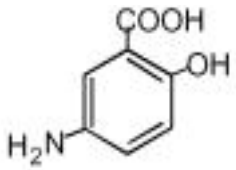
Asacol®
(mesalamine)
Delayed-Release Tablets

DESCRIPTION: Each **Asacol** delayed-release tablet for oral administration contains 400 mg of mesalamine, an anti-inflammatory drug. The **Asacol** delayed-release tablets are coated with acrylic based resin, Eudragit S (methacrylic acid copolymer B, NF), which dissolves at pH 7 or greater, releasing mesalamine in the terminal ileum and beyond for topical anti-inflammatory action in the colon. Mesalamine has the chemical name 5-amino-2-hydroxybenzoic acid; its structural formula is:



Molecular Weight: 153.1
Molecular Formula: $C_7H_7NO_3$

Inactive Ingredients: Each tablet contains colloidal silicon dioxide, dibutyl phthalate, edible black ink, iron oxide red, iron oxide yellow, lactose monohydrate, magnesium stearate, methacrylic acid copolymer B (Eudragit S), polyethylene glycol, povidone, sodium starch glycolate, and talc.

CLINICAL PHARMACOLOGY: Mesalamine is thought to be the major therapeutically active part of the sulfasalazine molecule in the treatment of ulcerative colitis. Sulfasalazine is converted to equimolar amounts of sulfapyridine and mesalamine by bacterial action in the colon. The usual oral dose of sulfasalazine for active ulcerative colitis is 3 to 4 grams daily in divided doses, which provides 1.2 to 1.6 grams of mesalamine to the colon.

The mechanism of action of mesalamine (and sulfasalazine) is unknown, but appears to be topical rather than systemic. Mucosal production of arachidonic acid (AA) metabolites, both through the cyclooxygenase pathways, i.e., prostanoids, and through the lipoxygenase pathways, i.e., leukotrienes (LTs) and hydroxyeicosatetraenoic acids (HETEs), is increased in patients with chronic inflammatory bowel disease, and it is possible that mesalamine diminishes inflammation by blocking cyclooxygenase and inhibiting prostaglandin (PG) production in the colon.

Pharmacokinetics: **Asacol** tablets are coated with an acrylic-based resin that delays release of mesalamine until it reaches the terminal ileum and beyond. This has been demonstrated in human studies conducted with radiological and serum markers. Approximately 28% of the mesalamine in **Asacol** tablets is absorbed after oral ingestion, leaving the remainder available for topical action and excretion in the feces. Absorption of mesalamine is similar in fasted and fed subjects. The absorbed mesalamine is rapidly acetylated in the gut mucosal wall and by the liver. It is excreted mainly by the kidney as N-acetyl-5-aminosalicylic acid.

Mesalamine from orally administered **Asacol** tablets appears to be more extensively absorbed than the mesalamine released from sulfasalazine. Maximum plasma levels of mesalamine and N-acetyl-5-aminosalicylic acid following multiple **Asacol** doses are about 1.5 to 2 times higher than those following an equivalent dose of mesalamine in the form of sulfasalazine. Combined