PRODUCT MONOGRAPH

PrMYLAN-BUDESONIDE AQ

Budesonide Aqueous Nasal Spray
64 mcg per metered dose

Mylan Std.

Corticosteroid for Nasal Use

Mylan Pharmaceuticals ULC
85 Advance Road
Etobicoke, Ontario
M8Z 2S9

DATE OF REVISION:
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Control Number: 197573
**Pr**MYLAN-BUDESONIDE AQ

Budesonide Aqueous Nasal Spray  
64 mcg per metered dose

**ACTIONS AND CLINICAL PHARMACOLOGY**

MYLAN-BUDESONIDE AQ contains budesonide which is a potent synthetic glucocorticosteroid with strong topical and weak systemic effects.

MYLAN-BUDESONIDE AQ 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 in the prevention of nasal polyps after polypectomy.

**CONTRAINDICATIONS**

- Hypersensitivity to any of the nasal spray’s components;
- 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 MYLAN-BUDESONIDE AQ (budesonide), 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 MYLAN-BUDESONIDE AQ therapy is not achieved until 2 to 3 days of treatment have been completed. In rare cases the full effect of MYLAN-BUDESONIDE AQ 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.

Treatment with MYLAN-BUDESONIDE AQ should not be stopped abruptly but tapered off gradually.

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 MYLAN-BUDESONIDE AQ, as 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.

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

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

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 MYLAN-BUDESONIDE AQ (see CONSUMER INFORMATION).

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

**Use in Pregnancy**

In experimental animal studies, budesonide was found to cross the placental 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 MYLAN-BUDESONIDE AQ to women who are breastfeeding should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

**Children Under 6 Years of Age**

MYLAN-BUDESONIDE AQ 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 Cmax (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 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 corticosteroids side-effects.
Omeprazole

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

ADVERSE REACTIONS

The adverse reactions reported with MYLAN-BUDESONIDE AQ (budesonide) are consistent with what one would expect when applying a topical treatment to an already inflamed membrane. All side effects were 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 MYLAN-BUDESONIDE AQ 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 budesonide. 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 MYLAN-BUDESONIDE AQ (budesonide) 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 a 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 MYLAN-BUDESONIDE AQ (budesonide).
Initially, MYLAN-BUDESONIDE AQ 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 MYLAN-BUDESONIDE AQ 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 cooperation 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 6 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 MYLAN-BUDESONIDE AQ therapy.

Although systemic effects are negligible at recommended doses, MYLAN-BUDESONIDE AQ treatment should not be continued beyond three weeks in the absence of significant symptomatic improvement. MYLAN-BUDEONSIDE AQ 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**

The recommended starting dose is 256 mcg daily. The dose can be administered once daily in the morning or divided into two administrations morning and evening. For example: 128 mcg (2 sprays) into each nostril in the morning or, 64 mcg (1 spray) into each nostril morning and evening.

**Maintenance Dose**

After the desired clinical effect is obtained, the maintenance dose should be reduced to the smallest amount necessary to control the symptoms.

**Treatment or Prevention of Nasal Polyps:**
The recommended dose is 64 mcg (1 spray) into each nostril morning and evening (total daily dose is 256 mcg).

**Children Under 6 Years**

Not recommended for children in this age group.
PHARMACEUTICAL INFORMATION

Drug Substance

Chemical Structure:

![Chemical Structure Image]

Generic Name: Budesonide

Chemical Name: Budesonide is a mixture of two isomers:
1. Pregna-1,4-diene-3,20-dione,16,17-butyldenebis(oxy)-11,21-dihydroxy-[11β,16α(R)] and
2. Pregna-1,4-diene-3,20-dione,16,17-butyldenebis(oxy)-11,21-dihydroxy-[11β,16α(S)]

Molecular Formula: C_{25}H_{34}O_{6}

Molecular Weight: 430.5 g/mol

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 64 mcg

Non-medicinal: hydrochloric acid, disodium edentate, potassium sorbate, dextrose anhydrous, polysorbate 80, Avicel RC-591.

Stability and Storage Recommendations

MYLAN-BUDESONIDE AQ should be stored at room temperature (15°C - 30°C).
AVAILABILITY OF DOSAGE FORMS

MYLAN-BUDESONIDE AQ 64 mcg/dose is a white to off-white, thixotropic suspension of budesonide in water supplied in amber glass bottles provided with a pump spray mechanism, nasal adapter and Patient Instruction leaflet in bottles of 120 doses.

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 bioavailability of oral budesonide in man is low (about 10%). With reference to the metered dose, the systemic availability of budesonide from MYLAN-BUDESONIDE AQ is 33%. 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 400 mcg budesonide from MYLAN-BUDESONIDE AQ is 1.0 nmol/L and is reached within 0.7 hours.

The distribution volume (Vd) of budesonide is 301.3 ± 41.7 L, indicating the high issue 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 the *in vitro* and *in vivo* metabolic patterns could be detected. Negligible biotransformation was observed in human lung and serum preparations.

**TOXICOLOGY**

**Acute Toxicity**

<table>
<thead>
<tr>
<th>Species</th>
<th>Sex</th>
<th>Route</th>
<th>LD₅₀ (mg/kg) After 3 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>mouse</td>
<td>male</td>
<td>s.c.</td>
<td>35 ± 18</td>
</tr>
<tr>
<td>mouse</td>
<td>male</td>
<td>p.o.</td>
<td>&gt;800</td>
</tr>
<tr>
<td>mouse</td>
<td>female</td>
<td>p.o.</td>
<td>&gt;800</td>
</tr>
<tr>
<td>rat</td>
<td>male</td>
<td>s.c.</td>
<td>15.1 ± 4.4</td>
</tr>
<tr>
<td>rat</td>
<td>female</td>
<td>s.c.</td>
<td>20.3±7.1</td>
</tr>
<tr>
<td>rat</td>
<td>male</td>
<td>p.o.</td>
<td>≈400</td>
</tr>
</tbody>
</table>

Surviving animals exhibited a marked decrease in body weight gain.
Toxicity After Repeated Administration Of Budesonide To Rats, Rabbits And Dogs

<table>
<thead>
<tr>
<th>Animal</th>
<th>No. of Dose Groups</th>
<th>Daily Dose Levels</th>
<th>Route of Administration</th>
<th>Duration</th>
<th>Toxic Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>4</td>
<td>0.05 0.5 5.0 50.0</td>
<td>p.o. 1 month</td>
<td></td>
<td>Atrophy of adrenal gland and lymphoid system. Gastric ulceration.</td>
</tr>
<tr>
<td>Rat</td>
<td>3</td>
<td>0.02 0.10 0.2-0.5</td>
<td>inhalation 3 months</td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td>Rat</td>
<td>3</td>
<td>0.005 0.01 0.05</td>
<td>inhalation 12 months</td>
<td></td>
<td>As above.</td>
</tr>
<tr>
<td>Rabbit</td>
<td>2</td>
<td>0.025 0.1</td>
<td>s.c. 1 month</td>
<td></td>
<td>High dose caused slight liver mass increase, slight decrease in adrenal mass, thymal regression.</td>
</tr>
<tr>
<td>Dog</td>
<td>3</td>
<td>0.01 0.1 1.0</td>
<td>p.o. 1 month</td>
<td></td>
<td>High dose – typical steroid effects – adrenal, lymphoid system atrophy, increased fat in myocardium, glycogen in liver.</td>
</tr>
<tr>
<td>Dog</td>
<td>3</td>
<td>0.02 0.06 0.2</td>
<td>inhalation 6 weeks</td>
<td></td>
<td>High dose – induced thymal atrophy, adrenal atrophy. No changes in respiratory system observed.</td>
</tr>
<tr>
<td>Dog</td>
<td>3</td>
<td>0.20 0.60 2.00</td>
<td>inhalation 6 months</td>
<td></td>
<td>High dose – decreased plasma cortisol, cortical atrophy of the adrenal gland, thymal regression. Slight visceral obesity.</td>
</tr>
<tr>
<td>Dog</td>
<td>3</td>
<td>0.20 0.60 2.00</td>
<td>inhalation 12 months</td>
<td></td>
<td>High dose – obesity, alopecia, females showed no evidence of estrous cycle. Systemic steroid effects – lymphoid and adrenal atrophy.</td>
</tr>
</tbody>
</table>

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/kg 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, 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

Budesonide Aqueous Nasal Spray

64 mcg per metered dose

Your nasal spray contains 120 doses.

WARNINGS AND PRECAUTIONS

BEFORE you use MYLAN-BUDESONIDE AQ talk to your doctor or pharmacist if you:

- are allergic to budesonide or any of the other ingredients in MYLAN-BUDESONIDE AQ;
- have or have had lung tuberculosis or any other recent infection. MYLAN-BUDESONIDE AQ may hide some symptoms of infection or may cause the symptoms of infection to worsen. You may be more likely to get an infection while taking MYLAN-BUDESONIDE AQ.
- have asthma;
- have thyroid problems;
- have open wounds after recent nasal surgery or trauma;
- have or had liver problems;
- are taking, or have previously taken steroids either as an injection or by mouth within the past several months;
- are pregnant or planning to become pregnant;
- are breastfeeding;
- about all health problems you have now or have had in the past.

Local corticosteroids such as MYLAN-BUDESONIDE AQ may cause:

- slower growth in children. Continuous long-term use in children is not recommended as the effects are not fully known. Your child’s doctor should regularly monitor their growth while they are taking MYLAN-BUDESONIDE AQ.
- symptoms of Cushing’s syndrome, such as thinning fragile skin that bruises easily, rapid weight gain around the body and face, excess sweating, and muscle and bone weakness.

Exposure to measles or chicken pox
You should avoid coming into contact with people who have measles or chicken pox while taking MYLAN-BUDESONIDE AQ. If you are exposed, tell your doctor right away.

Transfer to MYLAN-BUDESONIDE AQ from an oral corticosteroid
If you have been prescribed MYLAN-BUDESONIDE AQ and are taking oral steroid medication, your doctor may gradually reduce the dose of your tablets. This may happen over a period of weeks or months.
You should contact your doctor if you get symptoms such as:
- headache
- tiredness
- muscle and joint pain
- nausea or vomiting
- depression
- rash
- runny nose
- coughing, especially at night, during exercise or when laughing
- difficulty breathing
- chest tightness
- shortness of breath
- wheezing.

**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 MYLAN-BUDESONIDE AQ include:
- ritonavir used to treat HIV or AIDS;
- ketoconazole/itraconazole used to treat fungal infections.

**PROPER USE OF THIS MEDICATION**

This medicine is prescribed for you by your doctor. Never give it to someone else. It may harm them even if their symptoms are the same as yours.

**MYLAN-BUDESONIDE AQ:**
- Is for use in the nose only. Do not use it in your eyes or mouth.
- 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.

Take MYLAN-BUDESONIDE AQ exactly as recommended by your doctor. 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. Do not stop taking MYLAN-BUDESONIDE AQ even if you feel better unless told to do so by your doctor.

For seasonal allergic rhinitis, MYLAN-BUDESONIDE AQ 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.

This drug does not relieve allergy symptoms in the eyes. If your eyes bother you, your doctor may be able to give you some additional medicine to relieve these symptoms.

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

Children using MYLAN-BUDESONIDE AQ should be supervised by an adult. This is to ensure that the correct dose is given as prescribed by the doctor.

**Adults and Children (6 years and older)**

Depending on how MYLAN-BUDESONIDE AQ works for you, your doctor may change your dose.

**Rhinitis:**
MYLAN-BUDESONIDE AQ can be taken once a day or twice a day.

**Usual once a day starting dose:** 2 sprays into each nostril once a day (in the morning)

**Usual twice a day starting dose:** 1 spray into each nostril twice a day (in the morning and evening)

**Maintenance dose:** Use the lowest effective dose necessary to control symptoms.

**Nasal Polyps:**
**Usual Dose:** 1 spray into each nostril twice a day (in the morning and evening)

Treatment with MYLAN-BUDESONIDE AQ should not be stopped abruptly, but tapered off gradually.
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.

Missed Dose:

- If you miss a dose take it as soon as possible. Then go back to your regular schedule.
- If it is almost time to take your next dose, skip the missed dose and take the next dose at the usual time.
- **Do NOT take a double dose of MYLAN-BUDESONIDE AQ to make up for a missed dose.** If you are still unsure, check with your doctor or pharmacist to see what you should do.

How to use your MYLAN-BUDESONIDE AQ

Before you start using MYLAN-BUDESONIDE AQ for the first time, it is important that you read the instructions below and follow them carefully.

A. How to prepare a new sprayer for use:

When using the spray **for the first time**, you must prepare the spray.

Step 1
Turn the bottle upside-down 3 to 4 times. Remove the protective cap from the nose piece.

Step 2
Load the pump by pressing downwards on the collar. Use your index and middle fingers while supporting the base of the bottle with your thumb (Figure 1). Press down 5 to 10 times until a fine mist spray appears. Avoid spraying the mist into your eyes.

![Figure 1](image)

NOTE: If not used daily the pump must be loaded again. This time you just need to pump once into the air. The spray is now ready for use.

B. How to take a dose:

Step 1
Turn the bottle upside-down 3 to 4 times. Remove the protective cap from the nose piece.

Step 2
If you did not use your spray yesterday, make sure you prepare the pump by pressing down once only (Figure 1).

Step 3
Gently blow your nose. Hold the bottle as shown. Tilt your head forward slightly. Close one nostril with a finger and gently insert the tip of the nose piece into the other nostril (Figure 2).

![Figure 2](image)

Cleaning: Clean the nose piece and protective cap regularly. To clean the nose piece, remove the protective cap, press upwards on the collar and the nose piece will come off. Wash the nose piece and protective cap under lukewarm water. Air dry and replace the nose piece and the protective cap back on the bottle and reload as in Step #2. **Do not try to clean the nasal applicator by using a pin or sharp object.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Common side effects are:

- nose and throat irritation,
• nose bleeding and crusting

Other side effects include:
• itchy and sore throat
• cough
• fatigue
• nausea/dizziness
• headache

Uncommon side effects that may occur when also taking an oral steroid:
• asthma
• skin rash
• itching or swelling in the face
• Cushing’s syndrome (hypercorticism)

| 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 |

| Uncommon | 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 |

| Very rare | Small holes or ulcers in the skin inside the nose | X |

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

HOW TO STORE IT

Keep MYLAN-BUDESONIDE AQ out of the reach and sight of children.

Store the bottle at room temperature (15-30°C) in a dry place, away from moisture. Always replace the protective cap after using MYLAN-BUDESONIDE AQ.

Do not keep or use MYLAN-BUDESONIDE AQ after the expiry date indicated on the label.
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.

MORE INFORMATION

If you want more information about Mylan-Budesonide AQ:

- 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 (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); or by calling 1-844-596-9526

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