: Rifampicin Capsules; Rifampicin Oral Suspension;
USP 31: Rifampin and Isoniazid Capsules; Rifampin Capsules; Rifampin for Injection; Rifampin Oral Suspension; Rifampin, Isoniazid, and Pyrazinamide Tablets; Rifampin, Isoniazid, Pyrazinamide, and Ethambutol Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Moxina; Pharmaceutix†; Rifadecina†; Rifadin; ***Austral.:*** Rifadin; Rimycin; ***Austria:*** Eremfat; Rifoldin; Rimactan; ***Belg.:*** Rifadine; ***Braz.:*** Monicil; Rifaldin; Rifamp; ***Canad.:*** Rifadin; Rofact; ***Chile:*** Rifaldin; ***Cz.:*** Arficin; Benemicin; Eremfat; Rifamor†; Tubocin†; ***Denm.:*** Rimactan; ***Fin.:*** Rimapen; ***Fr.:*** Rifadine; Rimactan; ***Ger.:*** Eremfat; Rifa; ***Gr.:*** Rifadin; Rifaldin; ***Hong Kong:*** Ricin; Rifadin; Rifasynt; Rimactane; ***Hung.:*** Rifamed; ***India:*** R-Cin; Rifacilin; Rifacom E-Z; Rifamycin; Rimactane; Siticox; ***Indon.:*** Corifam; Famri; Lanarif; Medirif; Merimac; Prolung; Ramicin; RIF; Rifabiotic; Rifacin; Rifamtibi; Rimactane; ***Irl.:*** Rifadin; Rimactane; ***Israel:*** Rimactan; ***Ital.:*** Rifadin; Rifapiam†; ***Malaysia:*** Ramfin†; Rifasynt; Rimactane; ***Mex.:*** Eurifam; Finamicina; Pestarin; Rifadin; Rimactan; Turifam; ***Neth.:*** Rifadin; Rimactan†; ***Norw.:*** Rimactan; ***NZ:*** Rifadin; ***Philipp.:*** Crisarfam; Fampisec; Framacin; Medifam; Natricin; Odifam; Refam; Rexilan; Ricyn; Rifadin; Rifamax; Rimactane; Rimaped; Riprocin; ***Port.:*** Rifadin; Rifex; Rimactan; ***Rus.:*** Benemicin (Бенемицин); ***S.Afr.:*** Rifadin†; Rimactane; ***Singapore:*** Rimactane†; ***Spain:*** Rifagen†; Rifaldin; Rimactan; ***Swed.:*** Rifadin; Rimactan; ***Switz.:*** Rimactan; ***Thai.:*** Manorifcin; Myrin-P; Myrin†; Ramfin†; Rampicin†; Ricin; Rifadin; Rifagen; Rifam; Rifam-P†; Rifamcin; Rifasynt†; Rimactane; Rimecin; ***Turk.:*** Rifadin; Rifcap; Rifex; ***UK:*** Rifadin; Rimactane; ***USA:*** Rifadin; Rimactane; ***Venez.:*** Fampiz†; Rifadin; Rimactan.

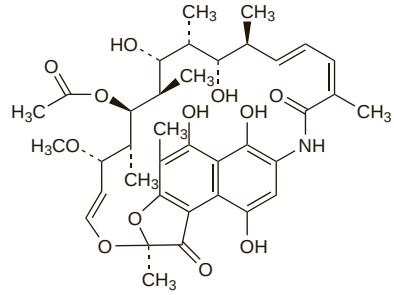
Multi-ingredient: ***Arg.:*** Bacifim; Rifaprim; Rifinah; Risoniac†; Ritroprim†; ***Austria:*** Rifater; Rifoldin INH; ***Braz.:*** Isoniaton; ***Canad.:*** Rifater; ***Denm.:*** Rimactazid; Rimstar; ***Fin.:*** Rimactazid; Rimstar; ***Fr.:*** Rifater; Rifinah; ***Ger.:*** Iso-Eremfat; Rifater; Rifinah; tebesium Duo; tebesium Trio; ***Gr.:*** Oboliz; Rifater; Rifinah; Rimactazid; ***Hong Kong:*** Rifater; Rifinah; ***Hung.:*** Rifazid; ***India:*** Akt-3; Akt-4; Arzide; Bicox-E†; Coxina-3; Coxina-4; Coxinex; Cx-3; Cx-4; Cx-5; Gocox Compound; Gocox-3; Gocox-4†; Ipcacin Kid; Isorifam; R-Cinex; R-Cinex Z; RHZ; RHZ-Plus; Rifa; Rifa E; Rifacomb Plus†; Rifacomb†; Rimactazid + Z; Rimpazid; Siticox-INH; Tibirim INH; Tricox; Wokex-2; Wokex-3; Wokex-4; Xeed-2; Xeed-3E; Xeed-4; ***Indon.:*** Ramicin-ISO; Rimactazid; Rimcure; Rimstar; ***Irl.:*** Rifater; Rifinah; Rimactazid; ***Ital.:*** Rifater; Rifinah; ***Malaysia:*** Rimactazid; Rimcure; ***Mex.:*** Arpisen; Finater; Finateramida; Isonid†; Rifaprim; Rifater; Rifinah; ***Neth.:*** Rifinah; ***NZ:*** Rifinah; ***Philipp.:*** 4D; Bifix; CombiKids; CombiPack; Continukit; Continukit Plus; Continupack; Econokit; Econokit-MDR; Econopack; Fixcom 3; Fixcom 4; Kidz Kit 2; Kidz Kit 3; Myrin; Myrin-P; Quadtab; Refam Duo; Refam Pedia Kit; Rifater; Rifinah; Rifzin; Rimactazid; Rimcure; Rimstar; SVM-Polypac-A; Tres; Triofix; Tritab; Viper; ***Pol.:*** Rifamazid; ***Port.:*** Rifater; Rifinah; ***Rus.:*** Isocomb (Изокомб); Repin B (Репин В); Rifacomb (Рифакомб); Rifacomb Plus (Рифакомб Плюс); Rimactazid (Римактазид); Rimecure 3-FDC (Римкур 3-ФДС); Rimstar 4-FDC (Римстар 4-ФДС); ***S.Afr.:*** Myrin Plus†; Myrin†; Rifafour; Rifater; Rifinah; Rimactazid; Rimcure; Rimstar; ***Singapore:*** Rimactazid; ***Spain:*** Rifater; Rifazida†; Rifinah; Rimactazid; Rimcure; Rimstar; Tisobrif; ***Swed.:*** Rimactazid; Rimcure; Rimstar; ***Switz.:*** Rifater; Rifinah; ***Thai.:*** Rifafour; Rifampyzid; Rifater; Rifinah; Rimactazid; Rimcure 3-FDC; Rimstar; ***UK:*** Rifater; Rifinah; Rimactazid†; ***USA:*** IsonaRif; Rifamate; Rifater; ***Venez.:*** Rimactazid; Rimcure.

Rifamycin Sodium *(BANM, rINNM)*

M-14 (rifamycin); Natrii Rifamycinum; Rifamicina sódica; Rifamicin-nátrium; Rifamicino natrio druska; Rifamycin sodná sůl; Rifamycin SV Sodium; Rifamycine sodique; Rifamycinnatrium; Rifamycinum natricum; Rifamysiininatrium; Ryfamycinum Natricum; Ryfamycyna sodowa. Sodium (12*Z*,14*E*,24*E*)-(2*S*,16*S*,17*S*,18*R*,19*R*,-20*R*,21*S*,22*R*,23*S*)-21-acetoxy-1,2-dihydro-6,9,17,19-tetrahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-1,11-dioxo-2,7-(epoxypentadeca-1,11,13-trienimino)-naphtho-[2,1-*b*]furan-5-olate.

Натрий Рифамицин

$C_{37}H_{46}NNaO_{12}$ = 719.8.
CAS — 6998-60-3 (rifamycin); 14897-39-3 (rifamycin sodium); 15105-92-7 (rifamycin sodium).
ATC — J04AB03; S01AA16; S02AA12.
ATC Vet — QJ04AB03; QS01AA16; QS02AA12.



(rifamycin SV)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Rifamycin Sodium). The monosodium salt of rifamycin SV, a substance obtained by chemical transformation of rifamycin B which is produced during growth of certain strains of *Amycolatopsis mediterranei*. Rifamycin SV may also be obtained directly from certain mutants of *A. mediterranei*. The potency is not less than 900 units/mg calculated with reference to the anhydrous substance. A red, fine or slightly granular powder. Soluble in water; freely soluble in dehydrated alcohol. A 5% solution in water has a pH of 6.5 to 8.0. Store in airtight containers at a temperature of 2° to 8°. Protect from light.

Adverse Effects and Precautions
Some gastrointestinal adverse effects have occurred after injections of rifamycin. High doses may produce alterations in liver function. Hypersensitivity reactions including rashes, pruritus, and anaphylaxis have occurred rarely, but prolonged use increases the risk of sensitisation. A reddish coloration of the urine and other body fluids has been reported. Rifamycin should be used with care in patients with hepatic dysfunction.

Antimicrobial Action
Rifamycin has similar antimicrobial actions to those of rifampicin (p.327).

Pharmacokinetics
Rifamycin is not effectively absorbed from the gastrointestinal tract. Plasma concentrations of 2 micrograms/mL have been achieved 2 hours after a dose of 250 mg by intramuscular injection; concentrations of about 11 micrograms/mL have been achieved 2 hours after an intravenous dose of 500 mg. Rifamycin is about 80% bound to plasma proteins and has a plasma half-life of about 1 hour.

Rifamycin is excreted mainly in the bile and only small amounts appear in the urine.

Uses and Administration
Rifamycin is a rifamycin antibacterial that has been used in the treatment of infections caused by susceptible organisms including Gram-positive organisms such as staphylococci. It has been given as the sodium salt by intramuscular injection and by slow intravenous infusion and is also given by local instillation and topical application.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Plusderm ATB†; Rifocina; ***Austria:*** Rifocin; ***Belg.:*** Rifocine; ***Braz.:*** Rifan; Rifocina; ***Fr.:*** Otofa; ***Ital.:*** Rifocin; ***Mex.:*** Rifocyna; ***Port.:*** Rifocina; ***Rus.:*** Otofa (Отофа); ***Switz.:*** Otofa; ***Turk.:*** Rif; Rifocin; ***Venez.:*** Rifocina.

Multi-ingredient: ***Braz.:*** Rifocort.

Rifapentine *(BAN, USAN, rINN)*

DL-473; DL-473-IT; L-11473; MDL-473; Rifapentina; Rifapentinum. 3-[*N*-(4-Cyclopentyl-1-piperazinyl)formimidoyl]rifamycin.

Рифапентин

$C_{47}H_{64}N_4O_{12}$ = 877.0.
CAS — 61379-65-5.
ATC — J04AB05.
ATC Vet — QJ04AB05.