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Azulfidine

(Sulfasalazine) - Pharmacia & Upjohn

THERAPEUTIC CLASS
5-aminosalicylic acid derivative/sulfapyridine

DEA CLASS
RX

INDICATIONS
Treatment of mild to moderate ulcerative colitis (UC). Adjunctive therapy in severe UC. To prolong remission period between acute attacks of UC.

ADULT DOSAGE
Adults: Individualize dose. Take preferably pc. Initial: 3-4g/day in evenly divided doses with intervals not >8 hrs. May initiate with a lower dose (eg, 1-2g/day) to reduce GI intolerance. Maint: 2g/day. When endoscopic examination confirms satisfactory improvement, reduce dose to a maintenance level. If diarrhea recurs, increase dose to previously effective levels. If symptoms of GI intolerance occur after 1st few doses, reduce daily dose by 1/2, then gradually increase over several days. If GI intolerance continues, d/c for 5-7 days, then reintroduce at a lower daily dose. Desensitization: Initial: 50-250mg/day. Titrate: Double every 4-7 days until desired therapeutic level is achieved. D/C if sensitivity recurs.

PEDIATRIC DOSAGE
Pediatrics: ≥6 Yrs: Individualize dose. Take preferably pc. Initial: 40-60mg/kg/24 hrs divided into 3-6 doses. Maint: 30mg/kg/24 hrs divided into 4 doses. When endoscopic examination confirms satisfactory improvement, reduce dose to a maintenance level. If diarrhea recurs, increase dose to previously effective levels. If symptoms of GI intolerance occur after 1st few doses, reduce daily dose by 1/2, then gradually increase over several days. If GI intolerance continues, d/c for 5-7 days, then reintroduce at a lower daily dose. Desensitization: Initial: 50-250mg/day. Titrate: Double every 4-7 days until desired therapeutic level is achieved. D/C if sensitivity recurs.

HOW SUPPLIED
Tab: 500mg* *scored

CONTRAINDICATIONS
Intestinal or urinary obstruction, porphyria.

WARNINGS/PRECAUTIONS
Caution with hepatic/renal damage, blood dyscrasias, severe allergy, bronchial asthma, history of recurring/chronic infections, or with underlying conditions or concomitant drugs that may predispose patients to infections. Deaths reported from hypersensitivity reactions, agranulocytosis, aplastic anemia, other blood dyscrasias, renal and liver damage, irreversible neuromuscular and CNS changes, and fibrosing alveolitis. Perform CBC, including differential WBC count, and LFTs before starting therapy, every 2nd week for the first 3 months, monthly for the next 3 months, then every 3 months thereafter, and as clinically indicated; d/c while awaiting the results of blood tests. Monitor urinalysis and renal function periodically. Oligospermia and infertility reported in males. Serious infections (eg, fatal sepsis, pneumonia) reported. D/C if serious infection or toxic/hypersensitivity reactions develop. Closely monitor for signs and symptoms of infection during and after treatment; if a new infection develops, perform a prompt and complete diagnostic workup for infection and myelosuppression. Serious skin reactions, some fatal (eg, exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis), reported; d/c at 1st appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity. Severe, life-threatening, systemic hypersensitivity reactions (eg, drug rash with eosinophilia and systemic symptoms) reported; evaluate immediately if signs/symptoms develop, and d/c if an alternative etiology cannot be established. Maintain adequate fluid intake to prevent crystalluria and stone formation. Closely monitor patients with G6PD deficiency for signs of hemolytic anemia. Do not attempt desensitization in patients who have a history of agranulocytosis, or who have experienced an anaphylactoid reaction with previous sulfasalazine (SSZ) therapy. Serum sulfapyridine (SP) levels >50mcg/mL appear to be associated with increased incidence of adverse reactions. Lab test interactions may occur.

ADVERSE REACTIONS
Anorexia, headache, N/V, gastric distress, reversible oligospermia.

DRUG INTERACTIONS
May reduce absorption of folic acid and digoxin.

PREGNANCY
Category B, caution in nursing.

MECHANISM OF ACTION
5-aminosalicylic acid (5-ASA) derivative/SP; not established. May be related to anti-inflammatory and/or immunomodulatory properties, to its affinity for connective tissue, and/or to the relatively high concentration it reaches in serous fluids, the liver, and intestinal walls.

PHARMACOKINETICS

Absorption: SSZ: Absolute bioavailability (<15%); C_{max}=6mcg/mL; T_{max}=6 hrs. SP: Well absorbed from colon. Bioavailability (60%); T_{max}=10 hrs. 5-ASA: Much less well absorbed from GI tract. Bioavailability (10-30%); T_{max}=10 hrs. **Distribution:** Crosses placenta; found in breast milk. SSZ: V_d=7.5L (IV); plasma protein binding (>99.3%). SP: Plasma protein binding (70%, 90% [acetylsulfapyridine]). **Metabolism:** SSZ: Intestinal bacteria and liver to SP (active) and 5-ASA (metabolites). SP: Acetylation to acetylsulfapyridine (principal metabolite). 5-ASA: Liver and intestine to N-acetyl-5-ASA. **Elimination:** Urine, feces. SSZ: $T_{1/2}$=7.6 hrs (IV). SP: $T_{1/2}$=10.4 hrs (fast acetylators), 14.8 hrs (slow acetylators).

ASSESSMENT

Assess for intestinal or urinary obstruction, porphyria, renal dysfunction, severe allergy, bronchial asthma, G6PD deficiency, pregnancy/nursing status, possible drug interactions, history of hypersensitivity to the drug, its metabolites, sulfonamides, or salicylates, history of recurring/chronic infections, and underlying conditions which may predispose patients to infections. Obtain CBC, including differential WBC count, and LFTs.

MONITORING

Monitor for GI intolerance, hypersensitivity/skin reactions, neuromuscular and CNS changes, fibrosing alveolitis, infection, signs of hemolytic anemia (in patients with G6PD deficiency), and other adverse reactions. Monitor CBC, including differential WBC count, and LFTs every 2nd week for the first 3 months, monthly for the next 3 months, then every 3 months thereafter, and as clinically indicated. Monitor urinalysis and renal function periodically, and serum SP levels. Monitor for diarrhea and/or bloody stools in infants fed milk from mothers taking SSZ. Monitor newborns for kernicterus.

PATIENT COUNSELING

Inform of possible adverse reactions and need for careful medical supervision. Instruct to seek medical advice if sore throat, fever, pallor, purpura, or jaundice occurs. Inform that UC rarely remits completely and that risk of relapse can be reduced by continued administration at a maintenance dosage. Advise that orange-yellow discoloration of urine or skin may occur.

ADMINISTRATION/STORAGE

Administration: Oral route. Take in evenly divided doses, preferably pc. **Storage:** 25°C (77°F); excursions permitted to 15-30°C (59-86°F).