1. NAME OF THE MEDICINE
Rifampicin

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
The capsules contain 150 mg or 300 mg of rifampicin as the active ingredient.
For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM
Rimycin 150 capsule: Presented as size 3 hard gelatin capsule, maroon body with black cap.
Rimycin 300 capsule: Presented as size 1 hard gelatin capsule with maroon body and cap.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Tuberculosis
In the initial treatment and in retreatment of patients with tuberculosis, rifampicin 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 non-infectious state which may be expected to occur in three to four months of treatment.
- As an alternative drug in lepromatous, dimorphous, indeterminate and tuberculoid leprosy resistant to sulfones and other anti-leprosy drugs.
- As an alternative drug in all those patients having true drug allergy to the more commonly used anti-leprosy drugs.

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

Haemophilus Influenzae
Prophylaxis of household contacts of patients with Haemophilus influenzae type B.

4.2. DOSE AND METHOD OF ADMINISTRATION

It is recommended that rifampicin 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.
RIMYCIN Product Information

**Leprosy**

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

**Prophylaxis of meningococcal disease (see Section 4.1 Therapeutic Indications)**

Dosage for contacts and carriers.

Adults: 600 mg daily for 4 days.

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

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

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

The NH & MRC 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 600 mg per day) for 4 days;
- Neonates (less than one month): 10 mg/kg once daily for 4 days.

**Other Information**

In the treatment of pulmonary tuberculosis, rifampicin 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 rifampicin is usually better tolerated than intermittent medication (see Section 4.4 Special warnings and precautions for use). The termination of long-term therapy with rifampicin and a subsequent resumption of medication may lead to immunopathological effects (see Section 4.8 Adverse effects (Undesirable 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.

**4.3. CONTRAINDICATIONS**

Jaundice

Known hypersensitivity to rifampicin or any of the rifamycins.

Rifampicin use is contraindicated when given concurrently with the combination of saquinavir / ritonavir (see Section 4.5 Interactions with other medicines and other forms of interactions).

**4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

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.

Rifampicin is a well characterised and potent inducer of drug metabolising enzymes and transporters and might therefore decrease concomitant drug exposure and efficacy (see Section 4.5 Interactions with other medicines and other forms of interactions). Therefore, patients should be advised not to take any other medication without medical advice.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics, including rifampicin. 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 moderate to severe cases, appropriate therapy with a suitable oral antibacterial agent effective against Clostridium difficile should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

For the treatment of tuberculosis, rifampicin is usually administered on a daily basis. High doses of rifampicin (greater than 600 mg) given once or twice weekly have resulted in a high incidence of adverse reactions, including the "flu syndrome" (fever, chills and malaise), haematopoietic reactions (leucopenia, thrombocytopenia, or acute haemolytic anaemia), cutaneous, gastrointestinal and hepatic reactions, shortness of breath, shock and renal failure. Recent studies indicate that regimens using twice-weekly doses of rifampicin 600 mg plus isoniazid 15 mg/kg are much better tolerated. Intermittent therapy may be used if the patient cannot or will not self-administer drugs on a daily basis. Patients on intermittent therapy should be closely monitored for compliance and cautioned against intentional or accidental interruption of prescribed therapy because of the risk of serious adverse reactions (see Warnings and Interactions sections).

Rifampicin should be used very carefully in patients with a known history of porphyria cutanea tarda or acute intermittent porphyria.

Rifampicin may precipitate acute renal crisis in patients with adrenal insufficiency. It may be necessary to increase the dose of adrenal steroids in patients with impaired adrenal function who are to receive rifampicin.

**Hepatotoxicity**

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
RIMYCIN Product Information

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.

**Drug resistance**

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.

Rifampicin 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, has not been adequately evaluated and, therefore, a second drug should be added to the treatment regimen as is done in the case of tuberculosis.

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.

**Immunological reactions/ Anaphylaxis**

Rifampicin is not recommended for intermittent therapy (less frequently than 2 to 3 times/week) because of the possibility of immunological reactions including anaphylaxis (see Section 4.8 Adverse effects (Undesirable 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 rifampicin should be stopped immediately and not reinstituted at any subsequent time.

**Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome**

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 Section 4.8 Adverse effects (Undesirable 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.

**Severe bullous reactions**

Cases of severe bullous skin reactions such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalised exanthematous pustulosis (AGEP) have been reported with rifampicin. If symptoms or signs of AGEP, SJS or TEN are present, rifampicin treatment must immediately be discontinued.

**Use in the elderly**

No data available.
Paediatric use

Use in Premature and Newborn Infants: As liver enzymes are not fully developed in this age group, treatment with rifampicin should be considered only in the most grave emergencies.

Effects 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.

Positive direct Coombs’ test may show a false positive during rifampicin therapy.

In the metyrapone test, rifampicin, by hepatic enzyme induction, may decrease the response to metyrapone.

Therapeutic levels of rifampicin have been shown to inhibit standard microbiological assays for serum folate and vitamin B₁₂. Thus, alternate assay methods should be considered.

Transient elevation 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.

Rifampicin may interfere with urinalysis based on spectrophotometry or colour reaction due to discoloration of the urine.

4.5. INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

When rifampicin is given concomitantly with combination saquinavir / ritonavir, the potential for hepatotoxicity is increased. Therefore, concomitant use of rifampicin with saquinavir / ritonavir is contraindicated (see Section 4.3 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 drug metabolising enzymes and transporters including cytochrome P450 enzymes 1A2, 2B6, 2C8, 2C9, 2C19, and 3A4, UDP-glucuronitransferases (UGT), sulfotransferases, carboxylesterases, and transporters including P-glycoprotein (P-gp) and multidrug resistance-associated protein 2 (MRP2). Most drugs are substrates for one or more of these enzyme or transporter pathways, and these pathways may be induced by rifampicin simultaneously. Co-administration of rifampicin with other drugs that are also metabolised by the cytochrome P-450 enzymes may accelerate metabolism and reduce the activity of these other drugs and has the potential to perpetuate clinically important drug-drug interactions against many drugs and across many drug classes. Therefore caution should be used when prescribing rifampicin with these drugs. 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, toremifien), 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, clonibrate, systemic hormonal contraceptives (see below), dapsone, doxycycline, oestrogens, fluoroquinolones, gestronone, oral hypoglycaemic agents (sulfonylureas), immunosuppressive agents (e.g. cyclosporin, tacrolimus), irinotecan, levethyroxine, narcotic analgesics, methadone, praziquantel, progestins, quinine, riluzole, selective 5-HT₃ 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.

Concurrent daily use of alcohol may result in increased incidence of rifampicin induced hepatotoxicity and increased metabolism of rifampicin; dosage adjustments of rifampicin may be necessary and patient monitoring for hepatotoxicity.

Concurrent use of hepatitis-C antiviral drugs (e.g. daclatasvir, simeprevir, sofosbuvir, telaprevir) and rifampicin should be avoided.

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.

Rifampicin treatment reduces the systemic exposure of oral contraceptives. 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 isoniazid with rifampicin should be monitored closely for hepatotoxicity.

Probenecid may increase rifampicin serum concentration and/or toxicity due to competition for hepatic uptake, however the effect on blood levels is inconsistent and concurrent use of probenecid to increase rifampicin serum concentration is not recommended.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

Rifampicin has enzyme-inducing 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 the induction of delta amino levullinic acid synthetase.

4.6. FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

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 child bearing potential, only if the potential benefit justifies the 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.

### 4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Rifampicin may cause undesirable effects which may reduce the capacity for the completion of certain tasks. Patients should be informed of the potential for these undesirable effects and if they experience these symptoms, consideration should be given not to drive or operate machinery.

### 4.8. ADVERSE EFFECTS (UNDESIRABLE 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 Section 4.4. Special warnings and precautions for use).

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 reported rarely.

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, acute generalised exanthematous pustulosis (AGEP) 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 Section 4.4 Special warnings and precautions for use). Tooth discoloration (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 (blood urea nitrogen), serum urea and serum uric acid have occurred. Rarely, haemolysis, haemoglobinuria, haematuria, renal insufficiency or acute renal 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 renal injury usually due to renal tubular necrosis or tubulointerstitial nephritis, but cortical
necrosis has been reported.

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

**Reporting suspected adverse effects**

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows
continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are

**4.9. OVERDOSE**

**Symptoms**

Nausea, vomiting, abdominal pain, pruritus, headache and increasing lethargy will probably occur within
a short time after ingestion; actual unconsciousness may occur with severe hepatic involvement.
Transient increases in hepatic 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 grams. 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.

For general advice on overdose management, contact the Poisons Information Centre, telephone number 13 11 26 (Australia).

5. **PHARMACOLOGICAL PROPERTIES**

5.1. **PHARMACODYNAMIC PROPERTIES**

Pharmacotherapeutic group: Antimycobacterials, antibiotic, ATC code: J04AB02

**Mechanism of action**

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.

**Clinical trials**

No data available.

5.2. **PHARMACOKINETIC PROPERTIES**

**Absorption**

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.

Absorption of rifampicin is reduced when the drug is ingested with food.

**Distribution**

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 placental barrier. Serum levels in the foetus equal 15 to 96% of the maternal serum levels. Rifampicin also appears in the breast milk of nursing mothers.
Metabolism

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

Excretion

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.

5.3. PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

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 humans, 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 have 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.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

The capsules also contain the following inactive excipients: lactose monohydrate, ascorbic acid, purified talc, magnesium stearate, brilliant blue FCF (CI 42090), erythrosine (CI 45430), titanium dioxide (CI 77891), sodium lauryl sulfate, colloidal anhydrous silica, potable water and gelatin. Additionally, the 150 mg capsules contain iron oxide yellow (CI 77492) and iron oxide red (CI 77491).

6.2. INCOMPATIBILITIES

No data available.

6.3. SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.
6.4. SPECIAL PRECAUTIONS FOR STORAGE

Store below 25 °C.

6.5. NATURE AND CONTENTS OF CONTAINER

HDPE Bottle packs of 10 capsules or 100 capsules.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7. PHYSICOCHEMICAL PROPERTIES

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

Chemical name : Rifamycin,3-[(4-methyl-1-piperazinyl)imino]methyl]-5,6,9,13,19,21-Hexahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-8-[(N-(4-methyl-1-piperazinyl)formimidoyl)2,7-(epoxypentadeca[1,11,13]trienimino)naphtho[2,1-b]furan-1,11-(2H)-dione 21-acetate

Structural formula : 

![Structural formula image]

Molecular formula : C_{43}H_{58}N_{4}O_{12} 
Molecular weight : 822.94

CAS number
13292-46-1

7. MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8. SPONSOR

Alphapharm Pty Limited
Level 1, 30 The Bond
30-34 Hickson Road
SUMMARY TABLE OF CHANGES

<table>
<thead>
<tr>
<th>Section changed</th>
<th>Summary of new information</th>
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</table>
| 4.4             | Addition of precaution statement about induction of metabolising enzymes and transporters  
|                 | Addition of Severe bullous reactions |
| 4.5             | Addition of interactions due to induction of metabolising enzymes and transporters  
|                 | Addition of Hepatitis-C antiviral drugs |
|                 | Addition of reduction in exposure to oral contraceptives |
| 4.8             | Addition of AGEP |
| 5.1             | Pharmacotherapeutic group and ATC code added |