APPROVED BY: _____ DATE _____

APPROVED BY: _____ DATE _____

FRONT

12.000 in

1.625 in

1.625 in

1.625 in

1.625 in

6.500 in

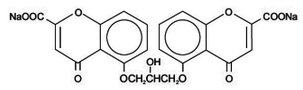
Cromolyn Sodium Oral Solution (Concentrate)

℞ Only

FOR ORAL USE ONLY – NOT FOR INHALATION OR INJECTION. MUST BE DILUTED.

DESCRIPTION: Each 5 mL ampule of Cromolyn Sodium Oral Solution (Concentrate) contains 100 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 Oral Solution (Concentrate) is clear, colorless, and sterile. It is intended for oral use.

Chemically, cromolyn sodium is disodium 5,5'-[(2-hydroxy-trimethylene) dioxy]bis[4-oxo-4H-1-benzopyran-2-carboxylate]. The empirical formula is $C_{23}H_{14}Na_2O_{11}$; 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 no intrinsic vasoconstrictor, antihistamine, or glucocorticoid activity.

Cromolyn sodium is poorly absorbed from the gastrointestinal tract. No 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 Oral Solution (Concentrate) in patients with either cutaneous or systemic mastocytosis; two of which utilized a placebo-controlled crossover design, 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 36 patients qualified for study entry, of whom 32 were considered evaluable. Consequently, formal statistical analyses were not performed. Clinically significant improvement in gastrointestinal symptoms (diarrhea, abdominal pain) were seen in the majority of patients with some improvement also seen for cutaneous manifestations (urticaria, pruritus, flushing) and cognitive function. The benefit seen with Cromolyn Sodium Oral Solution (Concentrate) 200 mg QID was similar to chlorpheniramine (4 mg QID) plus cimetidine (300 mg QID) for both cutaneous and systemic symptoms of mastocytosis.

Cromolyn Sodium Oral Solution (Concentrate)

Clinical improvement occurred within 2-6 weeks of treatment initiation and persisted for 2-3 weeks after treatment withdrawal. Cromolyn Sodium Oral Solution (Concentrate) did not affect urinary histamine levels or peripheral eosinophilia, although neither of these variables appeared to correlate with disease severity. Positive clinical benefits were also reported for 37 of 51 patients who received Cromolyn Sodium Oral Solution (Concentrate) in United States and foreign humanitarian programs.

INDICATIONS AND USAGE: Cromolyn Sodium Oral Solution (Concentrate) is indicated in the management of patients with mastocytosis. Use of this product has been associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients.

CONTRAINDICATIONS: Cromolyn Sodium Oral Solution (Concentrate) 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 may occur rarely in association with cromolyn sodium administration.

PRECAUTIONS: In view of the biliary and renal routes of excretion of Cromolyn Sodium Oral Solution (Concentrate), 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 adults and children on a mg/m^2 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 at subcutaneous doses up to 175 mg/kg in males (approximately equal to the maximum recommended daily oral dose in adults on a mg/m^2 basis) and 100 mg/kg in females (less than the maximum recommended daily oral dose in adults on a mg/m^2 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/m^2 basis) and 164 mg/kg in rats (less than the maximum recommended daily oral dose in adults on a mg/m^2 basis) or at intravenous doses up to 485 mg/kg in rabbits (approximately 4 times the maximum recommended daily oral dose in

Cromolyn Sodium Oral Solution (Concentrate)

adults on a mg/m^2 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/m^2 basis). Isoproterenol alone increased both resorptions and major malformations (primarily cleft palate) at a subcutaneous dose of 2.7 mg/kg (approximately 7 times the maximum recommended daily inhalation dose in adults on a mg/m^2 basis). The incidence of major malformations increased further when cromolyn sodium at a subcutaneous dose of 540 mg/kg was added to isoproterenol at a subcutaneous dose of 2.7 mg/kg. No such interaction was observed in rats or rabbits.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Cromolyn Sodium Oral Solution (Concentrate) is administered to a nursing woman.

Pediatric Use: In adult rats no adverse effects of cromolyn sodium were observed at oral doses up to 6144 mg/kg (approximately 25 times the maximum recommended daily oral dose in adults on a mg/m^2 basis). In neonatal rats, cromolyn sodium increased mortality at oral doses of 1000 mg/kg or greater (approximately 9 times the maximum recommended daily oral dose in infants on a mg/m^2 basis) but not at doses of 300 mg/kg or less (approximately 3 times the maximum recommended daily oral dose in infants on a mg/m^2 basis). Plasma and kidney concentrations of cromolyn after oral administration to neonatal rats were up to 20 times greater than those in older rats. In term infants up to six months of age, available clinical data suggest that the dose should not exceed 20 mg/kg/day. The use of this product in pediatric patients less than two years of age should be reserved for patients with severe disease in which the potential benefits clearly outweigh the risks.

Geriatric Use: Clinical studies of Cromolyn Sodium Oral Solution (Concentrate) did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

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 Oral Solution (Concentrate) during clinical studies were headache and diarrhea, each of which occurred in 4 of the 87

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

Patient Instructions

Cromolyn Sodium Oral Solution (Concentrate)

FOR ORAL USE ONLY – NOT FOR INHALATION OR INJECTION. MUST BE DILUTED.

How to Use Cromolyn Sodium Oral Solution (Concentrate):
As with all prescription drugs, follow the directions for dosage that your physician recommends.

The effect of Cromolyn Sodium Oral Solution (Concentrate) therapy is dependent upon its administration at REGULAR intervals, for as long as recommended by your physician.

Usual Starting Dose:

Adults and Adolescents (13 Years and Older):
Two ampules four times daily, taken one-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.

Note:
Your physician may decide to increase OR decrease your dosage to achieve optimum results with Cromolyn Sodium Oral Solution (Concentrate). However, do not change your dose or stop taking Cromolyn Sodium Oral Solution (Concentrate) without first consulting your physician.

Care & Storage:
Cromolyn Sodium Oral Solution (Concentrate) should be stored between 20°-25°C (68°-77°F) and protected from light. Do not use if it contains a precipitate (particles or cloudiness) or becomes discolored. Keep out of the reach of children.

Store ampules in foil pouch until ready for use.

(over)

3.0 in

3.0 in

3.0 in

3.0 in

JRCI
JR COLE INDUSTRIES
435 Minuet Lane
Charlotte, NC 28217
704-523-6622 jrcole.com

• ROLL LABEL DIVISION • JOB INFORMATION •

PO#: 22105756
LT#: L45428
ARTIST: alex
CORE SIZE:
MAX OD:
PN: RPIN0150
STOCK:
SCREEN: 150L HD
ESKO RIP DPI: 4000
LABEL: INSERT
CUSTOMER: THE RITEDOSE CORPORATION
ITEM DESC.: RDP Cromolyn Sodium Oral (Ailex ANDA)

JRCI PROOF NOTIFICATION

Due to the inherent nature of Digital Proofing, this proof does not reflect actual color achievable on press, refer to your Pantone Chart. Please examine this proof carefully for Copy, Layout, Die Size, Color Break, TTB, FDA, USDA, or any other agency regulations. **THE CONTENT AND ACCURACY ON THIS PROOF IS YOUR RESPONSIBILITY.** Please verify and sign this proof for approval. No production work will begin without signed approval.

ORDER OF COLOR SEPARATIONS

1 Black

DATE
10/6/2021
DATE CREATED
10/4/21
REVISIONS
R1: 10/6/21
R2:
R3:
R4:
R5:
R6:
PDF SIZE
DIELINE

QUALITY ASSURANCE

ART QA	DATE:
STEP	DATE:
STEP QA	DATE:
PLATE	DATE:
PLATE QA	DATE:

UNWIND #
N/A

APPROVED BY: _____ DATE _____

APPROVED BY: _____ DATE _____

BACK

12.000 in

6.500 in

Recycling Information: Cromolyn Sodium Oral Solution (Concentrate) ampules are made with a low density polyethylene plastic (recycling material code: ♳ LDPE).

Call your doctor for medical advice about side effects. You may report side effects to Ritedose Pharmaceuticals, LLC at 1-855-806-3300 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Directions for Use:

1. Open foil pouch by tearing at serrated edge as shown.

2. Remove ampule(s) from the strip.

3. Open the ampule by twisting off the tabbed top section.

4. Squeeze liquid contents into a glass of water.
Stir solution.
Drink all of the liquid.
Discard the empty ampule.

Distributed by:
Ritedose Pharmaceuticals, LLC
Columbia, SC 29203

Rev.: October 2021 RPIN0150

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

Cromolyn Sodium
Oral Solution
(Concentrate)

patients. Pruritus, nausea, and myalgia 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 Ritedose Pharmaceuticals, LLC at 1-855-806-3300 or FDA at 1-800-FDA-1088 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. In most cases the available information is incomplete and attribution to the drug cannot be determined. The majority of these reports involve the gastrointestinal system and include: diarrhea, nausea, abdominal pain, constipation, dyspepsia, flatulence, glossitis, stomatitis, vomiting, dysphagia, esophagospasm.

Other less commonly reported events (the majority representing only a single report) include the following:

Skin:	pruritus, rash, urticaria/angioedema, erythema/ burning, photosensitivity
Musculoskeletal:	arthralgia, myalgia, stiffness/weakness of legs
Neurologic:	headache, dizziness, hypoesthesia, pares - thesia, migraine, convulsions, flushing
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 lethargy, dysuria, urinary frequency, purpura, hepatic function test abnormal, polycythemia, neutropenia, pancytopenia, tinnitus, lupus erythematosus (LE) syndrome

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, taken one-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

Cromolyn Sodium
Oral Solution
(Concentrate)

40 mg/kg/day. Patients should be advised that the effect of Cromolyn Sodium Oral Solution (Concentrate) 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 Oral Solution (Concentrate) should be administered as a solution at least 1/2 hour before meals and at bedtime after preparation according to the following directions:

1. Break open ampule(s) and squeeze liquid contents of ampule(s) into a glass of water.
2. Stir solution.
3. Drink all of the liquid.

HOW SUPPLIED: Cromolyn Sodium Oral Solution (Concentrate) is an unpreserved, colorless solution supplied in a low density polyethylene plastic unit dose ampule with 8 ampules per foil pouch.

Each 5 mL ampule contains 100 mg cromolyn sodium, USP, in purified water.

NDC 76204-025-96 96 ampules x 5 mL
(12 pouches x 8 ampules)

Cromolyn Sodium Oral Solution (Concentrate) should be stored between 20° – 25°C (68° – 77°F) [see USP Controlled Room Temperature] and protected from light. Do not use if it contains a precipitate or becomes discolored. Keep out of the reach of children.

Store ampules in foil pouch until ready for use.

RITEDOSE PHARMACEUTICALS

Manufactured by:
The Ritedose Corporation
Columbia, SC 29203 for
Ritedose Pharmaceuticals, LLC
Columbia, SC 29203

Rev.: October 2021
RPIN0150

Cromolyn Sodium
Oral Solution
(Concentrate)

LBL052100

1.625 in
1.625 in
1.625 in
1.625 in

3.0 in
3.0 in
3.0 in
3.0 in

JRCI JR COLE INDUSTRIES
435 Minuet Lane
Charlotte, NC 28217
704-523-6622 jrcole.com

• ROLL LABEL DIVISION • JOB INFORMATION •

PO#: 22105756
LT#: L45428
ARTIST: alex
CORE SIZE:
MAX OD:
PN: RPIN0150
STOCK:
SCREEN: 150L HD
ESKO RIP DPI: 4000
LABEL: INSERT
CUSTOMER: THE RITEDOSE CORPORATION
ITEM DESC.: RDP Cromolyn Sodium Oral (Ailex ANDA)

DATE: 10/6/2021
DATE CREATED: 10/4/21
REVISIONS: R1: 10/6/21 R2: R3: R4: R5: R6:

QUALITY ASSURANCE

ART QA	DATE:
STEP	DATE:
STEP QA	DATE:
PLATE	DATE:
PLATE QA	DATE:

JRCI PROOF NOTIFICATION

Due to the inherent nature of Digital Proofing, this proof does not reflect actual color achievable on press, refer to your Pantone Chart. Please examine this proof carefully for Copy, Layout, Die Size, Color Break, TTB, FDA, USDA, or any other agency regulations. **THE CONTENT AND ACCURACY ON THIS PROOF IS YOUR RESPONSIBILITY.** Please verify and sign this proof for approval. No production work will begin without signed approval.

ORDER OF COLOR SEPARATIONS

1 Black

PDF SIZE

DIELINE

UNWIND #

N/A