COLOMINE®

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Mesalamine

1. Brand Name and Generic Name

COLOMINE -400: Mesalamine Delayed Release Tablets USP

COLOMINE-800: Mesalamine Delayed Release Tablets USP

COLOMINE-OD: Mesalamine Prolonged-release Tablets IP 1.2 g

2. Strength of Active Ingredient(s)

COLOMINE -400: Each enteric coated tablet contains Mesalamine USP 400 mg

COLOMINE-800: Each enteric coated tablet contains Mesalamine USP 800 mg

COLOMINE-OD Tablet: Each enteric coated prolonged-release tablet contains Mesalamine USP 1.2 g

3. Product Description

COLOMINE is Mesalamine, which is an aminosalicylate gastrointestinal anti-inflammatory drug used in the treatment of inflammatory bowel disease (IBD), including ulcerative colitis, or inflamed anus or rectum, and to maintain remission in Crohn's disease. It is considered to be the active moiety of Sulphasalazine.

4. Pharmacodynamics & Pharmacokinetics

Pharmacodynamics:

Mesalamine has a topical anti-inflammatory effect on the colonic epithelial cells. Mesalamine diminishes the inflammation by blocking mucosal production of arachidonic acid metabolites, both through cyclooxygenase and lipoxygenase pathways, such as prostaglandins and leukotrienes production which is increased in patients with chronic inflammatory bowel disease. Mesalamine has the potential to inhibit the activation of nuclear factor kappa B (NFkB) and consequently the production of key pro-inflammatory cytokines. Moreover, Mesalamine activates the Peroxisome proliferator-activated receptor (PPAR)-gamma (PPAR-γ) receptors which counteract activation of intestinal inflammatory responses. As a derivative of salicylic acid, it is also an antioxidant that traps free radicals, which are potentially damaging by-products of metabolism.

Pharmacokinetics

The mechanism of action of Mesalamine appears to be topical, and therefore the clinical efficacy of Mesalamine does not correlate with the pharmacokinetic profile. A major pathway of clearance of Mesalamine is via metabolism to N-acetyl-5-aminosalicylic acid (N-Ac-5-ASA), which is pharmacologically inactive. COLOMINE and COLOMINE-OD Tablets causes delayed release and prolonged release of Mesalamine respectively until it reaches the terminal ileum or beyond. COLOMINE-OD contains a core of Mesalamine formulated in a multi-matrix system (MMX).

Absorption

Approximately 21-22% of Mesalamine is systemically absorbed. Rest is available for the local action and eliminates in the faeces. The mean (t1/2) for Mesalamine and N-Ac-5-ASA are usually about 12 hours, but may vary from 2 to 15 hours. Complete disintegration and complete release of Mesalamine OD formulation occurs after approximately 17.4 hours.

Distribution

Absorbed Mesalamine has a relatively small volume of distribution of approximately 18L confirming minimal extravascular penetration of systemically available drug. Mesalamine is 43% bound and N-acetyl-5-aminosalicylic is 78-83% bound to plasma proteins when in vitro plasma concentrations are up to 2.5µg/mL and up to 10µg/mL respectively.

Metabolism

Mesalamine is metabolized to inactive metabolite N-Ac-5-ASA in liver and in the cytosol of intestinal mucosal cells by N-acetyltransferase-1 (NAT-1). About 96% of the drug recovered in the urine after oral administration is found as the main metabolite N-acetylmesalamine.

Excretion

Excretion of absorbed Mesalamine is mainly via the renal route as well as in the faecal form. Of the percentage of dose absorbed, less than 8% of the dose is excreted unchanged in the urine at steady state after 24 hours, compared with greater than 13% for N-Ac-5-ASA.

5. Indications:

Ulcerative colitis: For the treatment of mild to moderate, active acute exacerbations. For the maintenance of remission.Crohn's ileo-colitis:

For the maintenance of remission.

6. Recommended Dose and Administration

COLOMINE and COLOMINE-OD should be swallowed whole with water. The tablets must not be crushed or chewed and should be taken with food. COLOMINE-OD is intended for once daily, oral administration. If one or more doses have been missed, the next dose is to be taken as usual.

ADULTS:

Mild acute exacerbations of ulcerative colitis: 2.4g a day in divided doses. Moderate acute exacerbations of ulcerative colitis: 2.4 g to 4.8g a day in divided doses. Maintenance of remission of ulcerative colitis: 1.6 g to 2.4g a day once daily or in divided doses. Maintenance of remission of Crohn's ileocolitis: 2.4g a day in divided doses. The maximum adult dose should not exceed six tablets a day and not exceed 3 tablets taken together at any one time.

ELDERLY:

The normal adult dosage may be used unless renal function is impaired.

The highest dose of 4.8g/day is recommended for patients not responding to lower doses of Mesalamine. When using the highest dose (4.8g/day), the effect of the treatment should be evaluated at 8 weeks.

For COLOMINE-OD Tablets- two to four tablets (2.4 to 4.8 g) once daily for induction of remission. And two tablets (2.4 g) once daily for maintenance of remission.

7. Contraindication:

- In a history of hypersensitivity reaction to salicylates or renal sensitivity to sulfasalazine. Also in case of hypersensitivity to any of the ingredients.
- Confirmed severe renal impairment (GFR less than 20 ml/min).
- Severe hepatic impairment, gastric or duodenal ulcer, haemorrhagic tendency.

8. Warnings and Precautions

General:

Patients with pyloric stenosis may have prolonged gastric retention of Mesalamine tablets which could delay release of Mesalamine in the colon. Patients with chronic lung function impairment, especially asthma, are at risk of hypersensitivity reactions and should be closely monitored.

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Renal:

Mesalamine is excreted rapidly by the kidney, mainly as its metabolite, N-acetyl-5-aminosalicylic acid. Mesalamine should be used with extreme caution in patients with confirmed mild to moderate renal impairment. Patients on Mesalamine should have renal function monitored, (with serum creatinine levels measured) prior to treatment start. Renal function should then be monitored periodically during treatment, for example every 3 months for the first year, then every 6 months for the next 4 years and annually thereafter, based on individual patient history. Physicians should take into account risk factors such as prior and concomitant medications, duration and severity of disease and concurrent illnesses. Treatment with Mesalamine should be discontinued if renal function deteriorates. If dehydration develops, normal electrolyte and fluid balance should be restored as soon as possible.

Blood:

Following Mesalamine treatment, serious blood dyscrasias have been reported rarely. If the patient develops unexplained bleeding, bruising, purpura, anaemia, fever or sore throat, haematological investigations should be performed. If there is suspicion of blood dyscrasias, treatment should be terminated.

9. Special Populations

Geriatrics:

Use in the elderly should be cautious and subject to patients having normal renal function.

Pediatrics:

There is only limited documentation for an effect in children (age 6-18 years). Mesalamine is not recommended for children under 2 years of age. Mesalamine 1.2 g OD formulation is not recommended to children below 18 years.

Pregnancy and Lactation:

Pregnancy Category B. Use of Mesalamine during pregnancy should, unless essential, be avoided by nursing mothers.

10. Drug-Drug Interactions:

- Mesalamine tablets should not be given with lactulose or similar preparations, which lower stool pH and may prevent release of Mesalamine.
- Concurrent use of other known nephrotoxic agents, such as NSAIDs and Azathioprine, may increase the risk of renal reactions.
- Administration with coumarin-type anticoagulants e.g. warfarin, could result in decreased anticoagulant activity. Prothrombin time should be closely monitored if this combination is essential.
- Mesalamine inhibits thiopurine methyltransferase. In patients receiving azathioprine or 6-mercaptopurine, caution is recommended for concurrent use of Mesalamine as this can increase the potential for blood dyscriasis.

11. Undesirable Effects:

- Predominantly gastrointestinal, including nausea, vomiting, diarrhea, and abdominal pain, headache and arthralgia/myalgia.
- Rare reports of leucopenia, neutropenia, agranulocytosis, aplastic anaemia and thrombocytopenia, alopecia, peripheral neuropathy, pancreatitis, abnormalities of hepatic function and hepatitis, myocarditis and pericarditis, allergic and fibrotic lung reactions, lupus erythematosus-like reactions and rash (including urticaria), drug fever, interstitial nephritis and nephrotic syndrome with oral mesalamine treatment, usually reversible on withdrawal. Renal failure has been reported.
- Very rare reports with an exacerbation of the symptoms of colitis, Stevens Johnson syndrome and erythema multiforme.

12. Storage Condition

Store COLOMINE at room temperature, away from light and moisture.

- Keep the medication away from children and pets.
- Do not flush medications down the toilet or pour them into a drain unless instructed to do so.
- Properly discard this product when it is expired or no longer needed.

13. Dosage Forms and Packaging Available

COLOMINE-400 Tablet: Each box contains 20 Tablets x10 Blisters

COLOMINE-800 Tablet: Each box contains 10 Tablets x10 Blisters

COLOMINE-OD Tablet: Each box contains 10 Tablets x10 Blisters

DIVYAM
The Provider of Advance Care Solutions

Manufactured by:

Deurali-Janta Pharmaceuticals Pvt. Ltd.
Dhapasi, Kathmandu, Nepal
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