Sulphaprim (200 mg + 40 mg) / 5ml

Pharmaceutical form: Oral suspesion.

Composition: 5 ml oral suspension contains: 200 mg sulfamethoxazole and 40 mg trimethoprim, excipients: sucrose, microcrystalline cellulose, aerosil 200, polysorbate 80, xanthan, methylparaben, propylparaben, glycerin, liquid banana flavor, purified water.

Pharmacological group: Combinations of sulfonamides and trimethoprim, included derivatives.

Pharmacodynamics:

Combined antimicrobial drug, contains from sulfamethoxazole and trimethoprim. Sulfamethoxazole similar in structure to PABA, disrupts the synthesis of dihydrofolic acid in microbial cells, preventing the incorporation of PABA into its molecule.

Trimethoprim enhances the effect of sulfamethoxazole, distrupting the reduction of dihydrofolic acid to tetrahydrofolic acid, the active form of folic acid which is responsible for protein metabolism and microbila cell division. Due to this mechanism, the in vitro bactericidal effect of the drug is achieved at concentrations in which the individual components of the drug have a bacteriostatic effect.

Antibacterial spectrum

The sensitivity of trimethoprim/sulfamethoxazole to a number of pathogens is presented in the table below:

Antibiotic sensitivities of common pathogens:

Gram - positive aerobes:

Staphylococcus aureus

Staphylococcus saprophyticus

Streptococcus pyogenes

Gram - negative aerobes:

Enterobacter cloacae

Haemophilus influenzae

Klebsiella oxytoca

Moraxella catarrhalis

Salmonella spp.

Stenotrophomonas maltophilia

Yersinia spp.

Pathogens with problematic resistance:

Gram - positive aerobes:

Enterococcus faecalis

Enterococcus faecium

Nocardia spp.

Staphylococcus epidermidis

Streptococcus pneumonia

Gram - negative aerobes:

Citrobacter spp.

Enterobacter aerogenes

Escherichia coli

Klebsiella pneumoniae

Proteus mirabilis

Proteus vulgaris

Providencia spp.

Serratia marcescens

Resistant microorganisms:

Gram - negative aerobes:

Pseudomonas aeruginosa

Shigella spp.

Vibrio cholera

Pharmacokinetics:

Following oral administration trimethoprim and sulfamethoxazole are rapidly and almost completely absorbed from the gastrointestinal tract. The presence of food has almost no effect on the absorption process. Maximum plasma concentration is reached one to four hours after administration and depends from dose. Effective concentrations remain in the blood for 24 hours after taking a therapeutic dose. Minimum steady-state concentrations for adults are reached after a dose within 2-3 days. The elimination half-life is approximately 9 to 11 hours with normal kidney function.

Indications:

Infections of the respiratory system and ENT organs:

exacerbation of chronic bronchitis, otitis media in children, if there are sufficient reasons to prefer a combination of trimethoprim and sulfamethoxazole monotherapy with an antibiotic.

Infections of the urinary tract: infections of urinary tract, chancroid.

Infection of gastrointestinal tract: typhoid and paratyphoid, shigellosis (caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* if antibiotic therapy is indicated), traveler's diarrhea, caused by enterotoxic strains of *Escherichia coli,* cholera (in addition to fluid and electrolyte replacement).

Other bacterial infections: infections caused by a number of microorganisms (combination with other antibiotics is possible), for example: brucellosis, acute and chronic osteomyelitis, nocardiosis, actinomycosis, toxoplasmosis and South American blastomycosis.

Posology and method of administration:

Preferably to use with food or drinks. It is important to ensure that your child drinks plenty of fluid such as water, juices while they are taking Sulphaprim.

The daily dose is 6 mg/kg of trimethoprim and 30 mg/kg of sulfamethoxazole.

The course of treatment is usually at least 5 days. Standard dosing regimen recommendations for acute infections.

Age	**Pediatric suspension**
6 weeks to 5 months	2.5 ml each 12 hours
6 months to 5 years	5 ml each 12 hours
6 years to 12 years	10 ml each 12 hours

Standard dosing regimen provides up to approximately 6 mg of trimethoprim and 30 mg of sulfamethoxazole per kilogram of body weight over 24 hours. In severe infections, doses for children can be increased by 50%.

Treatment should be continued for two days after the disappearance of clinical symptoms, in most cases treatment is required for at least 5 days. If clinical improvement is not evident after 7 days of therapy, the patient should be reassessed. For uncomplicated infections of the lower urinary tract, the duration of treatment can be 1-3 days.

Special recommendations for dosing regimen

(Standard dosing regimen applies unless otherwise noted)

Pneumocystis pneumonia (P. Carinii): up to 20 mg trimethoprim and to 100 mg sulfamethoxazole in kg of body weight daily, divided into equal doses, each 6 hours during the 14 days.

Nocardiosis:

Adults: 12-16 measuring spoons of the suspension for at least 3 months. The dose should be adjusted depending on the age, body weight of the patient, kidney function and the severity of the disease. Sometimes treatment is continued up to 18 months.

Patients on hemodialysis:

After taking the usual loading dose, subsequent doses should be half or a third of the standard and administered every 24-48 hours.

Patients with impaired renal function:

With creatinine clearance > 30 ml / min, the usual dose is prescribed, with creatinine clearance of 15-30 ml / min - half the usual dose, and with creatinine clearance < 15 ml / min, Sulfaprim is not recommended.

Toxoplasmosis: There is no consensus on the most appropriate dosing regimen for the treatment or prevention of this condition. The decision should be based on clinical experience. However, for prevention, it may be appropriate to use a dosing regimen suggested for the prevention of pneumocystis pneumonia.

Contraindications:

- Hypersensitivity to sulfonamides, trimethoprim, and/or any of auxiliary components of the drug,
- Severe lesions of the liver parenchyma,
- Severe renal insufficiency (creatinine clearance <15 ml / min), if it is not possible to regularly determine the concentration of the drug in plasma,
- Acute allergy or astma,
- Diseases of liver and kidney,
- Hematopoietic disorders (history),
- Porphyria (increased levels of porphyrin in the blood),
- Deficiency of glucose-6-phosphate dehydrogenase,
- Metabolic disorders (phenylketonuria),
- Concomitant use of the following drugs: diuretics, pyrimethamine, cyclosporine, blood thinners, in particular warfarin, phenytoin, antidiabetic drugs, rifampicim, procainamide, amantadine, digoxin, zidovudine, lamivudine, potassium-regulating drugs or cytostatics, in particular methotrexate.

Side effect:

At recommended doses, Sulfaprim is generally well tolerated. The most common side effects are skin rash and gastrointestinal diseases.

The following classification is used to describe the frequency of adverse reactions:

Very common (≥10%), common (≥1% and <10%), nor common (≥0.1% and <1%), rarely (≥0.01% and <0.1%), very rarely (<0.01%), frequency unknown (cannot be calculated from available data).

Infectious and infestations: uncommon - Fungal infections such as candidosis

Immune system disorders: very rare - Hypersensitivity reactions, allergic reactions (fever, angioedema, anaphylactoid reactions, serum sickness).

Metabolism and nutrition disorders: rare – hypoglycemia.

Psychiatric disorders: rare – hallucinations.

From the organs of GIT: common - nausea, vomiting, not common - diarrhea, pseudomembranous enterocolitis, rarely - stomatitis, glossitis, the frequency is unknown - acute pancreatitis.

Blood and lymphatic system disorders:

rare - leukopenia, neutropenia, granulocytopenia and thrombocytopenia (most often mild or asymptomatic and disappear after discontinuation of the drug); very rare - agranulocytosis, anemia (megaloblastic, hemolytic / autoimmune or aplastic), methemoglobinemia, pancytopenia or purpura.

Renal and urinary disorders: rare - impaired renal function, interstitial nephritis, increased blood urea nitrogen, serum creatinine, crystalluria.

Hepatobiliary disorders: common - an increase in the activity of "liver" transaminases, uncommon - hepatitis, an increase in the concentration of bilirubin, rare - cholestasis, very rare - liver necrosis, "disappearing bile duct" syndrome - the frequency is unknown.

Hepatobiliary disorders: uncommon - convulsions, rare - neuropathy (including peripheral neuritis and paresthesias), very rare - ataxia, aseptic meningitis / meningeal symptoms, the frequency is unknown - cerebral vasculitis.

Eye disorders: very rare - uveitis, the frequency is unknown - retinal vasculitis.

Ear and labyrinth disorders: very rare - systemic and non-systemic dizziness.

Vascular disorders: very rare - allergic myocarditis, purpura, Henoch Shenlein purpura, the frequency is unknown - vasculitis, necrotizing vasculitis, granulomatosis with polyangiitis, periarteritis nodosa.

Respiratory, thoracic and mediastinal disorders: very rare - pulmonary infiltrates, the frequency is unknown - pulmonary vasculitis.

Musculoskeletal and connective tissue disorders: very rare - rhabdomyolysis, arthralgia, myalgia - the frequency is unknown.

Laboratory changes of parameters: Hyperkalemia, hyponatremia - frequency unknown.

General disorders and disorders at the injection site: rare - venous pain and phlebitis.

Allergic reactions: urticaria, rash, toxic epidermal necrolysis (Lyell's syndrome), Stevens-Johnson syndrome, allergic myocarditis, multiform erythema, exfoliative dermatitis, Quincke's edema, itching, redness of the sclera, fever.

Other: hyperkalemia, hyponatremia, aseptic meningitis, peripheral neuritis, arthralgia, myalgia, weakness, photosensitivity.

Description of individual adverse events:

Blood disorders are most often mild, asymptomatic and disappear after discontinuation of the drug. Allergic reactions may occur in patients with hypersensitivity to the components of the drug.

Disturbances from the skin and subcutaneous tissues are usually mild and quickly disappear after discontinuation of the drug.

Respiratory, Thoracic, and Mediastinal Disorders: Pulmonary infiltrates associated with eosinophilic or allergic alveolitis may present with symptoms such as cough and dyspnoea.

Metabolic and nutritional disorders: The use of high doses of trimethoprim for the treatment of pneumonia caused by Pneumocystis jirovecii may lead to a progressive but reversible increase in serum potassium concentration. Even at the recommended doses, trimethoprim may contribute to the development of hyperkalemia in patients with impaired potassium metabolism, renal insufficiency, or while taking drugs that contribute to the development of hyperkalemia. Cases of hypoglycemia have been observed in patients without a diagnosis of diabetes mellitus receiving trimethoprim-sulfamethoxazole, usually several days after the start of treatment. The risk of hypoglycemia is higher in patients with impaired renal function, liver disease, malnutrition, or those receiving high doses of trimethoprim-sulfamethoxazole.

Gastrointestinal Disorders: Cases of acute pancreatitis have been described during treatment with Sulfaprim. Adverse reactions in HIV-infected patients In the group of HIV-infected patients, adverse events are comparable to those in the general patient population, however, some adverse events may occur more frequently and differ in clinical presentation.

Blood and lymphatic system disorders: very common - leukopenia, granulocytopenia, thrombocytopenia.

Metabolism and nutrition disorders: rare – hypoglycemia.

Gastrointestinal disorders: very common - anorexia, nausea, vomiting, diarrhea.

Hepatobiliary disorders: very often - an increase in "liver" transaminases.

Skin and subcutaneous tissue disorders: very common - maculopapular rash, itching.

General disorders and administration site conditions: very common - fever (usually in combination with a maculopapular rash).

Investigations: very common - hyperkalaemia, uncommon - hyponatraemia.

Warnings and Precautions:

At the first appearance of a skin rash or any other severe adverse reaction, the drug should be discontinued. In patients with a tendency to allergic reactions and with bronchial asthma, Sulfaprim should be administered with caution.

Pregnancy and period of breastfeeding:

Since both trimethoprim and sulfamethoxazole pass the placental barrier, during pregnancy the drug should be prescribed only if the expected benefit from its use outweighs the possible risk to the fetus. In late pregnancy, the use of Sulfaprim should be avoided due to the possible risk of kernicterus in newborns.

Both trimethoprim and sulfamethoxazole pass into breast milk. If necessary, the appointment of the drug during lactation should decide on the termination of breastfeeding.

Shelf life:

3 years. You should not take the drug after their expiry date.

Storage conditions:

Store below 25° C. In a place protected from light.

Packaging:

100 ml glass bottle with dosage cup and Patient Information Leaflet completed in a Paperboard box.

Regulatory status:

Prescription only.