PRODUCT MONOGRAPH

Pr RHINOCORT® TURBUHALER®

Budesonide Dry Powder for Nasal Inhalation
100 mcg/metered dose

Corticosteroid for Nasal Use

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ACTIONS AND CLINICAL PHARMACOLOGY

RHINOCORT TURBUHALER contains pure budesonide which is a potent synthetic glucocorticosteroid with strong topical and weak systemic effects.

RHINOCORT TURBUHALER has a high topical anti-inflammatory potency and it is rapidly biotransformed in the liver. This favourable separation between topical anti-inflammatory activity and systemic effect is due to strong glucocorticosteroid receptor affinity and an effective first-pass metabolism with a short half-life. The mechanism of action of intranasally administered budesonide has not yet been completely defined.

INDICATIONS AND CLINICAL USE

The treatment of seasonal allergic and allergic/non-allergic perennial and vasomotor rhinitis unresponsive to conventional therapy. Also indicated for the treatment of nasal polyps and the prevention of nasal polyps after polypectomy.

CONTRAINDICATIONS

- Hypersensitivity to budesonide;
- Active or quiescent tuberculosis;
- Untreated fungal, bacterial or viral infections;
- Children under 6 years of age.

WARNINGS

In patients previously on prolonged periods or high doses of systemic steroids, withdrawal of steroids may cause symptoms such as tiredness, aches and pains, and depression. In severe cases, adrenal insufficiency may occur necessitating a temporary resumption of systemic steroids.

Careful attention must be given to patients with asthma or other clinical conditions in whom a rapid decrease in systemic steroids may cause a severe exacerbation of their symptoms.

Use in Pregnancy: see PRECAUTIONS.

PRECAUTIONS

In transferring patients from a systemic steroid to RHINOCORT TURBUHALER, the reduction of the systemic steroid must be very gradual and carefully supervised by the physician since systemic withdrawal symptoms (e.g., joint and/or muscular pain, lassitude, depression) may occur in spite of maintenance or improvement of respiratory functions (see DOSAGE and ADMINISTRATION).

Patients should be informed that the full effect of RHINOCORT TURBUHALER therapy is not achieved until 2 to 3 days of treatment have been completed. In rare cases the full effect of RHINOCORT TURBUHALER therapy is not achieved until 2 weeks of treatment have been completed. Treatment of seasonal rhinitis should, if possible, start before the exposure to allergens.

During long-term therapy, pituitary-adrenal function and hematological status should be periodically assessed. Use of excessive doses of, or long-term treatment with, glucocorticosteroids may lead to signs or symptoms of hypercorticism, suppression of HPA function and/or suppression of growth in children.

The long-term effects of nasal glucocorticosteroids in children are not fully known. Physicians should closely follow the growth of children taking glucocorticosteroids for longer term by any route, and weigh the benefits of the glucocorticosteroid therapy against the possibility of growth suppression. Until greater clinical experience has been gained, the continuous, long-term treatment of children is not recommended.

Treatment with RHINOCORT TURBUHALER should not be stopped abruptly but tapered off gradually.

Glucocorticosteroids may mask some signs of infection and new infections may appear during their use. A decreased resistance to localized infections has been observed during glucocorticosteroid therapy; this may require treatment with appropriate therapy or stopping the administration of RHINOCORT TURBUHALER.

Special care is needed in patients with fungal and viral nasal infections. Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chicken pox and measles, for example, can have a more serious or fatal course in children on immunosuppressant corticosteroids. In such children, or in adults who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG), as appropriate, may be indicated. If chicken pox develops, treatment with antiviral agents may be considered.

Concomitant treatment (topical histamines or cromones) may sometimes be required, as an add-on therapy to nasal corticosteroids, to counteract eye symptoms caused by allergy.

The long term effects of nasal corticosteroids in human subjects are still unknown, in particular, their local effects, and on developmental or immunologic processes. The nasal mucosa of those patients receiving long term, continuous therapy should be inspected at least twice a year. The possibility of atrophic rhinitis and/or pharyngeal candidiasis should be kept in mind.

When budesonide is administered intranasally, the following should be kept in mind:

- Glucocorticosteroid effects may be enhanced in patients with hypothyroidism and in those with cirrhosis. Reduced liver function may affect the elimination of corticosteroids. The intravenous pharmacokinetics of budesonide however, are similar in cirrhotic patients and in healthy subjects. The pharmacokinetics after oral ingestion of budesonide were affected by compromised liver function as evidenced by increased systemic availability. This is however, of limited clinical importance for RHINOCORT TURBUHALER, as after inhalation, the oral contribution to the systemic availability is relatively small.

- In hypoprothrombinemia, salicylates should be used cautiously in conjunction with glucocorticosteroids.

Because of the inhibitory effect of corticosteroids on wound healing in patients who have had recent nasal surgery or trauma, a nasal corticosteroid should be used with caution until healing has occurred.

Patients should be advised to inform subsequent physicians of the prior use of glucocorticosteroids.

Dose-related suppression of plasma and urinary cortisol has been observed in healthy volunteers after short-term administration of RHINOCORT TURBUHALER. Although no important changes in basal plasma cortisol levels were manifested in patients with rhinitis using RHINOCORT TURBUHALER at recommended doses, caution is advised.

To ensure the proper dosage and administration of the drug, the patient should be instructed by a physician or other health professional in the use of RHINOCORT TURBUHALER (see CONSUMER INFORMATION).

Use in Pregnancy

In experimental animal studies, budesonide was found to cross the blood-placenta barrier. Like other glucocorticosteroids, budesonide is teratogenic to rodent species. High doses of budesonide administered subcutaneously produced fetal malformations, primarily skeletal defects, in rabbits, rats, and in mice. Results from world-wide post marketing experience indicate inhaled budesonide during pregnancy has no adverse effects on the health of the fetus/new born child. Review of published literature of orally inhaled budesonide, including results from a large case control study performed with cases identified from 3 Swedish health registers showed that there was no association between exposure to inhaled budesonide and overall congenital malformations. Results from a similar study performed with intranasal

budesonide, using the same 3 Swedish health registers showed that the use of intranasal budesonide was associated with a subgroup "less severe cardiovascular defects"; however there was no statistically significant association between the use of intranasal budesonide during pregnancy and overall congenital malformations, or overall frequency of cardiovascular defects in the offspring. Budesonide should be used during pregnancy only if the potential benefits clearly outweigh the risk to the fetus. Infants born of mothers who have received substantial doses of corticosteroids, especially oral steroids, during pregnancy should be carefully observed for hypoadrenalism.

Lactation

Budesonide is excreted in breast milk. The administration of RHINOCORT TURBUHALER to women who are breastfeeding should only be considered if the expect benefit to the mother is greater than any possible risk to the child.

Children Under 6 Years of Age

RHINOCORT TURBUHALER is not presently recommended for children younger than 6 years of age due to limited clinical data in this age group.

Drug Interactions

To date budesonide has not been observed to interact with other drugs used for the treatment of rhinitis.

Cimetidine

The kinetics of budesonide were investigated in a study in healthy subjects without and with cimetidine, 1000 mg daily. After a 4 mg oral dose the values for C_{max} (nmol/L) and systemic availability (%) of budesonide without and with cimetidine (3.3 vs 5.1 nmol/L and 10 vs 12%, respectively) indicated a slight inhibitory effect on hepatic metabolism of budesonide, caused by cimetidine. This should be of little clinical importance.

Ketoconazole

The metabolism of budesonide is primarily mediated by CYP3A4, a subfamily of cytochrome P450. CYP3A4 inhibitors like ritonavir, cobicistat-containing products and azole antifungals (e.g. ketoconazole and itraconazole) increase the systemic exposure to budesonide. Therefore, concomitant use of budesonide and ritonavir or azole antifungals should be avoided unless the potential benefit outweighs the risk of systemic corticosteroid side-effects.

Omeprazole

At recommended doses, omeprazole has no effect on the pharmacokinetics of oral budesonide.

ADVERSE REACTIONS

The adverse reactions reported with RHINOCORT TURBUHALER are consistent with what one would expect when applying a topical treatment to an already inflamed membrane. All side effects are transient. The most commonly reported side effects include: nasal and throat

irritation, nasal bleeding and crusting. Other adverse events reported are itching throat, sore throat, cough, fatigue, nausea/dizziness, and headache. When patients are transferred to RHINOCORT TURBUHALER from a systemic steroid, allergic conditions such as asthma or eczema may be unmasked. Uncommon side effects such as immediate and delayed hypersensitivity reactions (urticaria, rash, dermatitis, angioedema, pruritus, etc.) may occur in association with local corticosteroid therapy. Very rare cases of anaphylactic reaction have been reported following the use of RHINOCORT TURBUHALER. Additionally, very rare cases of ulcerations of the mucous membranes and nasal septal perforation have been reported following the use of intranasal corticosteroids.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Like any other nasally administered corticosteroid, acute overdosing is unlikely in view of the total amount of active ingredient present. However, when used chronically in excessive doses or in conjunction with other corticosteroid formulations, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes recur, the dosage of RHINOCORT TURBUHALER should be discontinued slowly consistent with accepted procedures for discontinuation of chronic steroid therapy (see DOSAGE and ADMINISTRATION).

The restoration of the hypothalamic-pituitary-axis may be a slow process and during periods with pronounced physical stress such as severe infections, trauma, and surgical operations, a supplement with systemic steroids may be advisable.

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

DOSAGE AND ADMINISTRATION

See WARNINGS.

Careful attention must be given to patients previously treated for prolonged periods with systemic corticosteroids when transferred to RHINOCORT TURBUHALER. Initially, RHINOCORT TURBUHALER and the systemic corticosteroid must be given concomitantly, while the dose of the latter is gradually decreased. The usual rate of withdrawal of the systemic steroid is the equivalent of 2.5 mg of prednisone every four days if the patient is under close supervision. If continuous supervision is not feasible, the withdrawal of the systemic steroid should be slower, approximately 2.5 mg of prednisone (or equivalent) every ten days. If withdrawal symptoms appear, the previous dose of the systemic steroid should be resumed for a week before further decrease is attempted.

Patients should be informed that the full effect of RHINOCORT TURBUHALER therapy may not become evident until 2 to 3 days of treatment have been completed. Full therapeutic benefit requires regular usage. Explain the absence of an immediate effect to the patient in order to ensure co-operation and continuation of the treatment with a regular dosage regime. Treatment of seasonal rhinitis should, if possible, start before exposure to the allergens.

Concomitant treatment may sometimes be necessary to counteract eye symptoms caused by the allergy. In continuous long-term treatment, the nasal mucosa should be inspected regularly e.g. every six months.

If the nasal passages are severely blocked, the drug may fail to reach the site of action. In such cases, a course of oral steroids or decongestants may be required before initiating RHINOCORT TURBUHALER therapy.

The patient may not taste or feel any medication when using RHINOCORT TURBUHALER due to the small amount of drug dispensed.

Although systemic effects are negligible at recommended doses, RHINOCORT TURBUHALER treatment should not be continued beyond three weeks in the absence of significant symptomatic improvement. RHINOCORT TURBUHALER should not be used in the presence of untreated localized infections involving the nasal mucosa.

Adults and Children (6 Years and Older)

Rhinitis:

Initial Dose

Two inhalations into each nostril in the morning (total daily dose: 400 mcg).

Maintenance Dose

Use the lowest effective dose necessary to control symptoms.

Treatment or Prevention of Nasal Polyps:

One inhalation (100 mcg) into each nostril, morning and evening (total daily dose 400 mcg).

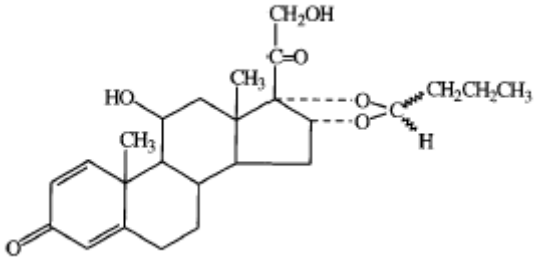
Children Under 6 Years

Not recommended for children in this age group.

PHARMACEUTICAL INFORMATION

Drug Substance

Chemical Structure:



Generic Name:	Budesonide
Chemical Name:	Budesonide is a mixture of two isomers: 1. Pregna-1,4-diene-3,20-dione,16,17-butylidenebis(oxy)-11,21-dihydroxy-,[11β,16α(R)] and 2. Pregna-1,4-diene-3,20-dione,16,17-butylidenebis(oxy)-11,21-dihydroxy-,[11β,16α(S)].
Molecular Formula:	$C_{25}H_{34}O_6$
Molecular Weight:	430.5
Description:	Budesonide is a glucocorticosteroid and consists of a 1:1 mixture of two epimers, 22R and 22S. It is a white to off-white crystalline powder and is freely soluble in chloroform, sparingly soluble in ethanol, practically insoluble in water and in heptane. Budesonide melts at 224°C to 231.5°C, with decomposition.

Dosage Form

Composition	per metered dose
Active:	budesonide 100 mcg
Non-medicinal:	none

Stability and Storage Recommendations

RHINOCORT TURBUHALER should be stored with the cover tightened, at room temperature (15-30°C).

AVAILABILITY OF DOSAGE FORMS

RHINOCORT TURBUHALER is a dry powder inhaler containing 200 doses of 100 mcg of micronized budesonide. Each inhalation from TURBUHALER will provide 100 mcg of budesonide active substance; no additives or carrier substances are included. RHINOCORT TURBUHALER cannot be refilled and should be discarded when finished.

PHARMACOLOGY

Studies with animals have shown that budesonide has a 2-10 times better ratio between topical anti-inflammatory and systemic glucocorticosteroid effects than that obtained with beclomethasone dipropionate or triamcinolone acetonide. In the blanching test for topical anti-inflammatory activity in humans, budesonide was about twice as potent as beclomethasone dipropionate. Beclomethasone dipropionate was, however, more active than budesonide with regard to systemic activity as measured by depression of morning plasma cortisol. The favourable topical anti-inflammatory activity to systemic effect ratio demonstrated by budesonide is due to its high glucocorticosteroid receptor affinity and high first-pass metabolism with a short half-life.

Budesonide has been shown to counteract the mainly "IgE" mediated lung anaphylaxis in guinea pigs. No significant bronchorelaxing activity, either *in vitro* or *in vivo*, could be demonstrated. Budesonide did not potentiate beta-mediated bronchorelaxation, and did not affect theophylline-induced relaxation or respiratory airway smooth muscle in guinea pigs.

Budesonide exhibits typical glucocorticosteroid effects in that subcutaneous administration to adrenalectomised rats induced glycogen deposition in the liver, increased urinary volume and only slightly affected sodium excretion.

Whole body autoradiography in mice has shown budesonide and its metabolites to have a similar distribution pattern to other glucocorticosteroids with a high distribution to endocrine organs.

HUMAN PHARMACOKINETICS

The systemic availability of oral budesonide in man is low (about 10%). With reference to the metered dose, the systemic availability of budesonide from RHINOCORT TURBUHALER is 22%. After application of budesonide in solution directly on the nasal mucosa, all the dose is systemically available, indicating that budesonide does not undergo local metabolism in the nose. The maximal plasma concentration after administration of 800 mcg budesonide from RHINOCORT TURBUHALER is 1.1 nmol/L and is reached within 0.4 hours.

The distribution volume (Vd) of budesonide is 301.3 ± 41.7 L, indicating the high tissue affinity of the drug. Plasma protein binding is estimated at 88.3 ± 1.5%.

After nasal administration of tritiated budesonide in human volunteers, 56.1% ± 2.6% of the discharged dose was recovered in the urine (0-96 hours) while during the same period, 33.4 ± 2.0% of the dose could be recovered in the feces. In those subjects who took the compound intravenously, 56.7 ± 1.2% was recovered in the urine, 34.0 ± 3.0% in the feces.

In vitro studies with human liver have shown that budesonide is rapidly metabolised to more polar compounds than the parent drug. Two major metabolites have been isolated and identified as 6β-hydroxybudesonide and 16α-hydroxyprednisolone. The metabolism of budesonide in the liver is primarily mediated by cytochrome P450 3A. The glucocorticosteroid activity of these two metabolites was at least 100-fold lower than the

parent compound as shown in the rat ear edema test. No qualitative differences between *in vitro* and *in vivo* metabolic patterns could be detected. Negligible biotransformation was observed in human lung and serum preparations.

TOXICOLOGY

Acute Toxicity

Species	Sex	Route	LD_{50} (mg/kg) After 3 Weeks
mouse	male	s.c.	35 ± 18
mouse	male	p.o.	> 800
mouse	female	p.o.	> 800
rat	male	s.c.	15.1 ± 4.4
rat	female	s.c.	20.3 ± 7.1
rat	male	p.o.	≈ 400

Surviving animals exhibited a marked decrease in body weight gain.

Toxicity After Repeated Administration Of Budesonide To Rats, Rabbits, And Dogs

Animal		Number and Sex Per Group	No. of Dose Groups	Daily Dose Levels		Route of Administration	Duration	Toxic Effects
Species	Strain			mg/kg	mg/animal			
rat	Sprague-Dawley	6 males 6 females	4	0.05 0.5 5.0 50.0		p.o.	1 month	Atrophy of adrenal gland and lymphoid system. Gastric ulceration.
rat	Wistar	10 males 10 females	3	0.02 0.10 0.2-0.5		inhalation	3 months	Hair loss, dose related reduction in lymphocytes, leukocytes, increase in neutrophils. In high dose group, reduced adrenal, thymic, splenic and hepatic weights. No pulmonary impairment observed.
rat	Wistar	40 males 40 females	3	0.005 0.01 0.05		inhalation	12 months	- as above
rabbit	New Zealand White	3 males 3 females	2		0.025 0.1	s.c.	1 month	High dose caused slight liver mass increase, slight decrease in adrenal mass, thymal regression.
dog	Beagle	1 male 1 female	3	0.01 0.1 1.0		p.o.	1 month	High dose - typical steroid effects - adrenal, lymphoid system atrophy, increased fat in myocardium, glycogen in liver.
dog	Beagle	2 males 2 females	3	0.02 0.06 0.2		inhalation	6 weeks	High dose - induced thymal atrophy, adrenal atrophy. No changes in respiratory system observed.
dog	Beagle	5 males 5 females	3		0.20 0.60 2.00	inhalation	6 months	High dose - decreased plasma cortisol, cortical atrophy of the adrenal gland, thymal regression. Slight visceral obesity.
dog	Beagle	5 males 5 females	3		0.20 0.60 2.00	inhalation	12 months	High dose - obesity, alopecia, females showed no evidence of estrous cycle. Systemic steroid effects - lymphoid and adrenal atrophy.

All effects observed were consistent with those expected during prolonged corticosteroid exposure.

Teratology and Reproduction Studies

Effects on Pregnancy

Rat

Daily doses of 20, 100, and 500 mcg/kg body mass were administered subcutaneously to pregnant rats during Days 6-15 of gestation. In the high dose group, all of the rats showed a deteriorated general condition including piloerection, drowsiness, decreased food consumption and decreased body mass gain. Fetal loss was increased and pup masses decreased in comparison to the control group. The frequency of fetal abnormalities was also increased. Doses in excess of 100 mcg/kg must be considered teratogenic in the rat.

Daily doses of 0.01, 0.05 and 0.1-0.25 mg/kg were administered by inhalation to pregnant rats during Days 6-15 of gestation. At the highest dose a slight significant reduction in fetal weight gain was observed, but there was no evidence of any effect on fetal development attributable to budesonide at any dose level.

Rabbit

Daily doses of 5, 25, and 125 mcg/body mass were administered subcutaneously during Days 6-18 of gestation. In the low and medium dose groups, food consumption and body mass gain were decreased during the fourth gestational week.

Some does also showed signs of diarrhea and vaginal bleeding. In the high dose group, all does aborted at the end of the gestation period. In the medium dose group, a marked increase in the frequency of abnormalities, mainly skeletal defects, was observed. Most commonly, defects were skull and vertebral abnormalities.

Effects on Fertility and General Reproductive Performance

Rat

To evaluate the effect of budesonide on fertility and general reproductive performance, daily doses of 0.01, 0.05, and 0.19 μmol/kg were given subcutaneously to males for 9 weeks prior to and throughout mating. Females received the same doses for two weeks before, throughout gestation and up to 21 days postpartum. The offspring of the high dose group showed a decrease of peri- and post-natal viability. Dams showed a decrease in body mass gain.

Mutagenicity Studies

Budesonide showed no mutagenic activity in the Ames Salmonella/microsome plate test or in the mouse micronucleus test.

Carcinogenicity

The carcinogenic potential of budesonide was evaluated in long-term mouse and rat studies.

Chronic Drinking Water Study in Mice

Budesonide was administered in the drinking water for 91 weeks to three groups of CD®-1 mice at dose levels of 10, 50, and 200 mcg/kg/day.

A statistically significant dose-related decrease in survival was noted for the males only. All other evaluation criteria were comparable in all groups. Upon microscopic examination, a variety of spontaneous lesions was observed which were not related to treatment. No carcinogenic effect was present.

Chronic Drinking Water Study (104 Weeks) with Budesonide in Rats

Three rat carcinogenicity studies have been performed. In the first study, budesonide was administered for 104 weeks in doses of 10, 25 and 50 mcg/kg/day.

A small but statistically significant increase in gliomas was noted in male animals from the high dose group. These results were considered equivocal since the S-D rat is very variable with regard to spontaneous glioma incidence.

To elucidate these results, two further 104-week carcinogenicity studies with budesonide 50 mcg/kg/day were performed, one using male S-D rats, and one using male Fischer rats (which have a lower and less variable incidence of gliomas). Prednisolone and triamcinolone acetonide were used as reference glucocorticosteroids in both studies.

The results from these new carcinogenicity studies in male rats did not demonstrate an increased glioma incidence in budesonide-treated animals as compared to concurrent controls or reference glucocorticosteroid-treated groups.

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PART III:
CONSUMER INFORMATION

Pr RHINOCORT® TURBUHALER®

budesonide (dry powder for nasal inhalation)

This leaflet is part III of a three-part "Product Monograph" published when RHINOCORT TURBUHALER was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about RHINOCORT TURBUHALER. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

This medicine is for you. Only a doctor can prescribe it for you. Never give it to someone else. It may harm them even if their symptoms are the same as yours.

What the medication is used for:
RHINOCORT TURBUHALER is used to treat:
- seasonal allergic rhinitis (hay fever);
- perennial (year-round) rhinitis;
- nasal polyps and/or prevent new nasal polyps from appearing after surgery (polypectomy).

What it does:
RHINOCORT TURBUHALER contains a medicinal ingredient that is a steroid (cortisone-like medicine). RHINOCORT TURBUHALER works by preventing and decreasing the inflammation that occurs on the lining of your nose.

When it should not be used:
Do not use RHINOCORT TURBUHALER:
- if you are allergic to budesonide;
- if you have an untreated infection:
  - fungal (yeast);
  - bacterial;
  - viral;
- if you have tuberculosis in your respiratory tract;
- if your child is younger than 6 years old.

What the medicinal ingredient is:
Budesonide.

What the nonmedicinal ingredients are:
RHINOCORT TURBUHALER contains no other ingredients.

What dosage form it comes in:
Dry powder for nasal inhalation: 100 mcg per metered dose (inhalation). Each inhaler contains 200 metered doses.

WARNINGS AND PRECAUTIONS

BEFORE you use RHINOCORT TURBUHALER talk to your doctor or pharmacist:
- if you are allergic to budesonide;
- if you have had lung tuberculosis or any other recent infection;
- if you have asthma;
- if you have thyroid problems;
- if you have or had liver problems;
- if you are taking, or have taken steroids either as an injection or by mouth within the past several months;
- if you are pregnant or planning to become pregnant;
- if you are breastfeeding;
- about **all** health problems you have now or have had in the past.

You should avoid coming into contact with people who have measles or chicken pox while taking RHINOCORT TURBUHALER. If you are exposed, tell your doctor right away.

It is not recommended to use RHINOCORT TURBUHALER for continuous, long-term treatment in children.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse, or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements, or alternative medicines.

Drugs that may interact with RHINOCORT TURBUHALER include:
- ritonavir and cobicistat-containing products (used to treat HIV or AIDS);
- ketoconazole, itraconazole (used to treat fungal infections).

PROPER USE OF THIS MEDICATION

- Take RHINOCORT TURBUHALER exactly as your doctor has told you to. **Follow your doctor's directions carefully. They may differ from the information in this leaflet.**
- **Do not** take more of your medicine or take it more often than your doctor tells you.
- RHINOCORT TURBUHALER is for use in the nose only. **Do not** use it in your eyes or mouth.
- RHINOCORT TURBUHALER does not relieve allergy symptoms in the eyes. If your eyes bother you, tell your doctor. He/she may be able to give you some additional medicine to relieve these symptoms.

- RHINOCORT TURBUHALER may take 2-3 days (and up to 2 weeks) to work. Take it each day without missing a dose to get the best results.
- For seasonal allergic rhinitis, RHINOCORT TURBUHALER works best if it is started before allergy season begins.
- If your nose is blocked, decongestant nose drops may be used during the first 2-3 days of the treatment.
- Do not stop taking RHINOCORT TURBUHALER even if you feel better unless told to do so by your doctor.

Tell your doctor if:
- your symptoms have not improved after 3 weeks of taking RHINOCORT TURBUHALER;
- your nose becomes irritated;
- you have a yellow or green discharge from your nose;
- you have repeated nose bleeds.

Adults and Children (6 years and older)

Rhinitis
Usual starting dose: 2 inhalations (200 mcg) into each nostril in the morning (total daily dose: 400 mcg).

Maintenance Dose: Your doctor will prescribe the lowest dose needed to control symptoms.

Depending on how RHINOCORT TURBUHALER works for you, your doctor may change your dose.

Nasal Polyps
Usual dose: 1 inhalation (100 mcg) into each nostril, morning and evening (total daily dose: 400 mcg).

If you have been prescribed RHINOCORT TURBUHALER and are taking oral steroid medication, your doctor may slowly (over a period of weeks or months) reduce the dose of your tablets. If your oral steroid medication is changed, you may experience the same symptoms you had earlier such as runny nose, and symptoms because of reduced oral steroid use such as rash, muscle and joint pain.

If your oral steroid is reduced, you should contact your doctor if you get symptoms such as:
- Headache;
- Tiredness;
- Nausea or vomiting.

Missed Dose:

Rhinitis
If you miss a dose and remember within 12 hours, you should take your usual dose as soon as possible. Then go back to your regular schedule. If it is more than 12 hours when you remember, do not take the missed dose. Take the next dose at the usual time.

Nasal Polyps
If you miss a dose and remember within 6 hours, you should take your usual dose as soon as possible. Then go back to your regular schedule. If it is more than 6 hours when you remember, do not take the missed dose. Take the next dose at the usual time.

Do NOT double the dose of RHINOCORT TURBUHALER to make up for a missed dose. If you are still unsure, check with your doctor or pharmacist to see what you should do.

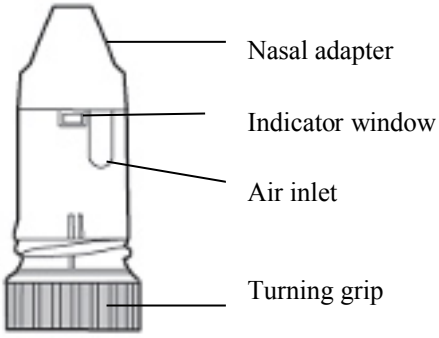
Overdose:

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

HOW TO USE YOUR RHINOCORT TURBUHALER INHALER (for nasal inhalation)

Before you start using RHINOCORT TURBUHALER for the first time, it is important that you read the instructions below and follow them carefully.

TURBUHALER is a multidose inhaler from which very small amounts of powder are administered. When you sniff RHINOCORT TURBUHALER the powder is delivered to your nasal passages.

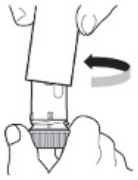


Before you use a **NEW** inhaler for the first time you must prepare the inhaler for use. Follow the steps under "**A. How to prepare a NEW inhaler for use:**".

For regular use of your inhaler follow the steps under "**B. How to take a dose:**".

A. How to prepare a NEW inhaler for use:
You only need to prepare your **NEW** inhaler for use **once**. You do not need to repeat these steps even if your inhaler is not used regularly.

STEP 1 Unscrew and lift off the cover (Figure 1). Figure 1



STEP 2 Hold the inhaler upright. Do not hold the inhaler by the nasal adapter.

- Turn the **grey grip** as far as it will go in one direction (clockwise or counter-clockwise, it does not matter which way you turn it first).
- Then turn the grey grip as far as it will go in the opposite direction (Figure 2).
- At some point when you are turning the grip you will hear a "**click**". This is part of the preparation process.

Figure 2

STEP 3 **Repeat STEP 2** one more time. Then, follow the steps under "**B. How to take a dose:", starting at STEP 2**.

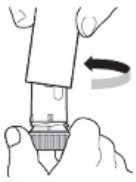
B. How to take a dose:

To properly take a dose, follow these 5 steps:

STEP 1 Blow your nose.

STEP 2 Unscrew and lift off the cover (Figure 1).

Figure 1



STEP 3 Hold the inhaler upright. Do not hold the inhaler by the nasal adaptor.

- Turn the **grey grip** as far as it will go in one direction (clockwise or counter-clockwise, it does not matter which way you turn it first).
- Then turn the grey grip as far as it will go in the opposite direction (Figure 2).

Figure 2

A dose has now been loaded.

- At some point when you are turning the grip you will hear a "**click**". This is part of the preparation process.

NOTE: If you accidentally drop, shake or breathe out into RHINOCORT TURBUHALER after the dose has been loaded, you will lose your dose. If this happens, repeat STEP 3 to load a new dose.

STEP 4 While your nose is away from the nasal adapter, **breathe out**. Then, place the adapter inside your nostril. Make sure it fits tightly around the adapter. Block the opposite nostril with your finger (Figure 3).

STEP 5 **Breathe in** (sniff) **quickly and hard** through your nose (Figure 3).

- When you breathe in, your indrawn breath provides the force needed to bring the drug to your nasal passages.
- Take the nasal adapter out from the nostril.
- When you breathe out, **do not** breathe into your TURBUHALER.
- The amount of medicine that you inhale is very small. You may not be able to feel it or taste it after you have used it. If you have followed the instructions, you will have inhaled the medicine.

Figure 3

Repeat STEPS 3 to 5 for the other nostril. When you have taken the prescribed amount of doses, **replace the cover of the inhaler by screwing it back on.**

I cannot remember how many times I turned the grey grip. What should I do?

The TURBUHALER is designed to load only one dose at a time. If you can't remember how many times you have turned the grey grip, you can start the process again. Follow the steps below. You will not end up loading two doses.

If you are using a **NEW** inhaler for the first time, start at the beginning of STEP 2 under the section "**A. How to prepare a NEW inhaler for use:**".

For regular use of your inhaler, start at the beginning of STEP 3 under the section "**B. How to take a dose:**".

How do I know my dose has been loaded?

By turning the grey grip all the way in <u>BOTH</u> directions, you will properly load a dose of your medication. At some point when you are turning the grip you will hear a "click". This is part of the loading process. If you are not sure you heard the "click", repeat from the beginning of STEP 3 under the section "**B. How to take a dose:**". This will not result in two doses being loaded. The TURBUHALER is designed to load only one dose at a time. If you do not hear the "click" sound when the turning grip is rotated, you will not receive any medication. If this problem persists, you need to replace the RHINOCORT TURBUHALER.

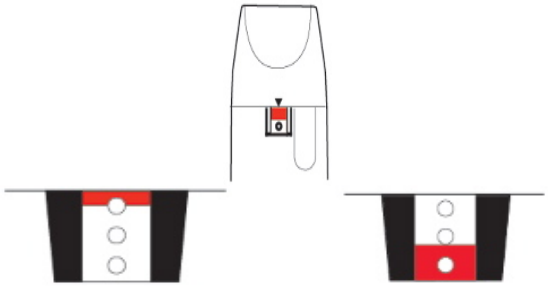
How do I clean my inhaler?

Clean the outside of the nasal adapter once a week with a **dry** tissue. **Never** use water or any other fluid.

How do I know when to start a new inhaler?

RHINOCORT TURBUHALER has a dose indicator. When a red mark first appears in the little window underneath the nasal adapter, there are approximately 20 doses left (Figure 4). Now is the time to obtain your next inhaler. When the red mark reaches the bottom of the window, you should discard your inhaler. The sound you hear if you shake the inhaler is produced by a drying agent, not the medication. RHINOCORT TURBUHALER cannot be refilled with drug and should be thrown away.

Figure 4



Approximately 20 doses left EMPTY

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- nose and throat irritation;
- nosebleeds and crusting;
- itchy and sore throat;
- cough;
- fatigue;
- nausea or dizziness;
- headache;
- skin rash.

Side effects that may occur with the use of local corticosteroids are:

- itching and swelling in the face;
- slower healing of wounds. Do not use RHINOCORT TURBUHALER until your nose has healed if you have a sore in your nose, if you have surgery on your nose, or if your nose has been injured;
- slower growth in children. Your doctor should monitor growth regularly for children;
- worsening of the symptoms of infections such as existing tuberculosis, fungal, bacterial or viral infections.

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 immediately seek emergency medical attention
		Only if severe	In all cases	
Very rare	small holes or ulcers in the skin inside the nose		X	
	Allergic reactions: such as swelling of the face, lips, tongue, and/or throat (which may cause difficulty in breathing or swallowing), hives, rash and itching			X
Un-known	**Cushing's Syndrome:** (hypercorticism) Rapid weight gain especially around the body and face; round "moon" face, excess sweating; thinning of the skin with easy bruising and dryness; muscle and bone weakness.		X	

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

HOW TO STORE IT

Keep RHINOCORT TURBUHALER out of the reach and sight of children.

Store the inhaler at room temperature (15-30°C).

Always replace the cover after using RHINOCORT TURBUHALER.

Do not keep or use RHINOCORT TURBUHALER after the expiry date indicated on the label.

REPORTING SUSPECTED 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 (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Call 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.

MORE INFORMATION

NOTE: This CONSUMER INFORMATION leaflet provides you with the most current information at the time of printing.

The Consumer Information Leaflet plus the full Product Monograph, prepared for health professionals can be found at: www.astrazeneca.ca, or by contacting the sponsor, AstraZeneca Canada Inc. at: 1-800-668-6000.

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