The use of sulfasalazine in pregnancy. In women with rheumatoid arthritis, the risk of miscarriage in the first and second trimesters was 1.4% and 2.7%, respectively, compared with 1.1% and 2.3% in the general population. However, the results of this study do not suggest a causal relationship between exposure to sulfasalazine and congenital malformations.

Sulfasalazine is excreted in human milk. The reported milk levels, however, are low when compared with the maternal plasma concentrations and the potential for adverse reactions to sulfasalazine in nursing infants is unknown. A decision must be made whether to discontinue the drug or to discontinue breastfeeding. If sulfasalazine is used in pregnancy or if the possibility of pregnancy exists, the patient should be apprised of the potential hazards to the fetus.

Sulfasalazine is a CYP2C9 and CYP2C19 inhibitor, and a weak inhibitor of CYP2B6, CYP3A4, and CYP2C19. Sulfasalazine is a substrate for CYP2C9 and CYP2C19. The inhibition of CYP2C9 and CYP2C19 by sulfasalazine may increase the plasma concentrations of drugs that are extensively metabolized by these enzymes, such as warfarin, diazepam, and alprazolam. The inhibition of CYP2B6 by sulfasalazine may increase the plasma concentrations of drugs that are extensively metabolized by this enzyme, such as phenytoin and carbamazepine. The effect of sulfasalazine on the plasma concentrations of drugs that are metabolized by CYP3A4 is unknown. Therefore, the concomitant use of drugs that are substrates or inhibitors of CYP2C9, CYP2C19, or CYP2B6 should be avoided or the dose of the affected drug should be decreased when sulfasalazine is used. The concomitant use of drugs that are substrates or inhibitors of CYP3A4 should be avoided when sulfasalazine is used.

Sulfasalazine is a substrate for P-glycoprotein, a protein that is involved in the efflux of drugs from the enterocyte. Therefore, the concomitant use of drugs that are substrates or inhibitors of P-glycoprotein should be avoided when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C19 enzyme, which is involved in the metabolism of warfarin. The concomitant use of warfarin and sulfasalazine may result in an increase in the anticoagulant effect of warfarin, which may require a reduction in the dose of warfarin. Therefore, the dose of warfarin should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C9 enzyme, which is involved in the metabolism of diazepam and alprazolam. The concomitant use of diazepam and alprazolam and sulfasalazine may result in an increase in the sedative effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of diazepam and alprazolam should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2B6 enzyme, which is involved in the metabolism of phenytoin and carbamazepine. The concomitant use of phenytoin and carbamazepine and sulfasalazine may result in an increase in the antiepileptic effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of phenytoin and carbamazepine should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP3A4 enzyme, which is involved in the metabolism of drugs that are substrates of this enzyme, such as cyclosporine, tacrolimus, and amiodarone. The concomitant use of these drugs and sulfasalazine may result in an increase in the plasma concentrations of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of these drugs should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C19 enzyme, which is involved in the metabolism of clopidogrel. The concomitant use of clopidogrel and sulfasalazine may result in an increase in the antiplatelet effect of clopidogrel, which may require a reduction in the dose of clopidogrel. Therefore, the dose of clopidogrel should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C9 enzyme, which is involved in the metabolism of warfarin, diazepam, and alprazolam. The concomitant use of warfarin, diazepam, and alprazolam and sulfasalazine may result in an increase in the anticoagulant effect, sedative effect, and antiepileptic effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of warfarin, diazepam, and alprazolam should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2B6 enzyme, which is involved in the metabolism of phenytoin and carbamazepine. The concomitant use of phenytoin and carbamazepine and sulfasalazine may result in an increase in the antiepileptic effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of phenytoin and carbamazepine should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP3A4 enzyme, which is involved in the metabolism of drugs that are substrates of this enzyme, such as cyclosporine, tacrolimus, and amiodarone. The concomitant use of these drugs and sulfasalazine may result in an increase in the plasma concentrations of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of these drugs should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C19 enzyme, which is involved in the metabolism of clopidogrel. The concomitant use of clopidogrel and sulfasalazine may result in an increase in the antiplatelet effect of clopidogrel, which may require a reduction in the dose of clopidogrel. Therefore, the dose of clopidogrel should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C9 enzyme, which is involved in the metabolism of warfarin, diazepam, and alprazolam. The concomitant use of warfarin, diazepam, and alprazolam and sulfasalazine may result in an increase in the anticoagulant effect, sedative effect, and antiepileptic effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of warfarin, diazepam, and alprazolam should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2B6 enzyme, which is involved in the metabolism of phenytoin and carbamazepine. The concomitant use of phenytoin and carbamazepine and sulfasalazine may result in an increase in the antiepileptic effect of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of phenytoin and carbamazepine should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP3A4 enzyme, which is involved in the metabolism of drugs that are substrates of this enzyme, such as cyclosporine, tacrolimus, and amiodarone. The concomitant use of these drugs and sulfasalazine may result in an increase in the plasma concentrations of these drugs, which may require a reduction in the dose of these drugs. Therefore, the dose of these drugs should be monitored and adjusted as necessary when sulfasalazine is used.

Sulfasalazine is a weak inhibitor of the CYP2C19 enzyme, which is involved in the metabolism of clopidogrel. The concomitant use of clopidogrel and sulfasalazine may result in an increase in the antiplatelet effect of clopidogrel, which may require a reduction in the dose of clopidogrel. Therefore, the dose of clopidogrel should be monitored and adjusted as necessary when sulfasalazine is used.
Central nervous system reactions: Transverse myelitis, convulsions, meningitis, transient lesions of the posterior spinal column, cauda equina syndrome, Guillain-Barré syndrome, peripheral neuropathy, mental depression, vertigo, lowering loss, insomnia, sleep, hallucination, tremors, and drowsiness.

Reactions: basic nephropathy with oliguria and anuria, nephritis, nephritic syndrome, urinary tract infections, hematuria, pyelonephritis, and hemolytic-uremic syndrome.

Other reactions: urine discoloration and skin discoloration.

The adverse events listed in the following table include some gastrointestinal, hepatic (jaundice and the bilirubin), and other hepatic and renal reactions. Other adverse reactions in patients receiving sulfasalazine may be observed.

Serum sulfapyridine concentrations may be used to monitor the progress of recovery from overdosage.

There are no documented reports of deaths due to ingestion of large single doses of sulfasalazine. Doses of 12 g/kg were not lethal to mice. In humans, fatalities have occurred following ingestion of as little as 6 g of sulfasalazine. In one case, 12 g/kg was not lethal to mice.

In patients who have experienced an anaphylactoid reaction while previously receiving sulfasalazine, discontinuation should not be attempted in patients who have a history of agranulocytosis, or who have experienced an anaphylactoid reaction while previously receiving sulfasalazine. Desensitization should not be attempted in patients who have a history of agranulocytosis, or who have experienced an anaphylactoid reaction while previously receiving sulfasalazine.

Metabolism and nutrition system disorders: Anemia, pallor

Vascular disorders: pallor

Central nervous system disorders: myoclonus

Hepatobiliary disorders: reports of hepatotoxicity, including elevated liver function tests (SGOT, SGPT, alkaline phosphatase), fulminating hepatic failure, cholestasis, cholestasis, and jaundice. Hepatocellular damage has been reported in patients taking sulfasalazine. There is evidence that the incidence and severity of toxicity following overdosage are directly related to the total serum sulfapyridine concentration. Symptoms of overdosage may include nausea, vomiting, gastric irritation, abdominal pain. In more advanced cases, central nervous system symptoms such as depression, vertigo, hearing loss, insomnia, ataxia, hallucinations, tinnitus, and drowsiness. There are no documented reports of death due to ingestion of large single doses of sulfasalazine. Doses of 16 g per day have been given to patients without mortality. A single oral dose of 12 g/kg was not lethal to mice.

Instructions for Overdosage: Gastric lavage or enemas plus cathartic as indicated. Administration of activated charcoal is not recommended. The low molecular weight of sulfasalazine and its metabolites may facilitate their removal by dialysis.

Dosage and Administration: The dosage of sulfasalazine tablets should be adjusted to each individual's response and tolerance.

Initial Therapy:

Adults: 3 to 6 g daily in evenly divided doses with storage intervals of at least eight hours. In some cases, it is advisable to initiate therapy with a smaller dosage, e.g., 1 to 2 g daily, to reduce possible gastrointestinal intolerance. If daily doses exceeding 4 g are required to achieve desired effects, the increased risk of toxicity should be kept in mind.

Children, six years of age and older: 45 to 60 mg/kg body weight in each 24-hour period, divided into 3 to 4 doses.

Maintenance Therapy:

Adults: 2 g daily.

Children, six years of age and older: 30 mg/kg body weight in each 24-hour period, divided into 3 to 4 doses.

The response of acute ulcerative colitis to sulfasalazine tablets can be evaluated by clinical criteria, including the presence of fever, weight change, and degree and frequency of diarrhea, as well as by sigmoidoscopic and the evaluation of biopsy samples. If necessary to continue medication even when clinical symptoms, including diarrhea, have been controlled. When endoscopic examination confirms improvement in the rectum, the dosage should be reduced to previously effective levels. If symptoms of gastric intolerance (anorexia, nausea, vomiting, or) occur after the first few doses of sulfasalazine, they are probably due to increased serum levels of sulfapyridine and may be alleviated by halving the daily dose of sulfasalazine and subsequently increasing it gradually over several days. If gastric intolerance continues, the drug should be discontinued for 5 to 7 days, then reintroduced at a lower daily dose.

Some patients may be sensitive to treatment with sulfasalazine. Various desensitization-like regimens have been reported to be effective in 20 to 50% of patients. The regimens suggest starting with small daily doses of 50 mg/kg (50 mg/kg initially and doubling every 1 to 3 days) until the desired therapeutic level is achieved. If the symptoms of sensitivity recur, sulfasalazine should be discontinued. Desensitization should not be attempted in patients who have a history of agranulocytosis, or who have experienced an anaphylactoid reaction while previously receiving sulfasalazine.

How Supplied:

Sulfasalazine Tablets USP: 500 mg are round, gold-colored, scored tablets, debossed "5904" and "V" on one side and plain on the reverse side. They are available in the following package sizes:

- Bottles of 180: 0603-5801-04
- Bottles of 100: 0603-5801-21
- Bottles of 50: 0603-5801-18
- Bottles of 100: 0603-5801-02

Storage:

Store at 25° C (77° F) [see USP Controlled Room Temperature].

References:


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Structure: CC7961A

Black

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