Swidar®

Sulfadoxine+Pyrimethamine

swipha

Composition

Each Tablet contains:
Sulfadoxine Int. Ph.:.....500mg
Pyrimethamine Int. Ph.:.....25mg

Description
White to off white, round bevelled tablet debossed with "SWIDAR swipha" above and Cross Break-mark below.

Clinical Pharmacology
Sulfadoxine and Pyrimethamine which are the constituents of **Swidar®** are folic acid antagonists. Sulfadoxine inhibits the activity of dihydropteroate synthase whereas, Pyrimethamine inhibits dihydrofolate reductase.

Pharmacokinetics

Absorption
After administration of 1 tablet, peak plasma levels for pyrimethamine (approximately 0.2 mg/L) and for sulfadoxine (approximately 60 mg/L) are reached after about 4 hours.

Distribution
The volume of distribution for sulfadoxine and pyrimethamine is 0.14 L/kg and 2.3 L/kg, respectively. Patients taking 1 tablet a week (recommended adult dose for malaria prophylaxis) can be expected to have mean steady state plasma concentrations of about 0.15 mg/L for pyrimethamine after about four weeks and about 98 mg/L for sulfadoxine after about seven weeks. Plasma protein binding is about 90% for both pyrimethamine and sulfadoxine. Both pyrimethamine and sulfadoxine cross the placental barrier and pass into breast milk.

Biotransformation
About 5% of sulfadoxine appears in the plasma as acetylated metabolite, about 2 to 3% as the glucuronide. Pyrimethamine is transformed to several unidentified metabolites.

Elimination
A relatively long elimination half-life is characteristic of both components. The mean values are about 100 hours for pyrimethamine and about 200 hours for sulfadoxine. Both pyrimethamine and sulfadoxine are eliminated mainly via the kidneys.

Indications
It is used for Intermittent Preventive Treatment in Pregnancy (IPT).
In combination with other antimalarials, it is used for treatment of falciparum malaria. **Swidar®** has also been found effective in infections with Toxoplasma gondii and in the prophylaxis of pneumonia due to Pneumocystis carinii.

Dosage and Administration

a. Intermittent Preventive Treatment of Malaria in Pregnancy
One full treatment dose during the second and third trimesters. The last dose should be given not later than one month before the expected date of delivery. (Second trimester starts sixteen weeks or when the pregnant woman notices the kicking of the baby).

b. As adjunct with other antimalarials.

Weight (kg)	No of Tablets (Stat. dose)
10-20	1 tablet
21-30	1 ½ tablets
31- less than 45	2 tablets
45 and above	3 tablets

Interactions
There have been reports which may indicate an increase in incidence and severity of adverse reactions when chloroquine is used with **Swidar®** as compared to the use of **Swidar®** alone. **Swidar®** is compatible with quinine and with antibiotics. However, antifolic drugs such as sulfonamides, trimethoprim, or trimethoprim-sulfamethoxazole combinations should not be used while the patient is receiving **Swidar®** for antimalarial prophylaxis. **Swidar®** has not been reported to interfere with antidiabetic agents. If signs of folic acid deficiency develop, **Swidar®** should be discontinued. When recovery of depressed platelets or white blood cell counts in patients with drug-induced folic acid deficiency is too slow, folinic acid (leucovorin) may be administered in doses of 5-15 mg intramuscularly daily for 3 days or longer.

Contraindication
- Hypersensitivity to pyrimethamine, sulfonamides, or any other ingredient of **Swidar®**
- Repeated prophylactic use of Swidar is contraindicated in patients with renal or hepatic failure or with blood dyscrasias;
- Patients with documented megaloblastic anemia due to folate deficiency;
- Infants less than 2 months of age;
- Hemopathies
- Prophylactic use of **Swidar®** in pregnancy in first semester, at term and during the nursing period.
- HIV- infected patients receiving cotrimoxazole prophyllaxis against opportunistic infection

Warnings / Precautions

WARNINGS
FATALITIES ASSOCIATED WITH THE ADMINISTRATION OF SWIDAR HAVE OCCURRED DUE TO SEVERE REACTIONS, INCLUDING STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS. SWIDAR PROPHYLAXIS MUST BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH, IF A SIGNIFICANT REDUCTION IN THE COUNT OF ANY FORMED BLOOD ELEMENTS IS NOTED, OR UPON THE OCCURRENCE OF ACTIVE BACTERIAL OR FUNGAL INFECTIONS.

Fatalities associated with the administration of sulfonamides, although rare, have occurred due to severe reactions, including fulminant hepatic necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias. **Swidar®** prophylactic regimen has been reported to cause leukopenia during a treatment of 2 months or longer. This leukopenia is generally mild and reversible.

PRECAUTIONS

General
Swidar® should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency and to those with severe allergy or bronchial asthma. As with some sulfonamide drugs, in glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur. Urinalysis with microscopic examination and renal function tests should be performed during therapy of those patients who have impaired renal function. Excessive sun exposure should be avoided.

Information for the Patient
Patients should be warned that at the first appearance of a skin rash, they should stop use of **Swidar®** and seek medical attention immediately. Adequate fluid intake must be maintained in order to prevent crystalluria and stone formation.

Patients should also be warned that the appearance of sore throat, fever, arthralgia, cough, shortness of breath, pallor, purpura, jaundice or glossitis may be early indications of serious disorders which require prophylactic treatment to be stopped and medical treatment to be sought.

Females should be cautioned against becoming pregnant (since **Swidar®** is not recommended in the first trimester) and should not breastfeed their infants during Swidar therapy or prophylactic treatment.

Patients should be warned to keep **Swidar®** out of reach of children.

Patients also should be advised:

- that malaria can be a life-threatening infection; that **Swidar®** is being prescribed to help prevent this serious infection;
- that no chemoprophylactic regimen is 100% effective;
- protective clothing, insect repellents, and bednets are important components of malaria prophylaxis;
- to seek medical attention for any febrile illness that occurs after return from a malarious area and inform their physician that they may have been exposed to malaria;
- that in a small percentage of cases, patients are unable to take this medication because of side effects, and it may be necessary to change medications;
- that if the patient experiences any symptom that may affect the patient's ability to take this drug as prescribed, the physician should be contacted and alternative antimalarial medication should be considered.

Laboratory Tests
Regularly scheduled complete blood counts, liver enzyme tests and analysis of urine for crystalluria should be performed whenever **Swidar®** is administered for more than three months.

Pregnancy and Lactation

Pregnancy
Sulfadoxine/Pyrimethamine showed reproductive toxicity in animal studies.

Teratogenic Effects
Pregnancy Category C. **Swidar®** has been shown to be teratogenic in rats when given in weekly doses approximately 12 times the weekly human prophylactic dose. Teratology studies with pyrimethamine plus sulfadoxine (1:20) in rats showed the minimum oral teratogenic dose to be approximately 0.9 mg/kg pyrimethamine plus 18mg/kg sulfadoxine. In rabbits, no teratogenic effects were noted at oral doses as high as 20 mg/kg pyrimethamine plus 400 mg/kg sulfadoxine.

Sulfadoxine/Pyrimethamines should not be used during the first trimester of pregnancy unless the benefit is considered to outweigh the risks and alternative drugs are not available.

During 2nd or 3rd trimesters of pregnancy, **Swidar®** may be used for intermittent preventive treatment of malaria.

Breastfeeding
Pyrimethamine is excreted in human milk. Some sulfonamides are excreted in human milk. Sulfonamides are avoided in premature infants and in infants with hyperbilirubinemia or glucose-6-phosphate dehydrogenase deficiency.

Adverse Reaction

Hematological Changes
Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia, methemoglobinemia and eosinophilia.

Skin and Miscellaneous Sites Allergic Reactions
Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, toxic epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia, allergic myocarditis, slight hair loss, Lyell's syndrome and allergic pericarditis.

Gastrointestinal Reactions
Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, hepatocellular necrosis, diarrhea, pancreatitis, feeling of fullness, and transient rise of liver enzymes.

Central Nervous System Reactions
Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness, nervousness and polyneuritis.

Respiratory Reactions
Pulmonary infiltrates resembling eosinophilic or allergic alveolitis.

Genitourinary
Renal failure, interstitial nephritis, BUN and serum creatinine elevation, toxic nephrosis crystalluria, toxic nephrososis with oliguria and anuria.

Miscellaneous Reactions
Drug fever, chills, periarteritis nodosa and LE phenomenon have occurred. The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides), and oral hypoglycemic agents. Diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

Symptoms of Overdosage and Management

Symptoms:
Headache, anorexia, nausea, vomiting, agitation, convulsions, hematologic changes (megaloblastic anemia, leucopoenia, thrombocytopenia), glossitis and crystalluria.

Management:
The patient should be urgently transferred to a specialized unit for close monitoring and supportive therapy including, where appropriate, activated charcoal and fluid administration; a parenteral benzodiazepine, phenytoin or a barbiturate can be given for convulsions. Liver and renal function should be monitored, and blood counts checked repeatedly for up to four weeks after the overdose. Should blood dyscrasia occur, folinic acid (leucovorin) may be used.

Storage Condition:
Store below 30^{o}C
Protect from moisture and Light

Presentation:
1 x 3 and 3 x 10 packs

NAFDAC REG NO.: A4-6639

Medicine: Keep out of reach of children

swipha

Manufactured by:
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