Long-term studies of cromolyn sodium have shown that cromolyn sodium inhibits the degranulation of sensitized mast cells which occurs after exposure to specific antigens. Cromolyn sodium acts by inhibiting the release of histamine and SRS-A (slow-reacting substance of anaphylaxis) from the mast cell. Another activity demonstrated in vitro is the capacity of cromolyn sodium to inhibit the degranulation of non-sensitized rat mast cells by phospholipase A and the subsequent release of chemical mediators. Another study showed that cromolyn sodium did not inhibit the enzymatic activity of released phospholipase A on its specific substrate. Cromolyn sodium has no intrinsic vasoconstrictor, antihistamine, or anti-inflammatory activity. Cromolyn sodium is poorly absorbed. When multiple doses of cromolyn sodium ophthalmic solution are instilled into normal rabbit eyes, less than 0.07% of the administered dose of cromolyn sodium is absorbed into the systemic circulation (presumably by way of the eye, nasal passages, buccal cavity and gastrointestinal tract). Treatment of rats (less than 0.01%) of the cromolyn sodium dose penetrate into the aqueous humor and clearance from this chamber is virtually complete within 24 hours after treatment is stopped. In normal volunteers, analysis of drug excretion indicates that approximately 0.003% of cromolyn sodium is absorbed following administration to the eye.

INDICATIONS AND USAGE
Cromolyn Sodium Ophthalmic Solution is indicated in the treatment of vernal keratoconjunctivitis, vernal conjunctivitis, and vernal keratitis.

CONTRAINDICATIONS
Cromolyn Sodium Ophthalmic Solution is contraindicated in those patients who have shown hypersensitivity to cromolyn sodium or to any of the other ingredients.

PRECAUTIONS
General: Patients may experience a transient stinging or burning sensation following application of Cromolyn Sodium Ophthalmic Solution. The recommended frequency of administration should not be exceeded (see DOSAGE AND ADMINISTRATION).

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENTS
Information for the Patient
Cromolyn Sodium Ophthalmic Solution, USP 4% (STERILE) is to be used only as directed by your physician.

1. Thoroughly wash your hands.
2. Remove safely seal (Figure 1).
3. Remove cap (Figure 2).
4. Sit or stand comfortably, with your head tilted back (Figure 3).
5. Open eyes, look up, and draw the lower lid of your eye down gently with your index finger (Figure 4).
6. Hold the Cromolyn Sodium Ophthalmic Solution, USP 4% bottle upside down. Place dropper tip as close as possible to the lower eyelid and gently squeeze out the prescribed number of drops (Figure 5).
7. Do not touch the eye or eyelid with the dropper tip.
8. Blink a few times to make sure the eye is covered with the solution.
9. Close your eye and remove any excess solution with a clean tissue.
10. Repeat process in the other eye.
Cromolyn sodium showed no mutagenic potential in the Ames Salmonella/microsome plate assays, mitotic gene conversion in Saccharomyces cerevisiae and in an in vitro cytogenetic study in human peripheral lymphocytes. No evidence of impaired fertility was shown in laboratory reproduction studies conducted subcutaneously in rats at the highest doses tested, 175 mg/kg/day (1050 mg/m²) in males and 100 mg/kg/day (600 mg/m²) in females. These doses are approximately 37 and 21 times the maximum daily human dose, respectively, based on mg/m².

**Pregnancy**

Teraotogenic effects: Pregnancy Category B. Reproduction studies with cromolyn sodium administered subcutaneously to pregnant mice and rats at maximum daily doses of 540 mg/kg (1620 mg/m²) and 164 mg/kg (586 mg/m²), respectively, and intravenously to rabbits at a maximum daily dose of 485 mg/kg (5850 mg/m²) produced no evidence of fetal malformation. These doses represent approximately 57, 35, and 205 times the maximum daily human dose, respectively, on a mg/m² basis. Adverse fetal effects (increased resorption and decreased fetal weight) were noted at virtually all perinatal doses that produced maternal toxicity. 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.

**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 ophthalmic solution is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness in pediatric patients below the age of 4 years have not been established.

**ADVERSE REACTIONS**

The most frequently reported adverse reaction attributed to the use of cromolyn sodium ophthalmic solution, on the basis of recurredence following readministration, is transient ocular stinging or burning upon instillation. The following adverse reactions have been reported as infrequent events. It is unclear whether they are attributed to the drug:

- Conjunctival injection; watery eyes; itchy eyes; dryness around the eye; puffy eyes; eye irritation; and styes.

Immediate hypersensitivity reactions have been reported rarely and include dyspnea, edema, and rash.

The following adverse reactions have been reported as infrequent events. It is unclear whether they are

attributed to the drug:

- Immediate hypersensitivity reactions have been reported rarely and include dyspnea, edema, and rash.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DOSE AND ADMINISTRATION**

The dose is 1 or 2 drops in each eye 4 to 6 times a day at regular intervals.

One drop contains approximately 1.6 mg cromolyn sodium.

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

Symptomatic response to therapy (decreased itching, tearing, redness, and discharge) is usually evident within a few days, but longer treatment for up to six weeks is sometimes required. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement.

If required, corticosteroids may be used concomitantly with Cromolyn Sodium Ophthalmic Solution.

**FOR OPHTHALMIC USE ONLY**

**HOW SUPPLIED**

Cromolyn Sodium Ophthalmic Solution, USP 4% is supplied in a plastic bottle individually cartoned with a white cap and controlled drop tip in the following sizes:

- 10 mL bottle (NDC 24208-961-10)


**KEEP OUT OF REACH OF CHILDREN.**

**SPECIAL TIPS**

1. Avoid placing Cromolyn Sodium Ophthalmic Solution, USP 4% solution directly on the cornea (the area just over the pupil), because it is especially sensitive. You will find the administration of eye drops more comfortable if you place the drops just inside the lower eyelid, as shown in Figure 5 on the previous page.

2. To avoid contamination of the solution, do not touch dropper tip to the eye, fingers or any other surface. Replace cap after use. It is recommended that any remaining contents be discarded after the treatment period prescribed by your physician.


5. Do not use with any other ocular medication unless directed by your physician. Do not wear contact lenses during treatment with Cromolyn Sodium Ophthalmic Solution, USP 4%.

**PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENTS**

- **DO NOT USE IF IMPRINTED NECKBAND IS NOT INTACT.**


**KEEP OUT OF REACH OF CHILDREN.**

Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC, Bridgewater, NJ 08807 USA

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