PRODUCT MONOGRAPH

^{Pr}NALCROM®
(Sodium Cromoglycate Capsules)

100 mg Capsules

Oral Anti-Allergic Agent

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PrNALCROM®

Sodium Cromoglycate Capsules

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	capsule 100 mg	gelatin, iron oxide

THERAPEUTIC CLASSIFICATION

Oral Anti-Allergic Agent

ACTIONS

Sodium cromoglycate is considered to exert a stabilizing effect upon mast cells capable of releasing mediators. In gastrointestinal disease the release of mediators causes a local inflammation which can either result in gastrointestinal symptoms or may allow absorption of antigenic material leading to systemic allergic reactions.

Sodium cromoglycate has no antihistaminic or anti-inflammatory activity.

INDICATIONS

NALCROM is indicated for the treatment of food allergy (where adequate investigations have been performed to determine sensitivity to one or more ingested allergens) in conjunction with restriction of main causative allergens.

CONTRAINDICATIONS

NALCROM is contraindicated in patients with known hypersensitivity to sodium cromoglycate or to any of the excipients (see the Summary Product Information table).

WARNINGS

The safety of capsules of granulated sodium cromoglycate (100 mg) in pregnancy, and for the treatment of children under two years, has not yet been established.

The recommended dosage should be decreased in patients with decreased renal or hepatic function. Severe anaphylactic reactions may occur rarely in association with sodium cromoglycate administration.

Withdrawal of NALCROM Therapy:

Patients should be warned against suddenly discontinuing therapy when symptoms have been partially or completely controlled.

The optimum dose required to maintain remission will need to be determined for each patient, but it is probably not less than two capsules four times daily.

PRECAUTIONS

Patients with a history of anaphylactic shock or similar life-threatening reaction to foods should not rely upon NALCROM to protect them.

The safety of capsules of granulated sodium cromoglycate (100 mg) in pregnancy, and for the treatment of children under two years, has not yet been established. The drug should not be used in such patients unless, in the opinion of the prescribing physician, the potential benefits outweigh the possible hazards.

Experience in patients is limited and therefore they should be carefully observed while undergoing treatment.

It is not known whether sodium cromoglycate is excreted in the breast milk but on the basis of its physico-chemical properties this is considered unlikely. There is no information to suggest that the use of sodium cromoglicate has any undesirable effects on the baby.

The effect of sodium cromoglycate has been studied on those antibody systems concerned with immunity. No effect was observed.

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

Drug Interactions
Interactions with other drugs have not been established.

Driving a vehicle or performing other hazardous tasks
NALCROM has no known effects on ability to drive or operate machinery.

ADVERSE REACTIONS

Nausea, vomiting, diarrhoea, abdominal discomfort, headache, insomnia, skin rashes, sneezing, cough, unpleasant taste in the mouth, and joint pains have been reported. Hypersensitivity reactions have been reported rarely**.**

Possible immunologic changes resulting in reactions such as polymyositis, pneumonitis and heart failure, urticaria and anaphylaxis, have been reported.

Cases of erythema, urticaria or maculopapular rash have been reported and these have cleared within a few days on withdrawal of the drug.

DOSAGE AND ADMINISTRATION

Food Allergy:

Initial Dose:
Adults:
Two capsules four times daily 15-20 minutes before meals.

Children (2-14 years of age):
One capsule four times daily 15-20 before meals.

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

Maintenance Dose:

Once a therapeutic response has been achieved the dose may be reduced to the minimum required to maintain the patient free of symptoms.

Prevention:
Patients who are unable to avoid allergenic foods under certain circumstances (i.e., school meals, restaurants) may be able to protect themselves against the effect of these foods by taking a single dose of NALCROM 15 minutes before the meal. The optimum dosage will need to be determined for each patient and a suitable starting dose would be 200 mg in adults and 100 mg in children.

Missed Dose:
Patients who forget a dose should take it as soon as they remember. However, if it is nearly time for the next dose, the missed dose must be skipped to avoid taking a double dose.

Administration:

Administration as a solution is the method of choice.

- Open the capsule(s) and put the powder in a cup, add 1 teaspoonful of very hot water and dilute it with 4 teaspoonfuls of cold water.

- Swallow the capsules whole.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

As NALCROM is absorbed only to a very limited extent, no action other than medical observation should be necessary alone or with symptomatic treatment if any symptoms appear.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

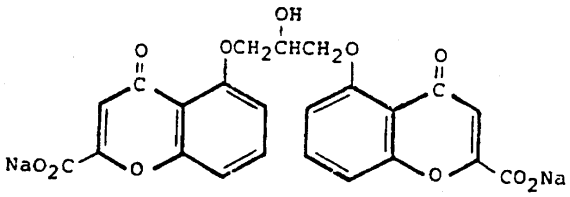
AVAILABILITY

NALCROM is a presentation of sodium cromoglycate for oral use. It is presented in clear, hard gelatin capsules printed Sodium Cromoglycate 100 mg in black. Each capsule contains 100 mg sodium cromoglycate, as a white powder. Tartrazine-free. Bottles of 100.

Non-medicinal ingredients: gelatin and iron oxide.

STRUCTURAL FORMULA AND CHEMISTRY

Structural Formula:



Molecular Formula: $C_{23}H_{14}Na_20_{11}$

Molecular Weight: 512

Chemical Name: Disodium 1,3-bis(2-carboxychromon-5-yloxy)-2-hydroxypropane

Description: White or creamy powder having little odour. Hygroscopic. It is tasteless at first but leaves a slightly bitter after-taste. It is soluble in water (1 in 10) and the resulting solution is neutral.

Storage conditions: Store between 15-30ºC.

PHARMACOLOGY

In Vivo Studies in Animals:

The principal effect of the drug is its specific ability to prevent disruption of sensitized cells and thus inhibit the release of the mediators of anaphylaxis initiated by the interaction of antigen with reagin-type antibodies.

The compound inhibited the passive cutaneous anaphylactic (PCA) reactions in monkeys (Macaca speciosa) sensitized with human reaginic serum when the compound was given intradermally with the antigen. It did not affect the skin reactions to intradermal histamine, 5-hydroxy-tryptamine or bradykinin. Antigen-induced bronchoconstriction in anaesthetized marmosets (Hapale jacchus) sensitized intravenously with human reaginic serum was substantially reduced by sodium cromoglycate compared with untreated controls.

In rats it was shown that sodium cromoglycate inhibited passive cutaneous anaphylactic (PCA)

reactions induced by antigen challenge in animals which had been sensitized with sera containing reaginic-like antibodies to either egg albumin combined with *B. pertussis* organisms or to the helminth *Nippostrongylus brasiliensis*. The local disruption of mast cells and the release of histamine caused by these reaginic-like antibodies were also inhibited by cromoglycate, but the drug did not inhibit PCA reactions induced in rats by rabbit serum containing non-reaginic antibodies (which were not dependent on mast cell disruption), or skin reactions induced by compound 48/80 (a known mast cell disruptor). These findings appear to suggest that sodium cromoglycate inhibits selectively only those reactions which involve reaginic antibodies and mast cells.

Homologous PCA reactions with precipitating antibody in guinea pigs were unaffected, as were aerosol or intravenous antigen-induced bronchospasm and the release of histamine and slow-reacting substance of anaphylaxis (SRS-A) from actively or passively sensitized guinea-pig lung *in vitro*.

Other Experiments:

The release of histamine and SRS-A from portions of fresh human lung passively sensitized with human reaginic serum was measured after exposure to specific antigens *in vitro*. Inhibition with sodium cromoglycate was found over a narrow range of concentrations.

Weighed portions of passively sensitized human lung were Ashocked@ in an organ bath containing an unsensitized human bronchial chain which contracted in response to the liberated spasmogens. Reproducible contractions were obtained by using fresh pieces of sensitized lung tissue of the same weight. Sodium cromoglycate caused a significant (40%) reduction in contraction compared with previous control responses.

A further series of experiments, using the isolated ileum of the guinea pig, confirmed that sodium cromoglycate has no antagonizing action against the following spasmogens: histamine, serotonin (5-HT), acetylcholine, nicotine, substance P, bradykinin, or SRS-A.

Sodium cromoglycate had no direct action on human bronchial chain *in vitro* nor did it antagonize the response to histamine, SRS-A, acetylcholine, or prostaglandin $F_2\alpha$.

These observations indicate that sodium cromoglycate interferes with the release of spasmogens in some way following the union of antigen and reaginic antibody, but does not directly antagonize these spasmogens.

These studies emphasize that sodium cromoglycate is most effective when given prior to antigen challenge.

Sodium cromoglycate is neither a bronchodilator nor an anti-inflammatory agent and has a few general pharmacological effects. Its action is distinct from that of corticosteroids in that is

appears to inhibit specifically the anaphylactic process initiated by reaginic antibody/antigen reactions.

Large doses of sodium cromoglycate had only weak inconsistent effects on the cardiovascular and respiratory systems of monkey, pig, cat, guinea pig and rat.

In conscious and anaesthetized dogs, the drug activated chemoreceptors originating in the pulmonary and coronary circulations, mediated by the vagi, producing bradycardia, hypotension, bradypnea and sometimes apnoea.

In the anaesthetized marmoset, sodium cromoglycate caused a rise in blood pressure and heart rate due to stimulation of post-ganglionic sympathetic fibres.

The compound showed no significant effect in several anti-inflammatory tests.

Other experiments showed that the drug does not affect steroid metabolism as indicated by plasma corticosterone and adrenal ascorbic acid levels.

In experiments on isolated frog oesophagus and human bronchial epithelium *in vitro* and on cat trachea *in vivo*, sodium cromoglycate was used in high concentrations. There was no evidence that the compound interfered with pulmonary clearance. Further work on this aspect of the drug is in progress.

ABSORPTION, DISTRIBUTION AND EXCRETION

The metabolism and tissue distribution of sodium cromoglycate has been studied in mouse, rat, guinea pig, rabbit, cat, dog, monkey (Macaca speciosa) and man. Sodium cromoglycate, labelled with a radioactive isotope, tritium (^{3}H), has been used for the animal experiments and chemical and spectrofluorometric methods of estimation for the experiments in man.

(a) Inhalation Studies:

Tritiated sodium cromoglycate has been introduced as a fine powder aerosol into the lungs of rats, rabbits and monkeys. All animals showed rapid clearance of the drug from the lungs, 50% being absorbed in 20 minutes, and 98% after 24 hours. The drug is taken up by the liver and kidneys and excreted unchanged via the bile and urine.

Human volunteers who inhaled the drug as a powder aerosol showed a peak plasma level at 10 minutes. This peak was followed by a fall in concentration similar to that demonstrated in the animal experiments. After inhalation, 3-5% of the administered dose was excreted in the urine over 6 hours. Assuming a similar biliary excretion, this would indicate that approximately 10% of the administered dose was absorbed.

(b) Other Routes of Administration:

Intravenous and intramuscular administration produces a rapid clearance of the compound from the plasma and a general distribution throughout the tissue followed by rapid excretion unchanged via the kidneys and in the bile. Intramuscular administration resulted in rapid absorption and excretion of a similar pattern to that following intravenous injection.

No tissue accumulation could be detected in the rat and dog after repeated intramuscular injections, the compound being excreted in the urine and bile. In the monkey, 6 hours after intravenous administration 80-90% of the total dose could be accounted for by renal and biliary excretion. At this stage there is a general distribution of the compound throughout the tissues with higher concentrations in the liver and kidney.

In man, oral administration of sodium cromoglycate was followed by a low rate of urinary excretion. The mean urinary excretion of the administered dose over 24 hours was only 0.5%. This indicates that little of the compound is absorbed from the gastrointestinal tract.

TOXICOLOGY

The method of clinical administration of the drug is orally as capsules of granulated sodium cromoglycate.

Toxic effects attributable to sodium cromoglycate have been found only at very high dose levels.

Acute Toxicity Studies:

In acute toxicity studies in mice, rats (including newborn and adult), guinea pigs, hamsters, rabbits and monkeys, the LD_{50} of sodium cromoglycate given by the intravenous or intraperitoneal routes was usually between 2000 and 4000 mg/kg, but with doses below 1000 mg/kg there was little apparent effect in any of these species. The highest dose it was feasible to administer by the oral route in rats and mice was 8000 mg/kg at which level no deaths occurred.

Long-Term Toxicity Studies:

Subcutaneous Injection - 90-day Test in Rats:

In a group of rats given subcutaneous injections of sodium cromoglycate on 90 consecutive days, the highest dose of 198 mg/kg produced one death in 24 animals. All but three rats at this level

showed renal damage, which in most cases was fairly severe. At a level of 78 mg/kg a quarter of the rats were affected, but at 30 mg/kg no histological abnormalities were observed. No histological changes were found in any other organ (at all dosage levels), and blood biochemical determinations failed to reveal any effect on kidney or liver function. The primary lesion in rats demonstrating evidence of renal damage was a tubular degeneration commencing in the proximal convoluted tubules. At lethal doses widespread necrosis was seen and death appeared to be due to acute renal failure.

Intravenous Injection - 180-day Test in Monkeys:

In this test, Rhesus monkeys were given daily intravenous injections of sodium cromoglycate for 180 days at dose levels up to 50 mg/kg. No compound-induced effects were observed.

Proliferative Arteriopathy in Macaque Monkeys:

In Macaque monkeys arterial lesions have been described during the course of toxicity studies on sodium cromoglycate. These lesions affected mainly the medium-sized arteries of the kidneys and were characterised by eccentric swellings of the tunica media, where normal smooth muscle was replaced by irregularly proliferating cells. No thrombosis or fibrinoid necrosis was observed in the lesions and there were no secondary effects such as infarction or glomerular or tubular degeneration.

Proliferative Arteritis in the Macaque Monkey in Sodium Cromoglycate Studies

ROUTE	DURATION	OVERALL	CONTROL	TREATED
Inhalation	3 Months	0 in 18	0 in 6	0 in 12
Inhalation	4 Months	5 in 30	1 in 18	4 in 12
Inhalation	4 Months	2 in 45	1 in 18	1 in 27
Inhalation	3 Months	1 in 25	0 in 17	1 in 8
Intravenous	Acute (7 days)	0 in 16	None	0 in 16
Intravenous	Acute (7 days)	1 in 8	0 in 2	1 in 6
Intravenous	6 Months	0 in 30	0 in 6	0 in 24
TOTAL		**9 in 172**	**2 in 67**	**7 in 105**

Although this condition was first observed during sodium cromoglycate toxicity studies it has subsequently been seen in Macaque monkeys which had not received the drug. Histological examinations of renal tissues from several sources (including untreated monkeys as well as those which had received sodium cromoglycate by various routes) showed that the lesions were spontaneous and not related to administration of the drug. Whilst the aetiology of this arteriopathy remains obscure, it appears to be a distinct entity confined to the genus Macaca.

Studies of Sodium Cromoglycate After Oral Administration:

Sodium cromoglycate has been given to rats at oral doses of 100, 300 and 1000 mg/kg/day for six months.

No effects were seen in body weight or food and water consumption which could be related to the administration of the drug.

In the haematology, urinalysis, blood biochemistry, serum protein electrophoresis and ophthalmoscopic studies there were no differences between test and control animals.

Organ weights were not affected by treatment.

There were no toxic morphological changes in the tissues of any rat in the vehicle control or high dose groups. Detailed examination of bone marrow preparations revealed no effects attributable to daily administration of sodium cromoglycate.

A detailed histopathological examination of every segment of the gastrointestinal tract revealed distinct alterations in the gastric mucosa of rats treated at 300 and 1000 mg/kg. The changes were a heightened incidence of increased cornification of the fore-stomach mucosa and basal cell proliferation at the level of the cardia. In addition, a further change noted in the cardia was referred to as mucinous microcyst formation. This latter lesion was not seen in the stomach of any of the high dose recovery animals at the end of the 30-day withdrawal period and appeared, therefore, to be fully reversible.

A test has been carried out in which neonatal rats have been given daily oral doses of sodium cromoglycate from five days of age to weaning at 22 days. This treatment, for 17 consecutive days, had no apparent effect on neonatal rats.

Young rats were given oral doses of 100, 400 and 1600 mg/kg of sodium cromoglycate for 56 consecutive days to investigate its possible effect on general endocrine function. The rats were 26 days old at the start of the dosing period.

Sodium cromoglycate did not appear to have any adverse effect on general endocrine development at the stated dose levels.

TERATOGENICITY

Studies of the effect of sodium cromoglycate on the various stages of the reproductive cycle have been carried out in rabbits, rats and mice. In rabbits, no teratogenic effects were observed following the intravenous administration of 500 mg/kg sodium cromoglycate daily throughout pregnancy. Although the dose proved lethal to some rabbits and produced renal lesions in all the survivors, there were no deformities in the 81 foetuses removed at full term. There was also no substantial increase in the resorption rate, but two partially resorbed foetuses did show developmental defects (limb flexures). In rats given daily doses of 185 mg/kg subcutaneously throughout pregnancy, one foetus (out of 272) showed a grossly shortened humerus, but no abnormalities were seen following daily doses of 90 mg/kg sodium cromoglycate given either with or without 0.05 mg/kg isoprenaline.

Similarly, no teratogenic effects were observed in mice following daily doses of up to 540 mg/kg subcutaneously, but doses in excess of 60 mg/kg significantly increased the incidence and severity of foetal abnormalities produced by doses of 0.9 mg/kg isoprenaline and above. However, there were no teratogenic effects when the daily dosage of the combination was reduced to 20 mg/kg sodium cromoglycate and 0.1 mg/kg isoprenaline.

No effect on mating or fertility was noted following the daily administration of 100 mg/kg sodium cromoglycate to male rats for a period of 80 days, and to female rats for a period of 14 days prior to mating.

CARCINOGENICITY

Long-term studies in hamsters and mice gave no evidence of drug-related neoplasia and indicated that sodium cromoglycate appears to be free of carcinogenic potential even at dose levels high enough to induce some expected renal damage.

Hamsters were given either 52.6 or 17.5 mg/kg three times a week intraperitoneally for 15 weeks and one-third of that dosage for the remainder of the one-year dosing period. The overall tumour incidence was 15% with no significant differences between the treated and control groups.

Two tests, one lasting 18 months and the other 12 months, were conducted in mice. In the 18-month study animals were treated intraperitoneally with 150 or 50 mg/kg three times a week for 12 months and were then sacrificed at 18 months. All animals, treated, untreated and saline-injected controls, were examined daily. Any which died before the end of the study, as well as the survivors, were subjected to detailed autopsy. Although the large doses given over a

period of one year were sufficient to cause some renal damage they had no observable effect on neoplasia. These sizeable doses also did not adversely affect survival.

Significant differences could not be detected between control and treated animals in the 12-month study.

CYTOTOXICITY

The effects of sodium cromoglycate were studied at the cellular level. Various types of cells were incubated with various concentrations of the drug for several days. No effects were observed at concentrations up to and including 100 μg/mL upon the following:

Migration characteristics of guinea-pig macrophages
Morphology of chick embryo fibroblasts
Morphology of human epithelial cells from a cell line
Ciliary activity of samples of human ciliated epithelium.

The tests on human respiratory epithelium were included to detect potential interference with pulmonary clearance mechanisms.

EFFECTS ON IMMUNE SYSTEMS

The effect of sodium cromoglycate was studied on those antibody systems concerned with immunity. In this context no effect was observed on:

Various antibody neutralizing or agglutinating systems
Development of active immunity or antibody production
Protection conferred by passive or active immunity.

No effect was found on the following virus/antibody neutralizing systems in vitro:

Influenza A. Polio Type II; with human or rabbit antisera
Vaccinia; with rabbit antisera
Herpes simplex; with human antisera

No effects were observed on the LD_{50} in mice of mouse-adapted polio virus; nor in their protection by Salk vaccine.

No effect was found on the neutralization of Clostridium welchii Type A α-toxin by specific antiserum, nor on the cytotoxic behaviour of rabbit anti-HeLa serum on HeLa cells in vitro.

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CONSUMER INFORMATION
PrNALCROM®
(sodium cromoglycate capsules)

This leaflet is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NALCROM. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

NALCROM is used to treat allergic reactions to certain foods.

NALCROM is only used if you have had a test to prove that you are allergic to these foods. As part of your treatment, your doctor should advise you to avoid eating certain foods which may cause an allergic reaction.

If you have life-threatening reactions to food, DO NOT RELY ON NALCROM, as it does not protect you from these serious conditions.

What it does:
NALCROM belongs to a group of medicines called anti-allergics. It works by stopping the release of the natural substances in your body that can cause an allergic reaction.

When it should not be used:

Do not take NALCROM if:

- You have an allergy to sodium cromoglycate, the active ingredient in NALCROM, or any of the ingredients NALCROM contains (see **What the nonmedicinal ingredients are**).

NALCROM should not be used in children under 2 years of age.

What the medicinal ingredient is:
sodium cromoglycate.

What the nonmedicinal ingredients are:
gelatin and iron oxide.

What dosage forms it comes in:
Capsules 100 mg

WARNINGS AND PRECAUTIONS

If you have life-threatening reactions to food, DO NOT RELY ON NALCROM, as it does not protect you from these serious conditions.
You should not stop taking NALCROM without talking to your doctor.

BEFORE you use NALCROM talk to your doctor or pharmacist if you:

- have any allergies to this drug or its ingredients
- are pregnant, think you are, or plan to get pregnant
- are breastfeeding, or planning to breastfeed
- have liver and kidney problems, as this may affect the dosage of NALCROM that you need

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products, and drugs prescribed by other doctors. Do not start a new medication without telling your doctor.

PROPER USE OF THIS MEDICATION

Always take NALCROM exactly as your doctor has told you.

Initial dose
Adults: 2 capsules four times a day 15-20 minutes before meals.

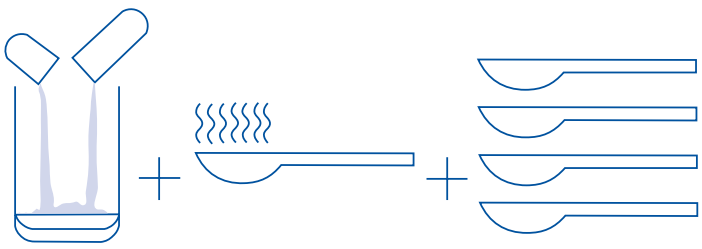
Children (2-14 years of age): 1 capsule four times a day 15-20 minutes before meals.

Maintenance dose:

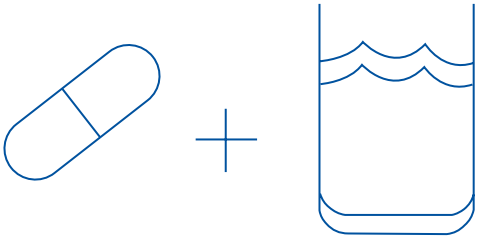
- Once the symptoms improve, the doctor may reduce the dose. Do not try to change the dose yourself. You should ask your doctor or pharmacist if you are not sure.
- If signs of allergy do not improve within 2-3 weeks, your doctor may double how much you take. Your dose should not be greater than 40 mg per kilogram of your body weight per day.

Prevention:
Patients who are unable to avoid allergenic foods under certain circumstances (i.e., school meals, restaurants) may be able to protect themselves against the effect of these foods by taking a single dose of NALCROM 15 minutes before the meal. Your doctor will determine the optimum dosage for you and a suitable starting dose would be 200 mg (2 capsules) in adults and 100 mg (1 capsule) in children.

How to use NALCROM
The best way to take NALCROM is to open the capsule(s) and put the powder in a cup, add 1 teaspoonful of very hot water and dilute it with 4 teaspoonfuls of cold water.



Alternatively, you can take the capsules by swallowing them whole with a drink of water.



Overdose:

In case of drug overdose, contact a heath care practitioner, hospital emergency department or Regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you forget a dose, take it as soon as you remember it. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for a forgotten dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects reported with NALCROM may include: vomiting, headache, insomnia, hives, skin rashes, sneezing, cough, unpleasant taste in the mouth, and joint pains.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
	Only if severe	In all cases	
Nausea, diarrhea, abdominal discomfort	√		
Heart Failure: shortness of breath, cough, leg swelling and fatigue			√
Polymyositis: progressive muscle weakness			√
Pneumonitis: difficulty breathing			√
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			√

This is not a complete list of side effects. For any unexpected effects while taking NALCROM, contact your doctor or pharmacist.

HOW TO STORE IT

Keep NALCROM and all other medications out of the reach and sight of children.

Keep the capsules in their original package and store at room temperature (15°-30°C).

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at:
www.healthcanada.gc.ca/medeffect

Call toll-free at 1-866-234-2345

Complete a Canada Vigilance Reporting Form and:
- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect .

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical

advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: http://www.sanofi-aventis.ca or by contacting the sponsor, sanofi-aventis Canada Inc., at: 1-800-265-7927

This leaflet was prepared by sanofi-aventis Canada Inc.

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