be administered, raised subsequently by 75 mg per day until the desired dosage level is attained. If, as may happen in exceptional cases the patient develops renal failure, thrombocytopenia, purpura or haemolytic anaemia, treatment with rifampicin should be stopped at once and not re-instituted at a later date.

Microbiological techniques for assaying the serum concentrations of folic acid vitamin B12 are not suitable for use during treatment with rifampicin.

Prevention of meningococcal meningitis
Owing to the possibility of bacterial resistance developing, contacts undergoing prophylactic treatment should be kept under careful surveillance; special attention should be paid to any signs of an overt meningococcal infection.

Royce Rifampicin Capsule must not be employed to treat an overt meningococcal infection.

Pregnancy and Lactation:
Pregnancy:
Rifampicin has been shown to have teratogenic effects in animals on very high doses, therefore during pregnancy the use of rifampicin should, if possible, be avoided. Particularly during the first 3 months of pregnancy, the drug's possible risks for the foetus must be carefully weighed against its therapeutic benefits for the mother.
When administered during the last few weeks of pregnancy, rifampicin can cause post-natal haemorrhages in mother and infant, for which treatment with vitamin K may be indicated.

Nursing Mother:
Rifampicin is excreted in breast milk. Mothers in whom its use proves unavoidable should refrain from breast feeding their infants.

Side Effects:
Reactions occurring with either daily or intermittent dosage regimens include:
Cutaneous reactions - Mild and self-limiting. Not appear to be hypersensitivity reactions. Consists of flushing and itching with or without a rash.

Gastrointestinal reactions - e.g. anorexia, nausea, vomiting, abdominal discomfort, and diarrhoae, Pseudomembranous colitis has been reported with rifampicin therapy. Hepatitis - Can be caused by rifampicin and liver function tests should be monitored.
Thrombocytopenia - With or without purpura may occur, usually associated with intermittent therapy, but is reversible if 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, leukopenia, edema, muscle weakness and myopathy occurred in a small percentage of patients treated with rifampicin.
Reactions usually occurring with intermittent dosage regimens and most probably of immunological origin include. "Flu Syndrome" consisting of episodes of fever, chills, headache, dizziness and bone pain. If serious complications arise, such as thrombocytopenia, purpura, renal failure or haemolytic anemia rifampicin should be stopped at once and never restart. Occasional disturbances of the menstrual cycle have been reported in women receiving long term antituberculosis therapy with regimens containing rifampicin. Rifampicin may produce a reddish discolouration of the urine, sputum and tears. The patient should be forewarned of this. Soft contact lenses may be permanently stained.
In common with other antibiotics, mild leucopenia and eosinophilia have been reported in a few patients, but appear to be of no particular clinical significance and no causal relationship has been established.

Interactions With Other Medicaments:
Rifampicin has been shown in animals and man to have liver enzyme inducing properties and may reduce the activity of anticoagulants, corticosteroids, cyclosporine, digitalis preparations, oral contraceptives, oral hypoglycaemic agents, dapsone phenytoin, quinidine, narcotics and analgesics. It may be necessary to adjust the dosage of these drugs if they aregiven concurrently with Rifampicin, particularly when it is initiated or withdrawn.

Patients on oral contraceptives should be advised to use alternative non-hormonal methods of birth control during Rifampicin therapy. Also diabetes may become more difficult to control.

If p-aminosalicylic acid and rifampicin are both included in the treatment regimen, they should be given not less than eight hours apart to ensure satisfactory blood levels.

Symptoms and Treatment of Overdose:
In cases of overdosage, gastric lavage should be performed. Intensive supportive measures should be instituted and individual symptoms treated as they arise.

Storage Condition:
Keep container tightly closed. Store in a dry place (below 30° C). Protect from light.

Pack Size:
Royce Rifampicin Capsule 150mg:
Blister pack of 1x10's,10x10's, 50x10's and 100x10's.

Royce Rifampicin Capsule 300mg:
Blister pack of 1x10's, 10x10's, 50x10's and 100x10's.

Registration Numbers:
Royce Rifampicin Capsule 150mg: MAL19860793AZ
Royce Rifampicin Capsule 300mg: MAL19860827AZ

Further information can be obtained from your doctor or pharmacist.

ROYCE®

Product Holder/Manufactured by:
ROYCE PHARMA MFG. SDN. BHD. (650435-X)
PT 1663, Nilai Industrial Estate,
71800 Nilai, Negeri Sembilan, Malaysia.

Revision date: 280417

ROYCE®

Rifampicin Capsule

(Rifampicin - Antibiotic)

Presentation:
Royce Rifampicin Capsule 150mg:
Size 2 capsule with opaque blue coloured cap and opaque green coloured body.

Royce Rifampicin Capsule 300mg:
Size 0 capsule with opaque brown coloured cap and opaque pink coloured body.

Content:
Royce Rifampicin Capsule 150mg:
Each capsule contains:
Rifampicin 150mg

Royce Rifampicin Capsule 300mg:
Each capsule contains:
Rifampicin 300mg

Pharmacological Information:
Rifampicin inhibits DNA-dependant RNA polymerize of mycobacteria and other microorganisms, leading to suppression of initiation of chain formation (but not chain elongation) in RNA synthesis. More specificall , the B subunit of this complex enzymes in the site of action of the drug. RNA polymerase from mammalian cells does not bind Rifampicin, and RNA synthesis is correspondingly unaffected.

It inhibits the growth of most gram-positive bacteria as well as gram-negative microorganisms as *Escherichia coli,* Pseudomonas, indole, positive and negative against *Neisseria miningitidis*. Minimal inhibitory concentrations range from 0.1 to 0.8µg/ml. It also inhibit the growth of certain types of virus.

Rifampicin is readily absorbed from the gastrointestinal tract and peak serum concentrations of about 8µg/ml have been

reported 2 hours after a dose of 450mg and 27µg/ml after a dose of 900mg. About 75% to 80% of Rifampicin in the circulation is bound to serum proteins. Rifampicin, but not its main metabolite, undergoes enterohepatic circulation. It is widely distributed in body tissues; it crosses the placenta and diffuses into milk and into the CSF when the meninges are inflame . Food may reduce and delay absorption.

Rifampicin is mainly metabolized to active desecetylrifampicin and it is excreted in the bile and to a lesser extent in the urine. Up to 30% of a dose of 900mg may be excreted in the urine; about ½ of it in 24 hours. It has a biological ½ life about 3 hours.

Indication:
Mycobacterial infections
•Tuberculosis (all forms)
Tuberculosis is the main indication for Royce Rifampicin Capsule.
Royce Rifampicin Capsule must always be combined with at least one other antituberculous agent.

•Leprosy
In combination with dapsone and clofazimine as treatment of multibacillary forms of leprosy (lepromatous [LL], borderline lepromatous [BL], borderline [BB]).
In combination with dapsone as treatment for paucibacillary forms of leprosy (tuberculoid [TT], borderline tuberculoid [BT]).

Non-mycobacterial infections
In non-mycobacterial infections, e.g. staphylococcal infections, Royce Rifampicin Capsule should only be employed:
-If the pathogens are resistant to the first-line antibiotics that normally prove effective,
-If the pathogens are demonstrably sensitive to rifampicin,
-If given in combination with other antibiotics/ chemotherapeutic agents to which the pathogens are sensitive,
-If a diagnosis of tuberculosis or leprosy has first been excluded.

Prevention of meningococcal meningitis
Prophylactic use in persons having had close contact (e.g. at home, in a day-nursery, at school, or while living in a mass accommodation) with a patient who develops meningococcal meningitis. In such persons, combating or eliminating the

pathogens (Neisseria meningitis) from the nasopharynx can reduce the significantly increased risk of infection. Since the pathogens may rapidly become resistant, a close watch should be kept for any initial signs of an overt infection.

Royce Rifampicin Capsule must not be employed to treat overt meningococcal meningitis (see Warning & Precautions).

Dosage and Administration:
Mycobacterial infections
•Tuberculosis
Adults weighing less than 50kg: Royce Rifampicin Capsule 450mg daily.
Adults weighing 50kg or more: Royce Rifampicin Capsule 600mg daily.
Infants and children: Royce Rifampicin Capsule 10-20mg/kg daily.
Maximum permissible daily dose: 600mg.

The chemotherapeutic agents usually employed today as combined therapy for tuberculosis are rifampicin (Royce Rifampicin Capsule) (RRC), isoniazid (INH), pyrazinamide (PZA), ethambutol (EMB), streptomycin (STM).
For the treatment of sputum-positive pulmonary tuberculosis, preference is nowadays given to the following regimens:
Continuous therapy (7 times a week)
Total duration 9 months:
First 2 months:
RRC + INH + PZA + EMB or STM
Next 7 months:
RRC + INH
A total duration of 9 months is recommended for tuberculosis with HIV infection, and for tuberculous meningitis, disseminated tuberculosis, or spinal involvement with neurological complications.
Total duration 6 months:
First 2 months:
RRC + INH + PZA + EMB or STM
Next 4 months:
RRC + INH
Partially intermittent therapy
Total duration 6 months:
First 2 months:
RRC + INH + PZA + EMB or STM daily

Next 4 months:
RRC + INH 2 or 3 times a week
Fully intermittent therapy
Total duration 6 months:
RRC + INH + PZA + EMB or STM 3 times a week. In the case of all regimens administered 2 or 3 times weekly, the patient should be monitored with directly observed therapy (i.e. administration of tablets under supervision). The same applies for relapses and treatment failures. Dosage recommendations for the treatment of sputum-negative pulmonary tuberculosis and extrapulmonary tuberculosis, and dosage recommendations for elderly and/or undernourished patients and for patients with severe liver damage can be found in the relevant literature.

•Leprosy
For the treatment of leprosy the WHO recommends the following regimens:
Multibacillary forms (LL, BL, BB):
Adults: rifampicin (Royce Rifampicin Capsule) 600mg once a month under supervision + dapsone 100mg once a day + clofazimine 300mg once a month under supervision + 50mg once a day.
Children: rifampicin (Royce Rifampicin Capsule) 10mg/kg once a month under supervision + dapsone 1-2mg/kg daily + clofazimine 200mg once a month under supervision + 50mg on alternate days.
Duration of treatment: at least 2 years and until the skin smears are negative where possible.

Paucibacillary forms (TT, BT):
Adults: rifampicin (Royce Rifampicin Capsule) 600mg once a month under supervision + dapsone 100mg (1-2mg/kg) once a day.
Children: rifampicin (Royce Rifampicin Capsule) 10mg/kg once a month under supervision + dapsone 1-2mg/kg daily.
Duration of treatment: at least 6 months.

Non-mycobacterial infections
In combination with other antibiotics/chemotherapeutic agents:
Adults:600-1200mg daily in 2 doses
Infants and children:10-20mg/kg daily

Prevention of meningococcal meningitis
Adults: 600mg twice a day every 12 hours for 2 days.
Children: 10mg/kg twice a day every 12 hours for 2 days. Infants: 5mg/kg twice a day every 12 hours for 2 days.
This prophylactic treatment should be started as soon as possible.

The dosage recommended by the Centers for Disease Control and Prevention are as follows:

Drug	Daily			Twice a week			Three times a week		
	mg/kg		max. mg	mg/kg		max. mg	mg/kg		max. mg
	Children	Adults		Children	Adults		Children	Adults	
RRC	10-20	10	600	10-20	10	600	10-20	10	600
INH	10-20	5	300	20-40	15	900	20-40	15	900
PZA	15-30	15-30	2000	50-70	50-70	4000	50-70	50-70	3000
EMB	15-25	5-25	2500	50	50	2500	25-30	25-30	2500
STM	20-30	15	1000	25-30	25-30	1500	25-30	25-30	1000

Contraindication:
Jaundice; hypersensitivity to rifampicin antibiotics; first trimester of pregnancy; premature and newborn infants.

Warning and Precautions:
As Rifampicin is excreted principally by the biliary tract, caution should be excreted in treating patients with hepatic disorders. Such patients should have liver function monitored during treatment.

In the presence of complete renal failure rifampicin is excreted entirely in the bile, provided hepatic function is not impaired the dosage of rifampicin need not be adjusted.

The occurrence of liver function abnormalities is more common when rifampicin and isoniazid are used in combination, special care us therefore required in patients with pre-existing liver impairment, or in the elderly, malnourished or very young patients.

When resuming treatment with Rifampicin after a temporary or a prolonged interval, the drug should be given in small, gradually increasing doses. In adults an initial dose of 75 mg daily should