SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

FECTRIM PAEDIATRIC/Co-Trimoxazole 20/100 mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Trimethoprim 20 mg
Sulphamethoxazole 100 mg.

3 PHARMACEUTICAL FORM

Tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prophylaxis (primary and secondary) of Pneumocystis carinii pneumonitis in adults and children.

Treatment and prophylaxis of toxoplasmosis, treatment of nocardia.

Treatment of urinary tract infections and acute exacerbations of chronic bronchitis where there is bacterial evidence of sensitivity to Co-trimoxazole and good reason to prefer this combination to a single antibiotic.

Treatment of acute otitis media in children, where there is good reason to prefer Cotrimoxazole to a single antibiotic.

4.2 Posology and method of administration

Children:

6-12 years: 4 tablets twice daily.
2-6 years: 2 tablets twice daily

In the case of severe infections, the dosage may be increased by 50%. FECTRIM should be taken with a little food to avoid gastro-intestinal disturbances.

The dosage regime should be continued for at least *5* days in acute infections or until the patient has become symptom-free for 2 days.

Long term prophylaxis of recurrent, or suppression of chronic infection following sterilisation of the urine. Children under 12: a single nightly dose equivalent to 2 mg Trimethoprim and 10 mg Sulphamethoxazole per kilo/body weight.

Treatment may be continued for 3-12 months or more as appropriate.

Pneumocystis carinii pneumonitis: Treatment: 20 mg Trimethoprim and 100mg Sulphamethoxazole per kilo/body weight per day in two or more divided doses for 2 weeks. For maximum efficacy and minimum toxicity the steady state peak plasma or serum level of Trimethoprim should be maintained at 5 micrograms per ml. Prophylaxis of Pneumocystis carinii pneumonia: 20 mg Trimethoprim and 100 mg Sulphamethoxazole per kilo/body weight per day in two or more divided doses (standard dose) for the duration of the period at risk.

Therapy in all acute infections should be continued until the patient is symptom-free for 2 days or for a minimum of 5 days, whichever is the longer.

Method of administration: Oral.

4.3 Contraindications

In patients exhibiting sensitivity to the product treatment should immediately be discontinued.

A history of sulphonamide or trimethoprim sensitivity is a contra-indication. Treatment must be stopped on the appearance of a rash.

Contra-indicated in blood dyscrasias or in patients showing marked liver parenchymal change.

Contra-indicated in renal insufficiency where measurement (repeated and regular) of the plasma concentration cannot be determined.

The medicament should not be given to premature infants under 6 weeks except in the treatment of Pneumocystis carinii pneumonitis.

4.4. Special warnings and precautions for use

- An adequate urinary output should be maintained in cases with renal impairment, and a reduced or more widely spaced dosage interval should be used so as to avoid accumulation of the drug.
- Hypersensitivity reactions may require treatment with steroids. Calcium folinate, 3 to 6 mg intramuscularly for five to seven days may be given to counteract the effect of Trimethoprim on haemopoiesis
- Fatalities may occur with Stevens Johnson syndrome, Lyell syndrome/toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anaemia, other blood dyscrasias, hypersensitivity of respiratory tract.
- Care in folate deficient patients and the elderly, who may require folate supplements.
- Haemolysis in glucose-6-phosphate dehydrogenase deficiency patients.
- Caution in patients with severe allergy and bronchial asthma.
- Do not use in Group A beta-haemolytic streptococci.
- May be used in phenylketonuria patients on diet.
- Avoid in acute porphyria risk patients.
- Regular blood counts are advised for patients on prolonged treatment;

Respiratory toxicity

Very rare, severe cases of respiratory toxicity, sometimes progressing to Acute Respiratory Distress Syndrome (ARDS), have been reported during co-trimoxazole treatment. The onset of pulmonary signs such as cough, fever, and dyspnoea in association with radiological signs of pulmonary infiltrates, and deterioration in pulmonary function may be preliminary signs of ARDS. In such circumstances, co-trimoxazole should be discontinued and appropriate treatment given.

Haemophagocytic lymphohistiocytosis (HLH)

Cases of HLH have been reported very rarely in patients treated with co-trimoxazole. HLH is a life- threatening syndrome of pathologic immune activation characterised by clinical signs and symptoms of an excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridaemia, hypofibrinogenaemia, high serum ferritin, cytopenias and haemophagocytosis). Patients who develop early manifestations of pathologic immune activation should be evaluated immediately. If diagnosis of HLH is established, cotrimoxazole treatment should be discontinued.

4.5 Interaction with other medicinal products and other forms of interaction

Patients receiving anti-coagulants of the coumarin group should be monitored to assess and ensure proper anti-coagulant control.

Patients taking anti-malarials particularly pyrimethamine at levels of 25 mg weekly (or more) should be monitored for the possibility of megaloblastic anaemia.

Diabetic patients on sulphonylurea may experience an increased hypoglycaemic action when taking Co-trimoxazole and care should be exercised when prescribing the drug to diabetics.

Cyclosporin increases risk of nephrotoxicity. Digoxin effect may be reduced and rifampicin may increase the metabolism of Co-Trimoxazole. Avoid concomitant use with methotrexate.

Co-trimoxazole increases the risk of ventricular arrhythmias with amiodarone, concomitant use should be avoided.

The antifolate effect and plasma concentration of phenytoin is increased by co-trimoxazole.

4.6 Pregnancy and lactation

The drug should not be given during pregnancy or lactation and caution should be exercised when prescribing the drug to women of child bearing age.

Safety is not established in pregnancy and Co-Trimoxazole is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Blood dyscrasias must be considered such as thrombocytopenia, purpura, leucopenia, neutropenia and, rarely, agranulocytosis. The elderly are most susceptible to these blood dyscrasias.

A blood count should be determined when treatment has continued for 4 weeks or longer.

Side effects reflect the components sulphonamide and trimethoprim in type and frequency.

Vascular disorders
Not known: Circulatory shock

Skin: rashes, photosensitivity, severe reactions of exfoliative dermatitis, erythema multiform, Stevens Johnson syndrome, Lyell syndrome/toxic epidermal necrolysis, which has a high mortality.

Allergic: serum sickness, anaphylaxis, allergic myocarditis, angioedema, drug fever, peri-arteritis nodosa, SLE.
Effects in treatment of Pneumocystis carinii pneumonitis may be more severe and severe hypersensitivity on re-exposure may occur.

Haematological: less commonly megaloblastic anaemia, aplastic anaemia, haemolytic anaemia, methaemoglobinaemia. Fatalities may occur. Haemolysis may occur in glucose-6-phosphate dehydrogenase deficiency.

Gastro-intestinal: hepatic elevated transaminases and bilirubin. Rarely cholestatic jaundice and hepatic necrosis, which may be fatal. Nausea, vomiting, diarrhoea, glossitis, stomatitis, anorexia, pseudomembranous colitis and pancreatitis.

Neurological: aseptic meningitis which is reversible on withdrawal, convulsions, peripheral neuritis, ataxia, vertigo, tinnitus, headache, depression, dizziness, hallucinations.

Genito-urinary: impaired renal function. Rarely interstitial nephritis.

Respiratory: cough, dyspnoea and pulmonary infiltrates, which suggest hypersensitivity, which may be fatal.

Metabolic: hyperkalaemia and hyponatraemia.

Musculoskeletal: arthralgia and myalgia.

Miscellaneous: monilial overgrowth.

Circulatory shock
Cases of circulatory shock, often accompanied by fever and not responding to standard treatment for hypersensitivity, have been reported with sulfamethoxazole + trimethoprim, mainly in immunocompromised patients.

4.9 Overdose

Symptoms of overdosage may include vomiting, mental and visual disturbances, petechiae, purpura and jaundice. Haematuria, crystalluria and anuria may occur in severe cases.

Treatment is symptomatic and may include gastric lavage and forced diuresis. Alkalinisation of the urine may aid the elimination of the Sulphamethoxazole component of FECTRIM.

Haemodialysis is effective but peritoneal dialysis is not.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The two components of Co-trimoxazole interfere with the bacterial synthesis of tetrahydrofolic acid, an essential stage in the production of thymidine, purines and, subsequently, nucleic acids. Sulphamethoxazole, like the other sulphonamides, inhibits the synthesis of dihydrofolic acid from p-aminobenzoic acid. Trimethoprim inhibits the action of dihydrofolate reductase and prevents the synthesis of tetrahydrofolic acid from dihydrofolic acid; although this stage also occurs in man, Trimethoprim is much less active against the mammalian enzyme. Enhanced antibacterial activity has been reported when Sulphamethoxazole and Trimethoprim are used together in vitro although there is doubt as to whether sequential blockage of the bacterial synthetic pathway is responsible. Co-trimoxazole has a wide spectrum of activity similar to that of the sulphonamides and Trimethoprim. It is also active against pneumocystis carinii.

5.2 Pharmacokinetic properties

When Co-trimoxazole is administered, plasma concentrations of Trimethoprim and Sulphamethoxazole are generally in the ratio of 1:20; in urine this ratio may vary from 1:1 to 1:5. About 50% of administered Trimethoprim and 50% of Sulphamethoxazole is excreted in the urine in 24 hours; a larger proportion of Sulphamethoxazole appears as inactive metabolite.

Sulphamethoxazole is readily absorbed from the gastro-intestinal tract and peak plasma concentrations are reached within 4 hours. Doses of 1 g twice daily should produce blood concentrations of unconjugated

Sulphamethoxazole in excess of 50 μg per ml. About 65% is bound to plasma albumin and the plasma half-life is about 10 hours. About 15% of Sulphamethoxazole in the blood is present as the acetyl derivative. Elimination in the urine is dependent on pH. About 25% of a single 2 g dose of Sulphamethoxazole has been reported to be excreted in the urine within 8 hours, about 60% being in the form of the acetyl derivative.

Trimethoprim is readily absorbed from the gastro-intestinal trace and peak concentrations in the circulation occur about 3 hours after a dose is taken. About 45% is bound to plasma proteins. Tissue concentrations are reported to be higher than serum concentrations, with particularly high concentrations occurring in the kidneys and lungs but concentrations in the cerebrospinal fluid are about one-half of those in the blood. The half-life is about 10 to 16 hours. About 40% to 50% of a dose is excreted unchanged in the urine within 24 hours, together with metabolites. Trimethoprim appears in breast milk.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in the other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Povidone K25
Crospovidone
Magnesium stearate.

6.2 Incompatibilities

None known.

6.3 Shelf life

Containers: 24 months.

6.4 Special precautions for storage

Store below 25°C in a dry place in well closed containers.

6.5 Nature and contents of container

High density polystyrene or polypropylene containers with polythene or polypropylene lids and polyurethane/polythene inserts. Pack sizes: 100.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
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