Each rectal suspension enema unit contains 4 grams of mesalamine.

In addition to mesalamine the preparation contains the inactive ingredients carbomer 934P, edetate disodium, hydroxypropyl methylcellulose, purified water and xanthan gum. Sodium benzoate is added as a preservative. The unit does not contain any added coloring, preservatives, or antimicrobial agents.

The unit has a one-way valve to prevent back flow of the dispensed product.

CLINICAL PHARMACOLOGY

Sulfasalazine is selectively absorbed in the colon into sulfapyridine (SP) and mesalamine (5-ASA). It is thought that the mesalamine component is therapeutically active in ulcerative colitis (A.K. Azad Khan et al. Lancet 2:922-925 (1977)). The active 5-ASA moiety is a prodrug which is converted to its metabolites via nonspecific colonic and hepatic enzymes. The 5-ASA is then released and absorbed from the colon. It has been demonstrated that the predominant 5-ASA metabolite is N-acetylsalicylic acid (NSA), which is converted to salicylic acid (SA), the active anti-inflammatory component of aspirin. The conversion is shown below:

\[
\text{5-ASA} \rightarrow \text{NSA} \rightarrow \text{SA}
\]

Mesalamine administered rectally as Mesalamine Rectal Suspension USP, Enema results in an effective 5-ASA concentration of 5-ASA and N-acetyl-5-ASA seen in ulcerative colitis patients.

Two pathways have been identified by which mesalamine is absorbed from the colon. The first is by the enterohepatic circulation where absorption occurs through the liver and enterohepatic recirculation occurs. The second is direct absorption from the colon. It has been determined that the absorbance is dependent on the retention time of the drug product. Mesalamine administered as an enema has a half-life of 2-4 hours. The compound is mainly eliminated as metabolites in the urine, with 30-50% of the dose being excreted as unchanged 5-ASA.

More than 90% of the dose is excreted in the urine as the N-acetyl-5-ASA metabolite. The poor colonic absorption of rectally administered mesalamine is substantiated by the low serum concentrations of mesalamine. However, elevation of mesalamine in the serum of patients after dosage with mesalamine. Under clinical conditions patients demonstrated plasma levels 10 to 12 hours post mesalamine administration of 2 mg/ml, about two-thirds of which was the N-acetyl metabolite. When mesalamine is excreted in the urine as the N-acetyl-5-ASA metabolite.

Mesalamine has been implicated in the production of an acute intolerance syndrome characterized by cramping, abdominal pain and bloody diarrhea, sometimes fever, headache, and rash; in such cases prompt withdrawal is required. The patient's history of sulfasalazine intolerance, if any, should be re-evaluated. If a relapse is performed later in order to confirm or exclude the diagnosis.

Although renal abnormalities were not in the clinical trials with Mesalamine Rectal Suspension USP, the possibility of increased absorption of mesalamine and consequent renal failure should be considered.

In addition, steady state plasma levels of up to 30% of the total dose were observed in the clinical trials with mesalamine. The clinical significance of this finding is unknown.

CONTRAINdications

Mesalamine Rectal Suspension, USP is contraindicated for patients known to have hypersensitivity to the drug or any component of this medication.

WARNINGS

Mesalamine Rectal Suspension, USP contains potassium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or fatal reactions, and sulfapyridine which may also produce severe skin reactions and cause the syndrome characterized by fever, skin rash and eosinophilia and may rarely cause hypersensitivity reactions, including anaphylactic shock, liver and kidney injury, and pulmonary and vascular reactions.

INDICATIONS AND USAGE

Mesalamine Rectal Suspension, USP is indicated for the treatment of active mild to moderate distal ulcerative colitis, proctosigmoiditis or proctitis.

CONTRAINDICATIONS

Mesalamine Rectal Suspension, USP is contraindicated for patients known to have hypersensitivity to the drug or any component of this medication.

PRECAUTIONS

In addition, the following adverse events have been identified during post-approval use of products which contain (or are metabolized to) mesalamine in clinical practice: nephrotoxicity, pancreatitis, fibrosing alveolitis and elevated liver enzymes. Cases of pancreatitis and fibrosing alveolitis have been reported as manifestations of inflammatory bowel disease as well. Published case reports and/or spontaneous post marketing surveillance have described rare instances of aplastic anemia, agranulocytosis, thrombocytopenia, eosinophilia, pancytopenia, neutropenia, oligospermia, and infertility in men. Amebiasis, leukocytosis and thrombocytosis can be part of the clinical presentation of inflammatory bowel disease.

Hair Loss - Mild hair loss characterized by ‘more hair in the comb’ but no withdrawal from clinical trials has been observed in seven of 817 mesalamine-treated patients but none of the placebo-treated patients. In the literature there are at least six additional patients with mild hair loss who received either mesalamine or sulfasalazine. Treatment is not always associated with complete hair loss.

DOSE AND ADMINISTRATION

The usual dosage of Mesalamine Rectal Suspension, USP, in 60 mL units is one rectal instillation (4 grams) once a day, preferably at bedtime, and retained for approximately eight hours. While the effect of Mesalamine Rectal Suspension, USP may be seen within three to twenty-one days, the usual course of therapy would be from three to six weeks depending on symptoms and sigmoidoscopic findings. Studies available to date have not associated Mesalamine Rectal Suspension, USP with major relapse rates after the 6-week short-term treatment. Mesalamine Rectal Suspension, USP is for rectal use only.

Mesalamine Rectal Suspension, USP contains potassium metabisulfite, a preservative. The disposable unit consists of an applicator tip protected by a polyethylene cover and lubricated with USP white petrolatum. The unit is attached to a disposable ensemble bottle containing the preparation. The patient should remove the protective cap from the ensemble bottle and insert the applicator tip. The patient should then discharge the preparation into the rectum. The position most often used is the left lateral position. The patient should then remain in this position for 2 minutes to allow the preparation to be absorbed. The ensemble bottle is then discarded. The unit is attached to a disposable ensemble bottle containing the preparation. The patient should remove the protective cap from the ensemble bottle and insert the applicator tip. The patient should then discharge the preparation into the rectum. The position most often used is the left lateral position. The patient should then remain in this position for 2 minutes to allow the preparation to be absorbed. The ensemble bottle is then discarded.

Patient instructions are included. Store at 20-25°C (68-77°F). [See USP Controlled Room Temperature]. Once the foil-wrapped unit of seven bottles is opened, all enemas should be used promptly as directed by your physician. Contents of enemas removed from the foil pouch may darken with time. Slight darkening will not affect potency, however, enemas with dark brown contents should be discarded.

NOTE: Mesalamine Rectal Suspension, USP will cause staining of direct contact surfaces, including but not limited to fabrics, flooring, painted surfaces, marble, granite, and vinyl, and enamel.

Keep out of reach of children.
PATIENT INSTRUCTIONS
How to Use this Medication.

Best results are achieved if the bowel is emptied immediately before the medication is given.
NOTE: Mesalamine Rectal Suspension, USP will cause staining of direct contact surfaces, including but not limited to fabrics, flooring, painted surfaces, marble, granite, vinyl, and enamel. Take care in choosing a suitable location for administration of this product.

1. Remove the Bottles
a. Remove the bottles from the protective foil pouch by tearing or by using scissors as shown, being careful not to squeeze or puncture bottles. Mesalamine Rectal Suspension USP is an off-white to tan colored suspension. Once the foil-wrapped unit of seven bottles is opened, all enemas should be used promptly as directed by your physician. Contents of enemas removed from the foil pouch may darken with time. Slight darkening will not affect potency, however, enemas with dark brown contents should be discarded.

2. Prepare the Medication for Administration
a. Shake the bottle well to make sure that the medication is thoroughly mixed.
b. Remove the protective sheath from the applicator tip. Hold the bottle at the neck so as not to cause any of the medication to be discharged.

3. Assume the Correct Body Position
a. Best results are obtained by lying on the left side with the left leg extended and the right leg flexed forward for balance.

b. An alternative to lying on the left side is the "knee-chest" position as shown here.

4. Administer the Medication
a. Gently insert the lubricated applicator tip into the rectum to prevent damage to the rectal wall, pointed slightly toward the navel.

b. Grasp the bottle firmly, then tilt slightly so that the nozzle is aimed toward the back, squeeze slowly to instill the medication. Steady hand pressure will discharge most of the medication. After administering, withdraw and discard the bottle.

c. Remain in position for at least 30 minutes to allow thorough distribution of the medication internally. Retain the medication all night, if possible.