

PRODUCT MONOGRAPH

OPTICROM®

Sodium Cromoglycate Ophthalmic Solution 2% w/v

ANTI-ALLERGIC

Allergan Inc.
Markham, Ontario
L3R 9R9

#049458

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February 17, 1997

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Sodium Cromoglycate Ophthalmic Solution 2% w/v

Therapeutic Classification:
ANTI-ALLERGIC

ACTIONS AND CLINICAL PHARMACOLOGY

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).

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.

INDICATIONS AND CLINICAL USE

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

CONTRAINDICATIONS

OPTICROM® (sodium cromoglycate) Ophthalmic Solution 2% is contraindicated in those patients who have shown hypersensitivity to sodium cromoglycate or to benzalkonium chloride.

WARNINGS

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.

PRECAUTIONS

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

Use in Children

Safety and effectiveness in children below the age of 5 years has not been established.

Use in Pregnancy

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

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 OPTICROM® is administered to a nursing woman.

Drug Interactions

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

ADVERSE REACTIONS

The most frequently reported adverse reaction attributed to the use of OPTICROM® on the basis of recurrence 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.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

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.

Dosage:

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.

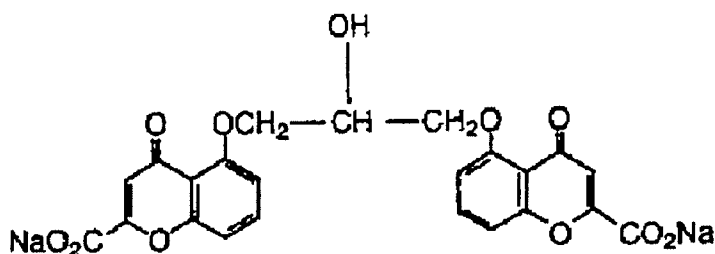
PHARMACEUTICAL INFORMATION

Drug Substance:

Proper Name: sodium cromoglycate

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

Structural Formula:



Molecular Formula: C₂₃H₁₄Na₂O₁₁

Molecular Weight: 512.3

Physical Form: sodium cromoglycate is a white hygroscopic powder.

Solubility: Soluble in 20 parts of water and the resulting solution is neutral.

Composition:

Contains sodium cromoglycate 2%, edetate disodium and benzalkonium chloride 0.01% as a preservative.

Stability and Storage Recommendations

Store at 15° to 30°C.

Protect from direct sunlight.

Discard opened bottle after 4 weeks.

AVAILABILITY OF DOSAGE FORMS

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

INFORMATION TO THE CONSUMER

OPTICROM®

Sterile sodium cromoglycate ophthalmic solution 2% w/v

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

What are Allergies?

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.

Why do they occur?

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.

How Can you Tell If You Have Allergies?

If this is the first time you have had the symptoms, you should confirm the diagnosis with your doctor.

It is likely that your symptoms are due to allergies if:

- Both eyes are affected
- You have a runny or congested nose as well
- Your sight is not affected

BUT if:

- Only one eye is affected
- You have no nose symptoms
- Your sight is affected
- You feel pain in your eye(s)

you cannot be sure your symptoms are due to allergies and should consult your doctor before you use OPTICROM®.

How does OPTICROM® work?

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.

How to Use OPTICROM®:

Adults and children over 5 years: *Two* drops into each eye 4 times daily. Do not exceed recommended dosage.

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. Discard the opened bottle after four weeks. Keep out of reach of children.

Caution:

Those people who are sensitive may experience mild irritation of the eye, during the first few days of use. These effects are infrequent, minimal and reversible.

OPTICROM® should not be used with any other eye treatment except on the advice of a doctor.

Warning:

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 injury 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 or milky (non-clear) discharge, abnormal pupils, if condition worsens or if relief is not obtained with 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 this product.

Contains: Sodium cromoglycate 2%, edetate disodium and benzalkonium chloride 0.01% as a preservative.

Store at 15° to 30°C and protect from direct sunlight.

Product Monograph is available to physician and pharmacists on request.

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PHARMACOLOGY

In vivo and *in vitro* animal studies have shown that sodium cromoglycate inhibits the degranulation of sensitized mast cells which occurs after exposure to specific antigens. Sodium cromoglycate acts by inhibiting the release of histamine and SRS-A (slow reacting substance of anaphylaxis) from the mast cells.

In vitro sodium cromoglycate demonstrated that it has the capacity to inhibit the degranulation of non-sensitized rat mast cells by phospholipase A and the subsequent release of chemical mediators. Sodium cromoglycate did not inhibit the enzymatic activity of released phospholipase A on its specific substrate.

Sodium cromoglycate has no intrinsic vasoconstrictor, antihistaminic or anti-inflammatory activity.

Absorption, Distribution and Excretion

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.

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.

Sodium cromoglycate is taken up by the liver and the kidneys and excreted unchanged via the bile and urine.

TOXICOLOGY

Acute Toxicity

The LD₅₀ 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 cytotoxicity 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.

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