

**ASPIRE PROPOSED DRAFT LABELING
ATTACHMENT 3**

Aspire Proposed Draft Albuterol Carton Labeling

I. Front Display Panel:

Andrx Pharmaceuticals, Inc.

NDC XXXX-XXXX-XX

17g 200 METERED INHALATIONS

Albuterol, USP Inhalation Aerosol

FOR ORAL INHALATION WITH ANDRX ALBUTEROL ACTUATOR ONLY

Contents: Each canister contains a microcrystalline suspension of albuterol, USP in propellants (trichloromonofluoromethane and dichlorodifluoromethane) with oleic acid. Each actuation delivers 90 mcg albuterol, USP from the mouthpiece.

Rx only

Usual Dosage (for adults and children 12 years and over): Two inhalations every 4 to 6 hours as necessary.

Aspire Proposed Draft Albuterol Carton Labeling

II. Left Informational Display Panel:

PATIENT'S INSTRUCTIONS FOR USE (*continued*)

DOSAGE: Use only as directed by your physician.

WARNINGS: The action of Albuterol Inhalation Aerosol may last up to 6 hours; therefore, it should not be used more frequently than recommended. Increasing the number or frequency of doses without consulting your physician can be dangerous. If recommended dosage does not provide relief of symptoms or symptoms become worse, seek immediate medical attention. While taking Albuterol Inhalation Aerosol, other inhaled medicines should be used only as prescribed by your physician.

Contents Under Pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children.

Aspire Proposed Draft Albuterol Carton Labeling

III. Right Informational Display Panel:

IMPORTANT: Read accompanying directions carefully.

Shake well before using.

Store between 15° and 30°C (59° and 86°F). Failure to use the product within this temperature range may result in improper dosing.

Attention Pharmacist-Detach Patient's Leaflet of Instructions from Package Insert and dispense Patient's Leaflet with inhaler.

Bar Code
Andrx Pharmaceuticals, Inc. , Davie, FL 33314
Rev. XXXX

Aspire Proposed Draft Albuterol Carton Labeling

IV. Top Panel:

17g 200 METERED INHALATIONS

Albuterol, USP Inhalation Aerosol

Aspire Proposed Draft Albuterol Carton Labeling

V. Back Panel:

PATIENT'S INSTRUCTIONS FOR USE

Before using your Albuterol Inhalation Aerosol, read complete instructions carefully.

1. SHAKE THE INHALER WELL immediately before each use. **Then remove the cap from the mouthpiece. Check mouthpiece for foreign objects prior to use.** Make sure the canister is fully and firmly inserted into the actuator.
2. BREATHE OUT FULLY THROUGH THE MOUTH, expelling as much air from your lungs as possible. Place the mouthpiece fully into the mouth, holding the inhaler in its upright position (see Figure 1) and closing the lips around it.
3. WHILE BREATHING IN DEEPLY AND SLOWLY THROUGH THE MOUTH, FULLY DEPRESS THE TOP OF THE METAL CANISTER with your index finger. (See Figure 2).
4. HOLD YOUR BREATH AS LONG AS POSSIBLE. Before breathing out, remove the inhaler from your mouth and release your finger from the canister.
5. Wait 1 minute and SHAKE the inhaler again. Repeat steps 2 through 4 for each inhalation prescribed by your physician.
6. CLEANSE THE INHALER THOROUGHLY AND FREQUENTLY. Remove the metal canister. Cleanse the plastic case and cap by rinsing thoroughly in warm running water, at least once a day. After thoroughly drying the plastic case and cap, gently replace the canister downward into the case **without using a twisting motion.** (See Figure 3). Replace the cap.
7. As with all aerosol medications, it is recommended to "test spray" into the air before using for the first time and in cases where the aerosol has not been used for a prolonged period of time.

(continued on right side panel)

Figure 1

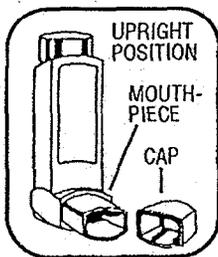


Figure 2

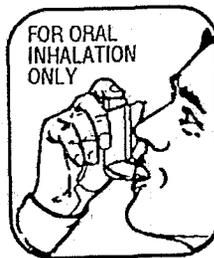
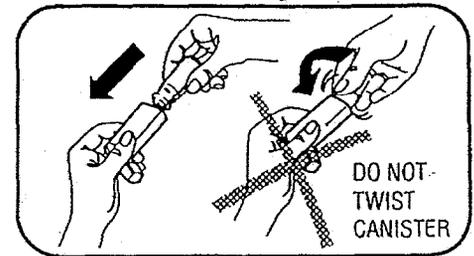


Figure 3



**Aspire Proposed Draft
Albuterol Carton Labeling**

VI. Bottom Panel:

Lot XXXXX

EXP XX/XX

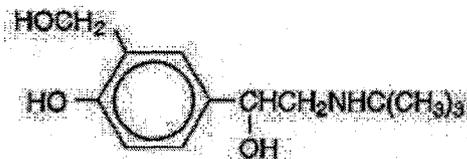
**ASPIRE'S PROPOSED DRAFT LABELING
PACKAGING INSERT**

Aspire's Proposed Physician Insert Draft Labeling

Albuterol, USP Inhalation Aerosol FOR ORAL INHALATION ONLY Rx ONLY

DESCRIPTION

The active component of Albuterol Inhalation Aerosol is albuterol, USP racemic α^1 -[(*tert*-butylamino)methyl]-4-hydroxy-*m*-xylene- α,α' -diol), a relatively selective beta₂-adrenergic bronchodilator, having the chemical structure:



The molecular weight of albuterol is 239.3, and the empirical formula is C₁₃H₂₁NO₃. Albuterol is a white to off-white crystalline solid. It is soluble in ethanol, sparingly soluble in water, and very soluble in chloroform. The World Health Organization recommended name for albuterol base is salbutamol.

Albuterol Inhalation Aerosol is a pressurized metered-dose aerosol unit for oral inhalation. It contains a microcrystalline suspension of albuterol in propellants (trichloromonofluoromethane and dichlorodifluoromethane) with oleic acid. Each actuation delivers 100 mcg albuterol, USP from the valve and 90 mcg of albuterol, USP from the mouthpiece. Each 17.0 g canister provides 200 oral inhalations.

CLINICAL PHARMACOLOGY

The primary action of beta-adrenergic drugs, including albuterol, is to stimulate adenylyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate (cyclic AMP) from adenosine triphosphate (ATP) in beta-adrenergic cells. The cyclic AMP thus formed mediates the cellular responses. Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

In vitro studies and *in vivo* pharmacologic studies have demonstrated that albuterol has a preferential effect on beta₂-adrenergic receptors compared with isoproterenol. While it is recognized that beta₂-adrenergic receptors are the predominant receptors in bronchial smooth muscle, data indicate that there is a population of beta₂-receptors in the human heart existing in a concentration between 10% and 50%. The precise function of these receptors has not been established.

In controlled clinical trials, albuterol has been shown to have more effect on the respiratory tract, in the form of bronchial smooth muscle relaxation than isoproterenol at comparable doses while producing fewer cardiovascular effects. Controlled clinical studies and other clinical experience have shown that inhaled albuterol, like other beta-adrenergic agonist drugs, can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or ECG changes.

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Albuterol is longer acting than isoproterenol in most patients by any route of administration because it is not a substrate for the cellular uptake processes for catecholamines nor for catechol-*O*-methyl transferase.

The effects of rising doses of albuterol and isoproterenol aerosols were studied in volunteers and asthmatic patients. Results in normal volunteers indicated that the propensity for increase in heart rate for albuterol is $\frac{1}{2}$ to $\frac{1}{4}$ that of isoproterenol. In asthmatic patients similar cardiovascular differentiation between the two drugs was also seen.

Preclinical Intravenous studies in rats with albuterol sulfate have demonstrated that albuterol crosses the blood-brain barrier and reaches brain concentrations that are amounting to approximately 5.0% of the plasma concentrations. In structures outside the blood-brain barrier (pineal and pituitary glands), albuterol concentrations were found to be 100 times those in the whole brain.

Studies in laboratory animals (minipigs, rodents, and dogs) have demonstrated the occurrence of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis) when beta-agonists and methylxanthines are administered concurrently. The clinical significance of these findings is unknown.

Pharmacokinetics Because of its gradual absorption from the bronchi, systemic levels of albuterol are low after inhalation at recommended doses.

Administration of tritiated albuterol by inhalation to four subjects resulted in maximum plasma concentrations within 2 to 4 hours. Due to the insensitivity of the assay method, the metabolic rate and half-life of elimination of albuterol in plasma could not be determined. However, data from urinary excretion studies indicated that albuterol has an elimination half-life of 3.8 hours. Approximately 72% of the inhaled dose is excreted in the urine within 24 hours, 28% as unchanged drug and 44% as metabolite.

Clinical Trials: In controlled clinical trials the onset of improvement in pulmonary function was within 15 minutes, as determined by both maximal midexpiratory flow rate (MMEF) and FEV₁. MMEF measurements also showed that near maximum improvement in pulmonary function generally occurs within 60 to 90 minutes, following 2 inhalations of albuterol and that clinically significant improvement generally continues for 3 to 4 hours in most patients. In clinical trials, some patients with asthma showed a therapeutic response (defined by maintaining FEV₁ values 15% or more above baseline) which was still apparent at 6 hours. Continued effectiveness of albuterol was demonstrated over a 13-week period in these same trials.

In clinical trials, 2 inhalations of albuterol taken approximately 15 minutes prior to exercise prevented exercise-induced bronchospasm, as demonstrated by the maintenance of FEV₁ within 80% of baseline values in the majority of patients. One of these studies also evaluated the duration of the prophylactic effect to repeated exercise challenges, which was evident at 4 hours in the majority of patients, and at 6 hours in approximately one third of the patients.

INDICATIONS AND USAGE

Albuterol Inhalation Aerosol is indicated in patients 12 years of age and older, for the prevention and relief of bronchospasm in patients with reversible obstructive airway disease, and for the prevention of exercise-induced bronchospasm.

CONTRAINDICATIONS

Albuterol Inhalation Aerosol is contraindicated in patients with a history of hypersensitivity to albuterol or any of its components.

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WARNINGS

Deterioration of Asthma: Asthma may deteriorate acutely over a period of hours, or chronically over several days or longer. If the patient needs more doses of Albuterol Inhalation Aerosol than usual, this may be a marker of destabilization of asthma and requires re-evaluation of the patient and the treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment, eg, corticosteroids.

Use of Anti-inflammatory Agents: The use of beta-adrenergic agonist bronchodilators alone may not be adequate to control asthma in many patients. Early consideration should be given to adding anti-inflammatory agents, eg, corticosteroids.

Paradoxical Bronchospasm: Albuterol Inhalation Aerosol can produce paradoxical bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs, Albuterol Inhalation Aerosol should be discontinued immediately and alternative therapy instituted. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister or vial.

Cardiovascular Effects: Albuterol Inhalation Aerosol, like all other beta-adrenergic agonists, can produce a clinically significant cardiovascular effect in some patients as measured by pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon after administration of Albuterol Inhalation Aerosol at recommended doses, if they occur, the drug may need to be discontinued. In addition, beta-agonists have been reported to produce electrocardiogram (ECG) changes, such as flattening of the T wave, prolongation of the QT_c interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, Albuterol Inhalation Aerosol, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Immediate Hypersensitivity Reactions: Immediate hypersensitivity reactions may occur after administration of albuterol, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema.

PRECAUTIONS

General: Albuterol, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Clinically significant changes in systolic and diastolic blood pressure have been seen and could be expected to occur in some patients after use of any beta-adrenergic bronchodilator.

Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis. As with other beta-agonists, albuterol may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects. The decrease is usually transient, not requiring supplementation.

Information For Patients: The action of Albuterol Inhalation Aerosol may last up to 6 hours or longer. Albuterol Inhalation Aerosol should not be used more frequently than recommended. Do not increase the dose or frequency of doses of Albuterol Inhalation Aerosol without consulting your physician. If you find that treatment with Albuterol Inhalation becomes less effective for symptomatic relief, your symptoms become worse, and/or you need to use the product more frequently than usual, you should seek medical attention immediately. While you are using Albuterol Inhalation Aerosol, other inhaled drugs and asthma medications should be taken only as directed by your physician. Common adverse effects include palpitations, chest pain, rapid heart rate, tremor, or nervousness. If you are pregnant or nursing, contact your physician about the use of Albuterol Inhalation Aerosol. Effective and safe use of Albuterol Inhalation Aerosol includes an understanding of the way that it should be administered. See illustrated **Patient's Instructions For Use.**

Aspire's Proposed Patient Insert Draft Labeling

The contents of Albuterol Inhalation Aerosol are under pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children. Avoid spraying in eyes.

Drug Interactions: Other short-acting sympathomimetic aerosol bronchodilators should not be used concomitantly with albuterol. If additional adrenergic drugs are to be administered by any route, they should be used with caution to avoid deleterious cardiovascular effects.

Beta Blockers: Beta-adrenergic receptor blocking agents not only block the pulmonary effect of beta-agonists, such as Albuterol Inhalation Aerosol but may produce severe bronchospasm in asthmatic patients. Therefore, patients with asthma should not normally be treated with beta-blockers. However, under certain circumstances, eg, as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-adrenergic blocking agents in patients with asthma. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

Diuretics: The ECG changes and/or hypokalemia that may result from the administration of nonpotassium-sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonist, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the coadministration of beta-agonists with nonpotassium-sparing diuretics.

Digoxin Mean decreases of 16% to 22% in serum digoxin levels were demonstrated after single dose intravenous and oral administration of albuterol, respectively, to normal volunteers who had received digoxin for 10 days. The clinical significance of this finding for patients with obstructive airway disease who are receiving albuterol and digoxin on a chronic basis is unclear. Nevertheless, it would be prudent to carefully evaluate the serum digoxin levels in patients who are currently receiving digoxin and albuterol.

Monoamine Oxidase Inhibitors or Tricyclic Antidepressants: Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents, because the action of albuterol on the vascular system may be potentiated.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: In a 2-year study in Sprague-Dawley rats, albuterol sulfate caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium at and above dietary doses of 2.0 mg/kg (approximately 15 times the maximum recommended daily inhalation dose for adults on a mg/m² basis). In another study this effect was blocked by the coadministration of propranolol, a non-selective beta-adrenergic antagonist.

In an 18-month study in CD-1 mice, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 500 mg/kg (approximately 1700 times the maximum recommended daily inhalation dose for adults on an mg/m² basis). In a 22-month study in the Golden Hamster, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 50 mg/kg (approximately 230 times the maximum recommended daily inhalation dose for adults on an mg/m² basis).

Albuterol sulfate was not mutagenic in the Ames test with or without metabolic activation using tester strains *S. typhimurium* TA1537, TA1538, and TA98 or *E. coli* WP2, WP2uvrA, and WP67. No forward mutation was seen in yeast strain *S. cerevisiae* S9 nor any mitotic gene conversion in yeast strain *S. cerevisiae* JD1 with or without metabolic activation. Fluctuation assays in *S. typhimurium* TA98 and *E. coli* WP2, both with metabolic activation, were negative. Albuterol sulfate was not clastogenic in a human peripheral lymphocyte assay or in an AH1 strain mouse micronucleus assay.

Reproduction studies in rats demonstrated no evidence of impaired fertility at oral doses of albuterol sulfate up to 50 mg/kg (approximately 340 times the maximum recommended daily inhalation dose for adults on an mg/m² basis).

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Teratogenic Effects--Pregnancy Category C: Albuterol sulfate has been shown to be teratogenic in mice. A study in CD-1 mice at subcutaneous (sc) doses at and above 0.25 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on an mg/m² basis), induced cleft palate formation in 5 of 111 (4.5%) fetuses. At an sc dose of 2.5 mg/kg (approximately 8 times the maximum recommended daily inhalation dose for adults on an mg/m² basis) albuterol sulfate induced cleft palate formation in 10 of 108 (9.3%) fetuses. The drug did not induce cleft palate formation when administered at an sc dose of 0.025 mg/kg (significantly less than the maximum recommended daily inhalation dose for adults on an mg/m² basis). Cleft palate also occurred in 22 of 72 (30.5%) fetuses from females treated with 2.5 mg/kg isoproterenol (positive control) administered subcutaneously.

A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) fetuses when albuterol sulfate was administered orally at a dose of 50 mg/kg (approximately 680 times the maximum recommended daily inhalation dose for adults on an mg/m² basis).

Studies in pregnant rats with tritiated albuterol demonstrated that approximately 10% of the circulating maternal drug is transferred to the fetus. Disposition in the fetal lungs is comparable to maternal lungs, but fetal liver disposition is 1% of the maternal liver levels.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients being treated with albuterol. Some of the mothers were taking multiple medications during their pregnancies. Because no consistent pattern of defects can be discerned, a relationship between albuterol use and congenital anomalies has not been established.

Use in Labor and Delivery-Use in Labor: Because of the potential for beta-agonist interference with uterine contractility, use of Albuterol Inhalation Aerosol for relief of bronchospasm during labor should be restricted to those patients in whom the benefits clearly outweigh the risk.

Tocolysis: Albuterol has not been approved for the management of preterm labor. The benefit:risk ratio when albuterol is administered for tocolysis has not been established. Serious adverse reactions, including maternal pulmonary edema, have been reported during or following treatment of premature labor with beta₂-agonists, including albuterol.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in some 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.

Pediatric Use: Safety and effectiveness in children below the age of 12 years have not been established.

ADVERSE REACTIONS

The adverse reactions of albuterol are similar in nature to those of other sympathomimetic agents, although the incidence of certain cardiovascular effects is less with albuterol.

Percent Incidence of Adverse Reactions in Patients ≥ 12 Years of Age in a 13-Week Clinical Trial * (n=147)		
Adverse Event	Albuterol Inhalation Aerosol	Isoproterenol Inhaler
Tremor	<15	<15
Nausea	<15	<15

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Tachycardia	10	10
Palpitations	<10	<15
Nervousness	<10	<15
Increased Blood Pressure	<5	<5
Dizziness	<5	<5
Heartburn	<5	<5
*A 13-week, double-blind study compared albuterol and isoproterenol aerosols in 147 asthmatic patients.		

Cases of urticaria, angioedema, rash, bronchospasm, hoarseness, oropharyngeal edema, and arrhythmias (including atrial fibrillation, supraventricular tachycardia, and extrasystoles) have also been reported after the use of inhaled albuterol. In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as hypertension, angina, vomiting, vertigo, central nervous system stimulation, insomnia, headache, unusual taste, and drying or irritation of the oropharynx.

OVERDOSAGE

The expected symptoms with overdosage are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the symptoms listed under **ADVERSE REACTIONS**, eg, angina, hypertension, tachycardia with rates up to 200 beats per minute, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, and insomnia. In addition, seizures, hypotension, arrhythmias, fatigue, malaise, and hypokalemia may also occur. As with all sympathomimetic aerosol medications, cardiac arrest and even death may be associated with abuse of Albuterol Inhalation Aerosol. Treatment consists of discontinuation of Albuterol Inhalation Aerosol together with appropriate symptomatic therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of Albuterol Inhalation Aerosol.

The oral median lethal dose of albuterol sulfate in mice is greater than 2000 mg/kg (approximately 6800 times the maximum recommended daily inhalation dose for adults on an mg/m² basis). In mature rats, the subcutaneous median lethal dose of albuterol sulfate is approximately 450 mg/kg (approximately 3000 times the maximum recommended daily inhalation dose for adults on an mg/m² basis). In small young rats, the subcutaneous median lethal dose is approximately 2000 mg/kg (approximately 14,000 times the maximum recommended daily inhalation dose for adults and children on an mg/m² basis). The inhalation median lethal dose has not been determined in animals.

DOSAGE AND ADMINISTRATION

Treatment of acute episodes of bronchospasm or prevention of asthmatic symptoms: The usual dosage for adults and children 12 years of age and older is 2 inhalations repeated every 4 to 6 hours; in some patients, 1 inhalation every 4 hours may be sufficient. More frequent administration or a larger number of inhalations is not recommended. For maintenance therapy or prevention of exacerbation of bronchospasm, 2 inhalations, 4 times a day should be sufficient.

The use of Albuterol Inhalation Aerosol can be continued as medically indicated to control recurring bouts of bronchospasm. During this time most patients gain optimal benefit from regular use of the inhaler. Safe usage for periods extending over several years has been documented.

If a previously effective dosage regimen fails to provide the usual response, this may be a marker of destabilization of asthma and requires re-evaluation of the patient and treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment, eg, corticosteroids.

Aspire's Proposed Physician Insert Draft Labeling

Exercise-Induced Bronchospasm Prevention: The usual dosage for adults and children 12 years and older is 2 inhalations, 15 minutes prior to exercise. For treatment, see above.

It is recommended to "test spray" Albuterol Inhalation Aerosol into the air before using for the first time and in cases where the aerosol has not been used for a prolonged period of time.

HOW SUPPLIED

Albuterol Inhalation Aerosol, 17.0 g canister contains 200 metered inhalations, box of one (NDC XXX-XXX-XX). Each actuation delivers 100 mcg of albuterol from the valve and 90 mcg of albuterol from the mouthpiece. Each canister is supplied with a plastic actuator with dust cap, and Patient's Instructions.

The correct amount of medication in each inhalation cannot be assured after 200 actuations from the 17.0 g canister even though the canister is not completely empty. The canister should be discarded when the labeled number of actuations have been used.

Store between 15° and 30°C (59° and 86°F). Failure to use the product within this temperature range may result in improper dosing. For optimal results, the canister should be at room temperature before use. Shake well before using.

Albuterol Inhalation Aerosol canister should be used only with the actuator provided. The actuator should not be used with other aerosol medication canisters.

NOTE: The indented statement below is required by the Federal government's Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFCs).

WARNING: Contains dichlorodifluoromethane (CFC-12) and trichloromonofluoromethane (CFC-11), substances which harm public health and the environment by destroying ozone in the upper atmosphere.

A notice similar to the above WARNING has been placed in the "Patient's Instructions for Use" portion of this package insert under the Environmental Protection Agency's (EPA's) regulations. The patient's warning states that the patient should consult his or her physician if there are questions about alternatives.

Andrx Pharmaceuticals, Inc.
Davie, FL 33314

Rev. XXXX

Aspire's Proposed Patient Insert Draft Labeling

PHARMACIST
TEAR AT PERFORATION
GIVE TO PATIENT

Albuterol, USP
Inhalation Aerosol
FOR ORAL INHALATION ONLY
Patient's Instructions
For Use

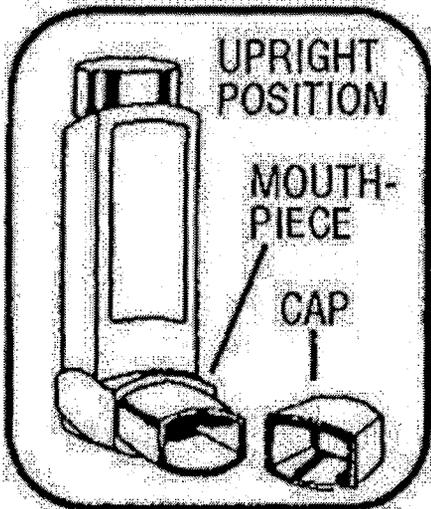


Figure 1

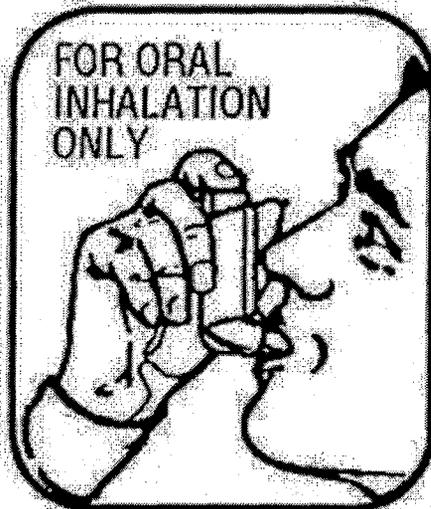


Figure 2

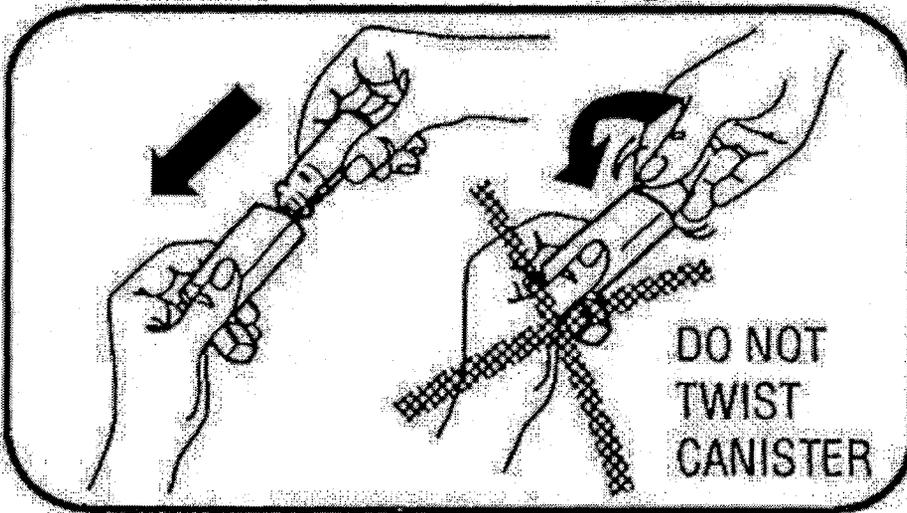


Figure 3

Aspire's Proposed Patient Insert Draft Labeling

Before using your Albuterol Inhalation Aerosol, read complete instructions carefully.

1. **SHAKE THE INHALER WELL** immediately before each use. **Then remove the cap from the mouthpiece. Check mouthpiece for foreign objects prior to use.** Make sure the canister is fully and firmly inserted into the actuator. The Albuterol Inhalation Aerosol canister should only be used with the Andrx Albuterol Inhalation Aerosol mouthpiece. This mouthpiece should not be used with any other inhalation drug product. Similarly, the canister should not be used with any other mouthpieces.
2. As with all aerosol medications, it is recommended to "test spray" into the air before using for the first time and in cases where the aerosol has not been used for a prolonged period of time.
3. **BREATHE OUT FULLY THROUGH THE MOUTH**, expelling as much air from your lungs as possible. Place the mouthpiece fully into the mouth, holding the inhaler in its upright position (See Figure 1) and closing the lips around it.
4. **WHILE BREATHING IN DEEPLY AND SLOWLY THROUGH THE MOUTH, FULLY DEPRESS THE TOP OF THE METAL CANISTER** with your index finger. (See Figure 2.)
5. **HOLD YOUR BREATH AS LONG AS POSSIBLE.** Before breathing out, remove the inhaler from your mouth and release your finger from the canister.
6. Wait one minute and **SHAKE** the inhaler again. Repeat steps 2 through 4 for each inhalation prescribed by your physician.
7. **CLEANSE THE INHALER THOROUGHLY AND FREQUENTLY.** Remove the metal canister and cleanse the plastic case and cap by rinsing thoroughly in warm running water, at least once a day. After thoroughly drying the plastic case and cap, gently replace the canister downward into the case **without using a twisting motion.** (See Figure 3.) Replace the cap.

DOSAGE: Use only as directed by your physician.

The correct amount of medication in each inhalation cannot be assured after 200 actuations from the 17.0 g canister even though the canister is not completely empty. The canister should be discarded when the labeled number of actuations have been used. Before you reach the specified number of actuations, you should consult your physician to determine whether a refill is needed. Just as you should not take extra doses without consulting your physician, you also should not stop using Albuterol Inhalation Aerosol without consulting your physician.

WARNINGS: The action of Albuterol Inhalation Aerosol may last up to 6 hours or longer. Albuterol Inhalation Aerosol should not be used more frequently than recommended. Do not increase the dose or frequency of Albuterol Inhalation Aerosol without consulting your physician. If you find that treatment with Albuterol Inhalation Aerosol becomes less effective for symptomatic relief, your symptoms become worse, and/or you need to use the product more frequently than usual, you should seek immediate medical attention. While taking Albuterol Inhalation Aerosol, other asthma drugs and inhaled medicines should be used only as prescribed by your physician.

Contents Under Pressure. Do not puncture. Do not store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children. Avoid spraying in eyes.

Store between 15° and 30°C (59° and 86°F). Failure to use the product within this temperature range may result in improper dosing. Shake well before using. For optimal results, the canister should be at room temperature before use.

Aspire's Proposed Patient Insert Draft Labeling

NOTE: The indented statement below is required by the Federal government's Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFCs).

This product contains dichlorodifluoromethane (CFC-12) and trichloromonofluoromethane (CFC-11), substances which harm the environment by destroying ozone in the upper atmosphere.

Your physician has determined that this product is likely to help your personal health. **USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR PHYSICIAN.** If you have any questions about alternatives, consult with your physician.

Andrx Pharmaceuticals, Inc.
Davie, FL 33314

Rev. XXXX

**ASPIRE PROPOSED DRAFT LABELING
ATTACHMENT 3
-CANISTER-**

Aspire Proposed Draft Albuterol Canister Labeling

Front Panel:

Andrx Pharmaceuticals, Inc.

NDC XXXX-XXXX-XX

17g 200 METERED INHALATIONS

Rx ONLY

Albuterol, USP Inhalation Aerosol

For Oral Inhalation with Andrx Albuterol Actuator Only

Read accompanying directions carefully.

Andrx Pharmaceuticals, Inc.
Davie, FL 33314

Rev. XXXX

Back Panel:

Contents: Each canister contains a microcrystalline suspension of albuterol in propellants (trichloromonofluoromethane and dichlorodifluoromethane) with oleic acid. Each actuation delivers 90 mcg albuterol, USP from the mouthpiece.

Usual Dosage (for adults and children 12 years and over):
Two inhalations every four to six hours as necessary.

WARNINGS: Do not exceed the dose prescribed by your physician. If difficulty in breathing persists, contact your physician immediately. Contents under pressure. Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children.

Store between 15° and 30°C (59° and 86° F). Failure to use the product within this temperature range may result in improper dosing. Shake well before using.

Lot XXXXX

EXP XXXX