HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROAIR RESPICLICK safely and effectively. See full prescribing information for PROAIR RESPICLICK.

PROAIR RESPICLICK (albuterol sulfate) inhalation powder, for oral inhalation use
Initial U.S. Approval: 1981

---------- INDICATIONS AND USAGE ----------
PROAIR RESPICLICK inhalation powder is a beta$_2$-adrenergic agonist indicated for:
- Treatment or prevention of bronchospasm in patients 12 years of age and older with reversible obstructive airway disease. (1.1)
- Prevention of exercise-induced bronchospasm in patients 12 years of age and older. (1.2)

---------- DOSAGE AND ADMINISTRATION ----------
For oral inhalation only
- Treatment or prevention of bronchospasm in adults and adolescents age 12 and older: 2 inhalations every 4 to 6 hours. In some patients, 1 inhalation every 4 hours may be sufficient. (2.1)
- Prevention of exercise-induced bronchospasm in adults and adolescents age 12 and over: 2 inhalations 15 to 30 minutes before exercise. (2.2)
- PROAIR RESPICLICK does not require priming. (2.3)
- Do not use with a spacer or volume holding chamber. (2.3)
- Keep the inhaler clean and dry at all times. Routine maintenance is not required. If the mouthpiece needs cleaning, gently wipe the mouthpiece with a dry cloth or tissue as needed. Never wash or put any part of the inhaler in water. (2.3)
- Discard when the dose counter displays 0 or after the expiration date on the product, whichever comes first. (2.3)

---------- DOSAGE FORMS AND STRENGTHS ----------
Inhalation powder: PROAIR RESPICLICK is a dry powder inhaler that meters 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) from the device reservoir and delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) from the mouthpiece per actuation. The inhaler is supplied for 200 inhalation doses. (3)

---------- CONTRAINDICATIONS ----------
- Patients with hypersensitivity to albuterol. (4)
- Patients with severe hypersensitivity to milk proteins. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Life-threatening paradoxical bronchospasm may occur. Discontinue PROAIR RESPICLICK immediately and treat with alternative therapy. (5.1)
- Need for more doses of PROAIR RESPICLICK than usual may be a sign of deterioration of asthma and requires reevaluation of treatment. (5.2)
- PROAIR RESPICLICK is not a substitute for corticosteroids. (5.3)
- Cardiovascular effects may occur. Use with caution in patients sensitive to sympathomimetic drugs and patients with cardiovascular or convulsive disorders. (5.4, 5.7)
- Excessive use may be fatal. Do not exceed recommended dose. (5.5)
- Immediate hypersensitivity reactions may occur. Discontinue PROAIR RESPICLICK immediately. (5.6)
- Hypokalemia and changes in blood glucose may occur. (5.7, 5.8)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions (≥1% and >placebo) are back pain, pain, gastroenteritis viral, sinus headache, and urinary tract infection. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Teva Respiratory, LLC at 1-888-482-9522 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------
- Other short-acting sympathomimetic aerosol bronchodilators and adrenergic drugs: May potentiate effect. (7)
- Beta-blockers: May decrease effectiveness of PROAIR RESPICLICK and produce severe bronchospasm. Patients with asthma should not normally be treated with beta-blockers. (7.1)
- Diuretics, or non-potassium sparing diuretics: May potentiate hypokalemia or ECG changes. Consider monitoring potassium levels. (7.2)
- Digoxin: May decrease serum digoxin levels. Consider monitoring digoxin levels. (7.3)
- Monoamine oxidase (MAO) inhibitors and tricyclic antidepressants: May potentiate effect of albuterol on the cardiovascular system. Consider alternative therapy in patients taking MAOs or tricyclic antidepressants. (7.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 03/2015

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Bronchospasm

PROAIR RESPICLICK (albuterol sulfate) inhalation powder is indicated for the treatment or prevention of bronchospasm in patients 12 years of age and older with reversible obstructive airway disease.

1.2 Exercise-Induced Bronchospasm

PROAIR RESPICLICK is indicated for the prevention of exercise-induced bronchospasm in patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Bronchospasm

For treatment of acute episodes of bronchospasm or prevention of symptoms associated with bronchospasm, the recommended dosage for adults and adolescents 12 years and older is 2 inhalations repeated every 4 to 6 hours. More frequent administration or a larger number of inhalations is not recommended. In some patients, 1 inhalation every 4 hours may be sufficient.

2.2 Exercise-Induced Bronchospasm

For prevention of exercise-induced bronchospasm, the recommended dosage for adults and adolescents 12 years of age or older is 2 inhalations 15 to 30 minutes before exercise.

2.3 Administration Information

Administer PROAIR RESPICLICK by oral inhalation only.

Priming: PROAIR RESPICLICK inhaler does not require priming.

Do not use PROAIR RESPICLICK with a spacer or volume holding chamber.

Cleaning:

- Keep the inhaler clean and dry at all times. **Never wash or put any part of your inhaler in water.**
- Routine maintenance is not required. If the mouthpiece needs cleaning, gently wipe the mouthpiece with a dry cloth or tissue as needed.

Dose Counter: The PROAIR RESPICLICK inhaler has a dose counter attached to the actuator. When the patient receives the inhaler, the number 200 will be displayed. The dose counter will count down each time the inhaler is actuated. When the dose counter reaches 20, the color of the numbers will change to red to remind the patient to contact their pharmacist for a refill of medication or consult their physician for a prescription refill. When the dose counter reaches 0, the background will change to solid red. Discard PROAIR RESPICLICK 13 months after opening the foil pouch, when the dose counter displays 0 or after the expiration date on the product, whichever comes first *[see Patient Counseling Information (17.8)]*.

3 DOSAGE FORMS AND STRENGTHS

Inhalation powder: PROAIR RESPICLICK is a multi-dose breath-actuated dry powder inhaler that meters 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) from the device reservoir and delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) from the mouth piece per actuation. Each inhaler is supplied for

200 inhalation doses. PROAIR RESPICLICK inhalation powder is supplied as a white dry powder inhaler with a red cap in a sealed foil pouch.

4 CONTRAINDICATIONS

Use of PROAIR RESPICLICK is contraindicated in patients with a history of hypersensitivity to albuterol and/or severe hypersensitivity to milk proteins. Rare cases of hypersensitivity reactions, including urticaria, angioedema, and rash have been reported after the use of albuterol sulfate. There have been reports of anaphylactic reactions in patients using inhalation therapies containing lactose *[see Warnings and Precautions (5.6)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Paradoxical Bronchospasm

PROAIR RESPICLICK can produce paradoxical bronchospasm that may be life threatening. If paradoxical bronchospasm occurs, PROAIR RESPICLICK should be discontinued immediately and alternative therapy instituted.

5.2 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 PROAIR RESPICLICK, 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.

5.3 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, to the therapeutic regimen.

5.4 Cardiovascular Effects

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

5.5 Do Not Exceed Recommended Dose

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 an unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

5.6 Immediate Hypersensitivity Reactions

Immediate hypersensitivity reactions may occur after administration of albuterol sulfate, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema. PROAIR RESPICLICK contains small amounts of lactose, which may contain trace levels of milk proteins. Hypersensitivity reactions including anaphylaxis, angioedema, pruritus, and rash have been reported with the use of therapies containing lactose (lactose is an inactive ingredient in PROAIR RESPICLICK). The potential for hypersensitivity must be considered in the clinical evaluation of patients who experience immediate hypersensitivity reactions while receiving PROAIR RESPICLICK.

5.7 Coexisting Conditions

PROAIR RESPICLICK, like 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 in individual patients 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 preexisting diabetes mellitus and ketoacidosis.

5.8 Hypokalemia

As with other beta-agonists, PROAIR RESPICLICK 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.

6 ADVERSE REACTIONS

Use of PROAIR RESPICLICK may be associated with the following:

- Paradoxical bronchospasm *[see Warnings and Precautions (5.1)]*
- Cardiovascular Effects *[see Warnings and Precautions (5.4)]*
- Immediate hypersensitivity reactions *[see Warnings and Precautions (5.6)]*
- Hypokalemia *[see Warnings and Precautions (5.8)*

6.1 Clinical Trials Experience

A total of 1120 subjects were treated with PROAIR RESPICLICK during the clinical development program. The most common adverse reactions (≥1% and >placebo) were back pain, pain, gastroenteritis viral, sinus headache, and urinary tract infection. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults and Adolescents 12 years of Age and Older: The adverse reaction information presented in Table 1 below concerning PROAIR RESPICLICK is derived from the 12-week blinded treatment period of three studies which compared PROAIR RESPICLICK 180 mcg four times daily with a double-blinded matched placebo in 653 asthmatic patients 12 to 76 years of age.

Table 1: Adverse Reactions Experienced by Greater Than or Equal to 1.0% of Patients in the PROAIR RESPICLICK Group and Greater Than Placebo in three 12-Week Clinical Trials[1]

Preferred Term	Number (%) of patients	
	PROAIR RESPICLICK 180 mcg QID N=321	Placebo N=333
Back pain	6 (2%)	4 (1%)
Pain	5 (2%)	2 (<1%)
Gastroenteritis viral	4 (1%)	3 (<1%)
Sinus headache	4 (1%)	3 (<1%)
Urinary tract infection	4 (1%)	3 (<1%)

1. This table includes all adverse events (whether considered by the investigator drug related or unrelated to drug) which occurred at an incidence rate of greater than or equal to 1.0% in the PROAIR RESPICLICK group and greater than placebo.

In a long-term study of 168 patients treated with PROAIR RESPICLICK for up to 52 weeks (including a 12-week double-blind period), the most commonly reported adverse events greater than or equal to 5% were upper respiratory infection, nasopharyngitis, sinusitis, bronchitis, cough, oropharyngeal pain, headache, and pyrexia.

In a small cumulative dose study, tremor, palpitations, and headache were the most frequently occurring (≥5%) adverse events.

6.2 Postmarketing Experience

In addition to the adverse reactions reported from clinical trials with PROAIR RESPICLICK, the following adverse events have been reported during use of other inhaled albuterol sulfate products: Urticaria, angioedema, rash, bronchospasm, hoarseness, oropharyngeal edema, and arrhythmias (including atrial fibrillation, supraventricular tachycardia, extrasystoles), rare cases of aggravated bronchospasm, lack of efficacy, asthma exacerbation (potentially fatal), muscle cramps, and various oropharyngeal side-effects such as throat irritation, altered taste, glossitis, tongue ulceration, and gagging. 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.

In addition, albuterol, like other sympathomimetic agents, can cause adverse reactions such as: angina, hypertension or hypotension, palpitations, central nervous system stimulation, insomnia, headache, nervousness, tremor, muscle cramps, drying or irritation of the oropharynx, hypokalemia, hyperglycemia, and metabolic acidosis.

7 DRUG INTERACTIONS

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

7.1 Beta Blockers

Beta-adrenergic-receptor blocking agents not only block the pulmonary effect of beta-agonists, such as PROAIR RESPICLICK, 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, consider cardioselective beta-blockers, although they should be administered with caution.

7.2 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. Although the clinical significance of these effects is not known, caution is advised in the coadministration of beta-agonists with non-potassium sparing diuretics. Consider monitoring potassium levels.

7.3 Digoxin

Mean decreases of 16% and 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 these findings 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 PROAIR RESPICLICK.

7.4 Monoamine Oxidase Inhibitors or Tricyclic Antidepressants

PROAIR RESPICLICK 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 cardiovascular system may be potentiated. Consider alternative therapy in patients taking MAO inhibitors or tricyclic antidepressants.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C:

There are no adequate and well-controlled studies of PROAIR RESPICLICK or albuterol sulfate in pregnant women. During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients treated with albuterol. Some of the mothers were taking multiple medications during their pregnancies. No consistent pattern of defects can be discerned, and a relationship between albuterol use and congenital anomalies has not been established. Animal reproduction studies in mice and rabbits revealed evidence of teratogenicity. PROAIR RESPICLICK should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In a mouse reproduction study, subcutaneously administered albuterol sulfate produced cleft palate formation in 5 of 111 (4.5%) fetuses at an exposure approximately eight-tenths of the maximum recommended human dose (MRHD) for adults on a mg/m^2 basis and in 10 of 108 (9.3%) fetuses at approximately 8 times the MRHD. Similar effects were not observed at approximately one-thirteenth of the MRHD. Cleft palate also occurred in 22 of 72 (30.5%) fetuses from females treated subcutaneously with isoproterenol (positive control).

In a rabbit reproduction study, orally administered albuterol sulfate induced cranioschisis in 7 of 19 fetuses (37%) at approximately 630 times the MRHD.

In a rat reproduction study, an albuterol sulfate/HFA-134a formulation administered by inhalation did not produce any teratogenic effects at exposures approximately 65 times the MRHD.

Non-Teratogenic Effects: A study in which pregnant rats were dosed with radiolabeled albuterol sulfate demonstrated that drug-related material is transferred from the maternal circulation to the fetus.

8.2 Labor and Delivery

Because of the potential for beta-agonist interference with uterine contractility, use of PROAIR RESPICLICK for relief of bronchospasm during labor should be restricted to those patients in whom the benefits clearly outweigh the risk. PROAIR RESPICLICK has not been approved for the management of pre-term labor. The benefit:risk ratio when albuterol is administered for tocolysis has not been established. Serious adverse reactions, including pulmonary edema, have been reported during or following treatment of premature labor with $beta_2$-agonists, including albuterol.

8.3 Nursing Mothers

Plasma levels of albuterol after inhaled therapeutic doses are very low in humans, but it is not known whether the components of PROAIR RESPICLICK are excreted in human milk.

Caution should be exercised when PROAIR RESPICLICK is administered to a nursing woman. Because of the potential for tumorigenicity shown for albuterol in animal studies and lack of experience with the use of PROAIR RESPICLICK by nursing mothers, 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.

8.4 Pediatric Use

The safety and effectiveness of PROAIR RESPICLICK for the treatment or prevention of bronchospasm in children 12 to 17 years of age and older with reversible obstructive airway disease is based on two 12-week clinical trials in 318 patients 12 years of age and older with asthma comparing doses of 180 mcg four times daily with placebo, one long-term safety study in children 12 years of age and older, and one single-dose crossover study comparing doses of 90 and 180 mcg with albuterol sulfate inhalation aerosol (ProAir® HFA) in 71 patients [*see Clinical Studies (14.1)]*. The safety and effectiveness of PROAIR RESPICLICK for treatment of exercise-induced bronchospasm in children 12 years of age and older is based on one single-dose crossover study in 38 patients age 16 and older with exercise-induced bronchospasm comparing doses of 180 mcg with placebo *[see Clinical Studies (14.2)]*. The safety profile for patients ages 12 to 17 was consistent with the overall safety profile seen in these studies.

The safety and effectiveness of PROAIR RESPICLICK in pediatric patients below the age of 12 years have not been established. Overall, 120 children with asthma ages 4 to 11 years have participated in the PROAIR RESPICLICK clinical program, including 76 patients evaluated in 2 single-dose crossover clinical trials comparing PROAIR RESPICLICK to ProAir HFA at doses up to 180 mcg.

8.5 Geriatric Use

Clinical studies of PROAIR RESPICLICK did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy *[see Warnings and Precautions (5.4, 5.7)]*.

All $beta_2$-adrenergic agonists, including albuterol, are known to be substantially excreted by the kidney, and the risk of toxic reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

10 OVERDOSAGE

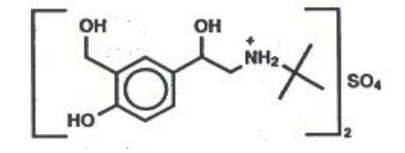
The expected symptoms with overdosage are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the symptoms listed under ADVERSE REACTIONS, eg, seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats per minute, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, and insomnia.

Hypokalemia may also occur. As with all sympathomimetic medications, cardiac arrest and even death may be associated with abuse of PROAIR RESPICLICK.

Treatment consists of discontinuation of PROAIR RESPICLICK 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 PROAIR RESPICLICK.

11 DESCRIPTION

The active ingredient of PROAIR RESPICLICK inhalation powder is albuterol sulfate, a racemic salt of albuterol. Albuterol sulfate is a beta2-adrenergic agonist. It has the chemical name α^1-[(*tert*-butylamino) methyl]-4-hydroxy-*m*-xylene-α,α'-diol sulfate (2:1) (salt), and the following chemical structure:



The molecular weight of albuterol sulfate is 576.7, and the empirical formula is $(C_{13}H_{21}NO_3)_2 \bullet H_2SO_4$. Albuterol sulfate is a white to off-white crystalline powder. It is soluble in water and slightly soluble in ethanol. Albuterol sulfate is the official U.S. Adopted Name in the United States, and salbutamol sulfate is the recommended World Health Organization international nonproprietary name.

PROAIR RESPICLICK is an inhalation-driven, multi-dose inhalation powder (dry powder inhaler) for oral inhalation only. It contains a formulation blend of albuterol sulfate with alpha-lactose monohydrate. Each actuation provides a metered dose of 2.6 mg of the formulation containing 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) and lactose from the device reservoir. Under standardized *in vitro* test conditions with fixed flow rates ranging from 58 to 71 L/min, and with a total air volume of 2 L, the PROAIR RESPICLICK inhaler delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) with lactose from the mouthpiece. The actual amount of drug delivered to the lung will depend on patient factors, such as inspiratory flow profile. In a study that investigated the peak inspiratory flow rate (PIFR) in asthma (n=27, ages 12 to 17 years old and n=50, ages 18 to 45 years old) and COPD (n=50, over 50 years old) patients, the mean PIFR achieved by subjects was >60 L/min (range = 31 to 110 L/min.), indicating that patients would be able to achieve the required inspiratory flow to operate the MDPI device correctly. The inhaler is provided for 200 actuations (inhalations).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Albuterol sulfate is a $beta_2$-adrenergic agonist. The pharmacologic effects of albuterol sulfate are attributable to activation of $beta_2$-adrenergic receptors on airway smooth muscle. Activation of $beta_2$-adrenergic receptors leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic-3',5'-adenosine monophosphate (cyclic AMP). This increase of cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Albuterol relaxes the smooth muscle of all airways, from the trachea to the terminal bronchioles. Albuterol acts as a functional antagonist to relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictor challenges. Increased cyclic AMP concentrations are also associated with the inhibition of release of mediators from mast cells in the airway. While it is recognized that $beta_2$-adrenergic receptors are the predominant receptors on bronchial smooth muscle, data indicate that there are beta-receptors in the human heart, 10% to 50% of which are cardiac $beta_2$-adrenergic receptors. The precise function of these receptors has not been established *[see Warnings and Precautions (5.4)]*.

Albuterol has been shown in most controlled clinical trials 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. However, 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 electrocardiographic changes [*see Warnings and Precautions (5.4)]*.

12.2 Pharmacodynamics

In a pharmacodynamic (PD) trial conducted in 47 patients, the PD and safety profiles were similar for PROAIR RESPICLICK and ProAir HFA. Comparable changes from baseline in the PD measures (serum glucose and potassium concentrations, QTcB, QTcF, heart rate, systolic blood pressure, and diastolic blood pressure) were observed following

cumulative dose administration up to 1440 mcg of both PROAIR RESPICLICK and ProAir HFA. The overall safety, efficacy and PD profile of PROAIR RESPICLICK and ProAir HFA were comparable.

In a single-dose Phase 2 study also assessing PD, 71 patients using PROAIR RESPICLICK had bronchodilator efficacy that was significantly greater than placebo and comparable to that of ProAir HFA at administered doses of 90 and 180 mcg in adolescent and adult subjects with persistent asthma.

Cardiac Electrophysiology
As with other $beta_2$-adrenergic agonists, PROAIR RESPICLICK prolonged QT intervals following a 1440 mcg cumulative dose. The prolongation was comparable to that of ProAir HFA.

12.3 Pharmacokinetics

Absorption
Albuterol was rapidly absorbed into the systemic circulation with peak plasma concentrations occurring at half an hour following single- or multiple-dose oral inhalation(s) of PROAIR RESPICLICK. In a cumulative dose study, the AUC_{0-t} was comparable between PROAIR RESPICLICK group and ProAir HFA group; C_{max} value was approximately one-third higher in PROAIR RESPICLICK group than ProAir HFA group.

Distribution
The volume of distribution has not been determined for PROAIR RESPICLICK. Published literature suggests that albuterol exhibits low *in vitro* plasma protein binding (10%).

Elimination
The accumulation ratio (~1.6 fold) was observed following one week QID dosing. The corresponding effective half-life was approximately 5 hours, which was consistent with the elimination half-life following both single- or multiple-dose administration.

Metabolism
Information available in the published literature suggests that the primary enzyme responsible for the metabolism of albuterol in humans is SULTIA3 (sulfotransferase). When racemic albuterol was administered either intravenously or via inhalation after oral charcoal administration, there was a 3- to 4-fold difference in the area under the concentration-time curves between the (R)- and (S)-albuterol enantiomers, with (S)-albuterol concentrations being consistently higher. However, without charcoal pretreatment, after either oral or inhalation administration the differences were 8- to 24-fold, suggesting that the (R)-albuterol is preferentially metabolized in the gastrointestinal tract, presumably by SULTIA3.

Excretion
The primary route of elimination of albuterol is through renal excretion (80% to 100%) of either the parent compound or the primary metabolite. Less than 20% of the drug is detected in the feces. Following intravenous administration of racemic albuterol, between 25% and 46% of the (R)-albuterol fraction of the dose was excreted as unchanged (R)-albuterol in the urine.

Specific Populations

Age: No pharmacokinetic studies for PROAIR RESPICLICK have been conducted in neonates or elderly subjects.

Sex: The influence of sex on the pharmacokinetics of PROAIR RESPICLICK has not been studied.

Race: The influence of race on the pharmacokinetics of PROAIR RESPICLICK has not been studied.

Renal Impairment: The effect of renal impairment on the pharmacokinetics of albuterol was evaluated in 5 subjects with creatinine clearance of 7 to 53 mL/min, and the results were compared with those from healthy volunteers. Renal disease

had no effect on the half-life, but there was a 67% decline in albuterol clearance. Caution should be used when administering high doses of PROAIR RESPICLICK to patients with renal impairment *[see Use in Specific Populations (8.5)]*.

Hepatic Impairment: The effect of hepatic impairment on the pharmacokinetics of PROAIR RESPICLICK has not been evaluated.

Drug Interaction Studies: In vitro and in vivo drug interaction studies have not been conducted with PROAIR RESPICLICK. Known clinically significant drug interactions are outlined in *Drug Interactions (7)*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year study in Sprague-Dawley rats, albuterol sulfate caused a dose-related increase in the incidence of benign leiomyomas of the mesovarium at and above dietary doses of 2 mg/kg (approximately 15 times the maximum recommended daily inhalation dose for adults on a mg/m^2 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 of up to 500 mg/kg (approximately 1,600 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). In a 22-month study in Golden Hamsters, albuterol sulfate showed no evidence of tumorigenicity at dietary doses of up to 50 mg/kg (approximately 210 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

Albuterol sulfate was not mutagenic in the Ames test or a mutation test in yeast. 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 up to 50 mg/kg (approximately 310 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

13.2 Animal Toxicology and/or Pharmacology

Preclinical: Intravenous studies in rats with albuterol sulfate have demonstrated that albuterol crosses the blood-brain barrier and reaches brain concentrations amounting to approximately 5% 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 β-agonists and methylxanthines were administered concurrently. The clinical significance of these findings is unknown.

14 CLINICAL STUDIES

14.1 Bronchospasm Associated with Asthma

Adult and Adolescent Patients 12 Years of Age and Older

In two 12-week, randomized, double-blind, placebo-controlled studies of identical design (Study 1 and Study 2), PROAIR RESPICLICK (153 patients) was compared to a matched placebo dry powder inhaler (163 patients) in asthmatic patients 12 to 76 years of age at a dose of 180 mcg albuterol four times daily. Patients were maintained on inhaled corticosteroid treatment. Serial FEV_1 measurements, shown below in Figure 1 as average of the mean changes from test-day baseline at Day 1 and Day 85, demonstrated that two inhalations of PROAIR RESPICLICK produced significantly greater improvement in FEV_1 $AUC_{0\text{-}6hr}$ over the pre-treatment value than placebo in Study 1. Consistent results were observed in Study 2.

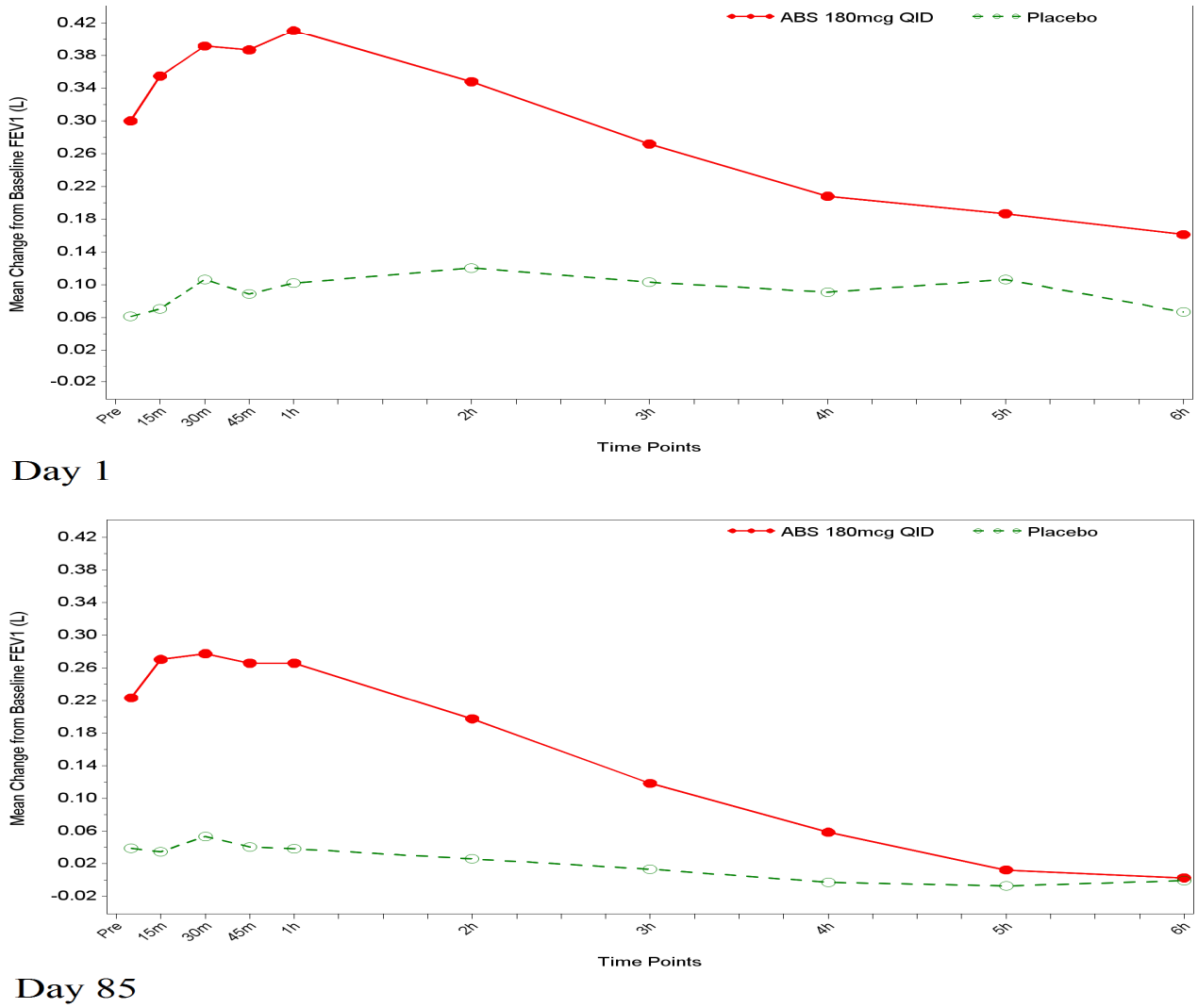


Figure 1: FEV_1 as Mean Change from Test-Day, Pre-Dose Baseline in a 12-Week Clinical Trial (Study 1)

In Study 1, 44 of 78 patients treated with PROAIR RESPICLICK achieved a 15% increase in FEV_1 within 30 minutes post-dose on Day 1. The median time to onset was 5.7 minutes, and median duration of effect as measured by a 15% increase was approximately 2 hours. Consistent results were observed in Study 2. In a double-blind, randomized, placebo–controlled, single-dose crossover study evaluating PROAIR RESPICLICK and ProAir HFA in 71 adult and adolescent subjects ages 12 and older with persistent asthma, PROAIR RESPICLICK had bronchodilator efficacy that was significantly greater than placebo at administered doses of 90 and 180 mcg.

14.2 Exercise-Induced Bronchospasm

In a randomized, single-dose, crossover study in 38 adult and adolescent patients with exercise-induced bronchospasm (EIB), two inhalations of PROAIR RESPICLICK taken 30 minutes before exercise prevented EIB for the hour following exercise (defined as the maintenance of FEV_1 within 80% of post-dose, pre-exercise baseline values) in 97% (37 of 38) of patients as compared to 42% (16 of 38) of patients when they received placebo.

Patients who participated in these clinical trials were allowed to use concomitant steroid therapy.

16 HOW SUPPLIED/STORAGE AND HANDLING

PROAIR RESPICLICK inhalation powder is supplied as a white dry powder inhaler with a red cap sealed in a foil pouch in boxes of one. Each inhaler contains 0.65g of the formulation and provides 200 actuations (NDC 59310-580-20).

Store at room temperature (between 15° and 25°C; 59° and 77°F). Avoid exposure to extreme heat, cold, or humidity.

Keep out of reach of children.

PROAIR RESPICLICK inhaler has a dose counter attached to the actuator. Patients should never try to alter the numbers for the dose counter. Discard the inhaler 13 months after opening the foil pouch, when the counter displays 0, or after the expiration date on the product, whichever comes first. The labeled amount of medication in each actuation cannot be assured after the counter displays 0, even though the inhaler is not completely empty and will continue to operate *[see Patient Counseling Information (17.8)]*.

17 PATIENT COUNSELING INFORMATION

See **FDA-Approved Patient Labeling** (Patient Information and Instructions for Using PROAIR RESPICLICK)

Patients should be given the following information:

Frequency of Use

The action of PROAIR RESPICLICK should last for 4 to 6 hours. Instruct patients to not use PROAIR RESPICLICK more frequently than recommended. Instruct patients to not increase the dose or frequency of doses of PROAIR RESPICLICK without consulting the physician. If patients find that treatment with PROAIR RESPICLICK becomes less effective for symptomatic relief, symptoms become worse, and/or they need to use the product more frequently than usual, they should seek medical attention immediately.

Caring for and Storing the Inhaler

Instruct patients to not open their inhaler unless they are taking a dose. Repeated opening and closing the cover without taking medication will waste medication and may damage the inhaler.

Advise patients to keep their inhaler dry and clean at all times. **Never wash or put any part of the inhaler in water**. Patient should replace inhaler if washed or placed in water.

Routine maintenance is not required. If the mouthpiece needs cleaning, instruct patients to gently wipe the mouthpiece with a dry cloth or tissue as needed.

Instruct patients to store the inhaler at room temperature and to avoid exposure to extreme heat, cold, or humidity.

Instruct patients to never take the inhaler apart.

Inform patients that PROAIR RESPICLICK has a dose counter attached to the actuator. When the patient receives the inhaler, the number 200 will be displayed. The dose counter will count down each time the mouthpiece cap is opened and closed. The dose counter window displays the number of actuations left in the inhaler in units of two (eg, 200, 198, 196, etc). When the counter displays 20, the color of the numbers will change to red to remind the patient to contact their pharmacist for a refill of medication or consult their physician for a prescription refill. When the dose counter reaches 0, the background will change to solid red. Inform patients to discard PROAIR RESPICLICK when the dose counter displays 0 or after the expiration date on the product, whichever comes first.

Paradoxical Bronchospasm

Inform patients that PROAIR RESPICLICK can produce paradoxical bronchospasm. Instruct patients to discontinue PROAIR RESPICLICK if paradoxical bronchospasm occurs.

Concomitant Drug Use

Inform patients that, while they are taking PROAIR RESPICLICK, they should take other inhaled drugs and asthma medications only as directed by a physician.

Common Adverse Events

Common adverse effects of treatment with inhaled albuterol include palpitations, chest pain, rapid heart rate, tremor, and nervousness.

Pregnancy

Inform patients who are pregnant or nursing that they should contact their physician about the use of PROAIR RESPICLICK.

General Information on Use

Effective and safe use of PROAIR RESPICLICK includes an understanding of the way that it should be administered. Do not use a spacer or volume holding chamber with PROAIR RESPICLICK. Patients should be instructed on the proper use of the inhaler. See the FDA-approved Patient Information and Patient Instructions for Use. Discard PROAIR RESPICLICK 13 months after opening the foil pouch, when the dose counter displays 0 or after the expiration date on the product, whichever comes first.

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Horsham, PA 19044

Manufactured by: Teva Pharmaceutical Industries Ltd.

Jerusalem, Israel
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United States Patent Nos. 6748947, 6871646, 6446627, 7540282, 8006690, 6701917, 6718972, 8651103

PROR-001

PATIENT INFORMATION
PROAIR RESPICLICK (prō´ār res-pē-klik)
(albuterol sulfate)
Inhalation Powder

What is PROAIR RESPICLICK?

PROAIR RESPICLICK is a prescription medicine used in people 12 years of age and older to:

- treat or prevent bronchospasm in people who have reversible obstructive airway disease
- prevent exercise-induced bronchospasm

It is not known if PROAIR RESPICLICK is safe and effective in children under 12 years of age.

Who should not use PROAIR RESPICLICK?

Do not use PROAIR RESPICLICK if you are allergic to albuterol sulfate, lactose, milk proteins, or any of the ingredients in PROAIR RESPICLICK. See the end of this leaflet for a complete list of ingredients in PROAIR RESPICLICK.

What should I tell my doctor before using PROAIR RESPICLICK?

Before you use PROAIR RESPICLICK, tell your doctor if you:

- have heart problems
- have high blood pressure (hypertension)
- have convulsions (seizures)
- have thyroid problems
- have diabetes
- have low potassium levels in your blood
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if PROAIR RESPICLICK will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if PROAIR RESPICLICK passes into your breast milk. Talk to your doctor about the best way to feed your baby if you are using PROAIR RESPICLICK.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

PROAIR RESPICLICK and other medicines may affect each other and cause side effects. PROAIR RESPICLICK may affect the way other medicines work, and other medicines may affect the way PROAIR RESPICLICK works.

Especially tell your doctor if you take:

- other inhaled medicines or asthma medicines
- beta blocker medicines
- diuretics
- digoxin
- monoamine oxidase inhibitors
- tricyclic antidepressants

Ask your doctor or pharmacist for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I use PROAIR RESPICLICK?

- For detailed instructions, see **"Instructions for Use"** at the end of this Patient Information.
- Use PROAIR RESPICLICK exactly as your doctor tells you to use it.
- Each dose of PROAIR RESPICLICK should last up to 4 hours to 6 hours.
- **Do not** increase your dose or take extra doses of PROAIR RESPICLICK without first talking to your doctor.
- Do not use a spacer or volume holding chamber with PROAIR RESPICLICK. PROAIR RESPICLICK does not need priming.
- Get medical help right away if PROAIR RESPICLICK no longer helps your symptoms.

- Get medical help right away if your symptoms get worse or if you need to use your inhaler more often.
- While you are using PROAIR RESPICLICK, **do not** use other inhaled rescue medicines and asthma medicines unless your doctor tells you to do so.
- Call your doctor if your asthma symptoms like wheezing and trouble breathing become worse over a few hours or days. Your doctor may need to give you another medicine (for example, corticosteroids) to treat your symptoms.

What are the possible side effects of PROAIR RESPICLICK?

PROAIR RESPICLICK may cause serious side effects, including:

- **worsening trouble breathing, coughing and wheezing (paradoxical bronchospasm).** If this happens stop using PROAIR RESPICLICK and call your doctor or get emergency help right away. Paradoxical bronchospasm is more likely to happen with your first use of a new asthma inhalation medicine.
- **heart problems, including faster heart rate and higher blood pressure**
- **possible death in people with asthma who use too much PROAIR RESPICLICK**
- **allergic reactions.** Call your doctor right away if you have the following symptoms of an allergic reaction:
  - itchy skin
  - swelling beneath your skin or in your throat
  - rash
  - worsening trouble breathing
- **low potassium levels in your blood**
- **worsening of other medical problems in people who also use PROAIR RESPICLICK including increases in blood sugar**

The most common side effects of PROAIR RESPICLICK include:

- back pain
- body aches and pain
- upset stomach
- sinus headache
- urinary tract infection
- your heart feels like it is pounding or racing (palpitations)
- chest pain
- fast heart rate
- shakiness
- nervousness
- headache
- dizziness
- sore throat
- runny nose

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of PROAIR RESPICLICK. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store PROAIR RESPICLICK?

- Store PROAIR RESPICLICK at room temperature between 59ºF and 77ºF (15ºC and 25ºC).
- Avoid exposure to extreme heat, cold, or humidity.
- Keep the cap on the inhaler closed during storage.
- Keep your PROAIR RESPICLICK inhaler dry and clean at all times.

Keep PROAIR RESPICLICK and all medicines out of the reach of children.

General Information about the safe and effective use of PROAIR RESPICLICK
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use PROAIR RESPICLICK for a condition for which it was not prescribed. Do not give PROAIR RESPICLICK to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information leaflet summarizes the most important information about PROAIR RESPICLICK. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about PROAIR RESPICLICK that is written for health professionals.

For more information, go to www.MyProAir.com or call 1-888-482-9522.

What are the ingredients in PROAIR RESPICLICK?

Active ingredient: albuterol sulfate
Inactive ingredients: lactose (may contain milk proteins)

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CODE# Rev. 03/15

Instructions for Use
PROAIR RESPICLICK (prō´ār res-pē-klik)
(albuterol sulfate)
Inhalation Powder

Your PROAIR RESPICLICK Inhaler

When you are ready to use PROAIR RESPICLICK for the first time, remove the PROAIR RESPICLICK inhaler from the foil pouch.

There are 2 main parts of your PROAIR RESPICLICK inhaler including:

- the white inhaler with the mouthpiece. See Figure A.
- red protective dust cap that covers the mouthpiece of the inhaler. See Figure A.

There is a dose counter in the back of the inhaler with a viewing window that shows you how many doses of medicine you have left. See Figure B.

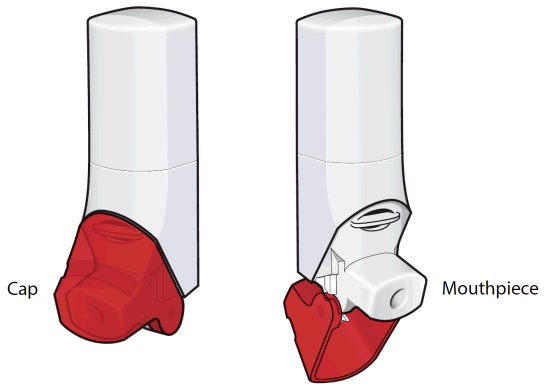

Figure A

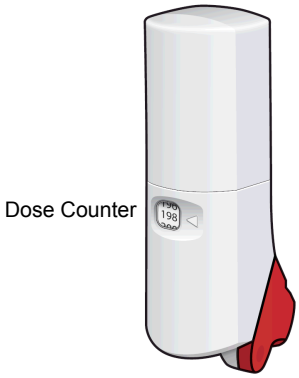

Figure B

- Your new PROAIR RESPICLICK inhaler contains ‘200’ doses (inhalations) of medication. See Figure C.
- When there are ‘20’ doses left, the dose counter will change to red and you should refill your prescription or ask your doctor for another prescription.

- When the dose counter displays ‘0’ your inhaler is empty and you should stop using the inhaler and throw it away. See Figure C.

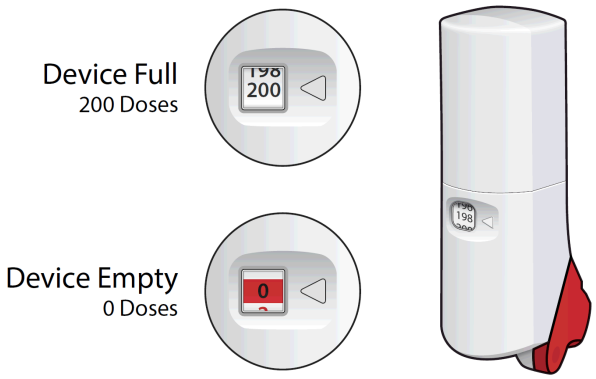

Figure C

IMPORTANT:

- Always close the cap after each inhalation so your inhaler will be ready for you to take your next dose. Do not open the cap unless you are ready for your next dose.
- You will hear a “click” sound when the cap is opened fully. If you do not hear the “click” sound the inhaler may not be activated to give you a dose of medicine.
- PROAIR RESPICLICK does not have an activation button or medicine canister. When you open the cap, a dose of PROAIR will be activated for delivery of the medicine.

Step-by-step instructions

Step 1. Make sure the cap is closed before each dose. See Figure D.

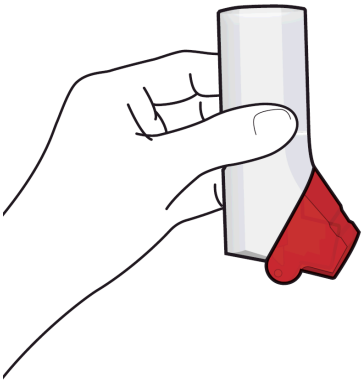

Figure D

- Before you use PROAIR RESPICLICK for the first time, look at the dose counter window to check that the inhaler is full and ‘200’ is in the window. The dose counter will count down by one number each time the mouthpiece cap is opened and closed. The dose counter only displays even numbers (example: 200, 198, 196, etc.) in the window.
- Throw away PROAIR RESPICLICK 13 months after removing it from the foil pouch for the first time, when the dose counter displays ‘0,’ or after the expiration date on the package, whichever comes first. See Figure E.

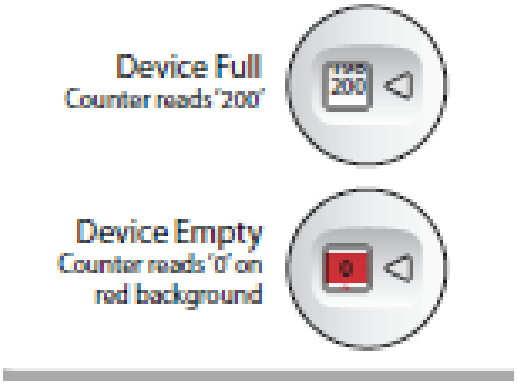

Figure E

Step 2. Hold the inhaler upright as you open the cap fully. See Figure F.

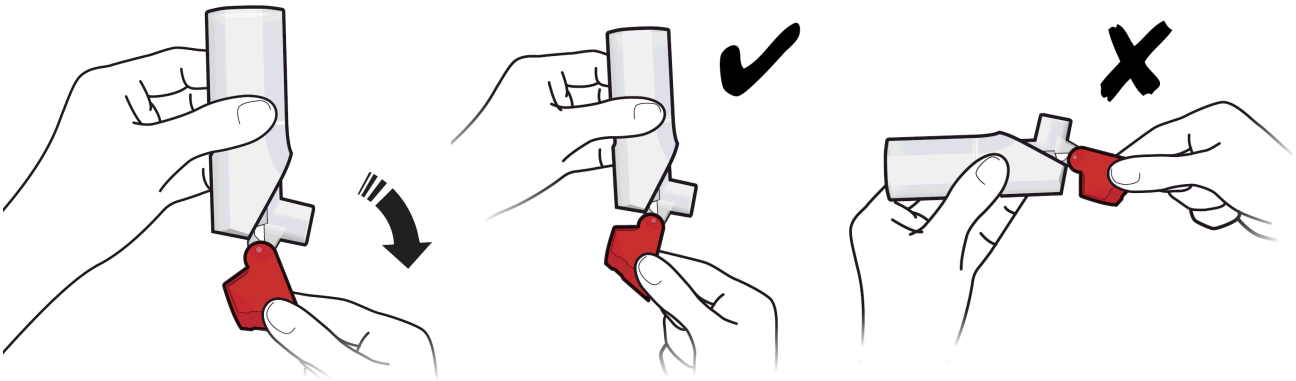

Figure F

- Open the cap all the way back until you hear a “click”.
- Your PROAIR RESPICLICK inhaler is now ready to use.
- Do not open the cap unless you are taking a dose.

Step 3. Breathe out through your mouth and push as much air from your lungs as you can. See Figure G.

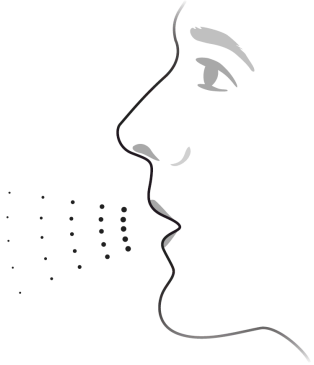

Figure G

- Be careful not to breathe out into the inhaler mouthpiece.

Step 4. Put the mouthpiece in your mouth and close your lips around it. Breathe in deeply through your mouth, until your lungs feel completely full of air

- Breathing in deeply through the mouthpiece will deliver the medication to your lungs.

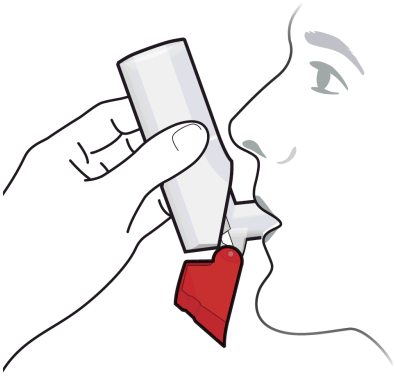

Figure H

- Do not let your lips or fingers block the vent above the mouthpiece. See Figure I.

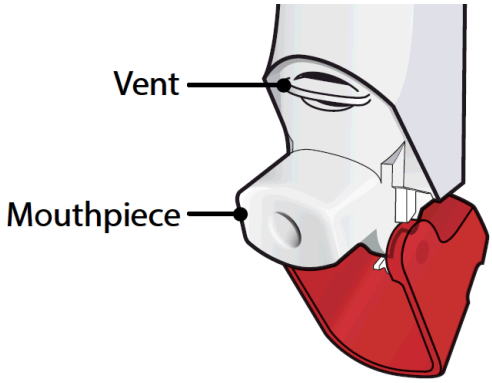

Figure I

Step 5. Hold your breath for about 10 seconds or as long as you comfortably can. See Figure J.

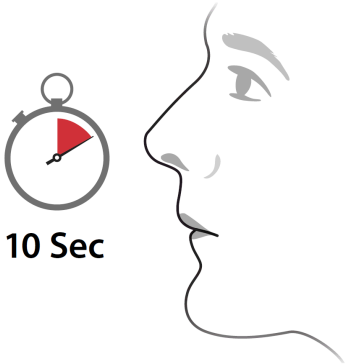

Figure J

- Remove the inhaler from your mouth.
- Check the dose counter on the back of the inhaler to make sure you received the dose.

Step 6. Close the cap over the mouthpiece after each use of the inhaler. Make sure the cap closes firmly into place. See Figure K.

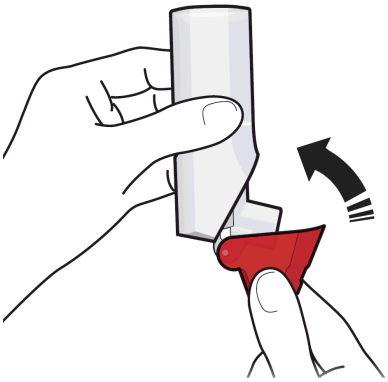

Figure K

- **Always close the cap after each inhalation so your inhaler will be ready for your next dose.**
- **If you need another dose close the cap and then repeat steps 1-6.**

How should I store PROAIR RESPICLICK?

- Store PROAIR RESPICLICK at room temperature between 59ºF and 77ºF (15ºC and 25ºC).
- Avoid exposure to extreme heat, cold, or humidity.
- Keep the cap on the inhaler closed during storage.
- Keep your PROAIR RESPICLICK inhaler dry and clean at all times.

Keep PROAIR RESPICLICK and all medicines out of the reach of children.

Cleaning your PROAIR RESPICLICK inhaler

- **Do not wash or put any part of your PROAIR RESPICLICK inhaler in water.**
- PROAIR RESPICLICK contains a powder and must be kept clean and dry at all times.
- If the mouthpiece needs cleaning, gently wipe it with a dry cloth or tissue.

Replacing your PROAIR RESPICLICK inhaler

- The counter on the back of your inhaler shows how many doses you have left.
- When there are '20' doses left, the dose counter will change to red and you should refill your prescription or ask your doctor for another prescription.

Important information

- Do not open the cap unless you are taking a dose. Opening and closing the cap without inhaling a dose will waste the medicine and may damage your inhaler.

Support

- If you have any questions about PROAIR RESPICLICK or how to use your inhaler, go to www.MyProAir.com or call 1-888-482-9522.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

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PRORIFU-001 Rev. 03/15

ProAir® RespiClick
SAMPLE 200 Inh. Carton
DRAFT

Side Opening

LOT NO./EXP. AREA

NDC 59310-580-21

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

NDC 59310-580-21

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

SAMPLE NOT FOR SALE

With Dose Counter

Refer to enclosed Patient Leaflet and Instructions for Use for detailed information on product use and handling.

For more information, visit www.MyProAir.com or call 1-888-482-9522.

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

CONTENTS: Each metered dose contains 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) from the device reservoir and delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) with lactose from the mouthpiece.

Usual Dosage: See package insert for full prescribing information.

IMPORTANT SAFETY INFORMATION

If recommended dosage does not provide relief of symptoms or symptoms become worse, seek medical attention immediately. While taking ProAir® RespiClick other inhaled medicines should be used only as prescribed by your physician.

NEVER WASH OR PUT ANY PART OF YOUR INHALER IN WATER.

Store inhaler at controlled room temperature between 15°C and 25°C (59°F and 77°F). Avoid exposure to extreme heat, cold, or humidity.

IMPORTANT

Discard inhaler when dose counter displays 0, or after the expiration date on the product, whichever comes first.

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Horsham, PA 19044

Mfd by: **Teva Pharmaceutical Industries, Ltd.**
Jerusalem, Israel

MANUFACTURED IN ISRAEL

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321K553070315 Rev. 03/15

NDC 59310-580-21
Rx Only

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

SAMPLE NOT FOR SALE

With Dose Counter

FOR ORAL INHALATION ONLY
200 METERED INHALATIONS
0.65 g NET CONTENTS

Refer to enclosed Patient Leaflet and Instructions for Use for detailed information on product use and handling.

EXP

OPEN HERE

NDC 59310-580-21

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

SAMPLE NOT FOR SALE

NDC 59310-580-21

1 2 3 4 5
6 7 8 9 0

ProAir® RespiClick Carton
200 inhalations SAMPLE

Size folding carton: 177x75x45 mm Die 230
Fonts: DIN OT Reg/Med/Bold/Cond, Helvetica Regular

Printed Colors

- PMS 186
- PMS 425
- PMS Green C
- Black
- Black 10%

ProAir® RespiClick
200 SAMPLE
Canister Label (Front)
DRAFT

For prominence comparison:

ProAir® RespiClick
200 SAMPLE Canister Label (Front)
200 inhalations

Size folding carton: 30.75–31.5 x 42 mm
Fonts: DIN OT Cond/Reg/Bold

Printed Colors

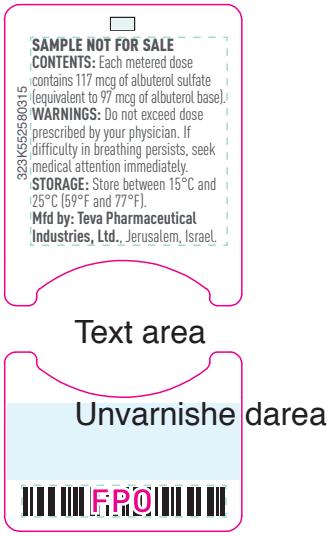
- PMS 186
- PMS 425
- Black

31.5x70 mm

ProAir® RespiClick 200 SAMPLE Canister Label (Back)

DRAFT

31.5 x 70 mm



safety

Lot No./Exp. Area (unvarnished)

ProAir® RespiClick
200 SAMPLE Canister Label (Back)
200 inhalations

Size folding carton: 31.5 x 70 mm
Fonts: DIN OT Cond Reg/Bold

Printed Colors

PMS 425

Black

ProAir® RespiClick Foil
200 SAMPLE

75 x 180 mm (folded panel)

DRAFT

P

(Half size of P above) P

albuteRol

NDC 59310-580-21 Rx Only

ProAir® RespiClick

(albuterol sulfate)

Inhalation Powder

SAMPLE NOT FOR SALE
For Oral Inhalation Only
200 Metered Inhalations
0.65 g Net Contents
Keep mouthpiece cover closed unless taking a dose.
CONTENTS: Each metered dose contains 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) from the device reservoir and delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) with lactose from the mouthpiece.
WARNINGS: Do not exceed dose prescribed by your physician. If difficulty in breathing persists, seek medical attention immediately.
STORAGE: Store between 15°C and 25°C (59°F and 77°F).
Mfd by: Teva Pharmaceutical Industries, Ltd., Jerusalem, Israel
328K999000215

FPO

N 3 59310-580-21 8

Lot No./Exp. Area (unvarnished)

ProAir® RespiClick Foil
200 SAMPLE
200 inhalations

Size foil: 75 x 180 mm
Fonts: DIN OT Cond/Reg/Bold

Printed Colors

Black

ProAir® RespiClick Carton
DRAFT

Side Opening

LOT NO./EXP. AREA

NDC 59310-580-20

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

NDC 59310-580-20

TEVA

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

With Dose Counter

Refer to enclosed Patient Leaflet and Instructions for Use for detailed information on product use and handling.

For more information, visit www.MyProAir.com or call 1-888-482-9522.

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

CONTENTS: Each metered dose contains 117 mcg of albuterol sulfate (equivalent to 97 mcg of albuterol base) from the device reservoir and delivers 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) with lactose from the mouthpiece.

Usual Dosage: See package insert for full prescribing information.

IMPORTANT SAFETY INFORMATION

If recommended dosage does not provide relief of symptoms or symptoms become worse, seek medical attention immediately. While taking ProAir® RespiClick other inhaled medicines should be used only as prescribed by your physician.

NEVER WASH OR PUT ANY PART OF YOUR INHALER IN WATER.

Store inhaler at controlled room temperature between 15°C and 25°C (59°F and 77°F). Avoid exposure to extreme heat, cold, or humidity.

IMPORTANT

Discard inhaler when dose counter displays 0, or after the expiration date on the product, whichever comes first.

Mktd by: **Teva Respiratory, LLC**
Horsham, PA 19044

Mfd by: **Teva Pharmaceutical Industries, Ltd.**
Jerusalem, Israel

MANUFACTURED IN ISRAEL

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321K553060315 Rev. 03/15

NDC 59310-580-20
Rx Only

TEVA

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

With Dose Counter

FOR ORAL INHALATION ONLY
200 METERED INHALATIONS
0.65 g NET CONTENTS

Refer to enclosed Patient Leaflet and Instructions for Use for detailed information on product use and handling.

N 3 59310-580-20 8

FPO

OPEN HERE

NDC 59310-580-20

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

117

ProAir® RespiClick
(albuterol sulfate)
Inhalation Powder

NDC 59310-580-20

1 2 3 4 5
6 7 8 9 0

ProAir® RespiClick Carton
200 inhalations

Size folding carton: 177x75x45 mm Die 230
Fonts: DIN OT Reg/Med/Bold/Cond, Helvetica Regular

Printed Colors

- PMS 186
- PMS 425
- PMS Green C
- Black
- Black 10%

ProAir® RespiClick
Canister Label (Front)
DRAFT

For prominence comparison:

ProAir® RespiClick
Canister Label (Front)
200 inhalations

Size folding carton: 30.75–31.5 x 42 mm
Fonts: DIN OT Cond/Reg/Bold

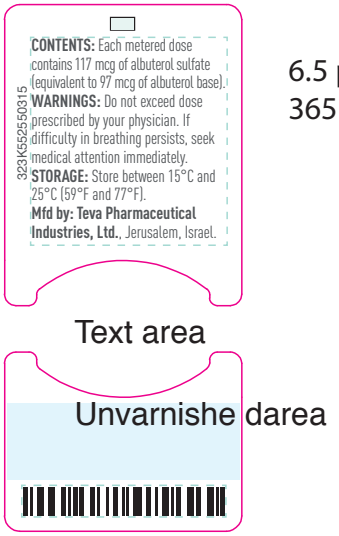
Printed Colors

- PMS 186
- PMS 425
- Black

31.5x70 mm

ProAir® RespiClick Canister Label (Back)
DRAFT

31.5 x 70 mm



6.5 pt type
365 characters

safety

Lot No./Exp. Area

ProAir® RespiClick Canister Label (Back) 200 inhalations

Size folding carton: 31.5 x 70 mm
Fonts: DIN OT Cond Reg/Bold

Printed Colors

PMS 425

Black

ProAir® RespiClick Foil

75 x 180 mm (folded panel)

DRAFT

P

(Half size of P above) P

albuteRol

NDC 59310-580-20 Rx Only

ProAir® RespiClick

(albuterol sulfate)

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328K998990315

N
3 59310-580-20 8

Lot No./Exp. Area

ProAir® RespiClick Foil
200 inhalations

Size foil: 75 x 180 mm
Fonts: DIN OT Cond/Reg/Bold

Printed Colors

Black