PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

OPTICROM®

Sodium Cromoglycate

Ophthalmic Solution 2% w/v

Manufacturer's standard

Manufacturer's standard

Allergan Inc.
Markham, Ontario
L6G 0B5

Date of Initial Approval:
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RECENT MAJOR LABEL CHANGES

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

OPTICROM® (sodium cromoglycate) Ophthalmic Solution 2% is indicated to help relieve and prevent symptoms associated with allergic conjunctivitis or hay fever conjunctivitis.

1.1 Pediatrics

Pediatrics (0 – 5 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of OPTICROM® in pediatric patients below the age of 5 years has not been established.

1.2 Geriatrics

Geriatrics (> 65 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

OPTICROM® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

The effect of OPTICROM® therapy is dependent upon its administration at regular intervals as directed in the labelling.

Symptomatic response to treatment (decreased itching, tearing, redness and discharge) is usually evident within 2-3 days. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement.

3.2 Recommended Dose and Dosage Adjustment

Adults and children over 5 years: *Two* drops in each eye 4 times daily at regular intervals. One drop contains approximately 0.8 mg sodium cromoglycate.

3.3 Missed Dose

No data available for this section.

4 OVERDOSAGE

There have been no reported cases in humans of overdosage of the drug. Symptomatic treatment is suggested should accidental ingestion occur.

For management of a suspected drug overdose, contact your regional poison control centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
topical ophthalmic	solution 2% w/v	benzalkonium chloride, edetate disodium and purified water

OPTICROM® is a clear, colourless to pale yellow sterile solution supplied in 10mL plastic dropper bottles.

6 WARNINGS AND PRECAUTIONS

General
The recommended frequency of administration should not be exceeded.

OPTICROM® should only be used for allergic conditions of the eye. In some instances irritation or redness may be due to serious eye conditions such as infection, foreign body in the eye, or other mechanical or chemical corneal trauma requiring the attention of a doctor. If you experience eye pain, changes in vision, pain on exposure to light, acute redness of the eye, excessive discharge, abnormal pupils, if condition worsens or if relief is not obtained within 72 hours consult your doctor immediately.

Any remaining contents should be discarded four weeks after opening. Do not touch dropper tip to any surface since this may contaminate the solution.

Ophthalmologic
During treatment with OPTICROM® (sodium cromoglycate) Ophthalmic Solution 2%, soft contact lenses should not be worn.

6.1 Special Populations

6.1.1 Pregnant Women

There has been to date, no adequate and well controlled studies in pregnant women.

6.1.2 Breast-feeding

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 OPTICROM® is administered to a nursing woman.

6.1.3 Pediatrics

Pediatrics (0 – 5 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of OPTICROM® in pediatric patients below the age of 5 years has not been established.

6.1.4 Geriatrics

No data available.

7 ADVERSE REACTIONS

7.1 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The most frequently reported adverse reaction attributed to the use of OPTICROM® on the basis of reoccurrence following administration is transient ocular stinging or burning upon instillation.

The following adverse reactions have been reported as infrequent events; conjunctival injection, watery eyes, itchy eyes, dryness around the eye, puffy eyes, eye irritation and sties. It is unclear whether they are attributable to the drug.

7.2 Post-Market Adverse Reactions

The reported post-marketing adverse reactions are as follows: blurred vision, and hypersensitivity reaction including generalized erythema, signs and symptoms related to angioedema and eye allergy.

8 DRUG INTERACTIONS

8.1 Drug-Drug Interactions

Sodium cromoglycate has been used in association with other ophthalmic solutions in the rabbit including mydriatrics, antibiotics, steroids, vasocontrictors and astringents. No drug-drug interactions have been observed in the rabbit eyes.

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

In the immediate allergic reaction (Type I), the union of antigen with reaginic antibody leads to the formation and release of mediators of the local anaphylactic reaction. The principal effect of sodium cromoglycate is its specific ability to stabilize the membrane of the mast cell and thus prevent the release of mediators of anaphylaxis. The action appears to be specific for reaginic (immediate type) antigen/antibody reactions. No direct effect has been demonstrated on other types of immune reactions (Type II, III, and IV).

9.2 Pharmacodynamics

Sodium cromoglycate has no vasoconstriction, anti-histaminic or anti-inflammatory activity. Within 2-3 days of commencing treatment one can expect improvement in the signs and symptoms of seasonal allergic conjunctivitis (itching, tearing, congestion, etc.) in most patients. Continued therapy will usually keep the patient free from ophthalmic allergy symptoms during the challenge period.

9.3 Pharmacokinetics

Absorption: Sodium cromoglycate is poorly absorbed. When multiple doses of sodium cromoglycate ophthalmic solution are instilled into the rabbit eyes less than 0.01% of the administered dose of sodium cromoglycate is absorbed into the systemic circulation (presumably by way of the eye, nasal passages, buccal cavity and gastrointestinal tract). Trace amounts (less than 0.01%) of the sodium cromoglycate dose penetrated 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 approximately 0.03% of sodium cromoglycate is absorbed following administration to the eye.

Distribution: A study on corneal epithelium wound healing in albino rabbits failed to demonstrate any significant difference in the rate of corneal re-epithelialisation between sodium cromoglycate ophthalmic solution, sterile saline solution, no treatment and an ophthalmic corticosteroid.

Metabolism: Sodium cromoglycate is taken up by the liver and the kidneys.

Elimination: Sodium cromoglycate is excreted unchanged via the bile and urine.

10 STORAGE, STABILITY AND DISPOSAL

Store at 15º to 30°C.
Protect from direct sunlight.
Discard opened bottle after 4 weeks.

11 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

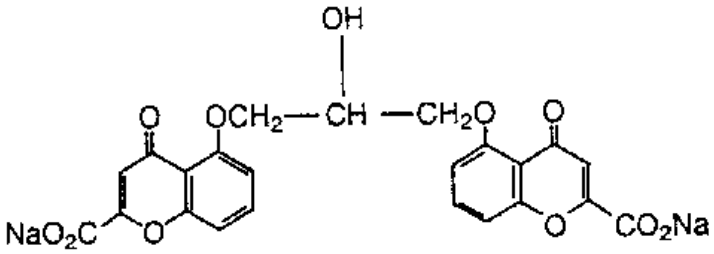
Drug Substance

Proper name: sodium cromoglycate (Ph. Eur.)
cromolyn sodium (USP)

Chemical name: Disodium 4, 4'-dioxo-5,5'-(2-hydroxytri-methylenedioxy) di (chromene-2-carboxylate)

Molecular formula and molecular mass: $C_{23}H_{14}Na_2O_{11}$ and 512.3

Structural formula:



Physicochemical properties: sodium cromoglycate is a white hygroscopic powder, soluble in 20 parts of water and the resulting solution is neutral.

13 NON-CLINICAL TOXICOLOGY

Acute Toxicity
The LD_{50} was approximately 4000 mg/kg administered peritoneally in mice, rats, guinea pigs, hamsters and rabbits, and intravenously in monkeys.

Subacute and Chronic Toxicity:

Studies of Sodium Cromoglycate Ophthalmic Solution:
A 4% solution of sodium cromoglycate was instilled into the rabbit eyes up to 4 times daily for 28 days. No signs of irritation to the cornea, iris or conjunctiva were seen. No drug related macroscopic or microscopic changes were observed.

New Zealand albino rabbits and squirrel monkeys received 2% sodium cromoglycate two to ten times daily for 3 months and 6 months respectively. No fundoscopic changes were seen. Detailed histopathological examination of the eyes and related structures revealed no local irritation or toxic effects of treatment. Rats received sodium cromoglycate subcutaneously for 90 days at daily doses of 30, 78 and 198 mg/kg. Renal tubular damage was noted in some rats at the two higher dose levels. Other toxic effects that were seen at the higher dose were that the growth rates were depressed and a significant increase in weight of the hearts and adrenals. No toxic effects were detected in the group dosed at 30 mg/kg.

Rhesus Monkeys were given intravenous injection of sodium cromoglycate for 180 days at daily doses of 2, 10 and 50 mg/kg. No toxic effects were observed.

Carcinogenesis, Mutagenesis and Reproduction
Long term studies in mice (12 months intraperitoneal treatment followed by six months observation), hamsters (12 months intraperitoneal treatment) followed by 12 months observation and rats (18 months subcutaneous treatment) showed no neoplastic effect of sodium cromoglycate.

No evidence of chromosomal damage or cytotoxity was obtained in various mutagenesis studies.

No evidence of impaired fertility was shown in laboratory reproduction studies.

Conclusion from the Toxicology Studies
Sodium cromoglycate has a remarkably low order of toxicity as demonstrated in many systems. The safety margin thus established, gives confidence that extended use in humans does not constitute a significant toxicological hazard.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

OPTICROM®
Sodium Cromoglycate Ophthalmic Solution

Read this carefully before you start taking **OPTICROM®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **OPTICROM®**.

What is OPTICROM® used for?

- **Helps prevent and relieve the symptoms of red, itchy, watery eyes due to allergies.**

How does OPTICROM® work?

Most allergic reactions are caused by exposure to substances in the environment. These include pollens, mold spores, house dust and animal dander. Allergy symptoms include irritation, grittiness, redness and excessive watering of the eyes. Your allergy symptoms may only occur at certain times of the year in reaction to a particular pollen. These are seasonal allergies.

Special (mast) cells which are present in the mucus membranes of your nose and eyes react to allergens such as pollen or dust by releasing histamine. This release of histamine then sets off the whole cycle of allergic symptoms.

OPTICROM® works by blocking the release of histamine from the mast cells. This helps prevent the allergic response from taking place and so helps prevent the symptoms of red, itchy, watery eyes. OPTICROM® use should be started prior to your usual allergy season to gain the maximum preventative effect. In the case of unexpected exposure, begin treatment immediately at the first onset of symptoms. To maintain the symptom-free effect, it should be taken continuously throughout the season even when you feel you are free from your symptoms.

What are the ingredients in OPTICROM®?

Medicinal ingredients: sodium cromoglicate.
Non-medicinal ingredients: benzalkonium chloride, ~~and~~ edetate disodium and purified water.

OPTICROM® comes in the following dosage forms:

Ophthalmic solution 2%.

Do not use OPTICROM® if:

- You are hypersensitive to sodium cromoglycate or any of the other ingredients in OPTICROM®.
- You are allergic to any component of the OPTICROM® container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take OPTICROM®. Talk about any health conditions or problems you may have, including if you:

- Have irritation or redness due to serious eye conditions such as infection, foreign body in the eye, or other mechanical or chemical corneal injury.
- Experience eye pain, changes in vision, pain on exposure to light, eye redness that does not last, excessive or milky (non-clear) discharge, abnormal pupils.
- Only one eye is affected.
- You have no nose symptoms.

Other warnings you should know about:
- OPTICROM® should only be used for allergic conditions of the eye.
- If condition worsens or if relief is not obtained within 72 hours consult your doctor immediately.
- Soft contact lenses should not be worn during treatment with OPTICROM®.
- As with any drug, if you are pregnant or nursing a baby, seek a doctor's advice before using OPTICROM®.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take OPTICROM®:
OPTICROM® are easily applied to the eye. First, you should tilt your head back and gently pull your lower lid down. Then carefully squeeze out two drops into each eye while looking up toward your forehead. Close your eyes gently for a few moments.

OPTICROM® should be used continually throughout your usual allergy season, even when you feel you are free from symptoms. Continued use will help ensure you remain symptom-free.

To maintain sterility, prevent touching the tip of the dropper with the eye or other surfaces.

Usual dose:
Adults and children over 5 years:
- Apply two drops into each eye 4 times per day at regular intervals.
- Do not use more than 8 drops in each eye in 24 hours.

Overdose:
There have been no reported cases in humans of overdose with OPTICROM®.

If you think you have taken too much OPTICROM®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you miss a dose, take it as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not take a double dose to make up for a missed dose.

What are possible side effects from using OPTICROM®?
These are not all the possible side effects you may feel when taking OPTICROM®. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:
Eye Disorders

- mild stinging in the eye
- burning sensation in the eye
- eye redness
- watery eyes
- itchy eyes
- dryness around the eye
- puffy eyes
- eye irritation
- blurred vision
- sties

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Allergic reaction: skin redness, difficulty breathing, and eye swelling			X

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at 15º to 30°C and protect from direct sunlight. Discard the opened bottle after four weeks.

Keep out of reach and sight of children.

If you want more information about OPTICROM®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and

includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website: www.allergan.ca, or by calling 1-800-668-6424.

This leaflet was prepared by Allergan Inc.

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