A 28-week, placebo-controlled US study comparing the safety of another LABA (salmeterol) with placebo, each added to usual asthma therapy, showed an increase in asthma-related deaths in patients receiving salmeterol (13/13,176 in patients treated with salmeterol vs. 3/13,179 in patients treated with placebo; RR 4.37, 95% CI 1.25, 15.34). The increased risk of asthma-related death is considered a class effect of LABAs, including ARCAPTA NEOHALER.

No study adequate to determine whether the rate of asthma-related death is increased in patients treated with ARCAPTA NEOHALER has been conducted. Serious asthma-related events, including death, were reported in clinical studies with ARCAPTA NEOHALER. The sizes of these studies were not adequate to precisely quantify the differences in serious asthma exacerbation rates between treatment groups *[see Adverse Reactions (6.2)]*.

Available data do not suggest an increased risk of death with use of LABA in patients with COPD.

5.2 Deterioration of Disease and Acute Episodes

ARCAPTA NEOHALER should not be initiated in patients with acutely deteriorating COPD, which may be a life-threatening condition. ARCAPTA NEOHALER has not been studied in patients with acutely deteriorating COPD. The use of ARCAPTA NEOHALER in this setting is inappropriate.

ARCAPTA NEOHALER should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. ARCAPTA NEOHALER has not been studied in the relief of acute symptoms and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled short-acting beta$_2$-agonist (SABA).

When beginning ARCAPTA NEOHALER, patients who have been taking inhaled, SABAs on a regular basis (e.g., four times a day) should be instructed to discontinue the regular use of these drugs and use them only for symptomatic relief of acute respiratory symptoms. When prescribing ARCAPTA NEOHALER, the healthcare provider should also prescribe an inhaled, SABA and instruct the patient on how it should be used. Increasing inhaled beta$_2$-agonist use is a signal of deteriorating disease for which prompt medical attention is indicated.

COPD may deteriorate acutely over a period of hours or chronically over several days or longer. If ARCAPTA NEOHALER no longer controls the symptoms of bronchoconstriction, or the patient's inhaled, SABA becomes less effective or the patient needs more inhalation of SABA than usual, these may be markers of deterioration of disease. In this setting, a reevaluation of the patient and the COPD-treatment regimen should be undertaken at once. Increasing the daily dosage of ARCAPTA NEOHALER beyond the recommended dose is not appropriate in this situation.

5.3 Avoid Excessive Use of ARCAPTA NEOHALER and Avoid Use with Other Long-Acting Beta$_2$-Adrenergic Agonists

As with other inhaled beta$_2$-adrenergic drugs, ARCAPTA NEOHALER should not be used more often, at higher doses than recommended, or in conjunction with other medications containing LABAs, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

5.4 Hypersensitivity Reactions, including Anaphylaxis

Immediate hypersensitivity reactions may occur after administration of ARCAPTA NEOHALER. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash, anaphylaxis) occur, ARCAPTA NEOHALER should be discontinued immediately and alternative therapy instituted.

5.5 Paradoxical Bronchospasm

As with other inhaled beta$_2$-agonists, ARCAPTA NEOHALER may produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, ARCAPTA NEOHALER should be discontinued immediately and alternative therapy instituted.

5.6 Cardiovascular Effects

ARCAPTA NEOHALER, like other beta$_2$-agonists, can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, or symptoms. If such effects occur,

ARCAPTA NEOHALER 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 QTc interval, and ST segment depression, although the clinical significance of these findings is unknown. Therefore, ARCAPTA NEOHALER, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

5.7 Coexisting Conditions

ARCAPTA NEOHALER, like other sympathomimetic amines, should be used with caution in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to sympathomimetic amines. Doses of the related beta$_2$-agonist albuterol, when administered intravenously, have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis.

5.8 Hypokalemia and Hyperglycemia

Beta$_2$-agonist medications may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects *[see Clinical Pharmacology (12.2)]*. The decrease in serum potassium is usually transient, not requiring supplementation. Inhalation of high doses of beta$_2$-adrenergic agonists may produce increases in plasma glucose.

Clinically notable decreases in serum potassium or changes in blood glucose were infrequent during clinical studies with long-term administration of ARCAPTA NEOHALER with the rates similar to those for placebo controls. ARCAPTA NEOHALER has not been investigated in patients whose diabetes mellitus is not well-controlled.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described in greater detail elsewhere in the labeling:

- Serious Asthma-Related Events – Hospitalizations, Intubations, Death *[see Warnings and Precautions (5.1)]*
- Paradoxical Bronchospasm *[see Warnings and Precautions (5.5)]*
- Hypersensitivity Reactions, including Anaphylaxis *[see Contraindications (4), Warnings and Precautions (5.4)]*
- Cardiovascular Effects *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience in Chronic Obstructive Pulmonary Disease

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.

The ARCAPTA NEOHALER safety database reflects exposure of 2516 patients to ARCAPTA NEOHALER at doses of 75 mcg or greater for at least 12 weeks in six confirmatory randomized, double-blind, placebo and active-controlled clinical trials *[see Clinical Studies (14)]*. In these trials, 449 patients were exposed to the recommended dose of 75 mcg for up to 3 months, and 144, 583, and 425 COPD patients were exposed to a dose of 150, 300, or 600 mcg for one year, respectively. Overall, patients had a mean pre-bronchodilator forced expiratory volume in one second (FEV_1) percent predicted of 54%. The mean age of patients was 64 years, with 47% of patients aged 65 years or older, and the majority (88%) was Caucasian.

In these six clinical trials, 48% of patients treated with any dose of ARCAPTA NEOHALER reported an adverse reaction compared with 43% of patients treated with placebo. The proportion of patients who discontinued treatment due to adverse reaction was 5% for ARCAPTA NEOHALER-treated patients and 5% for placebo-treated patients. The most common adverse reactions that lead to discontinuation of ARCAPTA NEOHALER were COPD and dyspnea.

The most common serious adverse reactions were COPD exacerbation, pneumonia, angina pectoris, and atrial fibrillation, which occurred at similar rates across treatment groups.

Table 1 displays adverse drug reactions reported by at least 2% of patients (and higher than placebo) during a 3-month exposure at the recommended 75 mcg once-daily dose. Adverse drug reactions are listed according to the Medical

Dictionary for Regulatory Activities [(MedDRA), version 13.0] system organ class and sorted in descending order of frequency.

Table 1: Number and Frequency of Adverse Drug Reactions Greater Than 2% (and higher than placebo) in COPD Patients Exposed to ARCAPTA NEOHALER 75 mcg for Up to 3 Months in Multiple Dose, Controlled Trials

	Indacaterol 75 mcg once daily	**Placebo**
	n = 449	**n = 445**
Adverse reaction	**n (%)**	**n (%)**
Respiratory, thoracic and mediastinal disorders		
- Cough	29 (6.5)	20 (4.5)
- Oropharyngeal pain	10 (2.2)	3 (0.7)
Infections and infestations		
- Nasopharyngitis	24 (5.3)	12 (2.7)
Nervous system disorders		
- Headache	23 (5.1)	11 (2.5)
Gastrointestinal disorders		
- Nausea	11 (2.4)	4 (0.9)

In these trials, the overall frequency of all cardiovascular adverse reactions was 2.5% for ARCAPTA NEOHALER, 75 mcg and 1.6% for placebo during a 3-month exposure. There were no frequently occurring specific cardiovascular adverse reactions for ARCAPTA NEOHALER 75 mcg (frequency at least 1% and greater than placebo).

Additional adverse drug reactions reported in greater than 2% (and higher than on placebo) in patients dosed with 150 mcg, 300 mcg, or 600 mcg for up to 12 months were as follows:

- Musculoskeletal and Connective Tissue Disorders: muscle spasm, musculoskeletal pain
- General Disorders and Administration-site Conditions: edema peripheral
- Metabolism and Nutrition Disorder: diabetes mellitus, hyperglycemia
- Infections and Infestations: sinusitis, upper respiratory tract infection

Cough Experienced Post-Inhalation

In the clinical trials, health care providers observed during clinic visits that an average of 24% of patients experienced a cough on at least 20% of visits following inhalation of the recommended 75 mcg dose of ARCAPTA NEOHALER compared to 7% of patients receiving placebo. The cough usually occurred within 15 seconds following inhalation and lasted for no more than 15 seconds. Cough following inhalation in clinical trials was not associated with bronchospasm, exacerbations, deteriorations of disease, or loss of efficacy.

6.2 Clinical Trials Experience in Asthma

In a 6-month randomized, active controlled asthma safety trial, 805 adult patients with moderate to severe persistent asthma were treated with ARCAPTA NEOHALER 300 mcg (n = 268), ARCAPTA NEOHALER 600 mcg (n = 268), and salmeterol (n = 269), all concomitant with inhaled corticosteroids, which were not co-randomized. Of these patients, there were 2 respiratory-related deaths in the ARCAPTA NEOHALER 300-mcg dose group. There were no deaths in the ARCAPTA NEOHALER 600-mcg dose group or in the salmeterol active control group. Serious adverse reactions related

to asthma exacerbation were reported for 2 patients in the indacaterol 300-mcg group, 3 patients in the indacaterol 600-mcg group, and no patients in the salmeterol active control group.

In addition, a two-week dose-ranging trial was conducted in 511 adult patients with mild persistent asthma taking inhaled corticosteroids. No deaths, intubations, or serious adverse reactions related to asthma exacerbation were reported in this trial.

6.3 Postmarketing Experience

The following adverse reactions have been identified during worldwide post-approval use of indacaterol, the active ingredient in ARCAPTA NEOHALER. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions are: hypersensitivity reactions, paradoxical bronchospasm, tachycardia/heart rate increase/palpitations, pruritus/rash, and dizziness.

7 DRUG INTERACTIONS

7.1 Adrenergic Drugs

If additional adrenergic drugs are to be administered by any route, they should be used with caution because the sympathetic effects of ARCAPTA NEOHALER may be potentiated *[see Warnings and Precautions (5.3, 5.6, 5.7, 5.8)]*.

7.2 Xanthine Derivatives, Steroids, or Diuretics

Concomitant treatment with xanthine derivatives, steroids, or diuretics may potentiate any hypokalemic effect of ARCAPTA NEOHALER *[see Warnings and Precautions (5.8)]*.

7.3 Non-Potassium Sparing Diuretics

The ECG changes or hypokalemia that 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 relevance of these effects is not known, caution is advised in the co-administration of ARCAPTA NEOHALER with non-potassium-sparing diuretics.

7.4 Monoamine Oxidase Inhibitors, Tricyclic Antidepressants, QTc Prolonging Drugs

Indacaterol, as with other beta$_2$-agonists, should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or other drugs known to prolong the QTc interval because the action of adrenergic agonists on the cardiovascular system may be potentiated by these agents. Drugs that are known to prolong the QTc interval may have an increased risk of ventricular arrhythmias.

7.5 Beta-Blockers

Beta-adrenergic receptor antagonists (beta-blockers) and ARCAPTA NEOHALER may interfere with the effect of each other when administered concurrently. Beta-blockers not only block the therapeutic effects of beta-agonists, but may produce severe bronchospasm in COPD patients. Therefore, patients with COPD should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-blockers in patients with COPD. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

7.6 Inhibitors of Cytochrome P450 3A4 and P-gp Efflux Transporter

Drug interaction studies were carried out using potent and specific inhibitors of CYP3A4 and P-gp (i.e., ketoconazole, erythromycin, verapamil, and ritonavir). The data suggest that systemic clearance is influenced by modulation of both P-gp and CYP3A4 activities and that the 1.9-fold AUC_{0-24} increase caused by the strong dual inhibitor ketoconazole reflects the impact of maximal combined inhibition. ARCAPTA NEOHALER was evaluated in clinical trials for up to one year at doses up to 600 mcg. No dose adjustment is warranted at the 75 mcg dose *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with ARCAPTA NEOHALER in pregnant women. Women should be advised to contact their physician if they become pregnant while taking ARCAPTA NEOHALER.

In animal reproduction studies, there was no evidence of fetal harm or structural abnormalities following subcutaneous administration of indacaterol maleate to pregnant Wistar rats and New Zealand White rabbits during the period of organogenesis at exposures approximately 180 and 410 times the maximum recommended human dose (MRHD of 75 mcg), respectively, on an exposure area under the curve (AUC) basis (*see Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Labor or Delivery

There are no adequate and well-controlled human studies that have investigated effects of ARCAPTA NEOHALER during labor and delivery. Because beta-agonist may potentially interfere with uterine contractility, ARCAPTA NEOHALER should be used during labor only if the potential benefit justifies the potential risk.

Data

Animal Data

In embryo-fetal development studies, pregnant Wistar rats received indacaterol maleate, during the period of organogenesis from Gestation Days 6 to 17, at exposures up to 180 times the MRHD (on an AUC basis with maternal subcutaneous doses up to 1 mg/kg/day) and pregnant New Zealand White rabbits received indacaterol maleate, during the period of organogenesis from Gestation Days 7 to 20, at exposures up to 1000 times the MRHD (on an AUC basis with maternal subcutaneous doses up to 3 mg/kg/day). Indacaterol maleate produced no evidence of fetal harm or structural abnormalities in rats and rabbits at exposures up to 180 and 410 times, respectively, the MRHD. Rabbit fetuses were observed with increased incidences of full supernumerary rib, a structural variation at an exposure approximately 1000 times the MRHD.

In a pre- and postnatal development study, pregnant Wistar rats received indacaterol maleate, throughout the period of organogenesis and lactation from Gestation Day 6 through Lactation Day 20, at doses up to 130 times the MRHD (on a mg/m^2 basis with maternal subcutaneous doses up to 1 mg/kg/day). F1 pups received subcutaneous doses of indacaterol maleate up to 1 mg/kg/day from postpartum Days 4 through 20. There was no evidence of maternal toxicity with doses up to 130 times the MRHD. There were no effects on the physical or behavioral development of F1 pups with doses up to 40 times the MRHD (on a mg/m^2 basis with maternal and F1 pup subcutaneous doses up to 0.3 mg/kg/day). There was a decrease in the number of F1 pregnant animals at a dose approximately 130 times the MRHD (on a mg/m^2 basis with maternal and F1 pup subcutaneous doses of 1 mg/kg/day); however, there were no effects on mating or other parameters of reproductive performance.

8.2 Lactation

Risk Summary

There is no data on the presence of indacaterol in human milk, effect on the breastfed infant, or the effects on milk production. Indacaterol is present in the milk of lactating rats (*see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ARCAPTA NEOHALER and any potential adverse effects on the breastfed child from ARCAPTA NEOHALER or from the underlying maternal condition.

Data

Animal Data

Indacaterol and its metabolites were detected in the milk within 1 hour following a single subcutaneous dose of 650 mcg radiolabeled indacaterol maleate administered to lactating rats postpartum days 8 and 9.

8.4 Pediatric Use

The safety and effectiveness of ARCAPTA NEOHALER in pediatric patients have not been established. ARCAPTA NEOHALER is not indicated for use in pediatric patients.

8.5 Geriatric Use

Based on available data, no adjustment of ARCAPTA NEOHALER dosage in geriatric patients is warranted. Of the total number of patients who received ARCAPTA NEOHALER at the recommended dosage of 75 mcg once daily in the clinical studies from the pooled 3-month database, 153 were 65 to 74 years, and 57 were ≥ 75 years of age.

No overall differences in effectiveness were observed, and in the 3-month pooled data, the adverse drug reaction profile was similar in the older population compared to the patient population overall.

8.6 Hepatic Impairment

Patients with mild and moderate hepatic impairment showed no relevant changes in C_{max} or AUC, nor did protein binding differ between mild and moderate hepatically impaired subjects and their healthy controls. Studies in subjects with severe hepatic impairment were not performed.

8.7 Renal Impairment

Due to the very low contribution of the urinary pathway to total body elimination, a study in renally impaired subjects was not performed.

10 OVERDOSAGE

In COPD patients, single doses of 40 times the 75 mcg dose were associated with moderate increases in pulse rate, systolic blood pressure and QTc interval.

The expected signs and symptoms associated with overdosage of ARCAPTA NEOHALER are those of excessive beta-adrenergic stimulation and occurrence or exaggeration of any of the signs and symptoms, e.g., angina, hypertension or hypotension, tachycardia, with rates up to 200 beats per minute, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, metabolic acidosis, and insomnia. As with all inhaled sympathomimetic medications, cardiac arrest and even death may be associated with an overdose of ARCAPTA NEOHALER.

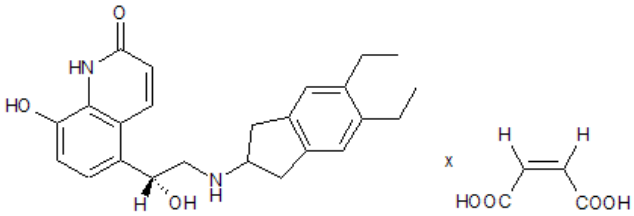
Treatment of overdosage consists of discontinuation of ARCAPTA NEOHALER together with institution of appropriate symptomatic and supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of ARCAPTA NEOHALER. Cardiac monitoring is recommended in cases of overdosage.

11 DESCRIPTION

ARCAPTA NEOHALER consists of a dry powder formulation of indacaterol maleate for oral inhalation only with the NEOHALER inhaler. The inhalation powder is packaged in clear gelatin capsules.

Each clear, hard gelatin capsule contains a dry powder blend of 75 mcg of indacaterol (equivalent to 97 mcg of indacaterol maleate) with approximately 25 mg of lactose monohydrate (which contains trace levels of milk protein) as the carrier.

The active component of ARCAPTA NEOHALER is indacaterol maleate, a (R) enantiomer. Indacaterol maleate is a selective $beta_2$-adrenergic agonist. Its chemical name is (R)-5-[2-(5,6-Diethylindan-2-ylamino)-1-hydroxyethyl]-8-hydroxy-1H-quinolin-2-one maleate; its structural formula is



Indacaterol maleate has a molecular weight of 508.56 g/mol, and its empirical formula is $C_{24}H_{28}N_2O_3 \bullet C_4H_4O_4$. Indacaterol maleate is a white to very slightly grayish or very slightly yellowish powder. Indacaterol maleate is freely soluble in N-methylpyrrolidone and dimethylformamide, slightly soluble in methanol, ethanol, propylene glycol and polyethylene glycol 400, very slightly soluble in water, isopropyl alcohol and practically insoluble in 0.9% sodium chloride in water, ethyl acetate and n-octanol.

The NEOHALER inhaler is a plastic device used for inhaling ARCAPTA. The amount of drug delivered to the lung will depend on patient factors, such as inspiratory flow rate and inspiratory time. Under standardized *in vitro* testing at a fixed flow rate of 60 L/min for 2 seconds, the NEOHALER inhaler delivered 57 mcg for the 75 mcg dose strength (equivalent to 73.9 mcg of indacaterol maleate) from the mouthpiece. Peak inspiratory flow rates (PIFR) achievable through the NEOHALER inhaler were evaluated in 26 adult patients with COPD of varying severity. Mean PIFR was 95 L/min (range 52-133 L/min) for adult patients. Approximately ninety-five percent of the population studied generated a PIFR through the device exceeding 60 L/min.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Indacaterol is a (LABA).

When inhaled, indacaterol acts locally in the lung as a bronchodilator. *In vitro* studies have shown that indacaterol has more than 24-fold greater agonist activity at $beta_2$-receptors compared to $beta_1$-receptors and 20-fold greater agonist activity compared to $beta_3$-receptors. This selectivity profile is similar to formoterol. The clinical significance of these findings is unknown. Although $beta_2$-receptors are the predominant adrenergic receptors in bronchial smooth muscle and $beta_1$-receptors are the predominant receptors in the heart, there are also $beta_2$-adrenergic receptors in the human heart comprising 10% to 50% of the total adrenergic receptors. The precise function of these receptors is not known, but their presence raises the possibility that even highly selective $beta_2$-adrenergic agonists may have cardiac effects.

The pharmacological effects of $beta_2$-adrenoceptor agonist drugs, including indacaterol, are at least in part attributable to stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate to cyclic-3', 5'-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels cause relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially mast cells.

12.2 Pharmacodynamics

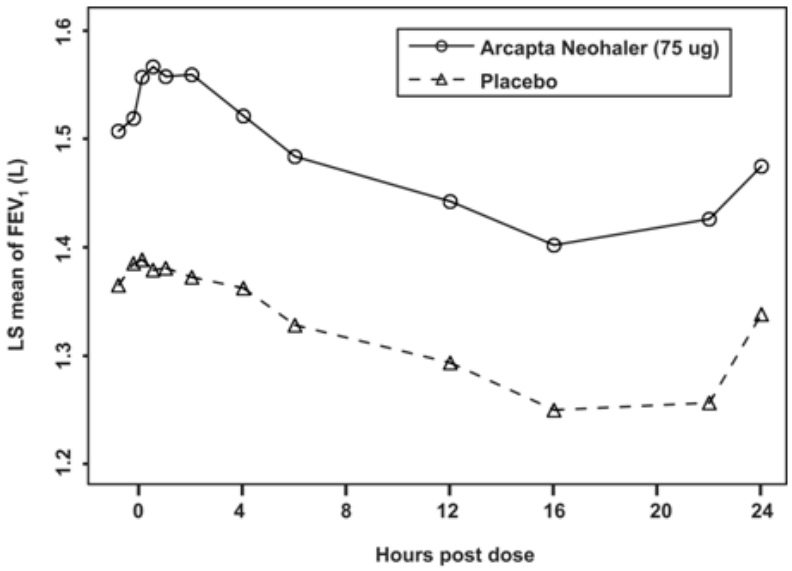
Systemic Safety

The major adverse effects of inhaled $beta_2$-adrenergic agonists occur as a result of excessive activation of systemic beta-adrenergic receptors. The most common adverse effects in adults include skeletal muscle tremor and cramps, insomnia, tachycardia, decreases in serum potassium and increases in plasma glucose.

Changes in serum potassium and plasma glucose were evaluated in COPD patients in double-blind studies. In pooled data, at the recommended 75 mcg dose, at 1 hour post-dose at Week 12, there was no change compared to placebo in serum potassium, and change in mean plasma glucose was 0.07 mmol/L.

Cardiac Electrophysiology

The effect of ARCAPTA NEOHALER on the QT interval was evaluated in a double-blind, placebo- and active (moxifloxacin)-controlled study following multiple doses of indacaterol 150 mcg, 300 mcg, or 600 mcg once-daily for 2 weeks in 404 healthy volunteers. Fridericia's method for heart rate correction was employed to derive the corrected QT interval (QTcF). Maximum mean prolongation of QTcF intervals were < 5 ms, and the upper limit of the 90% CI was



In both COPD clinical trials, including the 75 mcg dose (Trials 4 and 5), patients treated with ARCAPTA NEOHALER used less daily rescue albuterol during the trial compared to patients treated with placebo.

Health-related quality of life was measured using the SGRQ in all six confirmatory COPD clinical trials. SGRQ is a disease-specific patient reported instrument which measures symptoms, activities, and its impact on daily life. At Week 12, pooled data from these trials demonstrated an improvement over placebo in SGRQ total score of -3.8 with a 95% CI of (-5.3, -2.3) for the ARCAPTA NEOHALER 75 mcg dose, -4.6 with a 95% CI of (-5.5, -3.6) for 150 mcg, and -3.8 with a 95% CI of (-4.9, -2.8) for 300 mcg. The CI for this change are widely overlapping with no dose ordering. Results from individual studies were variable, but are generally consistent with the pooled data results.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

ARCAPTA NEOHALER (indacaterol) inhalation powder:

- contains 75 mcg indacaterol inhalation powder per capsule
- packaged in aluminum blister cards
- unit Dose (blister pack), Box of 30 (5 blister cards with 6 capsules each) NDC 63402-675-30
- NEOHALER inhaler consists of a white protective cap and a base with mouthpiece, capsule chamber and two translucent red push buttons

Storage and Handling

- Store in a dry place at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].
- Protect capsule from light and moisture.
- ARCAPTA capsules should be used with the NEOHALER inhaler only. The NEOHALER inhaler should not be used with any other capsules.
- Capsules should always be stored in the blister and only removed from the blister immediately before use.
- Always use the new NEOHALER inhaler provided with each new prescription.
- Keep out of the reach of children.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use)

Serious Asthma-Related Events

Patients should be informed that LABA, such as ARCAPTA NEOHALER, when used as monotherapy [without an inhaled corticosteroid], increase the risk of serious asthma-related events, including asthma-related death. ARCAPTA NEOHALER is not indicated for the treatment of asthma *[see Warnings and Precautions (5.1)]*.

Instructions for Administering ARCAPTA NEOHALER

It is important for patients to understand how to correctly administer ARCAPTA capsules using the NEOHALER device *[see Instructions for Use]*. Patients should be instructed that ARCAPTA capsules should only be administered via the NEOHALER device and the NEOHALER device should not be used for administering other medications. The contents of ARCAPTA capsules are for oral inhalation only and must not be swallowed.

ARCAPTA capsules should always be stored in sealed blisters. Only one ARCAPTA capsule should be removed immediately before use, or its effectiveness may be reduced. Additional ARCAPTA capsules that are exposed to air (i.e., not intended for immediate use) should be discarded.

Not for Acute Symptoms

ARCAPTA NEOHALER is not meant to relieve acute symptoms or exacerbations of COPD and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled, SABA, such as albuterol. The healthcare provider should provide the patient with such medication and instruct the patient in how it should be used.

Patients should be instructed to notify their healthcare provider immediately if they experience any of the following:

- worsening of symptoms
- decreasing effectiveness of inhaled, SABAs
- need for more inhalations than usual of inhaled, SABAs
- significant decrease in lung function as outlined by their healthcare provider.

Patients should not stop therapy with ARCAPTA NEOHALER without physician/healthcare provider guidance since symptoms may recur after discontinuation.

Do Not Use Additional Long-Acting $Beta_2$-Agonists

Patients who have been taking inhaled, SABAs on a regular basis should be instructed to discontinue the regular use of these products and use them only for the symptomatic relief of acute symptoms *[see Warnings and Precautions (5.2)]*.

When patients are prescribed ARCAPTA NEOHALER, other inhaled medications containing LABAs should not be used. Patients should not use more than the recommended once daily dose of ARCAPTA NEOHALER. Excessive use of sympathomimetics may cause significant cardiovascular effects, and may be fatal *[see Warnings and Precautions (5.3)]*.

Risks Associated with Beta-Agonist Therapy

Patients should be informed of adverse effects associated with $beta_2$-agonists, such as palpitations, chest pain, rapid heart rate, tremor, or nervousness.

Manufactured by:

Novartis Pharmaceuticals Corporation

East Hanover, New Jersey 07936

PATIENT INFORMATION

ARCAPTA® (ar-CAP-ta) NEOHALER®

(indacaterol inhalation powder)

Important: Do not swallow ARCAPTA capsules. ARCAPTA capsules are used only with the NEOHALER inhaler that comes with ARCAPTA NEOHALER. Do not place a capsule in the mouthpiece of the NEOHALER inhaler.

What is ARCAPTA NEOHALER?

- ARCAPTA NEOHALER is a long-acting $beta_2$-adrenergic agonist (LABA) used to control the symptoms of chronic obstructive pulmonary disease (COPD) in adults with COPD. COPD is a chronic lung disease that includes chronic bronchitis, emphysema, or both. LABA medicines, such as ARCAPTA NEOHALER help the muscles around the airways in your lungs stay relaxed to prevent symptoms, such as wheezing, cough, chest tightness and shortness of breath.
- ARCAPTA NEOHALER is for long-term use and should be taken 1 time each day, to improve the symptoms of COPD for better breathing.
- **ARCAPTA NEOHALER is not used to treat sudden symptoms of COPD**. Always have a short-acting $beta_2$-agonist medicine (rescue inhaler) with you to treat sudden symptoms of COPD. If you do not have a rescue inhaler, contact your healthcare provider to have one prescribed for you.
- **ARCAPTA NEOHALER is not for the treatment of asthma**. It is not known if ARCAPTA NEOHALER is safe and effective in people with asthma.
- **ARCAPTA NEOHALER should not be used in children**. It is not known if ARCAPTA NEOHALER is safe and effective in children.

Do not use ARCAPTA NEOHALER if you:

- have asthma.
- are allergic to indacaterol or any of the ingredients in ARCAPTA NEOHALER. Ask your healthcare provider if you are not sure. See "**What are the ingredients in ARCAPTA NEOHALER?**" at the end of this Patient Information leaflet for a complete list of ingredients in ARCAPTA NEOHALER.

Before using ARCAPTA NEOHALER, tell your healthcare provider about all of your medical conditions, including if you:

- have heart problems.
- have high blood pressure.
- have seizures.
- have thyroid problems.
- have diabetes.
- are pregnant or plan to become pregnant. It is not known if ARCAPTA NEOHALER can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if the medicine indacaterol in ARCAPTA NEOHALER passes into your breast milk and if it can harm your baby. You and your healthcare provider should decide if you will take ARCAPTA or breastfeed.
- are allergic to any of the ingredients in ARCAPTA NEOHALER, any other medicines, or food products.

ARCAPTA NEOHALER contains lactose (milk sugar) and a small amount of milk proteins. It is possible that allergic reactions may happen in patients who have a severe milk protein allergy.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ARCAPTA NEOHALER and certain other medicines may interact with each other. This may cause serious side effects.

Know the medicines you take. Keep a list of your medicines with you to show your healthcare provider and pharmacist each time you get a new medicine.

How should I use ARCAPTA NEOHALER?

Read the step-by-step instructions for using ARCAPTA NEOHALER at the end of this Patient Information leaflet.

- **Do not** use ARCAPTA NEOHALER unless your healthcare provider has taught you how to use the inhaler and you understand how to use it correctly. Ask your healthcare provider or pharmacist if you have any questions.
- Use ARCAPTA NEOHALER exactly as prescribed. **Do not use ARCAPTA NEOHALER more often than prescribed**.
- **Use 1 ARCAPTA capsule inhaled through the NEOHALER inhaler 1 time each day**, at the same time of the day.
- If you miss a dose of ARCAPTA NEOHALER, take it as soon as you remember. Do not take more than 1 dose in 24 hours.
- **Do not swallow ARCAPTA capsules**. ARCAPTA capsules are for oral inhalation use only.
- Only use ARCAPTA capsules with the NEOHALER inhaler.
- ARCAPTA capsules should always be stored in the sealed blisters and removed immediately before use. Throw away (discard) any ARCAPTA capsules that are removed from the blister and not used immediately.
- Always use the new NEOHALER inhaler that is provided with each new prescription.
- **ARCAPTA NEOHALER does not relieve sudden symptoms of COPD**. Always have a rescue inhaler medicine with you to treat sudden symptoms. If you do not have a rescue inhaler medicine, call your healthcare provider to have one prescribed for you.
- **Do not** stop using ARCAPTA NEOHALER or other medicines to control or treat your COPD unless told to do so by your healthcare provider because your symptoms might get worse. Your healthcare provider will change your medicines as needed.
- **Call your healthcare provider or get emergency medical care right away** if your breathing problems worsen with ARCAPTA NEOHALER, you need to use your rescue medicine more often than usual, or your rescue inhaler medicine does not work as well for you at relieving your symptoms.

What are the possible side effects with ARCAPTA NEOHALER?

ARCAPTA NEOHALER can cause serious side effects, including:

- **People with asthma who take LABA medicines, such as ARCAPTA NEOHALER, without also using medicine called an inhaled corticosteroid, have an increased risk of serious problems from asthma, including being hospitalized, needing a tube placed in their airway to help them breathe, or death.**
  - **Call your healthcare provider if breathing problems worsen over time while using ARCAPTA NEOHALER.** You may need a different treatment.
  - **Get emergency medical care if:**
    - breathing problems worsen quickly.
    - you use your rescue inhaler medicine, but it does not relieve your breathing problems.
- **COPD symptoms that get worse over time**. If your COPD symptoms worsen over time, do not increase your dose of ARCAPTA NEOHALER, instead call your healthcare provider.

Using too much of a LABA medicine may cause:

- chest pain
- fast and irregular heartbeat
- tremor
- increased blood pressure
- headache
- nervousness

- **Serious allergic reactions.** Stop using ARCAPTA NEOHALER and call your healthcare provider or get emergency medical care right away if you get any of the following symptoms of a serious allergic reaction.
  - rash
  - swelling of the tongue, lips, and face
  - hives
  - difficulty breathing or swallowing
- **Sudden shortness of breath can happen immediately after using ARCAPTA NEOHALER**. Sudden shortness of breath may be life-threatening. If you have sudden breathing problems immediately after inhaling your medicine, call your healthcare provider or go to the nearest hospital emergency room right away.
- **Effects on your heart:**
  - fast or irregular heartbeat, awareness of a heartbeat
  - increased blood pressure
  - chest pain
- **Changes in laboratory blood levels**, including high levels of blood sugar (hyperglycemia) and low levels of potassium (hypokalemia), which may cause symptoms of muscle spasm, muscle weakness or abnormal heart rhythm.

Common side effects of ARCAPTA NEOHALER include: runny nose, cough, sore throat, headache and nausea.

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of ARCAPTA NEOHALER. For more information, ask your healthcare provider 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 ARCAPTA NEOHALER?

- Store ARCAPTA NEOHALER (inhaler and blister-packaged capsules) at room temperature between 59°F to 86°F (15°C to 30°C).
- Store ARCAPTA NEOHALER in a dry place.
- Protect ARCAPTA capsules from light and moisture.
- **Do not** remove ARCAPTA capsules from their foil package until just before use.
- **Do not** store ARCAPTA capsules in the NEOHALER inhaler.

Keep ARCAPTA NEOHALER and all medicines out of the reach of children.

General Information about the safe and effective use of ARCAPTA NEOHALER.

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

You can ask your healthcare provider or pharmacist for information about ARCAPTA NEOHALER that is written for health professionals.

For more information about ARCAPTA NEOHALER or to report side effects, go to www.arcapta.com or call 1-888-669-6682

What are the ingredients in ARCAPTA NEOHALER?

Active ingredient: indacaterol
Inactive ingredients: lactose monohydrate (contains trace levels of milk protein)

Manufactured by:

Novartis Pharmaceuticals Corporation,

East Hanover, New Jersey 07936.

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 07/2021