PRODUCT INFORMATION

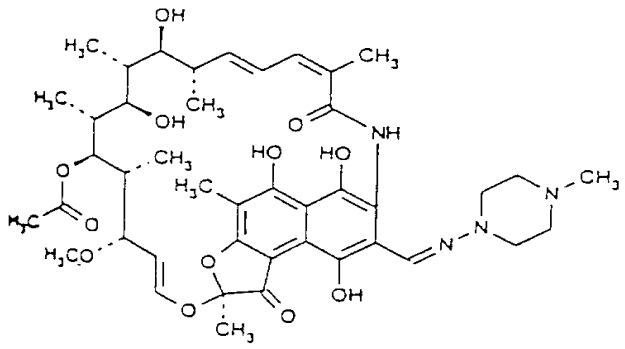
RIFADIN®

NAME OF THE MEDICINE

Non-Proprietary Name

rifampicin

Chemical Structure



$C_{43}H_{58}N_4O_{12}$

DESCRIPTION

Rifampicin is a semisynthetic antibiotic derivative of rifamycin B. Specifically, rifampicin is the hydrazone, 3-(4-methylpiperazinyliminomethyl) rifamycin SV. It is only slightly soluble in water and is rather unstable to light and moisture.

Excipients present in the capsules are maize starch, magnesium stearate, titanium dioxide, erythrosine, indigo carmine and gelatin.

Excipients present in the tablets are sodium lauryl sulfate, microcrystalline cellulose, lactose monohydrate, calcium stearate, carmellose sodium, maize starch, magnesium stearate, acacia, povidone, erythrosine, titanium dioxide, sucrose, purified talc, magnesium carbonate hydrate, kaolin, colloidal anhydrous silica and gelatin.

Excipients present in the injection are sodium formaldehyde sulfoxylate and sodium hydroxide, the diluent is water for injections.

Excipients present in the syrup are agar, sucrose, methyl hydroxybenzoate, propyl hydroxybenzoate, potassium sorbate, saccharin, sodium metabisulfite, polysorbate 80, raspberry essence (PI 458), diethanolamine and purified water.

PHARMACOLOGY

Rifampicin is particularly active against rapidly growing extracellular organisms but it also has bactericidal activity intracellularly and against slow and intermittently growing *Mycobacterium tuberculosis.* Rifampicin inhibits DNA dependent RNA polymerase activity in susceptible cells. Specifically, it interacts with bacterial RNA polymerase, but does not inhibit the mammalian enzyme. Cross resistance to rifampicin has only been shown with other rifamycins.

Pharmacokinetics

Rifampicin is readily absorbed from the stomach and the duodenum. Peak serum concentrations of the order of 7 microgram/mL (range 6 to 32 microgram/mL) occur about 2 to 4 hours after an oral dose of 600 mg on an empty stomach.

In normal subjects the biological half-life of rifampicin in serum averages about 3 hours after a 600 mg dose.

After absorption, rifampicin is rapidly eliminated in the bile, and an enterohepatic circulation ensues. During this process rifampicin undergoes progressive deacetylation, so that nearly all the drug in the bile

is in this form in about 6 hours. This metabolite retains essentially complete antibacterial activity. Intestinal reabsorption is reduced by deacetylation, and elimination is facilitated. Up to 30% of a dose is excreted in the urine, with about half of this being unchanged drug. Absorption of rifampicin is reduced when the drug is ingested with food.

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

Rifampicin crosses the placenta and serum levels in the foetus equal 15 to 96% of the maternal levels. It also appears in breast milk.

INDICATIONS

Tuberculosis

In the initial treatment and in re-treatment of patients with tuberculosis, RIFADIN must be used in conjunction with at least one other antituberculosis drug.

Leprosy

In the management of lepromatous leprosy and dimorphous leprosy to effect speedy conversion of the infectious state to the noninfectious state, which may be expected to occur in 3 to 4 months of treatment.

As an alternative drug in lepromatous, dimorphous, indeterminate and tuberculoid leprosy resistant to sulfones and other antileprosy drugs.

As an alternative drug in all those patients having true drug allergy to the more commonly used antileprosy drugs.

Meningococcal Disease

Prophylaxis of meningococcal disease in close contacts of known cases and in carriers (RIFADIN is not indicated for the treatment of meningococcal infections).

Haemophilus Influenzae

Prophylaxis of household contacts of patients with *H. influenzae* type B.

CONTRAINDICATIONS

Jaundice

History of hypersensitivity to any of the rifamycins.

Rifadin use is contraindicated when given concurrently with the combination of saquinavir / ritonavir (see **INTERACTIONS**).

PRECAUTIONS

Rifampicin has been shown to produce liver dysfunction. There have been fatalities associated with jaundice in patients with liver disease or receiving rifampicin concomitantly with other hepatotoxic agents. Since an increased risk may exist for individuals with liver disease, rifampicin should only be given to these patients in cases of necessity and under strict medical supervision. Periodic liver function monitoring in these patients, especially ALT and AST, should be carried out prior to therapy and then every 2 to 4 weeks during therapy. Dosage adjustment may be necessary. If signs of hepatocellular damage occur, rifampicin should be withdrawn. Similar precautions are recommended for undernourished patients.

In some cases, hyperbilirubinaemia resulting from competition between rifampicin and bilirubin for excretory pathways of the liver at the cell level can occur in 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.

Both in the treatment of tuberculosis and in meningococcal prophylaxis, small numbers of resistant cells, present within large populations of susceptible cells, can rapidly become the predominating type. Since

rapid emergence of resistance can occur, culture and susceptibility tests should be performed in the event of persistent positive cultures.

RIFADIN should not be used for the treatment of meningococcal disease. In the treatment of asymptomatic carriers, it should be reserved for situations where the risk of meningococcal meningitis is high.

The risks of drug resistance with rifampicin, when used in leprosy, have not been adequately evaluated and, therefore, a second drug should be added to the treatment regimen as is done in the case of tuberculosis.

RIFADIN is not recommended for intermittent therapy (less frequently than 2 to 3 times/week) because of the possibility of immunological reactions including anaphylaxis (see **ADVERSE EFFECTS**). The patient should be cautioned against intentional or accidental interruption of the daily dosage regimen since rare renal hypersensitivity reactions have been reported when therapy was resumed in such cases. If, as may happen in rare cases, a patient develops thrombocytopenia, purpura, haemolytic anaemia or renal failure, treatment with RIFADIN should be stopped at once and not reinstituted at any subsequent time.

It is necessary to exclude concomitant tuberculosis in any patient with leprosy who is to be given rifampicin. If tuberculosis exists concurrently, combined chemotherapy must be used.

Rifampicin syrup contains sodium metabisulfite which may cause allergic reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

Severe, systemic hypersensitivity reactions, including fatal cases, such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome have been observed during treatment with anti-tuberculosis therapy (see **ADVERSE EFFECTS**). It is important to note that early manifestations of hypersensitivity, such as fever, lymphadenopathy or biological abnormalities (including eosinophilia, liver abnormalities) may be present even though rash is not evident. If such signs or symptoms are present, the patient should be advised to consult their physician immediately.

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

Adults treated for tuberculosis with rifampicin should have baseline measurements of hepatic enzymes, bilirubin, serum creatinine, a complete blood count and a platelet count (or estimate). Baseline tests are unnecessary in children unless a complicating condition is known or clinically suspected.

Patients should be seen at least monthly during therapy and should be specifically questioned concerning symptoms associated with adverse reactions. All patients with abnormalities should have follow-up, including laboratory testing, if necessary. Routine laboratory monitoring for toxicity in people with normal baseline is generally not necessary.

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

Urine, faeces, saliva, sputum, sweat, tears and teeth may be coloured red-orange, yellow or brown by rifampicin and its metabolites. Soft contact lenses may be permanently stained. Individuals to be treated should be made aware of these possibilities in order to prevent undue anxiety.

Rifampicin has enzyme induction properties that can enhance the metabolism of endogenous substrates including adrenal hormones, thyroid hormones and vitamin D. Isolated reports have associated porphyria exacerbation with rifampicin administration as a result of induction of delta amino levulinic acid synthetase.

I.V. preparation is for intravenous infusion only and must not be administered by intramuscular or subcutaneous route. Avoid extravasation during injection; local irritation and inflammation due to extravascular infiltration of the infusion have been observed. If these occur, the infusion should be discontinued and restarted at another site.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics. A toxin produced by *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in severe cases,

appropriate therapy such as oral antibacterial agents effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement therapy should be provided when indicated.

Use in Pregnancy

Category C.

There are no well-controlled studies with rifampicin in pregnant women. Therefore, rifampicin should be used in pregnant women or in women of childbearing potential only if the potential benefit justifies the potential risk to the foetus.

In animal experiments, rifampicin, given during organ development, has caused skeletal malformations.

Although rifampicin has been reported to cross the placental barrier and appear in cord blood, the effect of rifampicin on the human foetus is not known.

Bleeding attributable to hypoprothrombinaemia has been reported in newborn infants and in mothers after the use of rifampicin during late pregnancy. If rifampicin is used during the last few weeks of pregnancy, vitamin K should be given to the mother and the newborn infant.

Use in Lactation

Rifampicin is excreted in breast milk and infants should not be breastfed by a patient receiving rifampicin.

Use in Premature and Newborn Infants

As liver enzymes are not fully developed in this age group, treatment with RIFADIN should be considered only in the most grave emergencies.

Carcinogenicity/Mutagenicity

There are no known human data on the long-term potential for carcinogenicity. 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.

Rifampicin was associated with an increased incidence of liver tumours in the females of one strain of mice at doses from 2 to 10 times the recommended human therapeutic doses administered for 60 weeks. In another strain of mice and in rats, no increase of tumours was found. All these studies were carried out during most of the animals' life span.

Rifampicin has been reported to possess immunosuppressive potential in rabbits, mice, rats, guinea pigs, human lymphocytes *in vitro* and humans.

There are no known human data on the long-term potential for mutagenicity. There was no evidence of mutagenicity in bacteria, *Drosophila melanogaster* or mice. An increase in chromatid breaks was noted when whole-blood cell cultures were treated with rifampicin. Increased frequency of chromosomal aberrations was observed *in vitro* in lymphocytes obtained from patients treated with combinations of rifampicin, isoniazid and pyrazinamide, and combinations of streptomycin, rifampicin, isoniazid and pyrazinamide.

INTERACTIONS WITH OTHER MEDICINES

When Rifadin is given concomitantly with combination saquinavir / ritonavir, the potential for hepatotoxicity is increased. Therefore, concomitant use of Rifadin with saquinavir / ritonavir is contraindicated (see **CONTRAINDICATIONS**).

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

Rifampicin is a potent inducer of certain cytochrome P-450 enzymes. Coadministration of rifampicin with other drugs that are also metabolized by the cytochrome P-450 enzymes may accelerate metabolism and reduce the activity of these other drugs. Therefore caution should be used when prescribing rifampicin with drugs metabolized by cytochrome P-450. To maintain optimum therapeutic blood levels, dosages of drugs metabolised by these enzymes may require adjustment when starting or stopping concomitantly administered rifampicin. Examples of drugs metabolised by cytochrome P-450 enzymes include: oral anticoagulants (e.g. warfarin), anticonvulsants (e.g. phenytoin), antiarrhythmics (e.g. disopyramide, mexiletine, quinidine, tocainide and propafenone), antioestrogens (e.g. tamoxifen, toremifen), antipsychotics (e.g. haloperidol), antifungals (e.g. fluconazole, itraconazole, ketoconazole -

see below), antiretroviral drugs (e.g. zidovudine, saquinavir, indinavir, efavirenz), barbiturates, beta-blockers, benzodiazepines (e.g. diazepam), benzodiazepine-related drugs (e.g. zopiclone, zolpidem), calcium channel blockers (e.g. diltiazem, nifedipine, verapamil), chloramphenicol, clarithromycin, corticosteroids, cardiac glycoside preparations, clofibrate, systemic hormonal contraceptives (see below), dapsone, doxycycline, oestrogens, fluoroquinolones, gestrinone, oral hypoglycaemic agents (sulfonylureas), immunosuppressive agents (e.g. cyclosporin, tacrolimus), irinotecan, levothyroxine, narcotic analgesics, methadone, praziquantel, progestins, quinine, riluzole, selective 5-HT_3 receptor antagonists (e.g. ondansetron), statins metabolized by CYP 3A4, telithromycin, theophylline, thiazolidinediones (e.g. rosiglitazone), tricyclic antidepressants (e.g. amitriptyline, nortriptyline) and losartan. It may be necessary to adjust the dosage of these drugs if they are given concurrently with rifampicin.

When atovaquone and rifampicin were taken concomitantly, decreased concentrations of atovaquone and increased concentrations of rifampicin were observed.

Concomitant use of ketoconazole and rifampicin has resulted in decreased serum concentrations of both drugs.

Concurrent use of rifampicin and enalapril has resulted in decreased concentrations of enalaprilat, the active metabolite of enalapril. Dosage adjustments should be made if indicated by the patient's clinical condition.

When rifampicin is taken with p-aminosalicylic acid (PAS), rifampicin levels in the serum may decrease. Therefore, the drugs should be taken at least 4 hours apart.

Patients using oral contraceptives should be advised to change to non-hormonal methods of birth control during rifampicin therapy. Diabetes may become more difficult to control in patients treated with rifampicin.

Combined administration of either halothane or isoniazid and rifampicin may give rise to more frequent and marked disorders of liver function than treatment with rifampicin alone. The concomitant use of rifampicin and halothane should be avoided. Patients receiving both rifampicin and isoniazid should be monitored closely for hepatotoxicity.

Effect on Laboratory Tests

Cross-reactivity and false-positive urine screening tests for opiates have been reported in patients receiving rifampicin when using the KIMS (Kinetic Interaction of Microparticles in Solution) method (e.g. Abuscreen On-Line opiates assay; Roche Diagnostic Systems). Confirmatory tests, such as gas chromatography / mass spectrometry, will distinguish rifampicin from opiates.

Therapeutic levels of rifampicin have been shown to inhibit standard microbiological assays for serum folate and vitamin B_{12}. Thus, alternate assay methods should be considered.

Transient elevations of bromsulfophthalein and serum bilirubin have been reported. Rifampicin may impair biliary excretion of contrast media used for visualization of the gallbladder, due to competition for biliary excretion. Therefore, these tests should be performed before the morning dose of rifampicin.

ADVERSE EFFECTS

Gastrointestinal disturbances such as heartburn, epigastric distress, abdominal discomfort, anorexia, decreased appetite, nausea, vomiting, gas, cramps and diarrhoea have been noted in some patients. Pseudomembranous colitis has been reported (see **PRECAUTIONS**).

Headache, drowsiness, fatigue, menstrual disturbances (in women receiving long-term antituberculosis therapy with regimens containing rifampicin), post-partum haemorrhage, fetal-maternal haemorrhage, ataxia, dizziness, inability to concentrate, mental confusion, visual disturbances, muscular weakness, fever, pains in the extremities and generalised numbness have also been noted. Psychoses have been rarely reported.

Encountered occasionally have been flushing, pruritus, urticarial rash, allergic dermatitis, pemphigus, pemphigoid, acneform lesions, sore mouth, sore tongue and exudative conjunctivitis. Rarely, hepatitis or a shock-like syndrome with hepatic involvement and abnormal liver function tests (e.g. elevations in serum bilirubin, bromsulfophthalein, alkaline phosphatase, serum transaminases) have also been observed. Elevations in blood bilirubin, aspartate aminotransferase and alanine aminotransferase have been commonly reported. An increase in blood creatinine and hepatic enzymes have also been reported.

Hypersensitivity reactions have been reported. Erythema multiforme including Stevens-Johnson syndrome, toxic epidermal necrolysis, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome and vasculitis have been reported rarely.

Rifampicin can cause certain bodily fluids such as sputum, urine, sweat and tears to become red-orange, yellow or brown in colour (see **PRECAUTIONS)**. Tooth discolouration (which may be permanent) has also been reported.

Thrombocytopenia with or without purpura may occur, usually associated with intermittent therapy, but is reversible if the drug is discontinued as soon as purpura occurs. Cerebral haemorrhage and fatalities have been reported when rifampicin administration has been continued or resumed after the appearance of purpura. Eosinophilia, leucopenia, oedema, muscle weakness and myopathy have been reported to occur in a small percentage of patients treated with rifampicin. Agranulocytosis has been reported very rarely. Disseminated intravascular coagulation has been rarely reported. Porphyria has been reported.

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

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

Reactions usually occurring with intermittent dosage regimens and most probably of immunological origin include the following:

- "Flu-like syndrome" consisting of episodes of fever, chills, headache, dizziness and bone pain appearing most commonly during the third to the sixth month of therapy. The frequency of the syndrome varies but may occur in up to 50% of patients given once weekly regimens with a dose of rifampicin of 25 mg/kg or more. These symptoms may be a prelude to more serious complications such as renal hypersensitivity reactions. It is preferable in such cases to change to daily medication.
- Shortness of breath/dyspnoea and wheezing.
- Anaphylaxis/anaphylactic reaction.
- Decrease in blood pressure and shock.
- Haemolytic anaemia.
- Acute kidney injury usually due to renal tubular necrosis or tubulointerstitial nephritis but cortical necrosis has been reported.

During the treatment of leprosy with RIFADIN, a lepromatous reaction may occur. Mild reactions do not require cessation of RIFADIN therapy; in other cases corticosteroid therapy may be required and withdrawal of rifampicin considered.

DOSAGE AND ADMINISTRATION

Oral

It is recommended that oral RIFADIN be administered once daily, either 30 minutes before or two hours after a meal.

Pulmonary Tuberculosis

Adults: 600 mg in a single daily administration.

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

Leprosy

Adults: 450 to 600 mg in a single daily administration.

Prophylaxis of Meningococcal Disease (see **INDICATIONS,** Meningococcal Disease).

Adults: 600 mg/day for 4 days.

Children, over 5 years: 10 mg/kg/day for 4 days, not to exceed 600 mg/day.

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

The NHMRC recommend that in any household in which a case of *H. influenzae* type B infection has occurred and in which another child less than 4 years resides, all members of the family, including adults, should receive rifampicin in a dose of 20 mg/kg per dose once daily (maximum dose 600 mg/day) for 4 days; the dose for neonates (less than 1 month) is 10 mg/kg once daily for 4 days.

In the treatment of pulmonary tuberculosis, RIFADIN must be used in conjunction with at least one other antituberculous agent. Similarly, in the treatment of leprosy, rifampicin should always be used in conjunction with at least one other antileprosy drug.

In general, therapy should be continued until bacterial conversion and maximal improvement have occurred.

Continuous daily treatment with RIFADIN is usually better tolerated than intermittent medication (see **PRECAUTIONS**). The termination of long-term therapy with rifampicin and a subsequent resumption of medication may lead to immunopathological effects (see **ADVERSE EFFECTS**). Intermittent therapy should be avoided but if this alternative is not possible therapy should be initiated with small incremental (150 mg/day) doses. Renal function should be monitored and corticosteroids may be useful.

Intravenous infusion

RIFADIN IV infusion is indicated in patients who are unable to tolerate oral therapy, e.g. postoperative or comatose patients, or patients in whom gastrointestinal absorption is impaired. Serum concentrations following single daily administration of 600 mg rifampicin given in an intravenous infusion drip over 1 to 3 hours are similar to those obtained after 600 mg by mouth.

Adults: Usual dose is 600 mg infused daily.

Children: 10 to 20 mg/kg/day, up to 600 mg/day.

In general, therapy should be continued until bacterial conversion and maximal improvement have occurred.

Preparation of intravenous infusion

RIFADIN IV is only intended to be administered via intravenous infusion and must not be administered by intramuscular or subcutaneous route. It should be freshly prepared by aseptically adding the solvent to the vial of rifampicin powder and swirling gently and continuously until the powder has completely dissolved. When the powder has completely dissolved, the solution should be immediately diluted in 500mL of 5% glucose solution or normal saline. It is suggested that the infusion is administered over a period of 1 to 3 hours.

Dilutions in glucose 5% for injections are stable for up to 4 hours at room temperature and should be prepared and used within this time. Precipitation of rifampicin from the infusion solution may occur beyond this time.

RIFADIN IV infusion is compatible with normal saline for up to 6 hours. Other infusion solutions are not recommended.

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

OVERDOSAGE

Symptoms

Nausea, vomiting, abdominal pain, pruritus, headache and increasing lethargy will probably occur within a short time after acute ingestion; actual unconsciousness may occur with severe hepatic involvement. Transient increases in liver enzymes and/or bilirubin may occur. Brownish-red or orange discolouration of the skin, urine, sweat, saliva, tears and faeces is proportional to amount ingested. Facial or periorbital oedema has also been reported in paediatric patients. Hypotension, sinus tachycardia, ventricular arrhythmias, seizures and cardiac arrest were reported in some fatal cases.

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

especially with prior impairment of hepatic function. A direct effect upon the haematopoietic system, electrolyte levels, or acid-base balance is unlikely.

Although it has not been observed in humans, animal studies suggest a possible neurodepressant action associated with very high doses of rifampicin. Where overdoses of other drugs, including such potentially hepatotoxic substances as isoniazid, pyrazinamide or ethionamide have occurred simultaneously, the signs and symptoms of acute poisoning may be aggravated and/or modified.

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 g of rifampicin. Fatal acute overdoses in adults have been reported with doses ranging from 14 to 60 gram. Alcohol or a history of alcohol abuse was involved in some of the fatal and nonfatal reports. Nonfatal overdoses in paediatric patients aged 1 to 4 years old of 100 mg/kg for one to two doses have been reported.

Treatment

Intensive supportive and symptomatic measures should be instituted. Since nausea and vomiting are likely present, activated charcoal slurry instilled into the stomach following evacuation of gastric contents could help absorb any remaining drug in the gastrointestinal tract. Antiemetic medication may be required to control severe nausea/vomiting.

Active diuresis (with measured intake and output) will help promote excretion of the drug. Bile drainage may be indicated in the presence of serious impairment of hepatic function lasting more than 24 to 48 hours; under these circumstances, extracorporeal haemodialysis may be required. In patients with previously adequate hepatic function, reversal of liver enlargement and impaired hepatic excretory function probably will be noted within 72 hours, with rapid return toward normal thereafter.

PRESENTATION AND STORAGE CONDITIONS

Capsules, 150 mg (blue/red, marked R-150): 100s; 300 mg (red, marked R-300): 100s

Tablets, 600 mg (cyclamen red):– packed in Al/Al blister strip in packs of 30.

Syrup, 100 mg/5 mL (red, raspberry flavoured): 60 mL - amber glass bottles.

IV infusion, 600 mg (with 10 mL solvent) - glass vials.

Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

S4. (PRESCRIPTION ONLY MEDICINE)

DATE OF APPROVAL

Date of TGA approval: 22 August 1996

DATE OF MOST RECENT AMENDMENT

31 July 2017