Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

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Pediatric Co-Trimoxazole Oral Suspension BP 240 mg/5ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml suspension contains

Sulfamethoxazole BP 200 mg

Trimethoprim BP 40 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Liquid Orals

Pink coloured suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Co-trimoxazole is indicated for the treatment of the following infections when owing to sensitive organisms:

Treatment and prevention of *Pneumocystis jiroveci. (P. carinii) pneumonitis*

Treatment and prophylaxis of toxoplasmosis

Treatment of nocardiosis

The following infections may be treated with Co-trimoxazole where there is bacterial evidence of sensitivity to Co-trimoxazole and good reason to prefer the combination of antibiotics in Co-trimoxazole to a single antibiotic:

Acute uncomplicated urinary tract infections

Acute otitis media

Acute exacerbation of chronic bronchitis.

4.2 Posology and Method of administration

Urinary Tract Infections and Shigellosis in Adults and Pediatric Patients and Acute Otitis Media in Pediatric Patients

Adults: The usual adult dosage in the treatment of urinary tract infections is one Co-trimoxazole DS (double strength) tablet, two Co-trimoxazole tablets or four teaspoonfuls (20 ml) Co-trimoxazole suspension every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Pediatric Patients: The recommended dose for pediatric patients with urinary tract infections or acute otitis media is 8 mg/kg Trimethoprim and 40 mg/kg Sulfamethoxazole per 24 hours given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

For Patients with Impaired Renal Function: When renal function is impaired, a reduced dosage should be employed

Acute Exacerbations of Chronic Bronchitis in Adults
The usual adult dosage in the treatment of acute exacerbations of chronic bronchitis is one Co-trimoxazole DS (double strength) tablet, two Co-trimoxazole tablets, or four teaspoonfuls (20 ml) Co-trimoxazole suspension every 12 hours for 14 days.

Travelers' Diarrhea in Adults
For the treatment of travelers' diarrhea, the usual adult dosage is one Co-trimoxazole DS (double strength) tablet, two Co-trimoxazole tablets, or four teaspoonfuls (20 ml) of Co-trimoxazole suspension every 12 hours for 5 days.

Pneumocystis Carinii Pneumonia
Treatment
Adults and Pediatric Patients: The recommended dosage for treatment of patients with documented Pneumocystis cariniipneumonia is 15 to 20 mg/kg Trimethoprim and 75 to 100 mg/kg Sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 to 21 days.

Prophylaxis

Adults: The recommended dosage for prophylaxis in adults is one Co-trimoxazole DS (double strength) tablet daily.

Pediatric Patients: For pediatric patients, the recommended dose is 150 mg/m^2/day Trimethoprim with 750 mg/m^2/day Sulfamethoxazole given orally in equally divided doses twice a day, on 3 consecutive days per week. The total daily dose should not exceed 320 mg Trimethoprim and 1,600 mg Sulfamethoxazole.

4.3 Contraindications

Co-trimoxazole should not be given to patients with a history of hypersensitivity to sulphonamides, Trimethoprim, Co-trimoxazole or any excipients of Co-trimoxazole.

Contra-indicated in patients showing marked liver parenchymal damage.

Contra-indicated in severe renal insufficiency where repeated measurements of the plasma concentration cannot be performed.

Co-trimoxazole should not be given to premature babies nor to full-term infants during the first 6 weeks of life except for the treatment/prophylaxis of PCP in infants 4 weeks of age or greater.

4.4 Special warnings and precautions for use

Fatalities associated with the administration of sulfonamides, although rare, have occurred due to severe reactions, including Stevens Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias. Sulfonamides, including

sulfonamide-containing products such as trimethoprim/ sulfamethoxazole, should be discontinued at the first appearance of skin rash or any sign of adverse reaction. In rare instances, a skin rash may be followed by a more severe reaction, such as Stevens Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis and serious blood disorder.

4.5 Interaction with other medicinal products and other forms of interact.

In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombocytopenia with purpura has been reported. In the literature, two cases of hyperkalemia in elderly patients have been reported after concomitant intake of trimethoprim/sulfamethoxazole and an angiotensin converting enzyme inhibitor.

It has been reported that Co-trimoxazole may prolong the prothrombin time in patients who are receiving the anticoagulant warfarin. This interaction should be kept in mind when Co-trimoxazole is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

Co-trimoxazole may inhibit the hepatic metabolism of phenytoin. Co-trimoxazole, given at a common clinical dosage, increased the phenytoin half-life by 39% and decreased the phenytoin metabolic clearance rate by 27%. When administering these drugs concurrently, one should be alert for possible excessive phenytoin effect.

4.6 Fertility, Pregnancy and Lactation

There are not any adequate data from the use of Co-trimoxazole in pregnant women. Case-control studies have shown that there may be an association between exposure to folate antagonists and birth defects in humans.

Trimethoprim is a folate antagonist and, in animal studies, both agents have been shown to cause foetal abnormalities.

Co-trimoxazole should not be used in pregnancy, particularly in the first trimester, unless clearly necessary. Folate supplementation should be considered if Co-trimoxazole is used in pregnancy.

Sulfamethoxazole competes with bilirubin for binding to plasma albumin. As significantly maternally derived drug levels persist for several days in the newborn, there may be a risk of precipitating or exacerbating neonatal hyperbilirubinaemia, with an associated theoretical risk of kernicterus, when Co-trimoxazole is administered to the mother near the time of delivery. This theoretical risk is particularly relevant in infants at increased risk of hyperbilirubinaemia, such as those who are preterm and those with glucose-6-phosphate dehydrogenase deficiency.

Lactation

The components of Co-trimoxazole (Trimethoprim and sulfamethoxazole) are excreted in breast milk. Administration of Co-trimoxazole should be avoided in late pregnancy and in lactating mothers where the mother or infant has, or is atparticular risk of developing, hyperbilirubinaemia. Additionally, administration of Co-trimoxazole should be avoided in infants younger than eight weeks in view of the predisposition of young infants to hyperbilirubinaemia.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Hematologic

Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, neutropenia, hemolytic anemia, megaloblastic anemia, hypoprothrombinemia, methemoglobinemia, eosinophilia.

Allergic

Stevens-Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, allergic myocarditis, erythema multiforme, exfoliative dermatitis, angioedema, drug fever, chills, Henoch- Schonlein purpura, serum sickness-like syndrome, generalized allergic reactions, generalized skin eruptions, photosensitivity, conjunctival and scleral injection, pruritus, urticaria, and rash. In addition, periarteritis nodosa and systemic lupus erythematosus have been reported.

Gastrointestinal

Hepatitis, including cholestatic jaundice and hepatic necrosis, elevation of serum transaminase and bilirubin, pseudo-membranous enterocolitis, pancreatitis, stomatitis, glossitis, nausea, emesis, abdominal pain, diarrhea and anorexia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Nausea, vomiting, dizziness and confusion are likely signs/symptoms of overdosage. Bone marrow depression has been reported in acute Trimethoprim overdosage.

If vomiting has not occurred, induction of vomiting may be desirable. Gastric lavage may be useful, though absorption from the gastrointestinal tract is normally very rapid and complete within approximately two hours. This may not be the case in gross overdosage. Dependant on the status of renal function administration of fluids is recommended if urine output is low.

Both Trimethoprim and active sulfamethoxazole are moderately dialysable by haemodialysis. Peritoneal dialysis is not effective

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

Co-trimoxazole is a combined chemotherapeutic agent consisting of Trimethoprim and the sulphonamide Sulphamethoxazole; their ratio is 1:5. It is bactericidal by virtue of a sequential blockade of the folic acid synthesis in micoorganisms. The antimicrobial spectrum of Co-trimoxazole includes many Gram-positive and Gram-negative aerobes, Chlamydias, nocardias, protozoas (Pneumocystis carinii), etc. In addition to its use for pneumocystis, Co-trimoxazole mainly has practical importance against Gram-positive aerobes (urinary tract infections), pneumococci, and Haemophilus influenzae (respiratory tract infections and otitis).

5.2 Pharmacokinetic properties

After oral administration Trimethoprim and Sulfamethoxazole are rapidly and nearly completely absorbed. The presence of food does not appear to delay absorption. Peak levels in the blood occur between one and four hours after ingestion and the level attained is dose related. Effective levels persist in the blood for up to 24 hours after a therapeutic dose. Steady state levels in adults are reached after dosing for 2-3 days. Neither component has an appreciable effect on the concentrations achieved in the blood by the other.

Trimethoprim is a weak base with a pKa of 7.4. It is lipophilic. Tissue levels of Trimethoprim are generally higher than corresponding plasma levels, the lungs and kidneys showing especially high concentrations. Trimethoprim concentrations exceed those in plasma in the case of bile, prostatic fluid and tissue, saliva, sputum and vaginal secretions. Levels in the aqueous humor, breast milk, cerebrospinal fluid, middle ear fluid, synovial fluid and tissue (intestinal) fluid are adequate for antibacterial activity. Trimethoprim passes into amniotic fluid and foetal tissues reaching concentrations approximating those of maternal serum.

Approximately 50% of Trimethoprim in the plasma is protein bound. The half-life in man is in the range 8.6 to 17 hours in the presence of normal renal function. It is increased by a factor of 1.5 to 3.0 when the creatinine clearance is less than 10 ml/minute. There appears to be no significant difference in the elderly compared with young patients.

The principal route of excretion of Trimethoprim is renal and approximately 50% of the dose is excreted in the urine within 24 hours as unchanged drug. Several metabolites have been identified in the urine. Urinary concentrations of Trimethoprim vary widely.

Sulfamethoxazole is a weak acid with a pKa of 6.0. The concentration of active Sulfamethoxazole in a variety of body fluids is of the order of 20 to 50% of the plasma concentration.

Approximately 66% of Sulfamethoxazole in the plasma is protein bound and the principal route of excretion of Sulfamethoxazole is renal. The half-life in man is approximately 9 to 11 hours in the presence of normal renal function. There is no change in the half-life of active Sulfamethoxazole with a reduction in renal function but there is prolongation of the half-life of the major, acetylated metabolite when the creatinine clearance is below 25 ml/minute.

The principle route of excretion of Sulphamethoxazole is renal; between 15% and 30% of the dose recovered in the urine is in the active form. In elderly patients there is a reduced renal clearance of Sulfamethoxazole.

5.3 Preclinical safety data

None stated.

6.0 Pharmaceutical particulars

6.1 List of excipients

Sucrose, Xanthan Gum, Sodium Methyl Hydroxybenzoate, Sodium Propyl Hydroxybenzoate, Bronopol, Citric Acid Monohydrate, Polysorbate 80, Sodium Benzoate, Flavour Peppermint, Colour Etythrosine, Liquid Sorbitol (Non Crysallising), Flavour Orange, Colloidal Anhydrous Silica, Purified Water.

6.2 Incompatibilities

None reported

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C in a dry place. Protect from light. Shake Well Before Use.

6.5 Nature and contents of container

60 ml and 100 ml PET Bottle

6.6 Special precautions for disposal and other handling

None reported

7. Marketing Authorisation Holder

MEDICAMEN BIOTECH LIMITED

SP-1192 A & B, Phase-IV,
Industrial Area, Bhiwadi-301019,
Distt Alwar, Rajasthan India

8. Number(s) in the national register of finished pharmaceutical products

Certificate No: 04723/07091/REN/2019

9. Date of first authorisation/renewal of the authorisation

Nov 4, 2019

10. Date of revision of the text

August 2023