Inactive ingredients: Docusate sodium 85%, sodium benzoate 15%, sodium stearate glycylglycine, magnesium stearate and pregelatinized starch.

**CLINICAL PHARMACOLOGY**

BACTRIM is rapidly absorbed following oral administration. Both sulfamethoxazole and trimethoprim exist in the blood as unbound, protein-bound and metabolized forms; sulfamethoxazole also exists as the conjugated form.

Sulfamethoxazole is rapidly absorbed following oral administration. It has a peak plasma level of 1.5 to 2.0 µg/mL in 1 hour, 1.5 to 2.0 µg/mL in 3 hours and 1.0 to 1.5 µg/mL in 6 hours. Approximately 70% of the dose is eliminated in the urine as sulfamethoxazole and 44% of trimethoprim is found in the plasma protein fraction.

**Pharmacokinetics**

BACTRIM is rapidly absorbed following oral administration. The maximum blood level of sulfamethoxazole is 1.5 to 2.0 µg/mL in 1 hour, 1.5 to 2.0 µg/mL in 3 hours and 1.0 to 1.5 µg/mL in 6 hours. Approximately 70% of the dose is eliminated in the urine as sulfamethoxazole and 44% of trimethoprim is found in the plasma protein fraction.

**Microbiology**

Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid (PABA).

**Renal Function**

Approximately 70% of sulfamethoxazole and 44% of trimethoprim are bound to plasma proteins. The presence of 10 mg percent sulfamethoxazole in plasma decreases the protein binding of trimethoprim by an insignificant degree; trimethoprim does not influence the protein binding of sulfamethoxazole.

**Hepatic Function**

The effects of sulfamethoxazole and trimethoprim on the liver are minimal. Both drugs are metabolized by the liver, primarily by glucuronidation and sulfation to inactive compounds.

**Dilution Techniques:**

Dilution Techniques:

Dilution techniques provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure 5 requires the use of standardized dilution methods that develop a range of values for zones or minimum inhibitory concentrations.

**MIC (µg/mL) Interpretation**

<table>
<thead>
<tr>
<th>Zone Diameter (mm)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥12</td>
<td>Susceptible (S)</td>
</tr>
<tr>
<td>10 - 12</td>
<td>Intermediate (I)</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Resistant (R)</td>
</tr>
</tbody>
</table>

**Zone Diameter Ranges (mm)**

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Zone Diameter Ranges (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>20 - 22</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
<td>15 - 18</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>10 - 12</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>10 - 12</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>10 - 12</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>10 - 12</td>
</tr>
</tbody>
</table>

**Indications and Usage**

**INDICATIONS**

BACTRIM is contraindicated in patients with known hypersensitivity to trimethoprim or sulfonamides and in patients with impaired renal function. It should not be used to treat methicillin-resistant Staphylococcus aureus (MRSAs) or drug-resistant strains of Haemophilus influenzae, Neisseria meningitidis, or Neisseria gonorrhoeae.

**WARNINGS**

There is a potential for neonatal hyperbilirubinemia and other blood dyscrasias.

Sulfonamide-induced hematologic abnormalities have been reported in patients treated with sulfamethoxazole and trimethoprim. The most common adverse reactions are leukopenia, thrombocytopenia, and eosinophilia. These reactions are dose-related, and patients who receive high doses of sulfamethoxazole and trimethoprim are at increased risk of developing hematologic complications.

**Pseudomembranous colitis**

Pseudomembranous colitis has been reported with BACTRIM therapy and is characterized by the sudden onset of profuse watery diarrhea, abdominal cramps, and fever. The possibility of pseudomembranous colitis should be considered in any patient who develops an unexplained moderate-to-severe diarrhea following the use of this or any other antibiotic. Pseudomembranous colitis usually responds to discontinuation of the drug and supportive therapy and does not usually require specific antibiotic treatment. If the diagnosis is suspected, appropriate diagnostic steps should be taken to exclude other causes of diarrhea. Treatment with metronidazole or vancomycin may be effective.

**PRECAUTIONS**

BACTRIM should not be used in patients with impaired renal or hepatic function, to those with folate-deficiency anemia, or in those who are known to be sensitive to sulfonamides. BACTRIM should not be used in patients with a history of porphyria or chronic alcoholism.

**Pneumocystis carinii pneumonia**

Sulfonamides are active against Pneumocystis carinii. The optimal dosage of BACTRIM for the treatment of Pneumocystis carinii pneumonia is not established. Treatment should be initiated with a dose of 160 mg/day of sulfamethoxazole and 80 mg/day of trimethoprim. Treatment should be continued for at least 2 weeks after the patient's clinical condition improves and the patient is afebrile. The patient should be monitored for clinical response and laboratory evidence of improvement. The optimal duration of therapy is not established. Pneumocystis carinii pneumonia is usually treated for at least 2 months. BACTRIM therapy should be continued for at least 2 months after the clinical condition improves. In cases of Pneumocystis carinii pneumonia, BACTRIM therapy should be continued for at least 2 months after the patient's clinical condition improves and the patient is afebrile. The patient should be monitored for clinical response and laboratory evidence of improvement.

**Cautions and contraindications**

BACTRIM should not be used in patients with a history of porphyria or chronic alcoholism.

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Contrary to common belief, the use of BACTRIM in children, particularly those whose mothers received sulfamethoxazole and trimethoprim at the time of conception or shortly thereafter, is not associated with teratogenic effects manifested mainly as cleft palates. In a separate survey, Brumfitt and Pursell also found no congenital abnormalities in 35 children born to women who had received sulfamethoxazole and amantadine during the first trimester.

Drug/Laboratory Test Interactions: BACTRIM, specifically the trimethoprim component, can interfere with a serum methotrexate assay as determined by the competitive binding protein technique (CBPT) when a bactidihydrofolate reductase inhibitors are used concomitantly. Similarly, BACTRIM has also been shown to interfere with the phenytoin assay by a radioimmunoassay (RIA). The presence of sulfamethoxazole and trimethoprim may also interfere with the Jaffe alkaline picrate reaction assay for creatinine, resulting in overestimations of about 10% in the range of normal values.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis: Long-term studies in animals to evaluate carcinogenic potential have not been conducted with BACTRIM. Mutagenesis: Bacterial mutagenic studies have not been performed with sulfamethoxazole and trimethoprim in combination. Trimethoprim was demonstrated to be mutagenic in the Ames assay. No chromosomal damage was observed in vivo in rats with sulfamethoxazole and trimethoprim alone or in combination. The offspring of rats exposed to trimethoprim concentrations used exceeded blood levels of these compounds following therapy with sulfamethoxazole and trimethoprim. Accordingly, no evidence of carcinogenic potential of BACTRIM was obtained from animal experiments.
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/s/

Janice Soreth
10/17/02 04:30:19 PM