

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

<sup>Pr</sup>Aermony RESPICLICK™

fluticasone propionate inhalation powder, Mfr. Std.

55 mcg, 113 mcg and 232 mcg fluticasone propionate / actuation

Corticosteroid for Oral Inhalation

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PrAermony RESPICLICK™

fluticasone propionate dry powder for oral inhalation

**PART I: HEALTH PROFESSIONAL INFORMATION**

**SUMMARY PRODUCT INFORMATION**

<b>Route of Administration</b>	<b>Dosage Form / Strength</b>	<b>Clinically Relevant Nonmedicinal Ingredients</b>
Oral inhalation	Dry powder for inhalation / 55 mcg, 113 mcg and 232 mcg fluticasone propionate / actuation	Lactose monohydrate (which contains milk protein).

**INDICATIONS AND CLINICAL USE**

Aermony RESPICLICK™ (fluticasone propionate) is indicated for:

- the maintenance treatment of steroid-responsive bronchial asthma as prophylactic therapy in patients 12 years of age and older.

Aermony RESPICLICK is **not** indicated for the relief of acute bronchospasm (see WARNINGS AND PRECAUTIONS, General).

**Geriatrics (> 65 years of age):**

No dose adjustment is needed in patients 65 years of age and older based on the available efficacy and safety data.

**Pediatrics (< 12 years of age):**

The efficacy and safety of Aermony RESPICLICK in children below 12 years of age have not been established.

## **CONTRAINDICATIONS**

The use of Aermony RESPICLICK is contraindicated in the following conditions:

- Patients with a history of hypersensitivity to any of its ingredients (see DOSAGE FORMS, COMPOSITION AND PACKAGING)
- Severe hypersensitivity to milk proteins (see WARNINGS AND PRECAUTIONS – Sensitivity/Resistance)
- The primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required.

## **WARNINGS AND PRECAUTIONS**

### **General**

It is essential that patients be instructed that Aermony RESPICLICK is a preventative agent which must be taken daily at the intervals recommended by their doctors.

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

### **Not for Acute Use**

Aermony RESPICLICK is not a bronchodilator and should not be used for rapid relief of acute episodes of bronchospasm. Patients will require an inhaled short-acting beta<sub>2</sub>-agonist (e.g. salbutamol) for treatment of acute asthmatic symptoms.

Patients should be instructed to contact their physicians immediately when episodes of asthma that are not responsive to bronchodilators occur during the course of treatment with Aermony RESPICLICK. During such episodes, patients may require therapy with oral corticosteroids.

There is no evidence that control of bronchial asthma can be achieved by the administration of Aermony RESPICLICK in amounts greater than the recommended dosages.

### **Discontinuance**

Treatment with Aermony RESPICLICK should not be stopped abruptly, but tapered off gradually due to a risk of exacerbation.

## **Endocrine and Metabolism**

### **Systemic Effects**

Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur with inhaled corticosteroids than with oral corticosteroids. Possible systemic effects of Aermony RESPICLICK include: Cushing's syndrome, Cushingoid features, hypothalamic-pituitary-adrenal (HPA) axis suppression, decrease in bone mineral density (BMD), growth retardation in children and adolescents, cataracts and glaucoma. It is important therefore, that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control is maintained.

### **Transferring Patients from Systemic Corticosteroid Therapy**

Particular care is needed for patients who have been transferred from systemically active corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function.

Patients who have been previously maintained on 20 mg or more of prednisone (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have been almost completely withdrawn. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Although Aermony RESPICLICK may control asthma symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of glucocorticoid systemically and does NOT provide the mineralocorticoid that is necessary for coping with these emergencies.

During periods of stress or a severe asthmatic attack, patients who have been withdrawn from systemic corticosteroids should be instructed to resume oral corticosteroids (in large doses) immediately and to contact their physician for further instruction. These patients should also be instructed to carry a warning card indicating that they may need supplementary systemic corticosteroids during periods of stress or a severe asthma attack. To assess the risk of adrenal insufficiency in emergency situations, routine tests of adrenal cortical function, including measurement of early morning and evening cortisol levels, should be performed periodically in all patients. An early morning resting cortisol level may be accepted as normal only if it falls at or near the normal mean level.

The replacement of a systemic corticosteroid with an inhaled corticosteroid must be gradual and carefully supervised by the physician. Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to Aermony RESPICLICK. Lung function (mean forced expiratory volume in 1 second [FEV<sub>1</sub>] or morning peak expiratory flow [AM PEF]), beta-agonist use, and asthma symptoms should be carefully monitored during withdrawal of oral corticosteroids. In addition, patients should be observed for signs and symptoms of adrenal insufficiency, such as fatigue, lassitude, weakness, nausea and vomiting, and hypotension.

During withdrawal from oral corticosteroids, some patients may experience symptoms of systemically active corticosteroid withdrawal (e.g., joint and/or muscular pain, lassitude, depression) despite maintenance or even improvement of respiratory function.

Transfer of patients from systemic corticosteroid therapy to Aermony RESPICLICK may unmask allergic conditions previously suppressed by the systemic corticosteroid therapy (e.g., rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions).

### **Hypercorticism and Adrenal Suppression**

Fluticasone propionate will often help control asthma symptoms with less suppression of HPA function than therapeutically equivalent oral doses of prednisone. Since fluticasone propionate is absorbed into the circulation and can be systemically active at higher doses, the beneficial effects of Aermony RESPICLICK in minimizing HPA dysfunction may be expected only when recommended dosages are not exceeded and individual patients are titrated to the lowest effective dose. A relationship between plasma levels of fluticasone propionate and inhibitory effects on stimulated cortisol production has been shown after 4 weeks of treatment with fluticasone propionate inhalation aerosol. Since individual sensitivity to effects on cortisol production exists, physicians should consider this information when prescribing Aermony RESPICLICK.

Because of the possibility of systemic absorption of inhaled corticosteroids in sensitive patients, patients treated with Aermony RESPICLICK should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response.

It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, the dosage of Aermony RESPICLICK should be reduced slowly, consistent with accepted procedures for reducing systemic corticosteroids, and other treatments for management of asthma symptoms should be considered.

### **Reduction in Bone Mineral Density**

Decreases in bone mineral density (BMD) have been observed with long-term administration of orally inhaled corticosteroids. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care, as Aermony RESPICLICK may pose an additional risk.

## **Effects on Growth**

Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to pediatric and adolescent patients. The effects of long-term treatment of children and adolescents with inhaled corticosteroids, including fluticasone propionate, on final adult height are not known. Routinely monitor the growth of pediatric patients receiving Aermony RESPICLICK (e.g., via stadiometry). To minimize the systemic effects of orally inhaled corticosteroids, including Aermony RESPICLICK, titrate each patient's dosage to the lowest dose that effectively controls his/her symptoms.

## **Hematologic**

### **Eosinophilic Conditions and Churg Strauss Syndrome**

In rare cases, patients on inhaled fluticasone propionate may present with systemic eosinophilic conditions. Some of these patients have clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition that is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction and/or withdrawal of oral corticosteroid therapy following the introduction of fluticasone propionate. Cases of serious eosinophilic conditions have also been reported with other inhaled corticosteroids in this clinical setting. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal relationship between fluticasone propionate and these underlying conditions has not been established.

## **Hypersensitivity**

Immediate hypersensitivity reactions (e.g., urticaria, angioedema, rash, bronchospasm, hypotension), including anaphylaxis, may occur after administration of Aermony RESPICLICK. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash) occur, Aermony RESPICLICK should be discontinued immediately and alternative therapy instituted. The patient should NOT be re-challenged with Aermony RESPICLICK if this is identified as the cause of the hypersensitivity reaction (see CONTRAINDICATIONS).

There have been reports of anaphylactic reactions in patients with severe milk protein allergy after inhalation of powder products containing lactose; therefore, patients with severe milk protein allergy should not use RESPICLICK.

## **Immune**

### **Candidiasis**

In clinical trials, the development of localized infections of the mouth and pharynx with *Candida albicans* has occurred in subjects treated with Aermony RESPICLICK. When such an infection develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy

while treatment with Aermony RESPICLICK continues. However, at times, therapy with Aermony RESPICLICK may need to be interrupted. Patients should be advised to rinse his/her mouth with water without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.

## **Infections**

Corticosteroids may mask some signs of infection and new infections may appear. An increased susceptibility to infections has been observed during corticosteroid therapy. This may require treatment with appropriate therapy or stopping the administration of fluticasone propionate until the infection is eradicated. Patients who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible children or adults using corticosteroids. In such children or adults who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chickenpox, prophylaxis with varicella-zoster immune globulin (VZIG) may be indicated. If a patient is exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. If chickenpox develops, treatment with antiviral agents may be considered.

Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral or parasitic infections; or ocular herpes simplex.

## **Ophthalmologic**

Glaucoma, increased intraocular pressure, cataracts and central serous chorioretinopathy (CSCR) have been reported in patients following the long-term administration of inhaled corticosteroids, including fluticasone propionate. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, cataracts and/or CSCR.

## **Respiratory**

### **Paradoxical bronchospasm**

As with other inhaled medicines, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. If bronchospasm occurs following dosing with Aermony RESPICLICK, it should be treated immediately with an inhaled, short-acting bronchodilator (e.g. salbutamol); Aermony RESPICLICK should be discontinued immediately, the patient assessed, and alternative therapy should be instituted (see ADVERSE REACTIONS).



## ***Special Populations***

### **Pregnant Women:**

There are no adequate and well-controlled studies with Aermony RESPICLICK in pregnant women and the safety of fluticasone propionate in pregnancy has not been adequately established. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels (See TOXICOLOGY). However, experience with oral corticosteroids suggests that rodents are more prone to teratogenic effects from corticosteroids than humans. Because animal reproduction studies are not always predictive of human response, Aermony RESPICLICK should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus. Women should be advised to contact their physicians if they become pregnant while taking Aermony RESPICLICK.

Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

### **Nursing Women:**

There are no data from controlled trials on the use of Aermony RESPICLICK by nursing mothers. It is not known whether fluticasone propionate is excreted in human breast milk. However, other corticosteroids have been detected in human milk. Furthermore, subcutaneous administration of tritiated fluticasone propionate to lactating rats resulted in excretion in the milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Aermony RESPICLICK and any potential adverse effects on the breastfed child from fluticasone propionate or from the underlying maternal condition.

### **Infertility:**

There are no human data to suggest any effects of fluticasone propionate on fertility.

### **Pediatrics (< 12 years of age)**

The safety and effectiveness of Aermony RESPICLICK in pediatric patients below the age of 12 years have not been established.

### **Geriatrics (> 65 years of age)**

Based on available data, no adjustment of the dose of RESPICLICK in geriatric patients is necessary, but greater sensitivity of some older individuals cannot be ruled out.

### **Hepatic Impairment**

Formal pharmacokinetic studies using Aermony RESPICLICK have not been conducted in patients with hepatic impairment. Since fluticasone propionate is predominantly cleared by hepatic metabolism, impairment of liver function may lead to accumulation of fluticasone propionate in plasma. Therefore, patients with hepatic disease should be closely monitored.

## Monitoring and Laboratory Tests

- **Monitoring control of asthma:** Increasing use of fast-acting inhaled bronchodilators to control symptoms indicates deterioration of asthma control. Sudden and progressive deterioration in asthma control is potentially life-threatening. The patient should be re-evaluated and consideration should be given to adjusting the asthma maintenance therapy. Patients should be instructed to contact their physicians if they find that relief with short-acting bronchodilator treatment becomes less effective or they need more inhalations than usual. During such episodes, patients may require therapy with systemic corticosteroids.
- During long-term therapy, HPA axis function and haematological status should be assessed periodically.
- Inhaled corticosteroids, including fluticasone propionate may cause a reduction in growth velocity in adolescents. The growth of adolescent patients receiving prolonged treatment with Aermony RESPICLICK should be monitored regularly.
- For patients at risk, monitoring of bone and ocular effects (cataract and glaucoma) should be considered in patients receiving maintenance therapy with Aermony RESPICLICK.
- Fluticasone propionate is predominantly cleared by hepatic metabolism. Therefore, patients with hepatic impairment should be monitored for corticosteroid effects due to potentially increased systemic exposure of fluticasone propionate.

## ADVERSE REACTIONS

### Adverse Drug Reaction Overview

Systemic and local corticosteroid use may result in the following (see WARNINGS AND PRECAUTIONS):

- Candidiasis
- Infections
- Hypercorticism and adrenal suppression
- Reduction in bone mineral density
- Effect on growth in pediatrics
- Glaucoma and cataracts

In general, inhaled corticosteroid therapy may be associated with dose dependent increases in the incidence of ocular complications, reduced bone density, suppression of HPA axis responsiveness to stress, and inhibition of growth velocity in children. Such events have been reported rarely in clinical trials with fluticasone propionate.

Glaucoma may be exacerbated by inhaled corticosteroid treatment for asthma or rhinitis. In elderly patients treated with inhaled corticosteroids, the prevalence of posterior subcapsular and nuclear cataracts is probably low but increases in relation to the daily and cumulative lifetime dose. Cofactors such as smoking, ultraviolet B exposure, or diabetes may increase the risk. Children may be less susceptible.

A reduction of growth velocity in children or teenagers may occur as a result of inadequate control of chronic diseases such as asthma or from use of corticosteroids for treatment.

Osteoporosis and fracture are the major complications of long-term asthma treatment with parenteral or oral steroids. Inhaled corticosteroid therapy is also associated with dose-dependent bone loss although the degree of risk is very much less than with oral steroid.

### **Clinical Trial Adverse Drug Reactions**

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

The incidence of adverse reactions associated with Aermony RESPICLICK in adult and adolescent patients 12 years of age and older with asthma (see Table 1) is based upon two randomized, placebo-controlled, 12-week, clinical studies (Study 1 and 2). A total of 822 patients (60% female patients) previously treated with inhaled corticosteroids or inhaled corticosteroid/LABA combination therapy were treated twice daily with Aermony RESPICLICK 55 mcg, 113 mcg, 232 mcg or placebo. The average duration of exposure was 82 days in Aermony RESPICLICK groups compared with 75 days in the placebo group.

**Table 1: Adverse Reactions with  $\geq 3\%$  Incidence with Aermony RESPICLICK, and More Common than Placebo in Subjects with Asthma**

Adverse Reaction	Aermony RESPICLICK 55 mcg (n=129) %	Aermony RESPICLICK 113 mcg (n=274) %	Aermony RESPICLICK 232 mcg (n=146) %	Placebo (n=273) %
<i>Infections and infestations</i>				
Nasopharyngitis	5.4	5.8	4.8	4.4
Upper respiratory tract infection	5.4	4.7	5.5	4.8
Oral candidiasis*	3.1	2.9	4.8	0.7
<i>Nervous system disorders</i>				
Headache	1.6	7.3	4.8	4.4
<i>Respiratory disorders</i>				
Cough	1.6	1.8	3.4	2.6

\* Oral candidiasis includes oropharyngeal candidiasis, oral fungal infection, and oropharyngitis fungal

Additional Adverse Reactions: Other adverse reactions not previously listed (and occurring in  $<3\%$  of patients and in three or more patients on Aermony RESPICLICK), whether considered drug-related or not by the investigators, that were reported more frequently by patients with asthma treated with Aermony RESPICLICK compared with patients treated with placebo include the following:

Oropharyngeal pain, hypertension, rhinitis allergic, influenza, pyrexia, dizziness, respiratory tract infection, muscle spasms, rhinitis, epistaxis, ligament sprain, musculoskeletal pain, pain in extremity, throat irritation, and vomiting.

### Safety Study (Study 3)

In a 26-week, randomized, open-label, active controlled safety study of 674 adult and adolescent patients (aged 12 years and older) previously treated with inhaled corticosteroids or inhaled corticosteroid/LABA combination therapy, 253 were treated twice daily with Aermony RESPICLICK 113 mcg or 232 mcg. The types of adverse reactions were similar to those reported above in placebo controlled studies.

## **Less Common Clinical Trial Adverse Drug Reactions (<1%)**

**Gastrointestinal Disorders:** Vomiting

**Injury, Poisoning and Procedural Complications:** Ligament sprain

**Respiratory, Thoracic and Mediastinal Disorders:** Throat irritation

### **Post-Market Adverse Drug Reactions**

In addition to adverse reactions reported from clinical trials, the following adverse reactions have been identified during post-approval use of fluticasone propionate, regardless of indication. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events have been chosen for inclusion due to either their seriousness, frequency of reporting, or causal connection to fluticasone propionate or a combination of these factors.

#### Endocrine and Metabolic:

*Rare:* Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children/adolescents, decreased bone mineral density.

Eye Disorders: Blurred vision and central serous chorioretinopathy, cataract, glaucoma.

#### Immune System Disorders:

*Uncommon:* Cutaneous hypersensitivity reactions.

*Very rare:* Hypersensitivity reactions manifesting as angioedema (mainly facial and oropharyngeal edema), respiratory symptoms (dyspnea and/or bronchospasm) and anaphylactic reactions.

#### Infections and Infestations:

*Rare:* Esophageal candidiasis.

#### Metabolism and Nutrition Disorders

*Very rare:* Hyperglycemia

#### Musculoskeletal and Connective Tissue Disorders

*Very Rare:* Osteonecrosis [particularly with previous or concurrent use of systemic steroids (e.g., IV or oral)].

### Psychiatry:

*Very rare:* Anxiety, sleep disorder and behavioral changes, including hyperactivity and irritability (primarily in children and adolescents).

### Respiratory, Thoracic and Mediastinal Disorders:

*Very rare:* Paradoxical bronchospasm (see WARNINGS AND PRECAUTIONS).

## **DRUG INTERACTIONS**

### **Overview**

Fluticasone propionate is a substrate of cytochrome P450 3A4 (CYP3A4). The use of strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with Aermony RESPICLICK is not recommended because increased systemic corticosteroid adverse effects may occur.

### **Inhibitors of CYP3A4**

Ritonavir: A drug interaction trial with fluticasone propionate aqueous nasal spray in healthy subjects has shown that ritonavir (a strong CYP3A4 inhibitor) can significantly increase plasma fluticasone propionate exposure, resulting in significantly reduced serum cortisol concentrations. During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression.

Ketoconazole: Coadministration of orally inhaled fluticasone propionate (1,000 mcg) and ketoconazole (200 mg once daily) resulted in a 1.9-fold increase in plasma fluticasone propionate exposure and a 45% decrease in plasma cortisol area under the curve (AUC), but had no effect on urinary excretion of cortisol.

## Drug-Drug Interactions

**Table 2 - Established or Potential Drug-Drug Interactions**

<Proper name>	Ref	Effect	Clinical comment
Ritonavir	CT	Systemic effects including Cushing's syndrome and adrenal suppression.	Concomitant use of fluticasone propionate and ritonavir should be avoided.
Other inhibitors of cytochrome P450 3A4	CT	Increased systemic exposure to fluticasone propionate.	Care is advised when co-administering potent cytochrome P450 3A4 inhibitors.
Acetylsalicylic acid	T		Use with caution in conjunction with corticosteroids in hypoprothrombinemia.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

## Drug-Food Interactions

Interactions with food have not been established.

## Drug-Herb Interactions

Interactions with herbal products have not been established.

## Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

## DOSAGE AND ADMINISTRATION

### Dosing Considerations

**The lowest dose of Aermony RESPICLICK required to maintain good asthma control should be used. When the patient's asthma is well controlled, a reduction in the dose of Aermony RESPICLICK should be attempted in order to identify the lowest possible dose required to maintain control. Such an attempt at dose reduction should be carried out on a regular basis.**

Patients using inhaled bronchodilators should be advised to use the bronchodilator before Aermony RESPICLICK in order to enhance the penetration of fluticasone propionate into the bronchial tree. Several minutes should lapse between the use of the two inhalers to allow for some bronchodilation to occur.

If asthma symptoms arise between doses, an inhaled short-acting beta<sub>2</sub>-agonist should be used for immediate relief.

In the presence of excessive mucous secretion, the drug may fail to reach the bronchioles. Therefore, if an obvious response is not obtained after ten days, a short course of systemic corticosteroid treatment might be in order. Continuation of treatment with inhaled fluticasone propionate usually maintains the improvement achieved, the systemic steroid being gradually withdrawn.

Treatment with Aermony RESPICLICK should not be stopped abruptly, but tapered off gradually.

### **Recommended Dose and Dosage Adjustment**

For patients aged 12 years and older, the recommended dosage of Aermony RESPICLICK is one inhalation twice daily, approximately 12 hours apart. Aermony RESPICLICK should be used at approximately the same time every day.

The recommended starting dosages are based on the patient’s asthma severity. For patients switching to Aermony RESPICLICK from another inhaled corticosteroid product, select the low (55 mcg), medium (113 mcg) or high (232 mcg) dose strength of Aermony RESPICLICK based on the strength of the previous inhaled corticosteroid product and level of disease severity (see Table 3).

**Table 3: Usual Recommended Starting Dosages of Aermony RESPICLICK**

<b>Current Therapy</b>	<b>Aermony RESPICLICK Recommended Starting Dose</b>
Bronchodilators alone	<b>55 mcg twice daily</b>
Inhaled corticosteroids	
- Low dose	<b>55 mcg twice daily</b>
- Medium dose	<b>113 mcg twice daily</b>
- High dose	<b>232 mcg twice daily</b>

Individual patients will experience a variable time to onset and degree of symptom relief. Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting treatment.

After asthma stability has been achieved, it is desirable to titrate to the lowest effective dosage to reduce the possibility of side effects.

If a dosage regimen of Aermony RESPICLICK fails to provide adequate improvement in asthma control, the therapeutic regimen should be reevaluated and additional therapeutic options (e.g., replacing the current strength of Aermony RESPICLICK with a higher strength, or adding additional controller therapies should be considered.



The maximum recommended dosage is one inhalation of Aermony RESPICLICK 232 mcg twice daily. The safety and efficacy of Aermony RESPICLICK when administered in excess of recommended dosages have not been established.

### **Missed Dose**

If a single dose is missed, instruct the patient to take the next dose when it is due.

### **Administration**

Aermony RESPICLICK should be administered by the orally inhaled route only in patients aged 12 years and older.

After inhalation, the patient should rinse his/her mouth with water without swallowing to help reduce the risk of oropharyngeal candidiasis.

### **The physician should instruct the patient as per the following points:**

- Aermony RESPICLICK does **not** require priming.
- Do not use Aermony RESPICLICK with a spacer or volume holding chamber.
- **Do not open your Aermony RESPICLICK cap unless you are taking a dose.** Repeated opening and closing the green cap without taking medication will waste medication and may damage the inhaler.
- **Immediately replace inhaler if mouthpiece cover is damaged or broken.**
- **Counter:** The Aermony RESPICLICK inhaler has a counter.
  - When the patient receives the inhaler, the number 60 will be displayed. The counter will count down each time the mouthpiece is opened and closed. The counter window displays the number of actuations (inhalations) left in the inhaler in units of two (e.g., 60, 58, 56, etc.). When the counter reaches 20, the colour of the numbers will change to red to remind the patient to contact their pharmacist for a refill of medication or consult their physician for a prescription refill. When the counter reaches 0, the background will change to solid red and the colour of the numbers will change to black.
  - Instruct the patient to discard Aermony RESPICLICK inhaler 30 days after opening the foil pouch, when the counter displays 0 or after the expiration date on the product, whichever comes first.
- **Cleaning:**
  - Keep the inhaler in a cool dry place. Never wash or put any part of the inhaler in water.
  - Gently wipe the mouthpiece with a dry cloth or tissue once a week.

## OVERDOSAGE

Chronic overdosage may result in signs/symptoms of hypercorticism.

Acute inhalation of Aermony RESPICLICK doses in excess of those approved may lead to temporary suppression of the hypothalamic-pituitary-adrenal axis. This does not usually require emergency action, as normal adrenal function typically recovers within a few days.

If higher than approved doses are continued over prolonged periods, significant adrenocortical suppression is possible. Situations which could potentially trigger acute adrenal crisis include exposure to trauma, surgery or infection or any rapid reduction in dosage. Patients receiving higher than approved dosages should be managed closely and the dose reduced gradually.

Chronic use of inhaled fluticasone propionate in daily doses in excess of the recommended dosage may lead to some degree of adrenal suppression. Monitoring of adrenal reserve may be indicated. Gradual reduction of the inhaled dose may be required. Treatment with Aermony RESPICLICK should be continued at a dose sufficient to control asthma.

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

## ACTION AND CLINICAL PHARMACOLOGY

### Mechanism of Action

Fluticasone propionate is a synthetic trifluorinated corticosteroid with anti-inflammatory activity. In comparison with beclomethasone dipropionate, fluticasone propionate has demonstrated greater topical potency.

Inflammation is an important component in the pathogenesis of asthma. Corticosteroids have been shown to have a wide range of actions on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation. These anti-inflammatory actions of corticosteroids contribute to their efficacy in asthma.

Though effective for the treatment of asthma, corticosteroids do not affect asthma symptoms immediately. Individual patients will experience a variable time of onset and degree of symptom relief. Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting treatment. When corticosteroids are discontinued, asthma stability may persist for several days or longer.

Trials in subjects with asthma have shown a favorable ratio between topical anti-inflammatory activity and systemic corticosteroid effects with recommended doses of orally inhaled fluticasone propionate. This is explained by a combination of a relatively high local anti-inflammatory effect, negligible oral systemic availability (<1%), and the minimal pharmacological activity of the only metabolite detected in man.

## **Pharmacodynamics**

### Hypothalamic Pituitary Adrenal Axis Effects

The potential systemic effects of Aermony RESPICLICK on the HPA axis were not fully studied, but other clinical trials evaluated the systemic effects of fluticasone propionate inhalation powder on the HPA axis in healthy subjects and in subjects with asthma.

There are no data from controlled trials using the Aermony RESPICLICK in healthy subjects or subjects with asthma regarding serum cortisol.

## **Pharmacokinetics**

### **Absorption:**

Fluticasone propionate acts locally in the lung; therefore, plasma levels do not predict therapeutic effect. Trials using oral dosing of labeled and unlabeled drug have demonstrated that the oral systemic bioavailability of fluticasone propionate was negligible (<1%), primarily due to incomplete absorption and presystemic metabolism in the gut and liver. In contrast, the majority of the fluticasone propionate delivered to the lung was systemically absorbed.

Following Aermony RESPICLICK administration the peak plasma concentration of fluticasone propionate occurs at approximately 1 hour after inhalation.

The mean peak concentration following a 232 mcg single oral inhalation of Aermony RESPICLICK to patients 12 years and older with persistent asthma was 73 pg/mL.

### **Distribution:**

Following intravenous administration, the initial disposition phase for fluticasone propionate was rapid and consistent with its high lipid solubility and tissue binding. The volume of distribution averaged 4.2 L/kg.

The percentage of fluticasone propionate bound to human plasma proteins averages 99%. Fluticasone propionate is weakly and reversibly bound to erythrocytes and is not significantly bound to human transcortin.

### **Metabolism:**

The total clearance of fluticasone propionate is high (average, 1,093 mL/min), with renal clearance accounting for less than 0.02% of the total. The only circulating metabolite detected in man is the 17 $\beta$  carboxylic acid derivative of fluticasone propionate, which is formed through the CYP3A4 pathway. This metabolite has less affinity (approximately 1/2,000) than the parent drug for the glucocorticoid receptor of human lung cytosol in vitro and negligible pharmacological activity in animal studies. Other metabolites detected in vitro using cultured human hepatoma cells have not been detected in man.

**Excretion:**

Terminal half-life estimate of fluticasone propionate following oral inhalation administration of Aermony RESPICLICK was approximately 11.2 hours.

Less than 5% of a radiolabeled oral dose of fluticasone propionate was excreted in the urine as metabolites, with the remainder excreted in the feces as parent drug and metabolites.

***Special Populations and Conditions***

**Pediatrics:** No pharmacokinetic studies have been performed with Aermony RESPICLICK in children. A subgroup analysis was conducted to compare patients aged 12-17 (n=16) and  $\geq 18$  (n=23) years following administration of 232 mcg Aermony RESPICLICK. No overall differences in fluticasone propionate pharmacokinetics were observed.

**Geriatrics:** No pharmacokinetic studies have been performed with Aermony RESPICLICK in geriatric patients.

**Gender:** A subgroup analysis was conducted to compare male (n=22) and female (n=17) patients following administration of 232 mcg Aermony RESPICLICK. No overall differences in fluticasone propionate pharmacokinetics were observed.

**Hepatic Insufficiency:** Formal pharmacokinetic studies using Aermony RESPICLICK have not been conducted in patients with hepatic impairment. Since fluticasone propionate is predominantly cleared by hepatic metabolism, impairment of liver function may lead to accumulation of fluticasone propionate in plasma. Therefore, patients with hepatic disease should be closely monitored.

**Renal Insufficiency:** The effect of renal impairment of the pharmacokinetics of Aermony RESPICLICK has not been evaluated.

**STORAGE AND STABILITY**

Store Aermony RESPICLICK at room temperature (between 15° and 25°C) in a dry place; excursions permitted from 15°C to 30°C. Avoid exposure to extreme heat, cold, or humidity.

Keep out of reach of children.

Aermony RESPICLICK should be stored inside the unopened moisture-protective foil pouch and only removed from the pouch immediately before initial use. Discard Aermony RESPICLICK 30 days after opening the foil pouch or when the counter reads “0”, whichever comes first. The inhaler is not reusable. Do not attempt to take the inhaler apart.

## **DOSAGE FORMS, COMPOSITION AND PACKAGING**

Aermony RESPICLICK is an inhalation driven, device metered, multidose dry powder inhaler containing fluticasone propionate and lactose monohydrate as the excipient.

Aermony RESPICLICK contains 60 actuations. Each actuation provides 55 mcg, 113 mcg or 232 mcg fluticasone propionate ex-valve equal to 51 mcg, 103 mcg, or 210 mcg of fluticasone propionate delivered from the mouthpiece.

Each inhaler has a green cap and is packaged individually in a foil pouch in a carton. Each inhaler contains 0.9 g of the formulation. The inhaler has a counter.

## PART II: SCIENTIFIC INFORMATION

### PHARMACEUTICAL INFORMATION

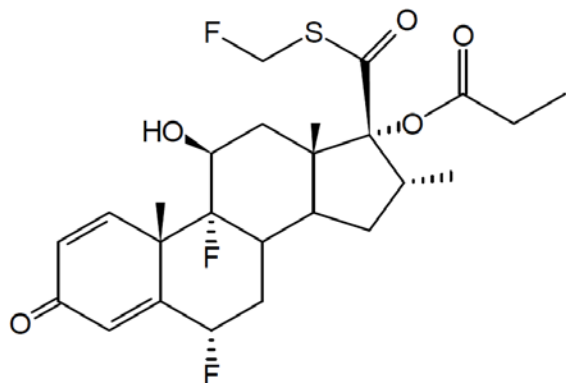
#### Drug Substance

Proper name: fluticasone propionate

Chemical name: S-(fluoromethyl) 6 $\alpha$ ,9-difluoro-11 $\beta$ ,17-dihydroxy-16 $\alpha$ -methyl-3-oxoandrosta-1,4-diene-17 $\beta$ -carbothioate, 17-propionate

Molecular formula and molecular mass: C<sub>25</sub>H<sub>31</sub>F<sub>3</sub>O<sub>5</sub>S      500.6

Structural formula:



Physicochemical properties: Fluticasone propionate is a white fine powder, practically insoluble in water, freely soluble in dimethyl sulfoxide and dimethylformamide, and slightly soluble in methanol and 95% ethanol.

## CLINICAL TRIALS

### **Study demographics and trial design**

#### Adult and Adolescent Patients Aged 12 Years and Older:

Two Phase 3 clinical trials were conducted-comparing Aermony RESPICLICK with placebo (Study 1 and Study 2). They were double-blind, parallel-group, placebo controlled, clinical trials, conducted in 1360 adult and adolescent patients (aged 12 years and older, with baseline FEV<sub>1</sub> 40% to 85% of predicted normal) with asthma that was not optimally controlled on their current therapy (Table 4). All treatments were given as 1 inhalation twice a day from the RESPICLICK inhaler device, and other maintenance therapies were discontinued.

**Table 4 - Summary of the Design and Patient Demographics in clinical trials patients with Asthma (FAS)**

<b>Study #</b>	<b>Trial design</b>	<b>Dosage, route of administration and duration</b>	<b>Study subjects (n)</b>	<b>Mean age (Range) (Years)</b>	<b>Gender (%)</b>
<b>Study 1</b>	Phase III: Randomized, double-blind, parallel group, placebo controlled, multicentre	Aermony RESPICLICK 55 mcg BID	128	41.6 (12-86)	Male: 279 (44) Female: 361(56)
		Aermony RESPICLICK 113 mcg BID	129		
		Fluticasone/Salmeterol Multidose Dry Powder Inhaler 55/14 mcg BID	128		
		Fluticasone/Salmeterol Multidose Dry Powder Inhaler 113/14 mcg BID	126		
		Placebo	129		
		Oral inhalation 12 weeks duration			
<b>Study 2</b>	Phase III: Randomized, double-blind, parallel group, placebo controlled, multicentre	Aermony RESPICLICK 113 mcg BID	145	44.9 (12-84)	Male: 284 (39) Female: 436 (61)
		Aermony RESPICLICK 232 mcg BID	146		
		Fluticasone/Salmeterol Multidose Dry Powder Inhaler 113/14 mcg BID	141		
		Fluticasone/Salmeterol Multidose Dry Powder Inhaler 232/14 mcg BID	145		
		Placebo	143		
		Oral inhalation 12 weeks duration			

**Study 1**

This randomized, double-blind, placebo-controlled, 12-week, global efficacy and safety trial that compared Fluticasone Propionate Multidose Dry Powder Inhaler (Aermony RESPICLICK) 55 mcg and 113 mcg (1 inhalation twice a day), Fluticasone/Salmeterol Multidose Dry Powder Inhaler 55/14 and 113/14 mcg (1 inhalation twice a day), and placebo in 640 adolescents and



adult patients with persistent symptomatic asthma despite low-dose inhaled corticosteroid (ICS) or ICS/LABA therapy.

Patients received single-blinded placebo MDPI and were switched from their baseline ICS or ICS/LABA therapy to beclomethasone dipropionate 40 mcg twice daily during the run-in period. Patients who met all randomization criteria were randomly assigned to receive treatment as detailed in Table 4. Baseline FEV<sub>1</sub> measurements were similar across treatments: Aermony RESPICLICK 55 mcg 2.134 L, Aermony RESPICLICK 113 mcg 2.166 L, and placebo 2.188 L. The primary endpoints for this trial were the change from baseline in trough FEV<sub>1</sub> at week 12 for all patients and standardized baseline-adjusted FEV<sub>1</sub> AUEC<sub>0-12h</sub> at week 12 analyzed for a subset of 312 patients who performed postdose serial spirometry.

## **Study 2**

This randomized, double-blind, placebo-controlled, 12-week, global efficacy and safety trial compared Fluticasone Propionate Multidose Dry Powder Inhaler (Aermony RESPICLICK) 113 mcg and 232 mcg (1 inhalation twice a day), Fluticasone/Salmeterol Multidose Dry Powder Inhaler 113/14 mcg and 232/14 mcg (1 inhalation twice a day), and placebo in 720 adolescents and adult patients with persistent symptomatic asthma despite medium or high strength ICS or ICS/LABA therapy.

Patients received single-blinded placebo MDPI and were switched from their baseline ICS therapy to Aermony RESPICLICK 55 mcg twice daily during the run-in period. Patients who met all randomization criteria were randomly assigned to receive treatment as detailed in Table 4. Baseline FEV<sub>1</sub> measurements were similar across treatments, as follows: Aermony RESPICLICK 113 mcg 2.069 L, Aermony RESPICLICK 232 mcg 2.075 L, and placebo 2.132 L. The primary endpoints for this trial were the change from baseline in trough FEV<sub>1</sub> at week 12 for all patients and standardized baseline-adjusted FEV<sub>1</sub> AUEC<sub>0-12h</sub> at week 12 analyzed for a subset of 312 patients who performed postdose serial spirometry.

## **Study results**

### **Study 1**

Patients receiving Aermony RESPICLICK 55 mcg and Aermony RESPICLICK 113 mcg had significantly greater improvements in trough FEV<sub>1</sub> compared with placebo at 12 weeks (Table 5). The mean trough FEV<sub>1</sub> results at each visit are displayed in Figure 1.

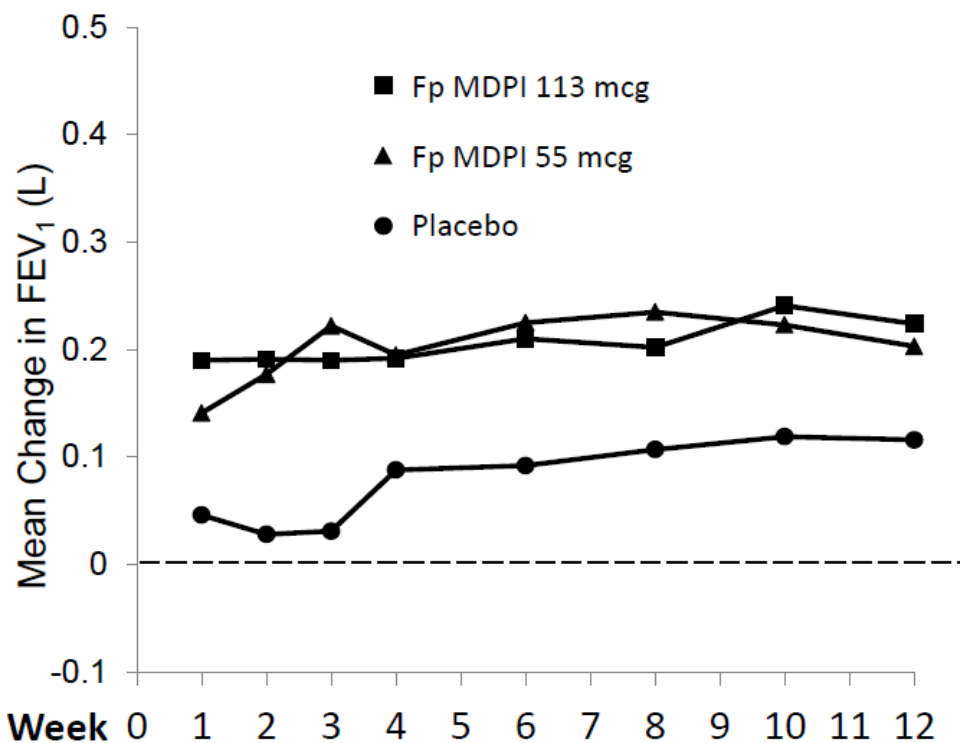
**Table 5: Study 1: Primary Analysis of Change from Baseline in Trough FEV<sub>1</sub> at Week 12 by Treatment Group (FAS)**

Variable Statistic	Placebo (N=130)	Aermony RESPICLICK	
		55 mcg BID (N=129)	113 mcg BID (N=130)
<b>Change in trough FEV<sub>1</sub> (L) at week 12</b>			
LS mean (SE)	0.053 (0.0350)	0.172 (0.0347)	0.204 (0.0340)
95% CI	(-0.015, 0.122)	(0.104, 0.240)	(0.137, 0.271)
<b>Comparison to placebo</b>			
Difference of LS mean		0.119	0.151
95% CI		(0.025, 0.212)	(0.057, 0.244)
p-value		0.0132	0.0017

Analysis performed using ANCOVA with effects due to baseline, sex, age, (pooled) center, previous therapy, and treatment.

**Figure 1:**

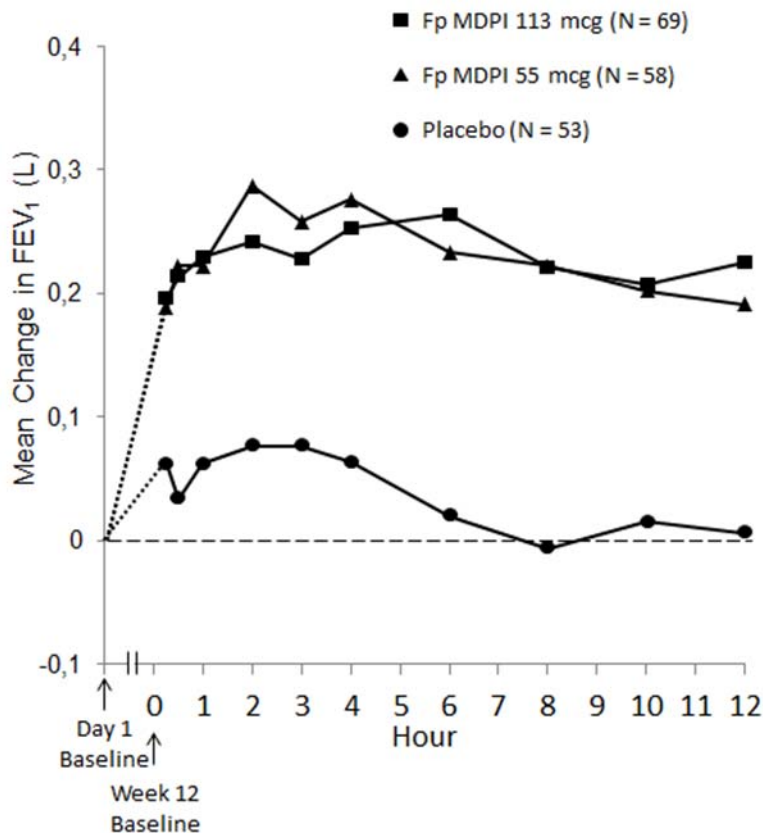
**Mean Change from Baseline in Trough FEV<sub>1</sub> at Each Visit by Treatment Group (Study 1)**



FEV<sub>1</sub> = forced expiratory volume in 1 second; Fp = fluticasone propionate

Improvements in FEV<sub>1</sub> for both Aermony RESPICLICK dose groups were sustained over the 12 hours of testing at week 12 (Figure 2) in the serial spirometry subset of patients. No diminution in the 12 hour bronchodilator effect was observed with Aermony RESPICLICK as assessed by FEV<sub>1</sub> following 12 weeks of therapy.

**Figure 2: Serial Spirometry: Mean Change from Baseline in FEV<sub>1</sub> (L) at Week 12 by Time Point and Treatment Group (Study 1: FAS; Serial Spirometry Subset)**



FAS = full analysis set; FEV<sub>1</sub> = forced expiratory volume in 1 second; Fp = fluticasone propionate.

There was supportive evidence of efficacy for Aermony RESPICLICK 55 mcg and 113 mcg bid compared with placebo for secondary efficacy variables such as the weekly average of daily trough morning peak expiratory flow (AM PEF), and total daily use of rescue medication. The Asthma Quality of Life Questionnaire (AQLQ) for patients' age ≥ 18 years or the pediatric AQLQ (PAQLQ) for patients aged 12 to 17 years demonstrated improvement compared to placebo.

## **Study 2**

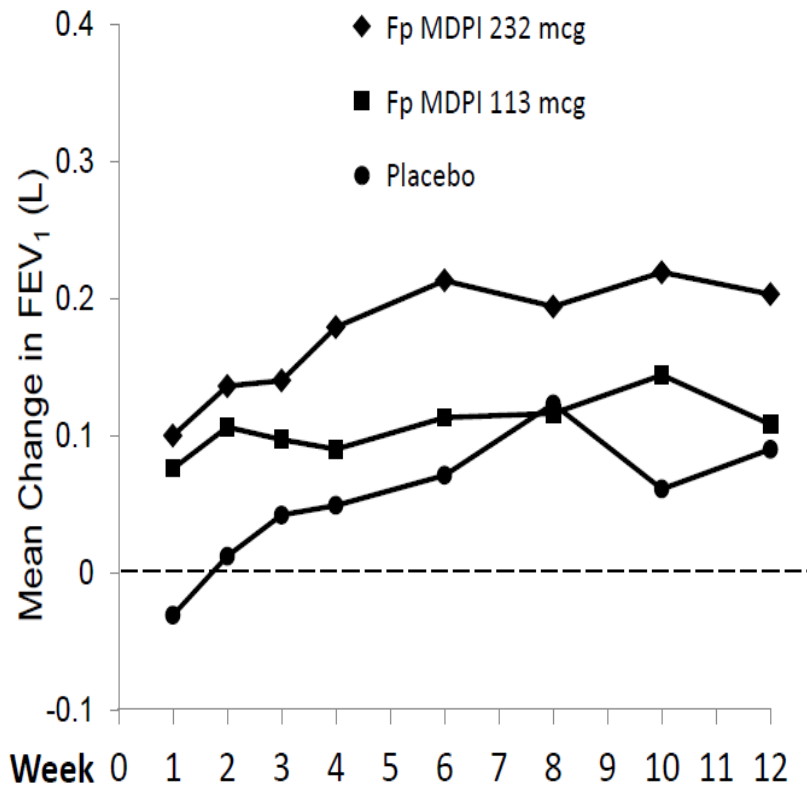
Efficacy results in this trial were similar to those observed in Study 1. Patients receiving Aermony RESPICLICK 113 mcg and Aermony RESPICLICK 232 mcg had significantly greater improvements in trough FEV<sub>1</sub> compared with placebo at 12 weeks (Table 6). The mean trough FEV<sub>1</sub> results at each visit are displayed in Figure 3.

**Table 6: Study 2: Primary Analysis of Change from Baseline in Trough FEV<sub>1</sub> at Week 12 by Treatment Group (FAS)**

Variable Statistic	Placebo (N=143)	Fp MDPI	
		113 mcg BID (N=145)	232 mcg BID (N=146)
<b>Change in trough FEV<sub>1</sub> (L) at week 12</b>			
LS mean (SE)	-0.004 (0.312)	0.119 (0.0311)	0.179 (0.0308)
95% CI	(-0.065, 0.057)	(0.058, 0.180)	(0.119, 0.240)
<b>Comparison to placebo</b>			
Difference of LS mean		0.123	0.183
95% CI		(0.038, 0.208)	(0.098, 0.268)
p-value		0.0047	0.0000

Analysis performed using ANCOVA with effects due to baseline, sex, age, (pooled) center, previous therapy (ICS or ICS/LABA), and treatment.

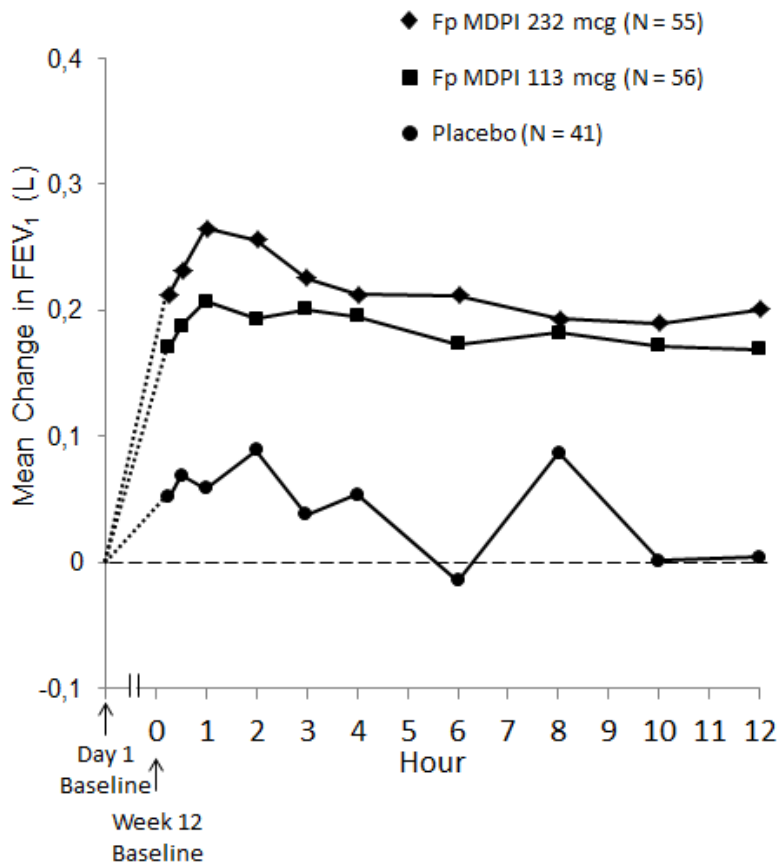
**Figure 3: Mean Change from Baseline in Trough FEV<sub>1</sub> at Each Visit by Treatment Group (Study 2)**



FEV<sub>1</sub> = forced expiratory volume in 1 second; Fp = fluticasone propionate

Improvements in FEV<sub>1</sub> for both Aermony RESPICLICK dose groups were sustained over the 12 hours of testing at week 12 in the serial spirometry subset of patients (Figure 4). No diminution in the 12 hour bronchodilator effect was observed with Aermony RESPICLICK as assessed by FEV<sub>1</sub> following 12 weeks of therapy.

**Figure 4: Serial Spirometry: Mean Change from Baseline in FEV<sub>1</sub> (L) at Week 12 by Time Point and Treatment Group (Study 2: FAS; Serial Spirometry Subset)**



FAS = full analysis set; FEV<sub>1</sub> = forced expiratory volume in 1 second; Fp = fluticasone propionate.

There was supportive evidence of efficacy for Aermony RESPICLICK compared with placebo for secondary endpoints such as the weekly average of daily trough AM PEF and total daily use of rescue medication. There were fewer withdrawals due to worsening asthma in patients treated with Aermony RESPICLICK than with placebo. The AQLQ and the PAQLQ demonstrated improvement compared to placebo.

## **DETAILED PHARMACOLOGY**

### **Pharmacology**

Fluticasone propionate is a synthetic trifluorinated corticosteroid with potent anti-inflammatory activity. The principal desired pharmacological activity of Fp is to reduce inflammatory reactions in the airways, thereby ameliorating the effects of allergic rhinitis and other respiratory conditions associated with inflammatory reactions to stimulation.

The anti-inflammatory activity of Fp has been demonstrated by its effects on a number of inflammatory mediators and markers *in vitro* and *in vivo*. *In vitro* assays using human lung cytosol preparations have established Fp as a human glucocorticoid receptor GR agonist with an affinity 18 times greater than dexamethasone, almost twice that of beclomethasone 17-monopropionate (BMP), the active metabolite of beclomethasone dipropionate, and over 3 times that of budesonide.

## **TOXICOLOGY**

### **Carcinogenesis**

Fluticasone propionate demonstrated no tumorigenic potential in mice at oral doses up to 1,000 mcg/kg (approximately 10 times the maximum recommended human daily inhaled dose [MRHDID] on a mg/m<sup>2</sup> basis) for 78 weeks or in rats at inhalation doses up to 57 mcg/kg (approximately equivalent to the MRHDID on a mg/m<sup>2</sup> basis) for 104 weeks.

### **Mutagenesis**

Fluticasone propionate did not induce gene mutation in prokaryotic or eukaryotic cells *in vitro*. No significant clastogenic effect was seen in cultured human peripheral lymphocytes *in vitro* or in the *in vivo* mouse micronucleus test.

### **Impairment of Fertility**

No evidence of impairment of fertility was observed in rats at subcutaneous doses up to 50 mcg/kg (approximately equivalent to the MRHDID on a mg/m<sup>2</sup> basis). Prostate weight was significantly reduced.

### **Reproductive and Developmental Toxicology**

In embryo/fetal development studies with pregnant rats and mice dosed by the subcutaneous route throughout the period of organogenesis, fluticasone propionate was teratogenic in both species. Omphalocele, decreased body weight, and skeletal variations were observed in rat fetuses, in the presence of maternal toxicity, at a dose approximately 2 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 100 mcg/kg/day). The rat no observed adverse effect level (NOAEL) was observed at approximately 0.6 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 30 mcg/kg/day). Cleft palate and fetal skeletal variations were observed in mouse fetuses at a dose approximately 0.5 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 45 mcg/kg/day). The mouse NOAEL was observed with a dose approximately 0.16 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 15 mcg/kg/day).

In an embryo/fetal development study with pregnant rats dosed by the inhalation route throughout the period of organogenesis, fluticasone propionate produced decreased fetal body weights and skeletal variations, in the presence of maternal toxicity, at a dose approximately 0.5 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal inhalation dose of 25.7 mcg/kg/day); however, there was no evidence of teratogenicity. The NOAEL was observed with a dose approximately 0.1 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal inhalation dose of 5.5 mcg/kg/day).

In an embryofetal development study in pregnant rabbits that were dosed by the subcutaneous route throughout organogenesis, fluticasone propionate produced reductions of fetal body weights, in the presence of maternal toxicity at doses approximately 0.02 times the MRHDID and higher (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 0.57 mcg/kg/day). Teratogenicity was evident based upon a finding of cleft palate for 1 fetus at a dose approximately 0.2 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 4 mcg/kg/day). The NOAEL was observed in rabbit fetuses with a dose approximately 0.004 times the MRHDID (on a mcg/m<sup>2</sup> basis with a maternal subcutaneous dose of 0.08 mcg/kg/day). Fluticasone propionate crossed the placenta following subcutaneous administration to mice and rats and oral administration to rabbits.

In a pre- and post-natal development study in pregnant rats dosed from late gestation through delivery and lactation (Gestation Day 17 to Postpartum Day 22), fluticasone propionate was not associated with decreases in pup body weight, and had no effects on developmental landmarks, learning, memory, reflexes, or fertility at doses up to approximate equivalence to the MRHDID (on a mcg/m<sup>2</sup> basis with maternal subcutaneous doses up to 50 mcg/kg/day).



## REFERENCES

1. Mansfield et al. A 6-month safety and efficacy study of fluticasone propionate and fluticasone propionate/salmeterol multidose dry powder inhalers in persistent asthma: Published online: *Allergy Asthma Proc* 38:1–13, 2017; doi: 10.2500/aap.2017.38.4061.
2. Sher et al. Fluticasone propionate and fluticasone propionate/salmeterol multidose dry powder inhalers compared with placebo for persistent asthma. Published online: (*Allergy Asthma Proc* 38:1–11, 2017; doi: 10.2500/aap.2017.38.4069).
3. ZuWallack R, Adelglass J, Clifford DP, Duke SP, Wire PD, Faris M, Harding SM. Long-term efficacy and safety of fluticasone propionate powder administered once or twice daily via inhaler to patients with moderate asthma. *Chest* 2000;118(2):303-12.

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE  
PATIENT MEDICATION INFORMATION**

**Pr Aermony RESPICLICK™**

**fluticasone propionate inhalation powder**

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

**What is Aermony Respiclick used for?**

**Aermony Respiclick** is used to treat and prevent asthma in people who are 12 years of age and older. It is used by people who need regular treatment for their asthma.

**Aermony Respiclick** is not meant to be used to provide immediate relief of an asthma attack. A fast acting ‘rescue’ medicine, such as salbutamol, should be used for any sudden asthma attacks.

**How does Aermony Respiclick work?**

Asthma is a lung disease. It is a condition that you can have for a long time. During an asthma attack the airways of your lungs react by swelling and becoming narrow. This makes it more difficult for the air to flow in and out of your lungs.

Fluticasone propionate belongs to a group of medicines called corticosteroids. They reduce the inflammation in the airways of the lungs. This helps you breathe easier.

**What are the ingredients in Aermony Respiclick?**

Medicinal ingredients: Fluticasone propionate

Non-medicinal ingredients: Lactose monohydrate

**Aermony Respiclick comes in the following dosage forms:**

Dry powder for inhalation: Each actuation contains: 55 mcg, 113 mcg or 232 mcg fluticasone propionate.

Each inhaler contains 60 actuations.

**Do not use Aermony Respiclick:**

- to treat sudden symptoms of an asthma attack. **Aermony Respiclick is not a rescue inhaler and should not be used to give you fast relief from your asthma attack**
- if you are allergic to fluticasone propionate
- if you have severe allergy to milk proteins
- if you are under 12 years of age

**To help avoid side effects and ensure proper use, talk to your healthcare professional**

**before you take Aermony Resplick. Talk about any health conditions or problems you may have, including if you:**

- have ever had to stop taking another medication for your breathing problems because you were allergic to it or it caused problems
- are allergic to lactose (milk sugar) or milk protein
- are taking other “steroids” by mouth or inhalation
- have ever had herpes simplex of the eye, a history of tuberculosis infections or any type of viral, bacterial, fungal (yeast) or parasitic infection
- have ever had a yeast infection (thrush) in your mouth
- if you have immune system problems
- are pregnant, or planning to become pregnant. Tell your doctor right away if you become pregnant while taking **Aermony Resplick**.
- are breastfeeding or plan to breastfeed. It is not known if the ingredients in **Aermony Resplick** can pass into breast milk
- are taking medicines used to treat HIV infection or AIDS, such as:
  - ritonavir
  - atazanavir
  - indinavir
  - nelfinavir
  - saquinavir

You should avoid taking **Aermony Resplick** if you are taking ritonavir.

- have liver problems or disease

**Other warnings you should know about:**

**Measles and Chickenpox:** While taking **Aermony Resplick**, you should avoid coming into contact with anyone who has measles or chicken pox. If you or your child(ren) do come into contact with someone who has it, tell your doctor right away.

**Effect on Growth:** All corticosteroids, especially when taken for a long time, may affect the usual growth pattern in adolescents. Your doctor should monitor you or your child(ren) regularly.

**Risk of Bone Fractures:** When using medicines like **Aermony Resplick** for long term treatment, you may be at risk of:

- breaking a bone
- osteoporosis (brittle bones)

You should take extra care to avoid any injuries, especially falls. Your doctor should also monitor you.

**Eye Disorders:** Medicines like **Aermony Respiclick** can cause eye disorders such as:

- Cataracts: clouding of the lens in the eye, blurry vision, eye pain;
- Glaucoma: an increased pressure in your eyes, eye pain. If untreated, it may lead to permanent vision loss.
- Central serous chorioretinopathy (CSCR): blurry vision or other changes in vision.

You should have regular eye exams.

**Monitoring:** Ask your doctor whether you need to be monitored in any special way, especially if you:

- were previously taking another form of corticosteroids (like an injection or an oral tablet) and have switched to an inhaled corticosteroid. Your doctor should look out for tiredness, weakness, nausea, vomiting and low blood pressure.
- are being treated for diabetes. You may need more frequent blood sugar monitoring or a change in the dose of your diabetes medication.

Tell your doctor right away if:

- there is a change in your symptoms such as more coughing, attacks of wheezing, chest tightness, or an unusual increase in the severity of the breathlessness
- you wake up at night with chest tightness, wheezing or shortness of breath
- you are using your rescue inhaler more often
- your rescue inhaler does not work well to relieve your symptoms

These could be warning signs that your condition may be getting worse.

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

**The following may interact with Aermony Respiclick:**

- Ketoconazole (a drug used to treat fungal infections)
- Drugs used to treat HIV and AIDS such as:
  - ritonavir
  - atazanavir
  - indinavir
  - nelfinavir
  - saquinavir
- Antifungal drugs (such as itraconazole)
- Clarithromycin (used to treat bacterial infections)
- Nefazodone (used to treat depression)
- Telithromycin (used to treat pneumonia)
- Acetylsalicylic acid (ASA) (used to treat pain and fever)

## **How to take Aermony Respiclick:**

### **Aermony Respiclick is for oral inhalation only.**

It may take up to 1 or 2 weeks for Aermony Respiclick to work. So is important that you use it:

- every day
- at about the same time each day

After you use it, you should rinse your mouth with water. Spit out the water. Do not swallow the water.

If you are also using an inhaled bronchodilator:

- use it first before you use Aermony Respiclick
- wait a few minutes and then use Aermony Respiclick

Do not stop taking Aermony Respiclick suddenly – even if you feel better. Your doctor will tell you how to slowly stop taking the medication if necessary.

Do not change the dose unless you are told to by your doctor.

### **Usual Dose (Adults and Adolescents 12 years of age and older):**

Take 1 inhalation twice a day, about 12 hours apart.

Do not take more than the recommended dose.

### **Instruction for Use:**

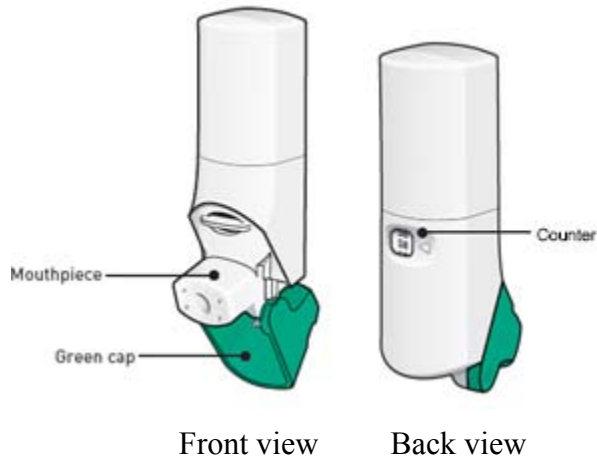
#### **About the inhaler:**

When you are ready to use **Aermony Respiclick** for the first time, remove the inhaler from the foil pouch. **Do not** remove the inhaler from the foil pouch until you are ready to use it.

There are 2 main parts of your inhaler: (see **Figure A**).

- the white inhaler with the mouthpiece
- the green cap that covers the mouthpiece of the inhaler

**Figure A:**



#### **IMPORTANT POINTS TO REMEMBER ABOUT USING YOUR INHALER:**

- **One actuation is equal to one dose.** An actuation is when you inhale the medication from the mouthpiece into your lungs.
- The **Aermomy Resplick** inhaler does not require priming.
- There is no button or canister that you need to press to load a dose. **Opening the green cap loads the dose.** Every time the green cap is opened and it “clicks”, one dose is ready to be inhaled. If you do not hear the “click” sound the inhaler may not be activated to give you a dose of medicine.
- Always close the green cap after using it so your inhaler will be ready for you to take your next dose.
- Do not open the cap unless you are ready to take your next dose. Opening and closing the cap without inhaling a dose will waste the medicine and may damage your inhaler.
- Your **Aermomy Resplick** inhaler contains dry powder so it is important that you do not blow or breathe into it.

#### **About the counter:**

- Your **Aermomy Resplick** inhaler contains 60 actuations (inhalations).
- There is a counter in the back of the inhaler with a viewing window that shows you how much of the medicine you have left (see **Figure A**).
- The counter will count down (in units of two) each time the green cap is opened and closed (for example, 60, 58, 56, etc.).
- When there are 20 actuations left, the colour of the numbers will change to red. You should refill your prescription or ask your doctor for another prescription.
- When the counter shows the number ‘0’ the background will change to red and the colour of the number ‘0’ will change to black. Your inhaler is empty and you should stop using the inhaler and throw it away (see **Figure B**).

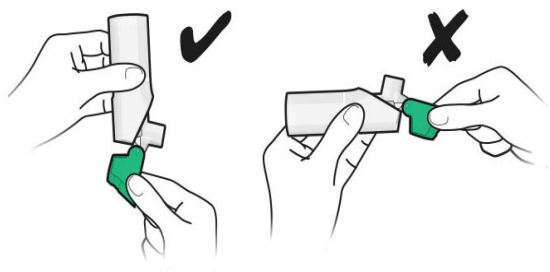
**Figure B:**



**How to use the Aermony Respiclick:**

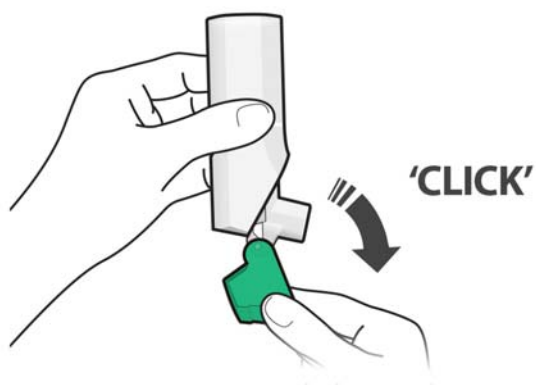
**STEP 1: Open**

**Figure C:**



- Make sure the cap is closed.
- Hold the inhaler upright (**see Figure C**).

**Figure D:**

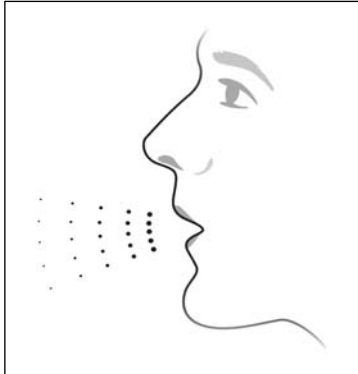


- Open the green cap all the way back until you feel and hear a “click” (**see Figure D**).
- Every time the green cap is opened and it clicks, one dose is ready to be inhaled.

**Do not open the green cap unless you are taking a dose.**

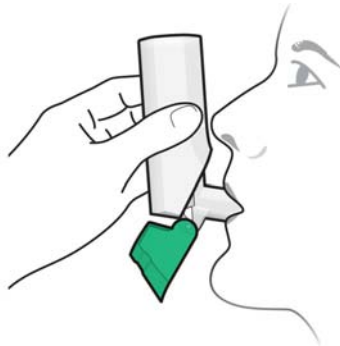
## STEP 2: Inhale

Figure E:



- Before inhaling, hold the inhaler away from your mouth and breathe out through your mouth as much air as you can and as is comfortable. **Never breathe out into the inhaler mouthpiece (see Figure E).**

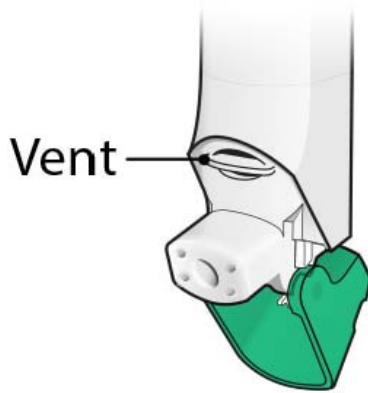
Figure F:



- **Place the mouthpiece in your mouth and close your lips around it so you form a good seal.**
- **Breathe in quickly and deeply through your mouth**, until your lungs feel completely full of air (see Figure F).



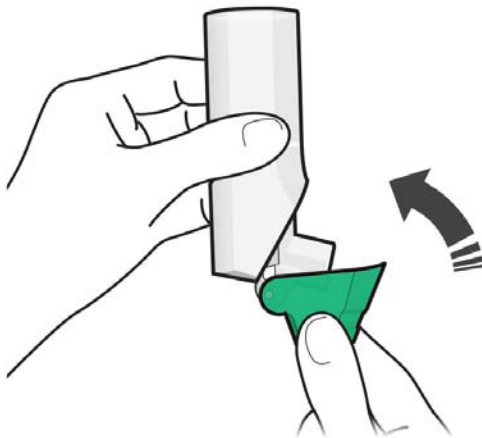
**Figure G:**



- Do not block the vent above the mouthpiece with your lips or fingers (**see Figure G**).
- Remove the inhaler from your mouth.
- Hold your breath for about 10 seconds or for as long as you comfortably can.
- Your Aermony Respiclick inhaler delivers your dose of medicine as a very fine powder that you may or may not taste or feel. **Do not** take an extra dose from the inhaler even if you do not taste or feel the medicine.

**STEP 3: Close**

**Figure H:**



- **Close the green cap after inhaling so that the inhaler will be ready for your next dose (see Figure H).**
- **Rinse your mouth with water after taking your dose.** Spit out the water. Do not swallow it.
- Throw the inhaler away 30 days after you have opened the foil pouch or when the counter reads '0,' whichever comes first.

**Cleaning your inhaler:**

- Never wash or put any part of the inhaler in water.
- Gently wipe the mouthpiece with a dry cloth or tissue once a week.

**Overdose:**

If you think you have taken too much **Aermony Respiclick**, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

If you have used larger doses than recommended by your doctor for a long period of time, you should talk to your doctor or pharmacist for advice. A gradual reduction of your dose may be needed. Do not stop taking the medication suddenly.

**Missed Dose:**

**It is very important that you use Aermony Respiclick regularly;** however, if you miss a dose, just skip that dose. Take the next dose at your usual time. **Do not take 2 doses at one time.**

**What are possible side effects from using Aermony Respiclick?**

These are not all the possible side effects you may feel when taking **Aermony Respiclick**. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- headache
- feeling anxious
- disturbed sleep
- behavioural changes (including hyperactivity and irritability)
- hoarseness and voice changes, inability to speak
- mild yeast infection of the mouth or throat (thrush, Candidiasis) or, rarely, in the esophagus. Common signs are white, slightly raised, sore patches on your tongue and inner cheeks. Remember to rinse and gargle your mouth with water and spit after using **Aermony Respiclick**. If you wear dentures, cleaning them may also help.
- increased bruising
- upper respiratory tract infection, viral infections
- stuffy/runny nose
- cough
- fever
- sore throat or irritation

<b>Serious side effects and what to do about them</b>			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>VERY COMMON</b>			
<b>Thrush:</b> Yeast infection of the mouth or throat; thick white patches in the mouth, tongue or on the throat, sore throat.		√	
<b>RARE</b>			
<b>Allergic Reactions:</b> Lumpy skin rash or hives anywhere on the body.			√
<b>Churg-Strauss Syndrome:</b> A flu-like illness, rash, pins and needles or numbness of arms or legs, severe sinusitis and worsening lung or breathing problems.		√	
<b>Esophageal candidiasis:</b> Yeast infection of the esophagus (food tube); difficulty swallowing		√	
<b>VERY RARE</b>			
Slowed growth in children and adolescents.		√	
<b>Cushing's Syndrome:</b> Round "moon face", rapid weight gain especially around the body. Excess sweating and thinning of the skin with easy bruising and dryness. Muscle and bone weakness.		√	
<b>Bone Fractures or Osteoporosis:</b> In situations where healthy people would not normally break a bone you may have sudden pain in any location and especially in the wrist, spine or hip. This may be a fracture.		√	
<b>Glaucoma:</b> Increased pressure in your eyes, eye pain.		√	
<b>Cataract:</b> Clouding of the lens in the eye, blurry vision, and/or eye pain.		√	

<b>Serious side effects and what to do about them</b>			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>Decreased Adrenal Function:</b> Tiredness, weakness, nausea and vomiting, low blood pressure.		√	
<b>Severe Allergic Reactions:</b> Sudden wheeziness and chest pain or tightness; or swelling of eyelids, face, lips, tongue or throat, difficulty swallowing or breathing.			√
<b>Hyperglycemia</b> (Increased amount of sugar in blood): Excessive thirst, frequent urination, dry skin, blurred vision and fatigue.		√	
<b>Osteonecrosis:</b> Persistent pain and/or limited range of motion of a joint or a limb.		√	
<b>UNKNOWN</b>			
Decreased ability to fight infections. Symptoms of infection may include fever, pain, chills, feeling tired, sore throat.	√		
Worsening of lung symptoms such as wheezing, shortness of breath, cough and chest tightness accompanied by fever and more phlegm.		√	

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

### **Reporting Side Effects**

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

#### **3 ways to report:**

- Online at <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program  
Health Canada, Postal Locator 1908C  
Ottawa, ON  
K1A 0K9
  - Postage paid labels and the Consumer Side Effect Reporting Form are available at <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>

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

### **Storage:**

- Store **Aermony Respiclick** at room temperature (between 15°C and 25°C) in a dry place.
- Keep the:
  - inhaler away from extreme heat, cold, or humidity.
  - green cap on the inhaler closed during storage.
  - inhaler dry and clean at all times.
- Throw the inhaler away 30 days after you have opened the foil pouch or when the counter reads '0,' whichever comes first.
- **Keep out of the reach and sight of children.**

### **If you want more information about Aermony Respiclick:**

- 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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website <http://www.tevacanadainnovation.ca>, or by calling 1-855-514-8382.

This leaflet was prepared by Teva Canada Innovation.

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