PACKAGE INSERT FOR RESCUVOLIN:

SCHEDULING STATUS:

Tablets: Not scheduled

Injection: S1

PROPRIETARY NAME (AND DOSAGE FORM):

RESCUVOLIN 15 mg Tablets

RESCUVOLIN POWDER FOR INJECTION 15 mg

RESCUVOLIN POWDER FOR INJECTION 50 mg

COMPOSITION:

Each tablet contains calcium folinate equivalent to 15 mg folinic acid.

Other excipients: Lactose monohydrate, potato starch, povidone, colloidal silicone dioxide, magnesium stearate.

Each vial contains calcium folinate equivalent to 15 mg or 50 mg folinic acid.

Other excipients: Sodium chloride.

PHARMACOLOGICAL CLASSIFICATION:

A 22.1.4 Vitamins - other.

PHARMACOLOGICAL ACTION:

Folinic acid is a fully reduced, metabolically functional folate co-enzyme. It enters cells via the specific carrier, mediated transport system and is convertible to other folate co-factors. Thus, it may function directly without the need for reduction by dihydrofolate reductase, in reactions such as those required for purine biosynthesis.

INDICATIONS:

As an antidote to folic acid antagonists, such as methotrexate, which block the conversion of folic acid to tetrahydrofolate by binding the enzyme dihydrofolate reductase.

CONTRAINDICATIONS:

Hypersensitivity to folinic acid or any of the ingredients in **RESCUVOLIN**.

Vitamin B_{12} deficiency (see **WARNINGS AND SPECIAL PRECAUTIONS**).

RESCUVOLIN is contraindicated in patients with stomach and bowel complaints (vomiting and diarrhoea).

WARNINGS AND SPECIAL PRECAUTIONS:

Warnings:

RESCUVOLIN should not be used for the treatment of pernicious anaemia or other megaloblastic anaemias secondary to a deficiency of Vitamin B_{12}. Its use can result in an apparent response of the haematopoietic system, but neurological damage may occur or progress if already present.

Special precautions:

This medicinal product contains lactose as an excipient, and patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

RESCUVOLIN has no or negligible influence on the ability to drive and use machines.

INTERACTIONS:

RESCUVOLIN enhances the toxicity, as well as the antineoplastic action of fluorouracil, especially on the gastro-intestinal tract.

RESCUVOLIN may increase the frequency of seizures in susceptible paediatric patients by counteracting the anticonvulsant effects of barbiturates, hydantoin anticonvulsants and primidone.

PREGNANCY AND LACTATION:

The safety of this medicine in pregnant and lactating women has not been established.

DOSAGE AND DIRECTIONS FOR USE:

In cases of inadvertent overdosage of a folic acid antagonist, **RESCUVOLIN** should be administered as soon as possible; if a period of more than 4 hours intervenes, the treatment may not be effective.

Where large doses of methotrexate have been given, **RESCUVOLIN** may be given by intravenous infusion in a dose equivalent to 75 mg of folinic acid within 12 hours, followed by 12 mg intramuscularly every 6 hours for 4 doses. Doses equal to or greater than the dose of methotrexate have been recommended. In less severe overdosage 6 to 12 mg of **RESCUVOLIN** intramuscularly every 6 hours for 4 doses may be adequate. **RESCUVOLIN** is used in conjunction with methotrexate to reduce the toxicity of the methotrexate ("folinic acid rescue"; "calcium leucovorin rescue"). **RESCUVOLIN** is given after an appropriate interval, usually of up to 24 hours, has elapsed for methotrexate to exert its antineoplastic effect. Doses of up to 120 mg have been given over 12 to 24 hours by intramuscular injection or intravenous injection or infusion, followed by 12 to 15 mg intramuscularly, or 15 mg by mouth, every 6 hours for the next 48 hours.

The required dose of **RESCUVOLIN** and duration of **RESCUVOLIN** treatment following high dose methotrexate treatment must be determined by regular (every 12 to 24 hours) measurements of the plasma methotrexate concentration. In general monitoring should continue until the plasma methotrexate concentration is below 5×10^{-8} Molar.

A larger dose and or longer administration may be required in patients with aciduria, ascites, dehydration, gastrointestinal obstruction, renal function impairment or pleural effusions because excretion of methotrexate is slowed and the length of time for plasma methotrexate levels to decrease to non-toxic levels is increased.

With lower doses of methotrexate, **RESCUVOLIN** 15 mg by mouth every 6 hours for 48 to 72 hours may suffice.

RESCUVOLIN POWDER FOR INJECTION may be reconstituted with sterile water for injection.

SIDE EFFECTS:

Immune system disorders:

Less frequent: Allergic reactions may occur; pyrexia has occurred after injections.

Central nervous system:

Less frequent: Seizures have been reported with use in cancer chemotherapy.

RESCUVOLIN should never be given alone or in conjunction with inadequate amounts of hydroxycobalamin for the treatment of pernicious anaemia.

Gastro-intestinal disorders:

Less frequent: High doses of **RESCUVOLIN** have given rise to gastro-intestinal complaints.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **SIDE EFFECTS**.

Treatment is symptomatic and supportive.

IDENTIFICATION:

Tablets: Each tablet is cream-coloured, flat-faced and scored.

Injection: Each colourless glass vial contains a virtually white, caked powdery mass. The reconstituted solution is clear and practically free of particles and is light yellow in colour.

PRESENTATION:

Tablets: Bottles containing 10 tablets, or blister strips containing 10 tablets. The blister strips are packed into an outer cardboard carton.

Injection: Single vials of powder for injection. The vials are packed into an outer cardboard carton.

STORAGE INSTRUCTIONS:

Tablets and dry powder: Store at or below 25 ºC and protect from light.

Shake well to dissolve.

Reconstituted solution: Store up to 8 hours at 15 – 25 ºC and protect from light.

Solution with precipitations are to be destroyed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

RESCUVOLIN 15 mg Tablets: S/22.1.4/339

RESCUVOLIN POWDER FOR INJECTION 15 mg: S/22.1.4/344

RESCUVOLIN POWDER FOR INJECTION 50 mg: S/22.1.4/345

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd

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