Bactrim

Trade mark

ROCHE

Dual-action chemotherapeutic agent with bactericidal properties

Composition. Active ingredients: trimethoprim (TM)and sulfamethoxazole (SMZ).

Form	TM	SMZ
1 tablet	80 mg	400 mg
1 forte tablet	160 mg	800 mg
1 measure (5 ml) pediatric syrup	40 mg	200 mg
1 measure (5 ml) adult syrup	80 mg	400 mg

Excipients. Forte tablets : macrogol in the coating. Pediatric syrup: preservatives (methylparaben, E218; propylparaben, E216); flavourings; sweetener (sorbitol). Adult syrup: preservatives (methylparaben, E218; propylparaben, E216); flavourings; sweeteners (sorbitol, saccharin sodium).

Properties, effects: "Bactrim" contains two active ingredients acting synergistically by blockade of two enzymes that catalyse successive stages in the biosynthesis of folinic acid in the microorganism. This mechanism usually results in bactericidal activity in vitro at concentrations at which the individual substances are only bacteriostatic. In addition, "Bactrim" is often effective against organisms that are resistant to one of the two components. Furthermore, the risk of development of widespread resistance is minimized.

The antibacterial effect of "Bactrim" in vitro covers a wide range of gram-positive and gram-negative pathogenic organisms:

Generally sensitive organisms (> 75% sensitive strains):

Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, Enterobacter spp., Acinetobacter spp., Salmonella typhi, nontyphi salmonellae, Shigella spp., Vibrio cholerae, Yersinia enterocolitica, Brucella spp., Aeromonas hydrophilia, Yersinia pestis, Haemophilus influenzae, Neisseria meningitidis, N. gonorrhea, Streptococcus pneumoniae, Str. pyogenes, Str. agalactiae, Str. viridans, staphylococcus aureus, St. epidermidis, Listeria monocytogenes, Chlamydia trachomatis, Nocardia spp., Pneumocystis carinii.

Partially sensitive organisms:

Indole-positive Proteus spp., Serratia marcescens, Pseudomonas spp. (non-aeruginosa), Providencia spp., Campylobacter fetus. Achromobacter spp., bacteroides spp., Str. faecalis, Toxoplasma gondii, Plasmodium spp., Mycobacterium marinum, Legionella spp.

As a rule, Mycoplasma spp., Mycobacterium tuberculosis, Pseudomonas aeruginosa and Treponema pallidum are resistant.

In the case of infections caused by partially sensitive pathogens a sensitivity test is recommended to exclude any resistance.

Sensitivityto "Bactrim" can be determined by standardized methods such as the disk or dilution tests recommended by the National Committee for Clinical Laboratory Standards (NCCLS). The following criteria for susceptibility are recommended by the NCCLS:

	Disktest*, diameter of inhibition zone (mm)	Dilution test**, MIC (µg/ml)	
		TM	SMZ
Sensitive	≥ 16	≤ 2	≤ 38
Partially sensitive	11 – 15	4	76
Resistant	≤ 10	≥ 8	≥ 152

* Disk: 1.25 µg TM and 23.75 µg TMZ. ** TM and SMZ in a ratio of 1 to 20.

Pharmacokinetics: The pharmacokinetic properties of TM and SMZ are very similar. Following a single dose of 160 mg TM+800 mg SMZ, the peak plasma concentrations are 1.5–3 µg/ml for TM and 40–80 µg/ml for SMZ. If administration is repeated every twelve hours the concentration stabilizes at this level, and there is thus no danger of accumulation. The volume of distribution of TM is 69–133 litres and that of SMZ 10–16 litres.

The half-lives of the two components are very similar (a mean of ten hours for TM and of eleven hours for SMZ).

At the above concentrations, 42–46% of TM and 66% of SMZ is bound to plasma proteins.

Studies in both animals and man have shown that diffusion of "Bactrim" into the tissue is good. Large amounts of TM and smaller amounts of SMZ pass from the bloodstream into the interstitial fluid and other extravascular body fluids. With the combination present in "Bactrim", however, the concentrations of TM and SMZ are higher than the minimum inhibitory concentrations for most pathogenic organisms.

Both substances, as well as their metabolites, are eliminated almost entirely by the kidneys, approximately 50% of the TM dose and 20% of the SMZ dose being excreted unchanged. The metabolites of SMZ are antibacterially inactive, while some of the metabolites of TM are active.

Indications: Upper and lower respiratory tract infections: Acute and chronic bronchitis, bronchiectasis, pneumonia (including Pneumocystis carinii pneumonia); pharyngitis, tonsillitis (in infections due to group A ß-hemolytic streptococci, the rate of eradication is not fully satisfactory), sinusitis, otitis media.

Renal and urinary tract infections: Acute and chronic cystitis, pyelonephritis, urethritis, prostatitis.

Genital infections in both sexes, including gonococcal urethritis,

Gastrointestinal tract infection, including typhoid and paratyphoid fever, and the treatment of persistent carriers; bacillary dysentery; cholera (as an adjunct to fluid and electrolyte replacement).

Skin and soft tissue infections: Pyoderma, furuncles, abscesses and infected wounds.

Other bacterial infections: Acute and chronic osteomyelitis, acute brucellosis, septicemia due to sensitive organisms. Nocardiosis, mycetoma (except when caused by the true fungi), South American blastomycosis.

Dosage: For adults and children over twelve years.

	Tablets, measures of adult syrup		Forte tablets	
	morning	evening	morning	evening
Standard dosage	2	2	1	1
Minimum dosage and dosage for long-term therapy (longerthan 14 days)	1	1	1/2	1/2
High dosage (for particularly severe cases)	3	3	1 1/2	1 1/2

"Bactrim" is best taken after meals with an adequate amount of fluid.

Special Dosage instructions:

a. Dosage for gonorrhea
5 tablets or measures of adult syrup both in the morning and in the evering, or 21/2 forte tablets twice on one day.

b. Dosage for acute uncomplicated urinary tract infections.
For women with acute uncomplicated infections of the urinary tract, a single dose of 3 forte tablets is recommended. The tablets should, if possible, be taken in the evening after a meal or before retiring.

c. The recommended dosage for patients with Pneumocystis carinii pneumonia is up to 20 mg TM per kg and up to 100 mg SMZ per kg in 24 hours, given in equal divided doses every six hours for 14 days.

d. Dosage for children.

	Measures of pediatric syrup	
	morning	evening
6 weeks to 5 months	1/2	1/2
6 months to 5 years	1	1
6 years to 12 years	2	2

The above schedules for children are approximately equivalent to a daily dose of 6 mg TM and 30 mg SMZ per kg bodyweight. For severe infections the dosage shown for children may be increased by 50%.

e. Dosage for patients with impaired renal function.

Creatinine clearance	Recommended dosage schedules
> 30 ml/min	Standard dosage
15 – 30 ml/min	Half the standard dosage
< 15 ml/min	Use of "Bactrim" not recommended

Restrictions on use: "Bactrim" is contraindicated in patients with marked liver parenchymal damage. It is also contraindicated in patients with severe renal insufficiency when repeated determinations of the plasma concentration cannot be made.

There is an increased risk of severe adverse reactions in elderly patients or when complicating conditions exist, e.g. impaired kidney and/or liver function, or concomitant use of other drugs (in which case the risk may be related to the dosage and duration of treatment). Fatal outcome, though rare, has been reported in connection with adverse reactions such as blood dyscrasias, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome) and fulminant liver necrosis.

In order to minimize the risk of undesirable reactions, the duration of treatment with "Bactrim" should be as short as possible, particularly in elderly patients. In the event of renal impairment, dosage should be adjusted according to the Special dosage instructions.

If "Bactrim" is given over a prolonged period, regular blood counts are required. If a significant reduction in the count of any formed blood element is noted, "Bactrim" should be discontinued.

Other than in exceptional cases "Bactrim" should not be given to patients with serious hematological disorders. The combination has occasionally been administered to patients receiving cytotoxic agents for the treatment of leukemia, without evidence of any adverse effect on the bone marrow or peripheral blood.

Owing to the possibility of hemolysis, "Bactrim" should not be given to patients with a G6PD deficiency unless absolutely essential, and then only in minimal doses.

Treatment should be discontinued immediately at the first appearance of skin rash or any other serious adverse reaction.

"Bactrim" should not be administered to patients with a history of hypersensitivity to sulfonamides or trimethoprim. For safety reasons, "Bactrim" is contraindicated during pregnancy. If pregnancy cannot be excluded, possible risks should be weighed against the expected therapeutic effect.

"Bactrim" must not be given to premature and newborn infants during the first few weeks of life.

Although TM and SMZ pass into the breast milk, the use of "Bactrim" by nursing mothers is virtually without risk for the infant.

In elderly patients, or in patients with preexisting folic acid deficiency or kidney failure, hematological changes indicative of folic acid deficiency may occur. These are reversible by folinic acid therapy.

Patients undergoing long-term treatment with "Bactrim" (in particular, patients with kidney failure) should be examined regularly for urine values and kidney function.

An adequate fluid intake should be ensured during treatment.

Undesirable effects: At the recommended dosage. "Bactrim" is usually well tolerated. Side effects, if any, are usually mild.

The following effects have been reported (in order of frequency): gastrointestinal side effects: nausea (with or without vomiting), stomatitis, diarrhea, rare cases of hepatitis, and isolated cases of pseudomembranous enterocolitis. Drug-induced skin rashes: These are generally mild and quickly reversible after withdrawal of medication. Like many other drugs, "Bactrim" has in rare cases been linked to erythema multiforme. Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome).

Most of the hematological changes observed were mild and asymptomatic; they proved to be reversible on withdrawal of the therapy. The changes most commonly seen were leukopenia, neutropenia and thrombocytopenia. Very rarely, agranulocytosis, megaloblastic anemia, pancytopenia or purpura may occur.

As with any other drug, allergic reactions may occur in patients who are hypersensitive to the substance.

Pulmonary infiltrates such as occur in eosinophilic or allergic alveolitis have been reported in rare instances. They may manifest themselves through symptoms such as cough or shortness of breath. Should such symptoms appear unexpectedly or worsen, the patient should be reevaluated and discontinuation of "Bactrim" therapy considered.

Rare cases of aseptic meningitis or meningitis-like symptoms have been described.

Interactions: An increased incidence of thrombocytopenia with purpura has been observed in elderly patients concurrently receiving certain diuretics, primarily thiazides.

It has been reported that "Bactrim" may prolong the prothrombin time in patients receiving the anticoagulant warfarin. This interaction should be borne in mind when "Bactrim" is given to patients already on anticoagulant therapy. In such cases, the coagulation time should be determined anew.

"Bactrim" may inhibit the hepatic metabolism of phenytoin. A 39% increase in phenytoin half-life and a 27% decrease in the metabolic clearance rate of phenytoin have been observed following administration of "Bactrim" at normal clinical dosages. If the two drugs are given concurrently, it is important to watch for an excessive phenytoin effect.

Sulfonamides can also displace methotrexate from plasma protein binding sites, thus increasing free methotrexate concentrations.

"Bactrim" may also affect the required dose of hypoglycemic drugs.

Occasional reports suggest that patients receiving pyrimethamine as malaria prophylaxis in doses exceeding 25 mg weekly may develop megaloblastic anemia if "Bactrim" is prescribed concurrently.

Reversible deterioration of renal function has been observed in patients treated with TM-SMZ and cyclosporin following renal transplantation.

Interference with laboratory tests: "Bactrim", specifically the TM component, can interfere with a serum methotrexate assay using the competitive protein-binding technique when bacterial dihydrofolate reductase is used as the binding protein. No interference occurs, however, if methotrexate is measured by radioimmunoassay.

The presence of TM and SMZ may also interfere with the Jaffé alkaline picrate reaction assay for creatinine, causing values in the normal range to be increased by about 10%.

Stability: This medicine should be used before the date shown after EXP on the pack.

Packs :

Tablets (scored)	20, 100
Forte tablet (scored)	10, 20, 50
Pediatric syrup	50, 100 ml
Adult syrup	100 ml

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacists who sold the medicament.
- The doctor and the pharmacists are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed foryou.
- Do not repeat the same prescription without consulting your doctor.

Keep medicaments out of the reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists