PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

PrAIROMIR®

Salbutamol Inhalation Aerosol, Mfr. Std.
100 mcg salbutamol (as Salbutamol Sulfate) per actuation

Bronchodilator
beta$_2$-adrenergic agonist

Bausch Health, Canada Inc.
2150 St-Elzear Blvd., West
Laval, Quebec H7L 4A8
Canada

Date of Revision:
December 22, 2020

Submission Control No: 241784

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION 3
SUMMARY PRODUCT INFORMATION 3
INDICATIONS AND CLINICAL USE 3
CONTRAINDICATIONS 3
WARNINGS AND PRECAUTIONS 3
ADVERSE REACTIONS 6
DRUG INTERACTIONS 9
DOSAGE AND ADMINISTRATION 9
OVERDOSAGE 11
ACTION AND CLINICAL PHARMACOLOGY 12
STORAGE AND STABILITY 13
SPECIAL HANDLING INSTRUCTIONS 13
DOSAGE FORMS, COMPOSITION AND PACKAGING 13

PART II: SCIENTIFIC INFORMATION 14
PHARMACEUTICAL INFORMATION 14
CLINICAL TRIALS 15
DETAILED PHARMACOLOGY 18
TOXICOLOGY 19
REFERENCES 22

PART III: PATIENT MEDICATION INFORMATION 23

PrAIROMIR®
Salbutamol Inhalation Aerosol, Mfr. Std.
100 mcg salbutamol (as Salbutamol Sulfate) per actuation

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral Inhalation	Inhalation aerosol/ 100 mcg salbutamol	1,1,1,2-Tetrafluoroethane (HFA-134a), Ethanol, and Oleic Acid

INDICATIONS AND CLINICAL USE

Adults and Children (6 years and older)
AIROMIR (salbutamol sulfate) Inhalation Aerosol is indicated for:

- the symptomatic relief and prevention of bronchospasm due to bronchial asthma, chronic bronchitis and other chronic bronchopulmonary disorders in patients in whom reversible bronchospasm is a complicating factor
- the prevention of exercise-induced asthma.

Pediatrics (<6 years of age)
Safety and effectiveness in children below the age of 6 years have not been established.

CONTRAINDICATIONS

AIROMIR (salbutamol sulfate) Inhalation Aerosol is contraindicated:

- in patients hypersensitive to salbutamol or any of the components in the AIROMIR Inhalation Aerosol (See **DOSAGE FORMS, COMPOSITION AND PACKAGING**)
- as a tocolytic in patients at risk of premature labour or threatened abortion.

WARNINGS AND PRECAUTIONS

General

Patients should be advised to always carry their AIROMIR Inhalation Aerosol to use immediately if an episode of bronchospasm or asthma is experienced.

If AIROMIR Inhalation Aerosol therapy does not produce a significant improvement or if the

patient's condition worsens, medical advice must be sought to determine a new plan of treatment. In the case of acute or rapidly worsening dyspnea, a physician should be consulted immediately.

Deterioration of Asthma
Asthma may deteriorate over time. If the patient needs to use inhaled salbutamol more often than usual, this may be a sign of worsening asthma. This requires re-evaluation of the patient and treatment plan and consideration of adjusting the asthma maintenance therapy. If inhaled salbutamol treatment alone is not adequate to control asthma, concomitant anti-inflammatory therapy should be part of the treatment regimen (see **DOSAGE AND ADMINISTRATION**). It is essential that the physician instruct the patient in the need for further evaluation if the patient's asthma becomes worse.

Cardiovascular

In individual patients, any beta$_2$-adrenergic agonist, including salbutamol, may have a clinically significant cardiac effect. Care should be taken with patients suffering from cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension. Special care and supervision are required in patients with idiopathic hypertrophic subvalvular aortic stenosis, in whom an increase in the pressure gradient between the left ventricle and the aorta may occur, causing increased strain on the left ventricle.

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma. The exact cause of death is unknown, but cardiac arrest following the unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

Endocrine and Metabolism

Large doses of intravenous salbutamol have been reported to aggravate pre-existing diabetes and ketoacidosis. Additionally, beta-agonists, including salbutamol given intravenously may cause a decrease in serum potassium possibly through intracellular shunting. The relevance of this observation to the use of AIROMIR Inhalation Aerosol given at the recommended daily dosing is unknown, since the aerosol dose is much lower than doses given intravenously. Caution is advised in acute severe asthma since hypokalemia may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics and by hypoxia. Hypokalemia will increase the susceptibility of digitalis-treated patients to cardiac arrhythmias. It is recommended that serum potassium levels be monitored in such situations.

Care should be taken in patients with hyperthyroidism.

Hypersensitivity

Immediate hypersensitivity reactions may occur after administration of salbutamol inhalation aerosol, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema.

Care should be taken in patients who are unusually responsive to sympathomimetic amines.

Neurologic

Care should be taken in patients with convulsive disorders.

Respiratory

With repeated excessive use of sympathomimetic inhalation preparations, some patients have been reported to have developed severe paradoxical bronchospasm, occasionally leading to death. The cause of either the refractory state or death is unknown. However, it is suspected in the fatal episodes that cardiac arrest occurred following the unexpected development of a severe acute asthmatic crisis and subsequent hypoxia.

Special Populations

Pregnant Women

Salbutamol has been in widespread use for many years in human beings without apparent ill consequence. However, there are no adequate or well-controlled studies in pregnant women, and there is little published evidence of its safety in the early stages of human pregnancy. Administration of any drug to pregnant women should only be considered if the anticipated benefits to the expectant woman are greater than any possible risks to the fetus.

During worldwide marketing experience, rare cases of various congenital anomalies, including cleft palate and limb defects have been reported in the offspring of patients being treated with salbutamol. Some of the mothers were taking multiple medications during their pregnancies. Because no consistent pattern of defects can be discerned, and baseline rate for congenital anomalies is 2-3%, a relationship with salbutamol use cannot be established.

A reproduction study in rats was performed with AIROMIR Inhalation Aerosol and no teratogenic effects were observed. Studies of propellant HFA-134a in pregnant rats or rabbits have not shown any specific hazard.

Labour and Delivery

Although there have been no reports concerning the use of AIROMIR Inhalation Aerosol during labor and delivery, it has been reported that high doses of salbutamol administered intravenously inhibit uterine contractions. Although this effect is extremely unlikely as a consequence of aerosol use, it should be kept in mind.

Nursing Women

Since salbutamol is likely excreted in breast milk, and because of the potential for tumorigenicity shown for salbutamol in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. It is not known whether salbutamol in breast milk has a harmful effect on the neonate.

Pediatrics (6 to < 12 years)
The use of metered-dose inhalers in children depends on the ability of the individual child to learn the proper use of this device.

Pediatrics (< 6 years of age)
Safety and effectiveness in children below the age of 6 years have not been established.

Geriatrics
As with other beta$_2$-agonists, special caution should be observed when using AIROMIR Inhalation Aerosol in elderly patients who have concomitant cardiovascular disease that could be adversely affected by this class of drug.

Monitoring and Laboratory Tests

In accordance with the present practice for asthma treatment, patient response should be monitored clinically and by lung function tests.

Monitoring Control of Asthma
Failure to respond for at least three hours to a previously effective dose of salbutamol indicates a deterioration of the condition and the physician should be contacted promptly. Patients should be warned not to exceed the recommended dose.

Increasing use of beta$_2$-agonists to control symptoms is usually a sign of worsening asthma. In worsening asthma it is inadequate to increase beta$_2$-agonist use only, especially over an extended period of time. Instead, a reassessment of the patient's therapy plan is required, and concomitant anti-inflammatory therapy should be considered (see **DOSAGE AND ADMINISTRATION**).

ADVERSE REACTIONS

Adverse Drug Reaction Overview

As with other bronchodilator inhalation therapy, the potential for paradoxical bronchospasm should be kept in mind. If it occurs, treatment should be discontinued immediately, and alternative therapy instituted.

Potentially serious hypokalemia may result from beta$_2$-agonist therapy primarily from parenteral and nebulised routes of administration (see **WARNINGS AND PRECAUTIONS**, **Endocrine and Metabolism**).

Peripheral vasodilation and a compensatory small increase in heart rate may occur in some patients. Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia, extrasystoles) have been reported, usually in susceptible patients.

Other adverse reactions associated with salbutamol are nervousness and tremor. In some patients inhaled salbutamol may cause a fine tremor of skeletal muscle, particularly in the hands. This

effect is common to all beta$_2$-adrenergic agonists. Adaptation occurs during the first few days of dosing and the tremor usually disappears as treatment continues.

In addition, salbutamol, like other sympathomimetic agents, can cause adverse effects such as drowsiness, flushing, restlessness, irritability, chest discomfort, difficulty in micturition, hypertension, angina, vomiting, vertigo, central nervous system stimulation, hyperactivity in children, unusual taste and drying or irritation of the oropharynx, headache, palpitations, transient muscle cramps, insomnia, nausea, weakness and dizziness.

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.

A 12-week double-blind study compared AIROMIR Inhalation Aerosol, VENTOLIN® salbutamol inhaler (US source), and HFA-134a placebo in 565 asthmatic patients. The following table lists the incidence of all adverse events (whether considered drug related or not related to drug by the investigator) from this study which occurred at a rate of at least 3% in the AIROMIR Inhalation Aerosol group. Only those adverse events which occurred more frequently in either the AIROMIR Inhalation Aerosol treatment group or the VENTOLIN® treatment group than the placebo group are listed.

Table 1: Adverse Experience Incidences (% of patients) in a Large 12-Week Clinical Trial[a]

Body System/ Adverse Event (Preferred Term)	AIROMIR Inhalation Aerosol N = 193	VENTOLIN® (US)-l Inhaler N = 186	HFA-134a Placebo Inhaler N= 186
Application Site Disorders			
Inhalation Site Sensation	6	9	2
Inhalation Taste Sensation	4	3	3
Body As A Whole			
Allergic Symptoms	6	4	<1
Back Pain	4	2	3
Fever	6	2	5
Central & Peripheral Nervous System			
Dizziness	5	8	6
Tremor	7	8	2

Gastrointestinal System			
Nausea	10	9	5
Vomiting	7	2	3
Heart Rate & Rhythm Disorder			
Tachycardia	7	2	<1
Psychiatric Disorders			
Nervousness	7	9	3
Respiratory System Disorders			
Respiratory Disorder	6	4	5
Rhinitis	16	22	14
Upper Resp Tract Infection	21	20	18
Urinary System Disorder			
Urinary Tract Infection	3	4	2

[a] *This table includes all adverse events (whether considered drug related or not related to drug) which occurred at an incidence rate of at least 3.0% in the AIROMIR Inhalation Aerosol group and more frequently in the AIROMIR Inhalation Aerosol group than in the HFA-134a placebo inhaler group.*

Adverse events reported by less than 3% of the patients receiving AIROMIR Inhalation Aerosol, and by a greater proportion of AIROMIR Inhalation Aerosol patients than placebo patients, which have the potential to be related to AIROMIR Inhalation Aerosol include: dysphonia, contact dermatitis, increased sweating, dry mouth, chest pain, edema, rigors, ataxia, leg cramps, hyperkinesia, eructation, flatulence, tinnitus, diabetes mellitus, anxiety, depression, somnolence, and rash.

In a small cumulative dose study, tremor, nervousness, and headache appeared to be dose-related. Palpitation has also been observed with AIROMIR.

Post-Market Adverse Drug Reactions

The following adverse reactions have been identified during post-approval use of inhaled salbutamol. 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.

Immediate hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension, rash, oropharyngeal oedema, anaphylaxis and collapse have been reported.

Rarely, in children, hyperactivity occurs and occasionally, sleep disturbances, hallucination or atypical psychosis have been reported.

Lactic acidosis has been reported very rarely in patients receiving intravenous and nebulised salbutamol therapy.

DRUG INTERACTIONS

Table 2: Established or Potential Drug-Drug Interactions

Drug type	Ref	Effect	Clinical comment
Monoamine oxidase inhibitors or tricyclic antidepressants	CS	May potentiate action of salbutamol on cardiovascular system.	AIROMIR should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants.
Other inhaled sympathomimetic bronchodilators or epinephrine	CS	May lead to deleterious cardiovascular effects.	Other inhaled sympathomimetic bronchodilators or epinephrine should not be used concomitantly with salbutamol. If additional adrenergic drugs are to be administered by any route to the patient using inhaled salbutamol, the adrenergic drugs should be used with caution. Such concomitant use must be individualized and not given on a routine basis. If regular co-administration is required then alternative therapy must be considered.
Beta-blockers	CS	May effectively antagonize the action of salbutamol.	Beta adrenergic receptor blocking agents, especially the non-cardio-selective ones, such as propranolol, should not usually be prescribed together.
Diuretics	CS	May lead to ECG changes and/or hypokalemia although the clinical significance of these effects is not known.	Caution is advised in the co-administration of beta-agonists with non-potassium sparing diuretics. The ECG changes and/or hypokalemia which may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded.
Digoxin	CS	May lead to a decrease in serum digoxin levels, although the clinical significance of these findings for patients with obstructive airways disease who are receiving salbutamol and digoxin on a chronic basis is unclear.	Careful evaluation of serum digoxin levels is recommended in patients who are currently receiving digoxin and salbutamol. Mean decreases of 16 and 22% in serum digoxin levels were demonstrated after single dose intravenous and oral administration of salbutamol, respectively, to normal volunteers who had received digoxin for 10 days.

Legend: CS = Class Statement

DOSAGE AND ADMINISTRATION

Dosing Considerations

Dosage should be individualized, and the patient's response should be monitored by the prescribing physician on an ongoing basis.

Increasing demand for inhaled salbutamol in bronchial asthma is usually a sign of poorly controlled or worsening asthma and indicates that the patient should be re-evaluated and the

treatment plan should be reviewed. If inhaled salbutamol treatment alone is not adequate to control asthma, concomitant anti-inflammatory therapy should be part of the treatment regimen.

If a previously effective dose fails to provide the usual relief, or the effects of a dose last for less than three hours, patients should seek prompt medical advice since this is usually a sign of worsening asthma.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice. However, if a more severe attack has not been relieved by the usual dose, additional doses may be required. In these cases, patients should immediately consult their doctors or the nearest hospital.

Recommended Dose and Dosage Adjustment

Relief of Acute Episodes of Bronchospasm
Adults and Adolescents (12 years and older): One to two inhalations (100 to 200 mcg of salbutamol).

Children (6 - 11 years of age): One inhalation (100 mcg salbutamol).

If a more severe attack has not been relieved by the usual dose (one to two inhalations), further inhalations may be required every 4 to 6 hours. In these cases, patients should immediately consult their doctors or the nearest hospital. More frequent administration or a larger number of inhalations is not recommended.

Prevention of Symptoms Associated with Bronchospasm:
If despite appropriate maintenance therapy, regular daily use of the inhalation aerosol remains necessary for the control of bronchospasm, the recommended dose is:

Adults and Adolescents (12 years and older): One to two inhalations (100 to 200 mcg of salbutamol) repeated every 4 to 6 hours, not exceeding eight inhalations (800 mcg salbutamol) per day.

Children (6 - 11 years of age): One inhalation (100 mcg salbutamol), repeated every 4 to 6 hours not exceeding four inhalations (400 mcg salbutamol) per day.

Prevention of Exercise-Induced Bronchospasm
Adults and Adolescents 12 years and older: Two inhalations (200 mcg of salbutamol) 30 minutes before exercise.

Children (6 - 11 years of age): One inhalation (100 mcg of salbutamol) 30 minutes before exercise.

Maximum Daily Dose
Adults and Adolescents (12 years and older): Eight inhalations (800 mcg salbutamol).

Children (6 - 11 years of age): Four inhalations (400 mcg salbutamol).

Missed Dose
If a single dose is missed, instruct the patient to take the next dose when it is due or if they become wheezy.

Administration
AIROMIR Inhalation Aerosol is to be administered by oral inhalation only.

It is important that patients be instructed on how to use AIROMIR Inhalation Aerosol correctly and how it should be used in relation to other medications they are taking as described in **PATIENT MEDICATION INFORMATION.**

The action of AIROMIR Inhalation Aerosol should last for four to six hours. AIROMIR Inhalation Aerosol should not be used more frequently than recommended. Do not increase the number of puffs or the frequency of doses of AIROMIR Inhalation Aerosol without consulting your physician. If you find that treatment becomes less effective for symptomatic relief, your symptoms become worse, and/or you need to use the product more frequently than usual, seek medical attention immediately. While you are taking AIROMIR Inhalation Aerosol, other inhaled drugs should be taken only as directed by your physician. If you are pregnant or nursing, contact your physician about the use of AIROMIR Inhalation Aerosol.

There is no tail-off phenomenon observed for AIROMIR since the propellant and drug exhaust simultaneously, providing consistent dosing from priming through to a few sprays beyond the planned maximum number of doses. Tail-off means that as most inhalers approach empty, the delivered dose becomes unpredictable and subject to wide variation.

The inhaler should be primed when new and after 2 or more weeks of non-use by discharging a minimum of 4 sprays into the air, away from the face.

The inhaler should be shaken well before using.

OVERDOSAGE

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

Symptoms and signs
Manifestations of overdosage may include anginal pain, hypertension, hypokalemia, tremor and tachycardia and exaggeration of other pharmacological effects as listed in **ADVERSE REACTIONS.**

As with all sympathomimetic aerosol medications, cardiac arrest and even death may be associated with abuse.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

The oral LD_{50} in male and female rats and mice was greater than 2,000 mg/kg. The aerosol LD_{50} could not be determined.

Treatment
Consideration should be given to discontinuation of treatment and appropriate symptomatic therapy. To antagonise the effect of salbutamol, the judicious use of a cardio-selective beta-adrenergic blocking agent (e.g. metoprolol, atenolol) may be considered, bearing in mind the danger of inducing an asthmatic attack. There is insufficient evidence to determine if dialysis is beneficial for overdosage of AIROMIR Inhalation aerosol.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Salbutamol produces bronchodilation through stimulation of $beta_2$-adrenergic receptors in bronchial smooth muscle, thereby causing relaxation of bronchial muscle fibers. This action results in improved pulmonary function as demonstrated by spirometric measurements. At therapeutic doses, salbutamol has little action on the $beta_1$-adrenergic receptors in cardiac muscle.

Clinical experience has shown that inhaled salbutamol, like other beta-adrenergic agonists, can produce significant cardiovascular effects in some patients, as measured by pulse rate, blood pressure and/or ECG changes. Other effects common to this class of drugs and probably mediated by beta-adrenoreceptors are tremor and hypokalemia.

The time to onset of a 15% increase in FEV_1 is five to 15 minutes after inhalation of salbutamol and the time to peak effect occurs within 60 to 90 minutes. The mean duration of effect as measured by a 15% increase in FEV_1 is about three hours. In some patients, duration of effect is as long as six hours.

Human Pharmacokinetics

Most of the inhaled salbutamol impacts on the throat and is swallowed. After absorption, it is extensively metabolized by sulfate conjugation, either in the intestinal wall or liver. Approximately 72% of the inhaled dose is excreted within 24 hours in the urine and consists of 28% unchanged drug and 44% as metabolite. Up to 12% of an inhaled dose may be excreted in the feces. Urinary excretion studies utilizing radioactive drug indicated that salbutamol has a half-life of 3.8 hours.

Salbutamol inhaled into the respiratory tract is absorbed within minutes. Systemic levels of salbutamol after inhalation of recommended doses are less than 10% of the oral recommended doses. Low systemic levels (1 ng/mL) of salbutamol after administration of a two-inhalation single dose were detected within the first 60 minutes post dosing in four of eight subjects given AIROMIR Inhalation Aerosol. Because the levels were transient, the metabolic rate and half-life of elimination of salbutamol in serum could not be determined.

Most of the propellant hydrofluoroalkane 134a administered with use of Inhalation Aerosol is exhaled and the elimination half-life of absorbed hydrofluoroalkane 134a is on the order of 5 minutes in man. No accumulation of the propellant hydrofluoroalkane 134a has been found with repeated dosing. Studies using liver microsomes from rat and rabbit have shown that hydrofluoroalkane 134a is metabolized primarily by cytochrome P-450 2E1. However, hydrofluoroalkane 134a metabolism is not significant in humans. After regular administration of large doses of propellant hydrofluoroalkane alone for up to 2 weeks to patients with either mild asthma or severe obstructive lung disease, the metabolite trifluoroacetic acid has not been detected in the urine.

STORAGE AND STABILITY

Store between 15^{o}C and 30^{o}C. Protect from direct sunlight and frost.

SPECIAL HANDLING INSTRUCTIONS

The contents of AIROMIR Inhalation Aerosol are under pressure. The aerosol container may explode if heated. Do not place in hot water or near radiators, stoves or other sources of heat or an open flame. Do not puncture or incinerate the inhaler even when empty. As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

DOSAGE FORMS, COMPOSITION AND PACKAGING

The AIROMIR Inhalation Aerosol is a pressurized inhalation aerosol delivering salbutamol sulfate, USP 120 mcg ex-valve (equivalent to 100 mcg salbutamol) into the mouthpiece of the adapter.

AIROMIR Inhalation Aerosol also contains and delivers the following inactive ingredients: oleic acid, ethanol and propellant HFA-134a. A metered dose from AIROMIR Inhalation Aerosol delivers 0.0054 milliliters of ethanol per puff.

AIROMIR Inhalation Aerosol is available in individual packages as 200-dose inhaler. The 200-dose product contains a minimum net content weight of 6.7 g and will provide a minimum of 200 inhalations.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

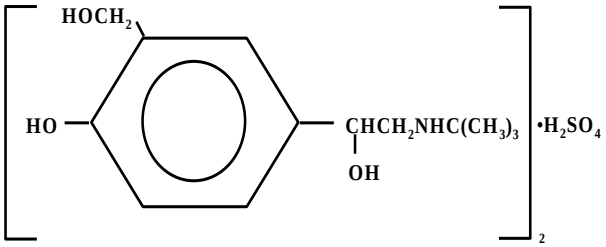
Proper name: Salbutamol sulfate

Chemical name: α^1-[(tert-butylamino)methyl]-4-hydroxy-m-xylene-α,α'-diol sulfate (2:1)(salt)

Molecular formula: $C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$

Molecular mass: 576.71 g/mol

Structural formula:



Physicochemical properties

Description: A white to off-white fine crystalline powder; odourless; specific rotation between -1.0° and +1.0°, calculated on the dried basis, determined in a 1 in 100 solution in alcohol.

Melting Point: Salbutamol melts at about 155°C with decomposition.

Solubility: Soluble in water, slightly soluble in ethanol (95%) and in ether and chloroform.

Stereoisomers: There is no known potential for stereoisomer production.

CLINICAL TRIALS

In a 12-week, randomized, double-blind, active- and placebo-controlled trial (1012-SILV), 565 asthmatic patients between 18 to 65 years of age were evaluated for the bronchodilator efficacy of AIROMIR Inhalation Aerosol (193 patients) in comparison with a CFC 11/12 propellant salbutamol inhaler (VENTOLIN®, US source; 186 patients) and an HFA-134a placebo inhaler (186 patients). Serial FEV_1 measurements demonstrated that two inhalations of AIROMIR Inhalation Aerosol produced significantly greater improvement in pulmonary function than placebo and produced outcomes which were clinically comparable to the VENTOLIN®.

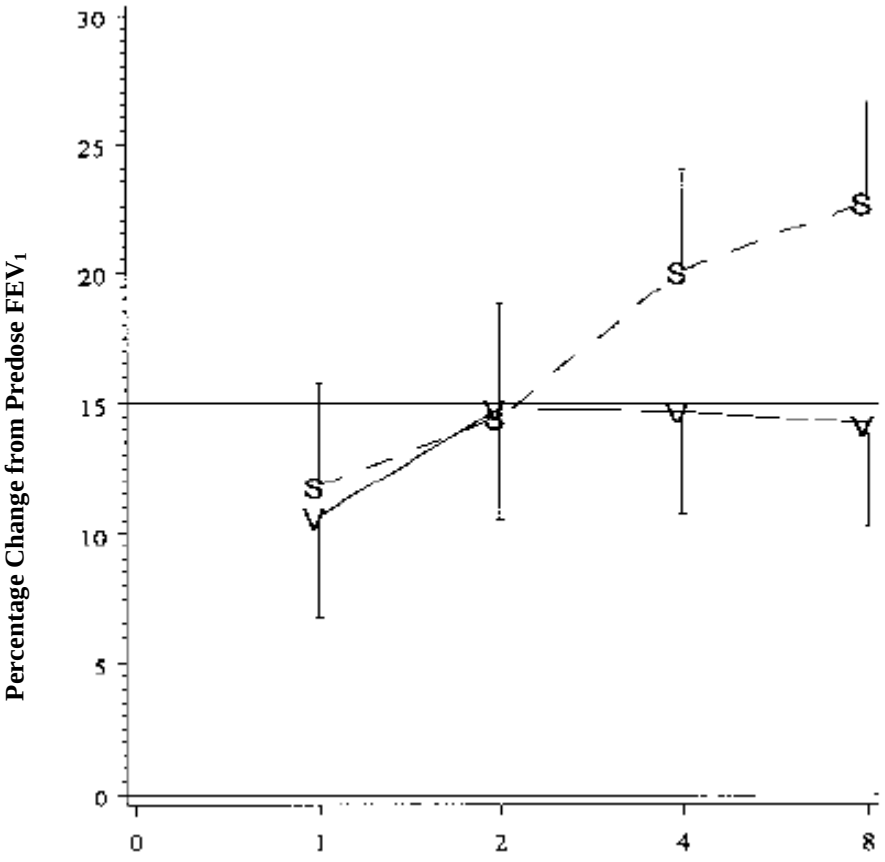
The mean time to onset of a 15 percent increase in FEV_1 was 6 minutes and the mean time to peak effect was 50 to 55 minutes. The mean duration of effect as measured by a 15 percent increase in FEV_1 was 3 hours. In some patients, duration of effect was as long as 6 hours. This study also demonstrated that there were no significant differences in these parameters between AIROMIR Inhalation Aerosol and the CFC-salbutamol inhaler (VENTOLIN®).

In a single-dose, randomized, single-blind, placebo-controlled, four-period crossover study (1150-SILV), 20 patients with exercise-induced asthma, aged 12-50 years, received two inhalations containing either HFA-134a salbutamol sulfate, VENTOLIN® (US source), Proventil® (US source) or HFA-134a placebo, followed 30 minutes postdose by an exercise challenge test. The mean smallest percent change from baseline FEV_1 were 2.0%, 2.0%, and 3.6% for the HFA-134a salbutamol sulfate, Proventil® and VENTOLIN® groups, respectively, while the HFA-134a placebo group had a mean smallest percent change of -23.7% ($p<.001$). Each of the active treatments was significantly different from HFA-134a placebo ($p<.001$) for the post exercise smallest absolute change from predose FEV_1. Safety data indicated no clinically meaningful differences between HFA-134a salbutamol sulfate, Proventil® and VENTOLIN®.

In a single-dose, randomized, single-blind, placebo-controlled, four-period crossover study (1247-SILV), 16 children with exercise-induced asthma, aged 6-11 years, received two inhalations containing either HFA-134a salbutamol sulfate, VENTOLIN® (US source), Proventil® (US source) or HFA-134a placebo, followed 30 minutes postdose by an exercise challenge test. Results showed that each active treatment group had significantly fewer patients who were unprotected (i.e., FEV_1 decreased by at least 20% at any of the eight times post-exercise) by the treatment than HFA-134a placebo ($p<.017$). The HFA salbutamol sulfate and Proventil® groups each had one (7%) unprotected patient. The VENTOLIN® group had no unprotected patients. In the HFA-134a placebo group, 10 (67%) patients were unprotected. The mean smallest percent change from baseline FEV_1 were 1.9%, -0.3%, and, -0.7% for the HFA-134a salbutamol sulfate, Proventil® and VENTOLIN® groups, respectively, while the HFA-134a placebo group had a mean smallest percent change of -25.5% ($p<.001$). Each of the active treatments was significantly different from HFA-134a placebo ($p<.001$) for the post exercise smallest absolute change from predose FEV_1. Safety data indicated no clinically meaningful differences between HFA-134a salbutamol sulfate, Proventil® and VENTOLIN®.

A single-blind, two-period crossover cumulative dose response study was carried out in children 6-11 years of age with asthma (1142-SILV). During each study period, patients self-administered individual dose levels of 1, 1, 2, and 4 inhalations (totaling 8 cumulative inhalations) of either

AIROMIR inhaler or VENTOLIN® (US source), at 30-minute intervals. AIROMIR performed as expected based on cumulative-dose studies in adults. The data (Figure 1) show that one puff of AIROMIR provided bronchodilation comparable to that obtained with one puff of VENTOLIN®. There was also comparable benefit after two cumulative puffs of AIROMIR or VENTOLIN®. There were no important clinical differences in the efficacy of AIROMIR and VENTOLIN® in the dose range advised for use of the product, namely one to two puffs. With increasing doses of AIROMIR beyond two puffs, there was increasing bronchodilation. However, with VENTOLIN®, there was a plateau of effect after 2 cumulative puffs most apparent with the FEV_1 response. All patients in this study were required to demonstrate at least a 15% reversibility to two puffs of VENTOLIN® to qualify for the study. The mean screening percent reversibility for patients in the study was 25.9% while the mean FEV_1 for VENTOLIN® after eight cumulative puffs was 14.2%. This cumulative dose study was performed under closely monitored conditions for the express purpose of studying extreme use and is not intended to reflect usual use. Indeed, if an asthma attack has not been relieved by one to two inhalations, patients should immediately consult their physicians or the nearest hospital.

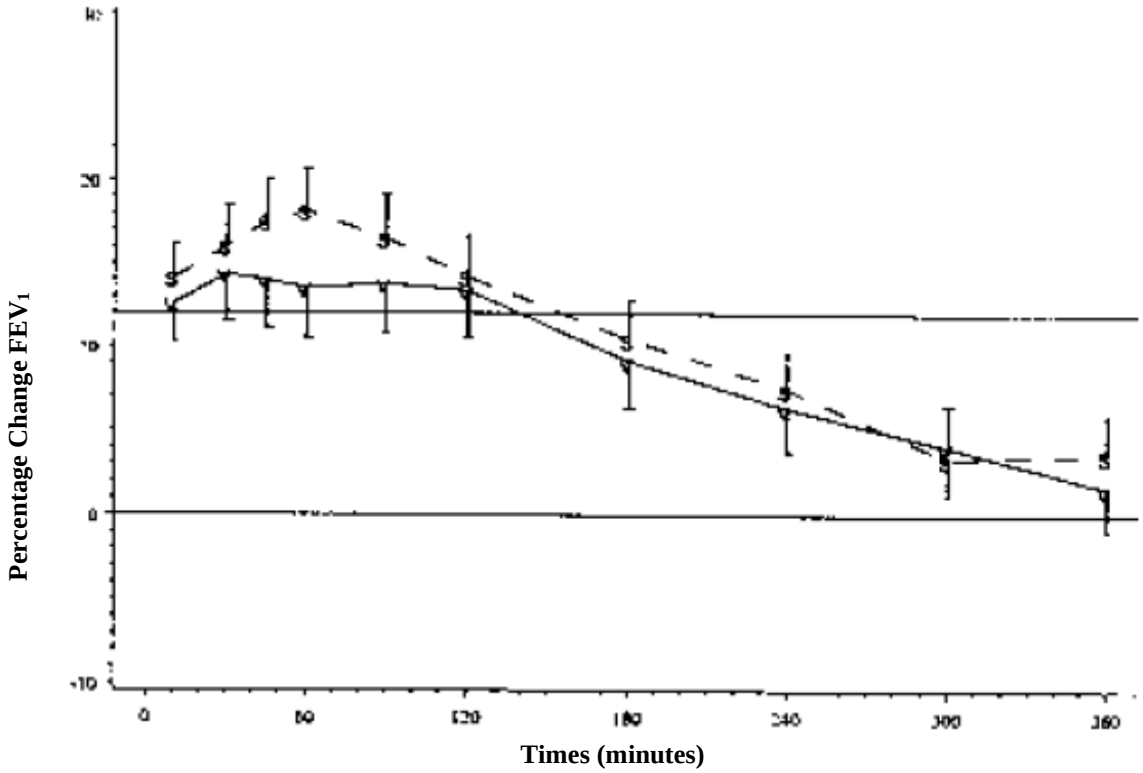


S = HFA-134a Salbutamol Sulfate
V = VENTOLIN® (CFC 11/12)

Figure 1: Mean (SE) Percentage Change from Predose FEV_1 (24 Patients Completing the Study)

Another pediatric study (1141-SILV) was designed as a rigorous test of the safety of AIROMIR at daily doses of two puffs, four-times a day for four weeks, in 63 children 4-11 years of age. AIROMIR was well tolerated and no safety concerns were detected. There was a trend for AIROMIR to have a greater bronchodilator response than VENTOLIN® at Study Week 4 as measured by FEV_1 (see Figure 2), but this difference could not be measured with a high degree of confidence.

A three-month, open label, observational post-marketing surveillance study (1178-SILV) was carried out in the U.K. to compare the safety of AIROMIR Inhalation Aerosol with that of CFC-salbutamol inhalers in primary care settings. In that study, 5,402 patients received AIROMIR Inhalation Aerosol, and 1,212 received CFC-salbutamol. The median age of patients was 38 years and 42 years for the AIROMIR Inhalation Aerosol and for the CFC-salbutamol groups, respectively. The cohort included 509 patients aged 6 months to 12 years, i.e. 409 patients in the AIROMIR group and 100 patients in the CFC-salbutamol group. There were no statistically significant differences between the AIROMIR Inhalation Aerosol and the CFC-salbutamol groups with respect to hospital admissions and other patient/doctor consultations, or in the overall incidence of adverse events. There was no evidence of an increased relative risk of safety problems in children receiving AIROMIR compared to those receiving CFC-salbutamol.



S= HFA-134a Salbutamol Sulfate (N = 33)
V = VENTOLIN® (CFC -11/12 Salbutamol) (N = 30)
The line at 12% represents a clinically meaningful effect

Figure 2: Mean (SE) Percentage Change from Predose FEV_1 at Study Week 4

DETAILED PHARMACOLOGY

Pharmacodynamics

Salbutamol stimulates beta-adrenergic receptors and has little or no effect on alpha-adrenergic receptors. Salbutamol appears to have a greater stimulating effect on beta-adrenergic receptors of the bronchial, uterine and vascular smooth muscles (β_2 receptors) than on beta-adrenergic receptors of the heart (β_1 receptors). The main effect following inhalation of salbutamol is bronchodilation resulting from relaxation of smooth muscles of the bronchial tree. In patients with reversible obstructive airway disease, salbutamol decreases resistance of the airways as measured by pulmonary function tests such as peak expiratory flow rate (PEFR) and forced expiratory volume in one second (FEV_1).

Ethanol
Ethanol has been previously used in inhaled medication, as a cosolvent. The small amounts used in inhalers are not known to cause safety problems in asthmatics. The ethanol in a metered dose is subject to evaporation as the aerosol expands and is diluted in body fluids as it expands.

Animal Pharmacology

The general class of halocarbons including HFA-134a is known to cause non-immunologic cardiac sensitization in dogs. Specifically, cardiac arrhythmias can be induced in dogs if, during exposure to halocarbons, the dogs are challenged with an intravenous injection of epinephrine. HFA-134a by itself did not cause cardiac, respiratory, or renal dysfunction in dogs exposed to 20,000 ppm of HFA-134a. Cardiac arrhythmias were noted at concentrations of 80,000 ppm and greater when dogs were challenged with epinephrine.

Animal Pharmacokinetics

Salbutamol
Absorption and Metabolism - after inhalation, the majority of salbutamol impacts on the throat and is swallowed and absorbed into the systemic circulation. It is almost exclusively metabolized by conjugation to a sulfate ester in the intestinal wall and liver.

Elimination - after inhalation about 70% of a dose is excreted in the urine as unchanged drug and metabolites within 24 hours. Up to 12% of an inhaled dose may be excreted in the feces. The fraction delivered to the lungs also appears in the circulation as free unmetabolized drug.

HFA-134a
The pulmonary pharmacokinetics of HFA-134a have been investigated in rat, dog, mouse, and rabbit.

Absorption and Distribution - following inhalation of ^{14}C labelled HFA-134a in rats a total of 1% of the inhaled dose was absorbed. Once absorbed, HFA-134a was distributed rapidly throughout the body. Unchanged HFA-134a was shown to rapidly equilibrate with all tissues in the body, and to be promptly eliminated once exposure was discontinued. In rats given ^{14}C labelled

HFA-134a by inhalation, the highest tissue concentrations were found in the lung, heart, kidney, liver, and spleen.

Distribution studies in the pregnant rat and rabbit showed that HFA-134a crosses the placental barrier and enters the embryo-foetal compartment. Amniotic fluid levels were less than the maternal blood level in both species.

Metabolism - very little metabolism of HFA-134a has been observed. Studies using liver microsomes from rat and rabbit have shown that HFA-134a is metabolized primarily by cytochrome P-450 2E1. The metabolite, trifluoroacetic acid, has been identified in urine from mouse and rat. An additional metabolite, trifluoroacetaldehyde, has been identified only in mouse urine. No metabolite of HFA-134a could be identified in dog urine.

Elimination - the initial elimination phase is rapid and the terminal half-life of HFA-134a averages about 5 minutes in the mouse, 15 to 25 minutes in the rat, and 15 to 20 minutes in the dog. No accumulation of HFA-134a was noted during daily exposures of 4 to 55 weeks.

TOXICOLOGY

Acute Toxicity

One dog was administered 250 metered aerosol doses of salbutamol sulfate in a single day. The dog tolerated the dosing without showing any adverse clinical reactions. No adverse or delayed reactions were detected during the 3-day post dosing observation period.

Repeated Dose Toxicity

Rats were exposed by inhalation to a maximum of 11.6 mg/kg/day of salbutamol sulfate for four days. There were no deaths during the study. Clinical signs generally observed included rapid and pronounced respiration and red staining around the snout. Body weight gains appeared higher than controls.

Dogs were exposed by inhalation of salbutamol sulfate to up to 250 metered doses per day for up to seven days. No significant adverse clinical signs were noted, although animals showed an increased heart rate during and after dosing. Occasional increased heart force determined by palpation was also observed. Electrocardiographic measurements immediately following exposure indicated a decrease in heart rate after the last exposure.

Rats were exposed to salbutamol sulfate by inhalation for 28 days at doses of 0.3, 1.1, and 9.5 mg/kg/day. The high dose group showed transient pronounced respiration and red oculo-nasal discharge. Organ weight analysis revealed an increase in heart and lung weights in the intermediate and high dose groups, although there were no histopathological abnormalities in any tissue.

Rats were exposed to salbutamol sulfate by inhalation for 90 days at doses of 0.3, 2.2, and

9.1 mg/kg/day. Clinical signs included hypoactivity, salivation, and nasal discharge. Epithelial metaplasia of the larynx and the first section of the nose was found proportional to the dose. The incidence rate and average severity of this lesion was similar for the placebo formulation and the high dose groups. The epithelial metaplasia in the larynx and nose was attributed to the purely physical nature of high exposures to any particulate matter which in turn causes an epithelial adaptive response. Thymic atrophy marked by depletion of lymphocytes was found in the high dose group.

Dogs were exposed by inhalation to salbutamol sulfate for 28 days at doses of 0.5, 1.1, and 2.3 mg/kg/day. There was a trend in male dogs to display a reduction in erythrocytic parameters. No comparable effect was noted for females. Treated males showed a trend toward lower liver weights and treated females showed a trend toward lower thymus weights. There were no treatment-related histological findings.

Dogs were exposed by inhalation to salbutamol sulfate for 90 days at doses of 0.1, 0.4, and 0.9 mg/kg/day. Treatment-related clinical signs included increased heart force which was most prominent in the high dose group. There was a general reduction in hemoglobin, hematocrit, and creatinine. There were significant decreases in spleen and heart weights, and non-statistically significant but apparent decreases in thymus weights. All parameters were normal in dogs allowed to recover for six weeks after the 90-day exposure. Histological examination revealed no treatment-related effects on any tissues.

Mutagenicity

In vitro tests of salbutamol have revealed no mutagenicity activity.

Carcinogenicity

A two-year rat carcinogenicity study showed a dose-related increase in benign leiomyomas of the mesovarium at doses equivalent to large multiples of the maximum anticipated human dosage. The relevance of this finding to man is not known.

Reproductive Studies

As a range-finding pilot study, salbutamol sulfate was administered by inhalation to timed-pregnant rats on gestation days 6 through 15. Measurable levels of salbutamol were detected in the serum and amniotic fluid from exposed rats thus indicating that salbutamol was absorbed by the dams and resulted in fetal exposure. No difference in litter weights or pup viability was detected. Gross external and soft tissue examinations did not show fetal malformations or anomalies.

Salbutamol sulfate was administered by inhalation to timed-pregnant rats on gestation days 6 through 15. The doses were 0.5, 1.1, and 2.3 mg/kg/day. Measurable levels of salbutamol were detected in the serum in a dose dependent manner. Salbutamol levels were also detected in the amniotic fluid in a dose related manner. Clinical signs consisting of ptosis and hypoactivity were observed in the high dose group. No biologically relevant changes in dam body or uterus weights

were present. No differences in litter weights or pup viability were detected. Gross external, skeletal, and soft tissue examinations did not show fetal malformations or anomalies.

Teratogenicity Studies

Salbutamol has been shown to be teratogenic in mice. A reproduction study in CD-1 mice given salbutamol sulfate subcutaneously (0.025, 0.25 and 2.5 mg/kg) showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg (approximately equal to the maximum recommended human daily inhalation dose on a mg/m^2 basis) and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg (approximately 10 times the maximum recommended human daily inhalation dose on a mg/m^2 basis). None was observed at 0.025 mg/kg (approximately one tenth the maximum recommended human daily inhalation dose on a mg/m^2 basis).

REFERENCES

1. Daly MJ, Farmer JB, Levy GP: Comparison of the bronchodilator and cardiovascular actions of salbutamol, iso prenaline and orciprenaline in guinea pigs and dogs. Br J Pharmacol 1971; 42:624-638.

2. Poynter D et al: Salbutamol: Lack of Evidence of Tumor Induction in Man. Br Med J 1978; 1:46.

3. Dockhorn R, Wagner DE, Burgess GL, Hafner KB et al: Proventil HFA provides protection from exercise-induced bronchoconstriction comparable to Proventil and VENTOLIN®. Annals Allergy, Asthma & Immunol 1997; 79(1): 85-88.

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

PrAIROMIR®
Salbutamol inhalation aerosol

Read this carefully before you start taking **AIROMIR** 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 **AIROMIR**.

What is AIROMIR used for?
AIROMIR is used in adults and children 6 years and older to:
- relieve bronchospasm symptoms
- prevent bronchospasm symptoms
- prevent bronchospasm symptoms caused by exercise

Bronchospasm is a sudden worsening of shortness of breath and wheezing.

The safety and effectiveness of AIROMIR in children under the age of 6 years is not known.

How does AIROMIR work?
AIROMIR belongs to a group of medicines called bronchodilators. It relaxes the muscles in the walls of the small air passages in the lungs. This helps to open up the airways and so helps to relieve chest tightness, wheezing and cough so that you can breathe more easily.

What are the ingredients in AIROMIR?
Medicinal ingredient: **S**albutamol Sulfate.
Non-medicinal ingredients: Ethanol, Oleic Acid, and Propellant HFA-134a.

AIROMIR comes in the following dosage forms:
AIROMIR is a pressurized inhalation aerosol. Each inhalation of aerosol from the canister contains 100 micrograms of salbutamol (as sulfate).

AIROMIR Inhalation Aerosol will deliver at least 200 sprays for the 200-dose size. However, after the labeled amount of sprays, the amount of drug delivered per spray may not be consistent. You should keep track of the number of sprays used from your canister of AIROMIR Inhalation Aerosol and discard the canister after 200 sprays (for the 200-dose inhaler).

Do not use AIROMIR:
- If you are allergic to salbutamol sulfate or any of the non-medicinal ingredients in the AIROMIR Inhalation Aerosol.
- For the treatment of preterm labour or miscarriage.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take AIROMIR. Talk about any health conditions or problems you may have,

including if you:

- have ever had to stop taking other medicines for this illness because you were allergic to them or they caused problems;
- have a thyroid condition;
- have a history of seizures;
- have high blood pressure or a heart problem;
- have diabetes;
- have low levels of potassium in your blood (hypokalemia), especially if you are taking:
    - drugs known as xanthine derivatives (such as theophylline) to treat breathing problems like COPD and asthma,
    - steroids to treat asthma,
    - water pills (diuretics);
- are pregnant or intend to become pregnant. Taking AIROMIR during pregnancy may cause harm to your baby. Your healthcare professional will consider the benefit to you and the risk to your baby of taking AIROMIR while you're pregnant;
- are breastfeeding. It is possible that AIROMIR passes into breast milk.

Other warnings you should know about:
The effects of AIROMIR should last for 4 to 6 hours. If the relief of wheezing or chest tightness is not as good as usual, or the effect lasts for less than three hours, contact your healthcare professional as soon as possible. It may be that your chest condition is worsening, and you may need to add another type of medicine to your treatment. If you notice a sudden worsening of your shortness of breath and wheeze shortly after taking your medicine, contact your healthcare professional or the nearest hospital immediately.

You should always carry your AIROMIR Inhalation Aerosol with you to use immediately in case you experience an asthma attack.

If you have to go to the hospital for an operation, take your inhaler with you and tell the healthcare professional about all the medicine(s) you are taking.

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 AIROMIR:

- anti-depressants;
- epinephrine;
- bronchodilators used to open the airways (such as other asthma medication);
- diuretics ('water pills');
- drugs to lower blood pressure such as propranolol;
- digoxin, a heart medication.

How to take AIROMIR:
AIROMIR should only be inhaled. Do not swallow.

Use AIROMIR only as directed by your healthcare professional.

If you are also using an inhaled corticosteroid:

- Always use AIROMIR first.
- Wait a few minutes.
- Then use your inhaled corticosteroid.

You should call your doctor immediately if:

- the effects of one dose last less than 3 hours;
- you notice a sudden worsening of your shortness of breath;
- your symptoms get worse;
- your usual dose does not provide relief of wheezing or chest tightness;
- you need to use AIROMIR more often than before.

These may be signs that your asthma or chest condition is getting worse. Your doctor may want to reassess your treatment plan.

Do not increase the dose or the number of times you use your medicine without asking your doctor, as this may make you feel worse.

Usual dose:
For relief of bronchospasm symptoms:
Adults and Adolescents 12 years and older: 1 to 2 inhalations of AIROMIR Inhalation Aerosol as needed.

Children (6 - 11 years of age): 1 inhalation of AIROMIR Inhalation Aerosol as needed.

If you have a more severe attack, you can repeat the dose every 4 to 6 hours, and immediately consult your doctor or the nearest hospital.

For prevention of bronchospasm symptoms:
Adults and Adolescents 12 years and older: 1 to 2 inhalations of AIROMIR Inhalation Aerosol repeated every 4 to 6 hours as needed, not exceeding 8 inhalations per day.

Children (6 - 11 years of age): 1 inhalation of AIROMIR Inhalation Aerosol, repeated every 4 to 6 hours as needed, not exceeding 4 inhalations per day.

For prevention of bronchospasm symptoms caused by exercise:
Adults and Adolescents 12 years and older: 2 inhalations of AIROMIR Inhalation Aerosol 30 minutes before exercise.

Children (6 - 11 years of age): 1 inhalation of AIROMIR Inhalation Aerosol 30 minutes before exercise.

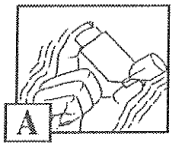
Maximum Dose per 24-hour period:
Adults and Adolescents 12 years and older: 8 inhalations of AIROMIR Inhalation Aerosol.

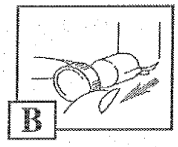
Children (6 - 11 years of age): 4 inhalations of AIROMIR Inhalation Aerosol.

How to prime AIROMIR Inhalation Aerosol:
Before using AIROMIR for the first time, or if your inhaler has not been used for 2 weeks or more, shake the inhaler well and release 4 sprays into the air, away from your face, to insure that it works properly.

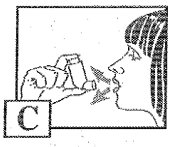
How to use AIROMIR Inhalation Aerosol:
AIROMIR should only be used with the mouthpiece supplied with the product. You should test the mouthpiece and aerosol canister before using them for the first time, or if you have not used your inhaler for more than 2 weeks.

1 SHAKE THE INHALER WELL right before each use (see figure A). Then take the cap off of the mouthpiece (see figure B). Check the mouthpiece for dirt or other objects before you use it. Make sure the aerosol canister is pushed all the way into the actuator (the small vertical cylinder in the mouthpiece). It should fit tightly, without wobbling.

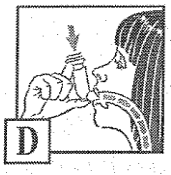




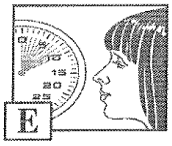
2 BREATHE OUT AS BIG A BREATH AS YOU CAN THROUGH YOUR MOUTH, pushing as much air out of your lungs as possible. Place the mouthpiece in your mouth between your teeth and close your lips around it. Make sure the inhaler stays straight up (see figure C).



3 AT THE BEGINNING OF A DEEP, SLOW BREATH THROUGH YOUR MOUTH, PUSH ALL THE WAY DOWN ON THE TOP OF THE AEROSOL CANISTER. (See figure D).



4 HOLD YOUR BREATH FOR AS LONG AS YOU CAN. Before breathing out, take the inhaler out of your mouth and stop squeezing down on the aerosol canister. (See figure E).

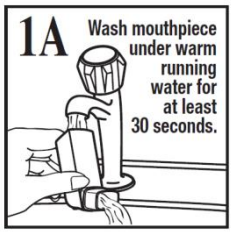


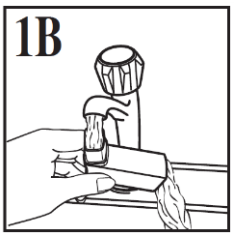
5 If your healthcare professional has told you to take two puffs, wait one minute and shake the inhaler again. Repeat steps 2 through 4. Replace the cap after you are finished using the inhaler.

6 KEEPING THE PLASTIC MOUTHPIECE CLEAN IS VERY IMPORTANT TO PREVENT THE INHALER FROM BECOMING DIRTY AND CLOGGED.

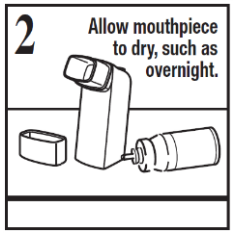
Routine Cleaning Instructions:

Step 1A & 1B. To clean, remove the canister and mouthpiece cap. Rinse the mouthpiece through the top and bottom with warm running water for at least 30 seconds. Let the water run through the mouthpiece as shown in figure 1A. Turn the mouthpiece unit around and let the water run through the unit as shown in figure 1B for another 30 seconds. Look into the mouthpiece to make sure any medicine build-up has been completely washed away. If there is any build-up, repeat steps in figure 1A & 1B. **Never put the metal canister in water.**



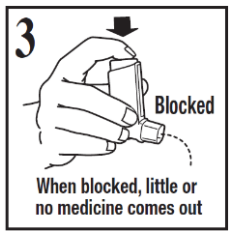


Step 2. To dry, shake off as much excess water as you can and let the mouthpiece air dry thoroughly, such as overnight. When the mouthpiece is dry, put the canister back in and make sure it fits firmly without wobbling. Replace the cap. **If you use the inhaler before it is dry, you may cause it to clog.**

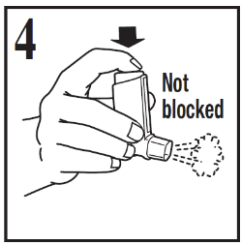


These cleaning and drying instructions are very important and should be performed at least once a week to prevent clogging of the unit.

IF YOUR INHALER HAS BECOME BLOCKED (little or no medication coming out of the mouthpiece, see figure 3 and 4), wash the mouthpiece as described in STEP 1A & 1B and air dry thoroughly as described in STEP 2.



If you need to use your inhaler right after you have washed it, shake off excess water, put the canister back in and test spray it into the air twice, away from your face, to remove most of the water remaining in the mouthpiece. Then take your dose as prescribed. **After such use, re-wash and air dry thoroughly as described in STEPS 1A & 1B and 2.**



Overdose:

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

If you accidentally take a larger dose than prescribed, you are more likely to get side effects like a faster heartbeat, headaches and feeling shaky or restless. These effects usually wear off within a few hours, but you should tell your healthcare professional as soon as possible.

Missed Dose:
If you forget a dose, just inhale the next dose when it is due or if you become wheezy.

What are possible side effects from using AIROMIR?
These are not all the possible side effects you may feel when taking AIROMIR. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:
- chest pain or discomfort
- tremor, feeling shaky
- nervousness
- restlessness, feeling anxious or irritable
- headache
- dizziness, feeling as though you are spinning or loss of balance (vertigo)
- drowsiness
- feeling tired or weak
- trouble sleeping (insomnia)
- flushing
- nausea, vomiting
- diarrhea
- trouble passing urine
- unusual taste in your mouth
- dry or irritated throat
- cough
- infection and/or inflammation in your airways or lungs
- muscle cramps or pain
- high blood pressure

Side effects in children may also include:
- changes in sleep patterns
- changes in behavior such as restlessness and excitability (hyperactivity)

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<u>VERY RARE</u> **Bronchospasm:** Sudden worsening of shortness of breath and wheezing shortly after using AIROMIR			✓

Allergic reactions: Sudden wheezing and chest pain or tightness; or swelling of eyelids, face, lips, tongue or throat			✓
RARE: **Low levels of potassium in the blood (Hypokalemia):** muscle weakness and muscle spasms		✓	
Hallucinations in children: see or hear things that are not there		✓	
COMMON: Heart palpitations, faster than normal heartbeat		✓	
UNKNOWN: Irregular heartbeat		✓	

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 report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- 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.

Storage:
Store AIROMIR between 15°C and 30°C. Protect it from direct sunlight and freezing.

Warning: The contents of AIROMIR inhalation aerosol are under pressure. The canister may explode if heated. Do not place in hot water or near radiators, stoves or other sources of heat. Do not puncture or incinerate the aerosol canister, even when it seems to be empty. As with most inhaled medications in aerosol canisters, AIROMIR may not work as well when the canister is cold.

If your healthcare professional changes your treatment and you no longer require AIROMIR

Inhalation Aerosol, please return your inhaler to your pharmacy for disposal.

Keep out of reach and sight of children.

If you want more information about AIROMIR:

- 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 at www.healthcanada.gc.ca; or by calling 1-800-361-4261.

You may need to read this leaflet again. **Please do not throw it away** until you have finished your medicine.

This leaflet was prepared by Bausch Health, Canada Inc.

Last Revised: December 22, 2020