For Oral Use Only — Not for Inhalation or Injection.

DESCRIPTION: Each 5 mL ampule of Cromolyn Sodium, USP contains 540 mg cromolyn sodium, USP, in purified water. Cromolyn sodium is a hygroscopic, white powder having little odor. It may leave a slightly bitter aftertaste. Cromolyn Sodium, USP Oral Concentrate is clear, colorless, and sterile. It is intended for oral use.

Clarithromycin, cromolyn sodium is disodium 5,5’-[2-hydroxy-trimethylenedioxy]bis[4-oxo-4H-1-benzopyran-2-carboxylate]. The empirical formula is C_{22}H_{22}O_{12}, the molecular weight is 512.34. Its chemical structure is:

Pharmacologic Category: Mast cell stabilizer
Therapeutic Category: Antiallergic

CLINICAL PHARMACOLOGY: In vitro and in vivo animal studies have shown that cromolyn sodium inhibits the release of mediators from sensitized mast cells. Cromolyn sodium acts by inhibiting the release of histamine and leukotrienes (SRS-A) from the mast cell.

Cromolyn sodium has inotropic vasconstrictor, antihistamine, or glucocorticoid activity. Cromolyn sodium is poorly absorbed from the gastrointestinal tract. More than 1% of an administered dose is absorbed by humans after oral administration, the remainder being excreted in the feces. Very little absorption of cromolyn sodium was seen after oral administration of 500 mg by mouth to each of 12 volunteers. From 0.28 to 0.50% of the administered dose was recovered in the first 24 hours of urinary excretion in 3 subjects. The mean urinary excretion of an administered dose over 24 hours in the remaining 9 subjects was 0.45%.

CLINICAL STUDIES: Four randomized, controlled clinical trials were conducted with Cromolyn Sodium, USP in patients with either cutaneous or systemic mastocytosis; two of which utilized a placebo-controlled crossover design, and one utilized an active-controlled (chlorpheniramine plus cimetidine) crossover design, and one utilized a placebo-controlled parallel group design. Due to the rare nature of this disease, only 32 patients qualified for study entry, of whom 32 were considered evaluable.

Clinically significant improvement in gastrointestinal symptoms (diarrhea, abdominal pain) were seen in the majority of patients with either cutaneous or systemic mastocytosis; two of which showed no mutagenic potential in Ames Salmonella/microsome plate assays, mitotic gene conversion in Saccharomyces cerevisiae and in an in vitro cytogenetic study in human peripheral lymphocytes.

In rats, cromolyn sodium showed no evidence of impaired fertility or increased resorptions or major malformations at subcutaneous doses up to 540 mg/kg (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 53 mg/kg three days per week for 15 weeks followed by 17.5 mg/kg three days per week for 37 weeks in hamsters, and at subcutaneous doses up to 75 mg/kg six days per week for 18 months in rats. These doses in mice, hamsters, and rats are less than the maximum recommended daily oral dose in children and adults on a mg/m² basis.

Pregnancy: Pregnancy Category B. In reproductive studies in pregnant mice, rats, and rabbits, cromolyn sodium produced no evidence of fetal malformations at subcutaneous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) and 164 mg/kg in rats (less than the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 485 mg/kg in rabbits (approximately 4 times the maximum recommended daily oral dose in adults on a mg/m² basis). There are, however, no adequate and well controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Drug Interaction During Pregnancy: In pregnant mice, cromolyn sodium alone did not cause significant increases in resorptions or major malformations at subcutaneous doses up to 540 mg/kg (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis). Isopropyl alcohol alone increased both resorptions and major malformations (pymartic cleft palate) at a subcutaneous dose of 2.7 mg/kg (approximately 7 times the maximum recommended daily oral dose in adults on a mg/m² basis).

Information for Patients:

Cromolyn Sodium Oral Concentrate is intended for use in the management of patients with mastocytosis. Use of this product may be associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients. Use of this product may be associated with improvement in abdominal pain, nausea, and itching in some patients.

Important Information:

Indications and Usage:

Cromolyn Sodium, USP is indicated in the management of patients with mastocytosis. Use of this product may be associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients.

Contraindications:

Cromolyn Sodium, USP is contraindicated in those patients who have shown hypersensitivity to cromolyn sodium.

Warnings:

The recommended dosage should be decreased in patients with decreased renal or hepatic function. Severe anaphylactic reactions have occurred rarely in association with cromolyn sodium administration.

Precautions:

In view of the biliary and renal routes of excretion of Cromolyn Sodium, USP, consideration should be given to decreasing the dosage of the drug in patients with impaired renal or hepatic function.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

In carcinogenicity studies in mice, hamsters, and rats, cromolyn sodium had no neoplastic effects at intraperitoneal doses up to 150 mg/kg three days per week for 12 months in mice, at intraperitoneal doses up to 53 mg/kg three days per week for 15 weeks followed by 17.5 mg/kg three days per week for 37 weeks in hamsters, and at subcutaneous doses up to 75 mg/kg six days per week for 18 months in rats. These doses in mice, hamsters, and rats are less than the maximum recommended daily oral dose in children and adults on a mg/m² basis.

Cromolyn sodium showed no mutagenic potential in Ames Salmonella/microsome plate assays, mitotic gene conversion in Saccharomyces cerevisiae and in an in vitro cytogenetic study in human peripheral lymphocytes.

In rats, cromolyn sodium showed no evidence of impaired fertility or increased resorptions or major malformations at subcutaneous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) and 164 mg/kg in rats (less than the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 485 mg/kg in rabbits (approximately 4 times the maximum recommended daily oral dose in adults on a mg/m² basis). There are, however, no adequate and well controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Drug Interaction During Pregnancy: In pregnant mice, cromolyn sodium alone did not cause significant increases in resorptions or major malformations at subcutaneous doses up to 540 mg/kg (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis). Isopropyl alcohol alone increased both resorptions and major malformations (pymartic cleft palate) at a subcutaneous dose of 2.7 mg/kg (approximately 7 times the maximum recommended daily oral dose in adults on a mg/m² basis).

Information for Patients:

Cromolyn Sodium Oral Concentrate is intended for use in the management of patients with mastocytosis. Use of this product may be associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients. Use of this product may be associated with improvement in abdominal pain, nausea, and itching in some patients.

Important Information:

Indications and Usage:

Cromolyn Sodium, USP is indicated in the management of patients with mastocytosis. Use of this product may be associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients.

Contraindications:

Cromolyn Sodium, USP is contraindicated in those patients who have shown hypersensitivity to cromolyn sodium.

Warnings:

The recommended dosage should be decreased in patients with decreased renal or hepatic function. Severe anaphylactic reactions have occurred rarely in association with cromolyn sodium administration.

Precautions:

In view of the biliary and renal routes of excretion of Cromolyn Sodium, USP, consideration should be given to decreasing the dosage of the drug in patients with impaired renal or hepatic function.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

In carcinogenicity studies in mice, hamsters, and rats, cromolyn sodium had no neoplastic effects at intraperitoneal doses up to 150 mg/kg three days per week for 12 months in mice, at intraperitoneal doses up to 53 mg/kg three days per week for 15 weeks followed by 17.5 mg/kg three days per week for 37 weeks in hamsters, and at subcutaneous doses up to 75 mg/kg six days per week for 18 months in rats. These doses in mice, hamsters, and rats are less than the maximum recommended daily oral dose in children and adults on a mg/m² basis.

Cromolyn sodium showed no mutagenic potential in Ames Salmonella/microsome plate assays, mitotic gene conversion in Saccharomyces cerevisiae and in an in vitro cytogenetic study in human peripheral lymphocytes.

In rats, cromolyn sodium showed no evidence of impaired fertility or increased resorptions or major malformations at subcutaneous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) and 164 mg/kg in rats (less than the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 485 mg/kg in rabbits (approximately 4 times the maximum recommended daily oral dose in adults on a mg/m² basis). There are, however, no adequate and well controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Drug Interaction During Pregnancy: In pregnant mice, cromolyn sodium alone did not cause significant increases in resorptions or major malformations at subcutaneous doses up to 540 mg/kg (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis). Isopropyl alcohol alone increased both resorptions and major malformations (pymartic cleft palate) at a subcutaneous dose of 2.7 mg/kg (approximately 7 times the maximum recommended daily oral dose in adults on a mg/m² basis).

Information for Patients:

Cromolyn Sodium Oral Concentrate is intended for use in the management of patients with mastocytosis. Use of this product may be associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients. Use of this product may be associated with improvement in abdominal pain, nausea, and itching in some patients.
Cromolyn Sodium, USP
Oral Concentrate

Psychiatric: psychosis, anxiety, depression, hallucinations, behavior change, insomnia, nervousness.

Heart Rate: tachycardia, premature ventricular contractions (PVCs), palpitations.

Respiratory: pharyngitis, dyspnea.

Miscellaneous: fatigue, edema, unpleasant taste, chest pain, postprandial lightheadedness and lassitude, dysuria, urinary frequency, purpura, hepatic function test abnormal, polycythemia, neutropenia, pancytopenia, tinnitus.

DOSAGE AND ADMINISTRATION: NOT FOR INHALATION OR INJECTION. SEE DIRECTIONS FOR USE.

The usual starting dose is as follows:

Adults and Adolescents (13 Years and Older): Two ampules four times daily, 15 minutes half-hour before meals and at bedtime.

Children 2-12 Years: One ampule four times daily, taken one-half hour before meals and at bedtime.

Pediatric Patients Under 2 Years: Not recommended.

If satisfactory control of symptoms is not achieved within two to three weeks, the dosage may be increased but should not exceed 40 mg/kg/day.

Patients should be advised that the effect of Cromolyn Sodium, USP therapy is dependent upon its administration at regular intervals, as directed.

Maintenance Dose: Once a therapeutic response has been achieved, the dose may be reduced to the minimum required to maintain the patient with a lower degree of symptomatology. To prevent relapses, the dosage should be maintained.

Administration: Cromolyn Sodium, USP should be administered as a solution at least 1/2 hour before meals and at bedtime. After preparation according to the following directions:

1. Open foil pouch by tearing at serrated edge as shown.
2. Remove ampule(s) from the strip.
3. Drink all of the liquid.

Other Adverse Events: Additional adverse events have been reported during studies in other clinical conditions and from worldwide postmarketing experience, and include: dizziness, lightheadedness, rash, pruritus, urticaria, angioedema, anaphylaxis, rash, edema, peptic ulcer disease, mental depression, somnolence, and insomnia. Other less commonly reported events include: conjunctivitis, pharyngitis, cough, rhinitis, sinusitis, viral infections, otitis media, increased sweating, anxiety, dyspepsia, flatulence, glossitis, stomatitis, vomiting, dysphagia, esophagospasm. The incidence of major malformations in neonates born to mothers who had received Cromolyn Sodium, USP during clinical studies were headache and diarrhea, nausea, vomiting, anorexia, and abdominal pain. Neonatal and infantile deaths occurred in 4 of the 87 patients. Pruritus, nausea, vomiting, abdominal pain, and diarrhea occurred in 3 patients and abdominal pain, rash, and irritability in 2 patients each. One report of malaise was also recorded.

To report SUSPECTED ADVERSE REACTIONS, contact Wallace Pharmaceuticals Inc. at 1-877-899-8467 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

ADVERSE REACTIONS: Most of the adverse events reported in mastocytosis patients have been transient and could represent symptoms of the disease. The most frequently reported adverse events in mastocytosis patients who have received Cromolyn Sodium, USP during clinical studies were headache and diarrhea, each of which occurred in 4 of the 87 patients. Pruritus, nausea, and vomiting were each reported in 3 patients and abdominal pain, rash, and irritability in 2 patients each. One report of malaise was also recorded.

To report SUSPECTED ADVERSE REACTIONS, contact Wallace Pharmaceuticals Inc. at 1-877-899-8467 or FDA at 1-800-FDA-4636 or www.fda.gov/medwatch.

Other Adverse Events: Additional adverse events have been reported during studies in other clinical conditions and from worldwide postmarketing experience, and include: dizziness, lightheadedness, rash, pruritus, urticaria, angioedema, anaphylaxis, rash, edema, peptic ulcer disease, mental depression, somnolence, and insomnia. Other less commonly reported events include: conjunctivitis, pharyngitis, cough, rhinitis, sinusitis, viral infections, otitis media, increased sweating, anxiety, dyspepsia, flatulence, glossitis, stomatitis, vomiting, dysphagia, esophagospasm. The incidence of major malformations in neonates born to mothers who had received Cromolyn Sodium, USP during clinical studies were headache and diarrhea, nausea, vomiting, anorexia, and abdominal pain. Neonatal and infantile deaths occurred in 4 of the 87 patients. Pruritus, nausea, vomiting, abdominal pain, and diarrhea occurred in 3 patients and abdominal pain, rash, and irritability in 2 patients each. One report of malaise was also recorded.

Directions for Use:

1. Open foil pouch by tearing at serrated edge as shown.
2. Remove ampule(s) from the strip.
3. Break open ampule(s) and squeeze liquid contents of ampule(s) into a glass of water.
4. Stir solution.
5. Drink all of the liquid.

Pharmacist – Detach Here and Give Instructions to Patient

CPS STW STW-PRS7096-642R01_ec2

Date: 7_20_2015

Wallace Pharmaceuticals Inc.
Somerset, New Jersey 08873-4120

Essentra

1224 N. Church Rd • Somerton, NJ 08087 • 854-439-7300

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

Directions for Use:

1. Open for dust at bottom edge as shown.
2. Remove ampule(s).
3. Open the ampule off the tabbed top section by twisting off the tabbed top section of the ampule into a glass.
4. Squeeze liquid into a glass. Swirl to mix. Discard the empty ampule.