Co-trimoxazole 480 mg 960mg , tablets

Qualitative And Quantitative Composition
Co-trimoxazole CF 480 mg, tablets: Each tablet contains 80 mg of trimethoprim and 400 mg of sulfamethoxazole (= 480 mg of co-trimoxazole).Excipients with known effect: Each tablet contains 40 mg of lactose.

Co-trimoxazole forte CF 960 mg, tablets: Each tablet contains 160 mg of trimethoprim and 800 mg of sulfamethoxazole (= 960 mg of co-trimoxazole). Excipients with known effect: Each tablet contains 20 mg of lactose.

Therapeutic indications
Co-trimoxazole CF is indicated for the prevention and treatment of the infections listed below in adults and children aged 6 years and older. Co-trimoxazole is used to treat infections caused by microorganisms sensitive to co-trimoxazole. Co-trimoxazole should only be used when the use of a single antibacterial agent is undesirable or inadequate. To exclude resistance, especially if infections are (likely) caused by partially susceptible organisms, the isolate should be tested for susceptibility to co-trimoxazole.

Respiratory tract infections
Treatment of otitis media, acute exacerbations of chronic bronchitis, treatment and prevention of Pneumocystis jiroveci pneumonia (PJP).

Urinary tract infections: Treatment of acute uncomplicated urinary tract infections.

Other bacterial infections caused by susceptible microorganisms

Co-trimoxazole can be used in combination with other antimicrobial agents for acute brucellosis (see also: Special dosage instructions). Official guidelines on the appropriate use of antibacterial agents should be taken into account.

Dosage and administration

Dosage: Adults and children over 12 years

The oral standard dose for adults and children over 12 years is 2 tablets of Co-trimoxazole CF 480 mg or 1 tablet of Co-trimoxazole forte CF 960 mg every 12 hours. In case of severe infections, one and a half times this dose can be given. To reduce possible gastrointestinal complaints, take preferably after a meal.

Pediatric patients: Dosage per body weight: The oral standard dose for children under 12 years of age is approximately 6 mg of trimethoprim plus 30 mg of sulfamethoxazole per kg of body weight per day, divided into two doses.

Dosage per age category: The oral standard dosage for children under 12 years of age according to age is given in the table below.

Dosage for children based on age

- Age Dosage every 12 hours
- From 6 weeks to 6 months 120 mg
- From 6 months to 6 years 240 mg
- From 6 years to 12 years 480 mg

In case of severe infections, one and a half times this dose can be given. To reduce possible gastrointestinal complaints, take preferably after a meal.

Co-trimoxazole CF tablets are not suitable for use in children under 6 years of age.

Elderly patients: No dose adjustment is necessary for normal liver and kidney function. For reduced kidney function, see "Dosage in patients with reduced kidney function".

Duration of treatment: In general, the standard dose should be reduced by half after 14 days of treatment. See also "Special dosage instructions".

For acute infections, co-trimoxazole should be administered for up to 2 days after symptoms disappear, but for a minimum of 5 consecutive days.

Special dosage instructions

Patients with impaired liver and/or kidney function
In patients with liver and/or kidney dysfunction, the dosage should be reduced or the dosing interval should be adjusted as shown in the table below .

Patients with impaired kidney function

More than 30 ml/min - Standard dosage

15-30 ml/min - One standard dose every 12 hours for 3 days, followed by one standard dose every 24 hours for as long as allowed by control analyses.

Less than 15 ml/min - The use of co-trimoxazole is contraindicated

There is insufficient data on the administration of co-trimoxazole to children with impaired kidney function.

It is recommended to measure the plasma concentration of sulfamethoxazole every 2 to 3 days, 12 hours after administration. If it exceeds 150 micrograms per ml, the treatment should be interrupted until the plasma concentration drops below 120 micrograms per ml.

Pneumocystis jiroveci pneumonia (PJP)

Treatment
For the treatment of PJP, administer 90-120 mg co-trimoxazole per kg body weight per day, divided into 3-4 doses for 14 days. Parenteral administration is preferred.

Prophylaxis in adults and children aged 12 years and older
The recommended dose is 960 mg co-trimoxazole once daily on every day of the week.

If this dose is not well tolerated, one of the following dosing schedules may be used:

• 480 mg co-trimoxazole once daily on every day of the week
• 960 mg co-trimoxazole per day divided into two doses, given every other day, on 3 days per week

Prophylaxis in children under 12 years of age

The recommended dose is 18 mg co-trimoxazole per kg body weight once daily, which may be divided into two doses, on every day of the week. Alternative dosing schedules are:

• 2 x 18 mg/kg/day, divided into two doses, on 3 consecutive days per week
• 2 x 18 mg/kg/day, divided into two doses, given every other day, on 3 days per week

The total daily dose should not exceed 1920 mg co-trimoxazole.

Acute brucellosis
Co-trimoxazole should only be given in combination with other antimicrobial agents (doxycycline, gentamicin, rifampicin).

Adults
The recommended dose is 160 mg trimethoprim and 800 mg sulfamethoxazole (= 960 mg co-trimoxazole) twice daily for 6 weeks. For complicated infections such as osteomyelitis, meningoencephalitis, and endocarditis, a treatment duration of 3 months is recommended.

Pediatric patients
The recommended dosage is twice daily approximately 5 mg/kg trimethoprim and 25 mg/kg sulfamethoxazole (= 30 mg/kg co-trimoxazole) for 6 weeks. For complicated infections such as osteomyelitis, meningoencephalitis, and endocarditis, a treatment duration of 3 months is recommended.

Contraindications
Co-trimoxazole CF should not be administered in the following cases:

• hypersensitivity to the active substances (sulfonamides, trimethoprim or co-trimoxazole, • in patients with severe renal impairment and oliguria (creatinine clearance ≤ 15 ml/min, • severe damage to the hepatic parenchyma • hematological abnormalities (particularly anemia, thrombocytopenia, and agranulocytosis) unless under close monitoring, • in the first six weeks of life,• in concomitant use with dofetilide

Special warnings and precautions for use
There is an increased risk of serious adverse reactions in elderly patients or when complicating factors are present, such as reduced renal and/or hepatic function, or when other medications are used concomitantly (in which case there may be a relationship with the dosage and duration of treatment).

There have been some cases of fatal outcomes reported in relation to serious adverse reactions such as blood dyscrasias, extensive exudative erythema multiforme (Stevens-Johnson syndrome), toxic epidermal necrolysis (Lyell's syndrome), DRESS (drug reaction with eosinophilia and systemic symptoms), and fulminant hepatic necrosis.

Concretion formation
Concretion formation in the kidneys and urinary tract due to aggregation of N-acetylsulfamethoxazole crystals has been described, particularly in patients with hypoalbuminemia due to intestinal and renal disorders associated with high protein loss and malnutrition. Urine analysis and kidney function tests should be regularly performed in patients undergoing long-term co-trimoxazole treatment (particularly in patients with renal failure). To prevent concretion formation during treatment, adequate fluid intake and urine production should be ensured.

AIDS patients
Although co-trimoxazole is contraindicated in severe hematological abnormalities, it may be necessary to administer co-trimoxazole in certain cases, such as in AIDS patients. In these cases, regular blood monitoring is advisable.

Drug-induced thrombocytopenia

In patients with a history of drug-induced thrombocytopenia with diuretics or other sulfonamides, alternative treatment other than co-trimoxazole should be considered if possible. If this is not possible, the number of platelets should be regularly monitored.

Long-term treatment
If treatment with co-trimoxazole lasts longer than 14 days, regular blood monitoring is recommended. Progressive changes in blood counts are a reason to stop treatment with co-trimoxazole.

Respiratory toxicity: Severe cases of respiratory toxicity have been reported very rarely, which sometimes worsened during treatment with co-trimoxazole and progressed to acute respiratory distress syndrome (ARDS). The onset of pulmonary symptoms such as cough, fever, and dyspnea, combined with radiological signs of lung infiltrates and deterioration of lung function, may be indicative of ARDS. In such circumstances, treatment with co-trimoxazole should be discontinued and appropriate treatment administered.

Hemophagocytic lymphohistiocytosis (HLH): Very rare cases of HLH have been reported in patients treated with co-trimoxazole. HLH is a life-threatening syndrome of pathological immune activation characterized by clinical signs and symptoms of excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridemia, hypofibrinogenemia, high serum ferritin, cytopenia, and hemophagocytosis). Patients who develop early manifestations of pathological immune activation should be evaluated immediately. If the diagnosis of HLH is confirmed, treatment with co-trimoxazole should be stopped.

Pharyngitis:C o-trimoxazole should not be used to treat pharyngitis caused by group A beta-hemolytic streptococci because they are eliminated less quickly than with some other antibacterial agents.

Exanthem: Treatment with co-trimoxazole should be discontinued in case of exanthem.

Folic acid deficiency: Patients who are at risk of or have manifest folic acid deficiency, especially older patients or patients with renal insufficiency, should receive folic acid supplementation. These disorders are reversible after administration of folinic acid.

Liver and/or kidney dysfunction: In patients with liver and/or kidney dysfunction, the dosage should be reduced or the dosing interval adjusted to prevent any potential accumulation of co-trimoxazole. In patients who are treated with co-trimoxazole for a long period, regular urine analysis and kidney function tests should be performed, especially in patients with reduced kidney function. To reduce the risk of crystalluria during treatment with co-trimoxazole, a generous diuresis of at least 1200 ml per 24 hours is recommended.

Microbial infections: Superinfections with non-sensitive microorganisms may occur.

Hypersensitivity to oral hypoglycemic agents: Caution is advised when administering co-trimoxazole to patients with a known hypersensitivity to oral hypoglycemic agents of the sulfonylurea type or to aminobenzoic acid derivatives.

Acute porphyria: Administration of co-trimoxazole to patients with a known or suspected risk of acute porphyria should be avoided. Trimethoprim and sulfonamides - although not specifically sulfamethoxazole - have been associated with clinical exacerbation of porphyria.

Thyroid dysfunction: Caution should be exercised in patients with thyroid dysfunction because co-trimoxazole may decrease thyroid hormone serum concentrations.

Phenylalanine metabolism: It is known that trimethoprim can reduce the metabolism of phenylalanine. However, this is not clinically important in phenylketonuria patients who are on an adequate diet.

Glucose-6-phosphate dehydrogenase deficiency: As the sulfonamide component of co-trimoxazole can cause hemolysis, co-trimoxazole should not be given to patients with glucose-6-phosphate dehydrogenase deficiency, unless strictly indicated and in the minimum required dose.

Hyperkalemia: High doses of trimethoprim, as used in the treatment of Pneumocystis jiroveci pneumonia (PJP), can lead to a progressive but reversible increase in serum potassium levels. Lower doses of trimethoprim can also cause severe hyperkalemia in patients with underlying abnormalities in potassium metabolism, renal dysfunction, or simultaneous use of agents that can cause hyperkalemia, such as spironolactone (see also section 4.5). Accurate monitoring of serum potassium levels is necessary in these patients. When hyperkalemia occurs, medication should be discontinued.

Hypoglycemia: Hypoglycemia may occur in some patients, often after several days. This should be taken into account especially in patients with impaired renal function, liver disease, poor nutritional status, or high doses. When hypoglycemia occurs, medication should be discontinued and appropriate corrective measures should be taken. It should be noted that hypoglycemia can persist for a longer period of time.

Pancytopenia: Cases of pancytopenia have been reported in patients receiving trimethoprim together with methotrexate (see section 4.5).

Excipients: Co-trimoxazole contains lactose as an excipient. Patients with rare hereditary conditions such as galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption should not use this medication.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, i.e. essentially 'sodium-free'.

Fertility, Pregnancy, and Breastfeeding

Pregnancy: So far, there is no evidence of an increased risk of congenital abnormalities when using co-trimoxazole in clinical doses during pregnancy in humans. However, when using sulfonamides before delivery, there is a risk of hyperbilirubinemia in the newborn because sulfonamides displace bilirubin from binding sites on albumin in the blood. In animal studies, co-trimoxazole has been shown to be harmful at high doses due to antagonism of folate synthesis.

When using Co-trimoxazole CF during the first trimester of pregnancy, folic acid supplementation should be given, otherwise, in doses customary for all pregnant women. Caution should be exercised when using co-trimoxazole during the second and third trimesters of pregnancy.

Breastfeeding: Co-trimoxazole is excreted in small amounts in breast milk. In premature neonates and children with glucose-6-phosphate dehydrogenase deficiency, there may be an increased risk of hyperbilirubinemia. In all other cases, breastfeeding can be given during treatment with Co-trimoxazole CF.

Fertility: Combinations of sulfonamides and trimethoprim caused a decrease in the amount of sperm in men after one month of treatment. There are no data on possible effects on fertility in women.

Effects on ability to drive and use machines: There is no information available on the effect of this medicine on driving ability. When driving vehicles and operating machinery, one should consider the possibility of occasional dizziness.

Overdose
Acute overdose is characterized by nausea, vomiting, diarrhea, headache, dizziness, confusion, and visual disturbances. In severe cases, crystalluria, hematuria, and anuria may occur. Bone marrow depression has been reported after acute overdose of trimethoprim.

Chronic overdose can lead to bone marrow depression, manifested by thrombocytopenia or leukopenia and other blood dyscrasias due to folate deficiency.

Depending on the symptoms, the treatment of overdose is as follows: discontinue administration, induce vomiting if desired, and perform gastric lavage depending on the symptoms. The latter may be useful, although absorption is normally rapid (within 2 hours) and complete. This may not be the case with gross overdose.

As general supportive measures, stimulation of renal excretion by forced diuresis (alkalinization of the urine increases the elimination of sulfamethoxazole but decreases the elimination of trimethoprim) and hemodialysis, in which both trimethoprim and active sulfamethoxazole are removed from the body, should be used. It is important to know that peritoneal dialysis is not effective.

In addition, monitoring of the blood count and electrolytes is necessary. If a clear blood dyscrasia or jaundice occurs, specific treatment for these complications is required.

If there is an effect of trimethoprim on the bone marrow, calcium folinate in a dose of 5-10 mg i.m. for 5 to 7 days will counteract the effect of trimethoprim on hematopoiesis.

Special precautions for storage:

- Blister packaging: Store below 25°C in the original packaging.
- Tablet container: Store below 25°C in the tightly closed packaging.