8031680-9093

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

BALACOL

(Balsalazide Disodium Capsules U.S.P.)

COMPOSITION

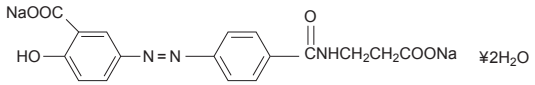
Each hard gelatin capsule contains :

Balsalazide Disodium (Dihydrate) U.S.P. 750 mg

Approved colours used in hard gelatin capsule shell

PROPERTIES

Balsalazide disodium dihydrate is a pro-drug of mesalamine, which has an inert carrier molecule. It is a stable, odourless orange to yellow microcrystalline powder, freely soluble in water and isotonic saline, sparingly soluble in methanol and ethanol and practically insoluble in all other organic solvents. The empirical formula of Balsalazide disodium dihydrate is $C_{17}H_{13}N_3O_6Na_2.2H_2O$ and molecular weight is 437.32. Chemically it is (E)-5-[[-4-[[(2-carboxyethyl) amino] carbonyl] phenyl]azo]-2-hydroxybenzoic acid, disodium salt, dihydrate. Its structural formula is:



CLINICAL PHARMACOLOGY

MECHANISM OF ACTION

Balsalazide remains intact until it reaches the colon where bacterial action within the colon reduces Balsalazide to the active component mesalamine [5-amino salicylic acid i.e. 5-ASA]. The exact mechanism of action of mesalamine is unknown. It is believed, however, that 5-ASA blocks production of arachidonic acid metabolites in the colon. This action appears to be topical rather than systemic in nature.

PHARMACOKINETICS

Absorption

In healthy individuals, the systemic absorption of intact Balsalazide was very low and variable. The mean Cmax occurs approximately 1-2 hours after single oral doses of 1.5 grams or 2.25 grams. The absolute bioavailability of this compound was not determined. In a study of ulcerative colitis patients receiving Balsalazide, 1.5 grams twice daily, for over one year, systemic drug exposure, based on mean AUC values, was up to 60 times greater (8 ng.hr/mL to 480 ng.hr/mL) after equivalent multiple doses of 1.5 grams twice daily when compared to healthy subjects who received the same dose. There was a large intersubject variability in the plasma concentration of Balsalazide versus time profiles in all studies, thus its half-life could not be determined. Fasting slightly increases the systemic uptake of balsalazide and its metabolites.

Distribution

The binding of Balsalazide to human plasma proteins was ‡99%.

Metabolism

The products of the azoreduction of this compound, 5-aminosalicylic acid and 4-aminobenzoyl-b-alanine, and their N-acetylated metabolites have been identified in plasma, urine and feces.

Elimination

Less than 1% of an oral dose was recovered as parent compound, 5-aminosalicylic acid or 4-aminobenzoyl- -alanine in the urine of healthy subjects after single and multiple doses of Balsalazide , while up to 25% of the dose was recovered as the N-acetylated metabolites. In a study with 10 healthy volunteers, 65% of a single 2.25 grams dose of Balsalazide was recovered as 5-aminosalicylic acid, 4-aminobenzoyl- -alanine, and the N-acetylated metabolites in feces, while <1% of the dose was recovered as parent compound. In a study that examined the disposition of Balsalazide in patients who were taking 3-6 grams of Balsalazide daily for more than one year and who were in remission from ulcerative colitis, less than 1% of an oral dose was recovered as intact Balsalazide in the urine. Less than 4% of the dose was recovered as 5-aminosalicylic acid, while virtually no 4-aminobenzoyl-b-alanine was detected in urine. The urinary recovery of the N-acetylated metabolites comprised 20-25% of the Balsalazide dose. No fecal recovery studies were performed in this population.

INDICATIONS

BALACOL is indicated for the treatment of mild to moderate ulcerative colitis and maintenance of remission.

CONTRAINDICATIONS

BALACOL is contraindicated in :

- Patients with Hypersensitivity to any component of the product or its metabolites, including mesalazine. History of hypersensitivity to salicylates. Hypersensitivity reactions may include, but are not limited to the following: anaphylaxis, bronchospasm, and skin reaction.
- Severe hepatic impairment, moderate-severe renal impairment.
- Pregnant and breast feeding women.

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WARNINGS AND PRECAUTIONS

General: Balsalazide capsules should be used with caution in patients with asthma, bleeding disorders, active ulcer disease, mild renal impairment, ulcerative colitis, pyloric stenosis or those with established hepatic disease. During treatment with Colazide blood counts, BUN/creatinine and urine analysis should be performed. Patients receiving balsalazide should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment. A blood count should be performed and the drug stopped immediately if there is suspicion of a blood dyscrasia.

Pyloric Stenosis : Patients with pyloric stenosis may have prolonged gastric retention of Balsalazide capsules.

Exacerbations of Ulcerative Colitis : In the adult clinical trials, 3 out of 259 patients reported exacerbation of the symptoms of ulcerative colitis. In the pediatric clinical trials, 4 out of 68 patients reported exacerbation of the symptoms of ulcerative colitis. Observe patients closely for worsening of these symptoms while on treatment.

patients taking Balsalazide at doses up to 2000 mg/kg (approximately 21 times the recommended 6.75 grams/day dose on a mg/kg basis for a 70 kg person). Balsalazide had no nephrotoxic effects in rats or dogs. Renal toxicity has been observed in animals and patients given other mesalamine products, therefore, caution should be exercised when administering Balsalazide to patients with known renal dysfunction or a history of renal disease.

Use in pregnancy, nursing mothers and children

Pregnancy: [Category B]

There are no adequate and well-controlled studies with Balsalazide in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers:

It is not known whether Balsalazide is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when Balsalazide is administered to a nursing woman.

Pediatric Use:

Safety and effectiveness of Balsalazide in pediatric patients have not been established.

ADVERSE REACTIONS

The adverse effects are expected to be those of mesalazine. Reactions reported during treatment with oral mesalazine are listed below.

General

Fatigue, Fever, Flu-like disorder, Dry mouth,

Blood and lymphatic system disorders

Blood dyscrasias, Aplastic anaemia, Leucopenia, Neutropenia, Agranulocytosis, Thrombocytopenia

Nervous system disorders

Headache, Neuropathy, Insomnia

Cardiac disorders

Myocarditis, Pericarditis

Respiratory, thoracic and mediastinal disorders

Bronchospasm, Allergic alveolitis, Rhinitis, Pharyngitis, Coughing

Gastrointestinal disorders

Abdominal pain, Diarrhoea, Nausea, vomiting, Aggravation of ulcerative colitis, Acute pancreatitis, Flatulence, Dyspepsia, Anorexia, Constipation

Hepatobiliary disorders

Hepatitis, Cholelithiasis

Skin and subcutaneous tissue disorders

Alopecia, Angioedema, Rash

Musculoskeletal and connective tissue disorders

Systemic lupus erythematosus-like syndrome, Arthralgia, Myalgia

Renal and urinary disorders

Interstitial nephritis, Urinary tract infection

Immune system disorders

Hypersensitivity

DRUG INTERACTIONS

No drug interaction studies have been conducted for Balsalazide, however, the use of orally administered antibiotics could, theoretically, interfere with the release of mesalamine in the colon.

The acetylated metabolites of balsalazide are actively secreted in the renal tubule to a high degree. Therefore, plasma levels of co-prescribed drugs also eliminated by this route may be raised and this should be noted in the case of those with a narrow therapeutic range, such as methotrexate. Pharmacodynamic interactions have not been studied. However, while balsalazide, mesalazine, and N-acetylmesalazine are salicylates chemically, their properties and kinetics make classical salicylate interactions such as those found with acetylsalicylic acid very unlikely. The uptake of digoxin has been impaired in some individuals by concomitant treatment with sulphasalazine. Even if it is not known whether this would occur also during treatment with balsalazide, it is recommended that plasma levels of digoxin should be monitored in digitalised patients starting Colazide. Mesalazine inhibits thiopurine methyltransferase. In patients receiving azathioprine or 6-mercaptopurine, caution is recommended for concurrent use of mesalazine as this can increase the potential for blood dyscrasias.

DOSAGE AND ADMINISTRATION

To be swallowed whole with or after food.

Adults:

Treatment of active disease:

2.25g Balsalazide disodium (3 capsules) three times daily (6.75g daily) until remission or for 12 weeks maximum. Rectal or oral steroids can be given concomitantly if necessary.

Maintenance treatment:

The recommended starting dose is 1.5g Balsalazide disodium (2 capsules) twice daily (3g daily). The dose can be adjusted based on each patient's response; there may be an additional benefit with a dose up to 6g daily.

Elderly: No dose adjustment is anticipated.

Children: Balsalazide capsules is not recommended in children

OVERDOSAGE

No case of overdose has occurred with Balsalazide. If an overdose occurs with Balsalazide use, treatment should be supportive, with particular attention to correction of electrolyte abnormalities.

EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store protected from moisture, at a temperature not exceeding 25°C.

PRESENTATION

BALACOL is available as brown / brown hard gelatin capsule containing brown granular powder, in blister strips of 10 capsules.

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured by :
Acme Formulation Pvt. Ltd.
Ropar Road, Nalagarh, Dist. Solan H. P.-174101