Once COPD symptoms appear, lung function is already lost.[1]

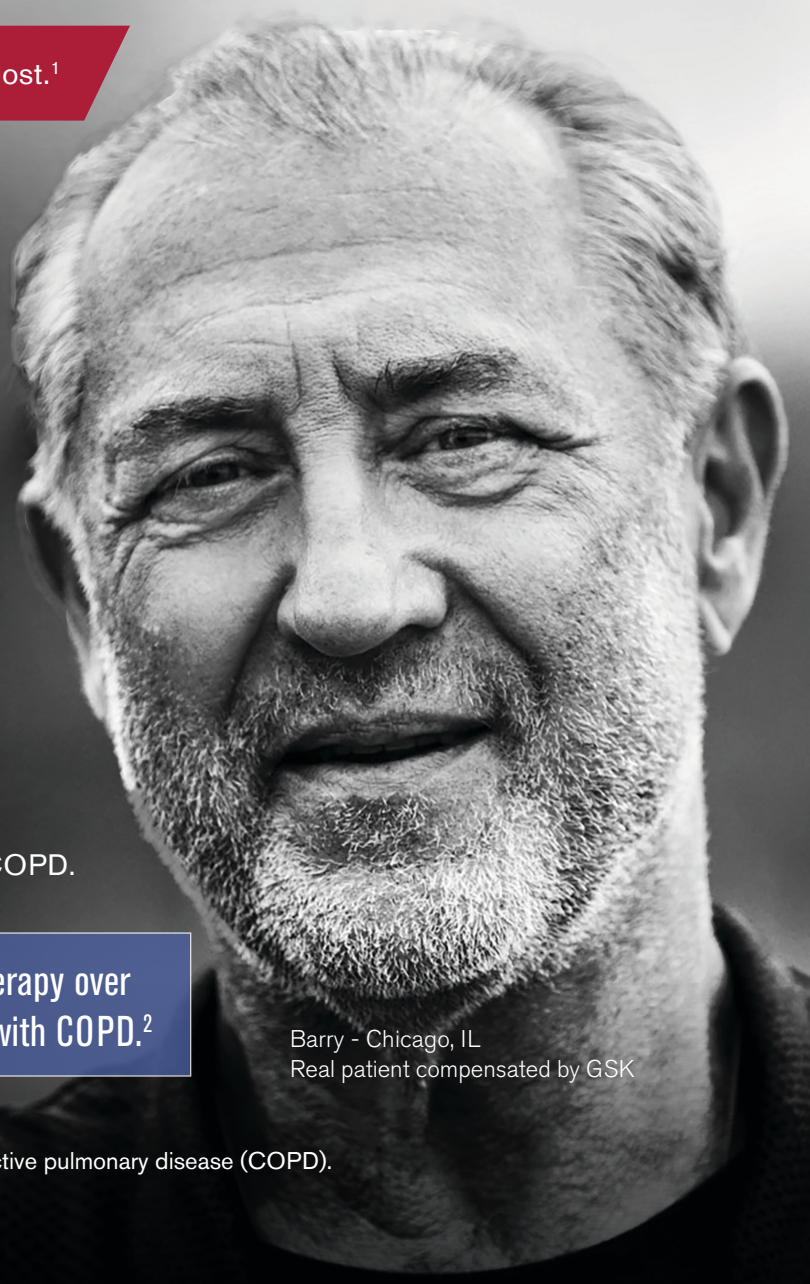
START STRONG
with ANORO

In patients who may experience:

- **COUGH**
- **WHEEZING**
- **SHORTNESS OF BREATH**
- **LEADING TO**
  - Regular rescue medication use
  - Pulling away from normal activities

ANORO was studied in patients with moderate or worse COPD.

ATS strongly recommends LABA/LAMA combination therapy over LABA or LAMA monotherapy for symptomatic patients with COPD.[2]



Barry - Chicago, IL
Real patient compensated by GSK

INDICATION

ANORO is for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).
ANORO is NOT for the relief of acute bronchospasm or for asthma.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- ANORO is contraindicated in patients with severe hypersensitivity to milk proteins or with hypersensitivity to umeclidinium, vilanterol, or any of the excipients.
- Use of a long-acting $beta_2$-adrenergic agonist (LABA) without an inhaled corticosteroid (ICS) is contraindicated in patients with asthma.

WARNINGS AND PRECAUTIONS

- The safety and efficacy of ANORO in patients with asthma have not been established. ANORO is not indicated for the treatment of asthma. Use of LABA as monotherapy (without ICS) for asthma is associated with an increased risk of asthma-related death, and in pediatric and adolescent patients, available data also suggest an increased risk of asthma-related hospitalization. These findings are considered a class effect of LABA monotherapy. Available data do not suggest an increased risk of death with use of LABA in patients with COPD.
- ANORO should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD.
- ANORO is NOT a rescue medication and should NOT be used for the relief of acute bronchospasm or symptoms. Acute symptoms should be treated with an inhaled, short-acting $beta_2$-agonist.

Please see additional Important Safety Information for ANORO throughout this brochure.
Please see accompanying full Prescribing Information, including Patient Information, for ANORO.

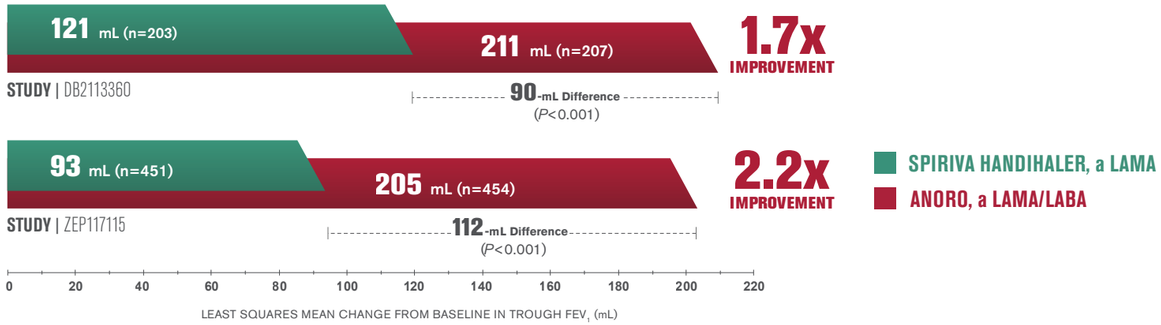
ANORO ELLIPTA
(umeclidinium 62.5 mcg and
vilanterol 25 mcg inhalation powder)

gsk | INNOVIVA

START STRONG WITH **ANORO** FOR SUPERIOR LUNG FUNCTION IMPROVEMENT VS **SPIRIVA HANDIHALER**[3-5]

ANORO delivers nearly 2X Lung Function vs SPIRIVA, a single bronchodilator[3-5]

Trough FEV_1 at Day 169



Studied in patients with moderate or worse COPD (GOLD 2-4).[4,5]

In a separate study (DB2113374), ANORO ELLIPTA (n=217) compared with SPIRIVA HANDIHALER (n=215) showed a 60-mL difference* (208 mL and 149 mL, respectively), but due to testing hierarchy, statistical significance cannot be inferred.[4]
*Reflects rounding.

DESCRIPTION OF STUDIES[4-6]
The efficacy and safety of a once-daily dose of ANORO ELLIPTA and SPIRIVA HANDIHALER (tiotropium bromide inhalation powder) were evaluated in 24-week, multicenter, randomized, blinded, active-controlled, double-dummy, parallel-group studies in patients (mean age range: 62 to 65 years) with COPD. At screening, patients had a mean postbronchodilator FEV_1 range of 46.4% to 47.7% predicted. The studies were not powered to compare safety profiles of the products.

PRIMARY ENDPOINT
Trough (predose) FEV_1 at Day 169 (defined as the mean of the FEV_1 values obtained 23 and 24 hours after dosing on Day 168).

FEV_1= forced expiratory volume in 1 second; GOLD=Global Initiative for Chronic Obstructive Lung Disease.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- ANORO should not be used more often or at higher doses than recommended or with another LABA (eg, salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs, like LABA.
- Caution should be exercised when considering the coadministration of ANORO with ketoconazole and other known strong CYP3A4 inhibitors (eg, ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole) because increased cardiovascular adverse effects may occur.
- If paradoxical bronchospasm occurs, discontinue ANORO and institute alternative therapy.
- Hypersensitivity reactions such as anaphylaxis, angioedema, rash, and urticaria may occur after administration of ANORO. Discontinue ANORO if such reactions occur.
- Vilanterol can produce clinically significant cardiovascular effects in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, or symptoms. If such effects occur, ANORO may need to be discontinued. ANORO should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.
- Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis, and in patients who are unusually responsive to sympathomimetic amines.

ANORO REDUCED RESCUE MEDICATION USE VS SPIRIVA HANDIHALER[4,5]

Patients taking ANORO had fewer rescue albuterol puffs per day over 24 weeks compared with patients taking SPIRIVA[4-6]

↓22% REDUCTION in albuterol puffs vs SPIRIVA[4,5]
0.7 puffs per day† (over 24 weeks)

†In DB2113360, least square (LS) mean number of rescue albuterol puffs per day over Weeks 1 to 24: ANORO ELLIPTA=2.5, SPIRIVA HANDIHALER=3.2. Difference=0.7.[6]

Other endpoint. Endpoint was not adjusted for multiplicity.

Studied in patients with moderate or worse COPD (GOLD 2-4).[4,5]

In ZEP117115, LS mean number of rescue albuterol puffs per day was 1.8 for ANORO ELLIPTA (n=454) and 2.3 for SPIRIVA HANDIHALER (n=451), which corresponds to a 0.5 difference or a 22% reduction. Other endpoint not adjusted for multiplicity.[5,6]

In DB2113374, as part of a predefined hierarchy, one comparison for the primary endpoint did not achieve statistical significance, and therefore subsequent comparisons are descriptive only. In this study, the LS mean number of rescue albuterol puffs per day for ANORO ELLIPTA (n=217) and SPIRIVA HANDIHALER (n=215) was 2.9 vs 3.5, respectively.[4,6]

DESCRIPTION OF STUDIES[4-6]
See Description of Studies on preceding page.

OTHER EFFICACY ENDPOINT
Rescue albuterol use (puffs/day), Weeks 1 to 24.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- Use with caution in patients with narrow-angle glaucoma. Instruct patients to contact a healthcare provider immediately if signs or symptoms of acute narrow-angle glaucoma develop.
- Use with caution in patients with urinary retention, especially in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to contact a healthcare provider immediately if signs or symptoms of urinary retention develop.
- Be alert to hypokalemia and hyperglycemia.

ADVERSE REACTIONS

- The most common adverse reactions (≥1% and more common than placebo) reported in four 6-month clinical trials with ANORO (and placebo) were: pharyngitis, 2% (<1%); sinusitis, 1% (<1%); lower respiratory tract infection, 1% (<1%); constipation, 1% (<1%); diarrhea, 2% (1%); pain in extremity, 2% (1%); muscle spasms, 1% (<1%); neck pain, 1% (<1%); and chest pain, 1% (<1%).
- In addition to the 6-month efficacy trials with ANORO, a 12-month trial evaluated the safety of umeclidinium/vilanterol 125 mcg/25 mcg in subjects with COPD. Adverse reactions (incidence ≥1% and more common than placebo) in subjects receiving umeclidinium/vilanterol 125 mcg/25 mcg were: headache, back pain, sinusitis, cough, urinary tract infection, arthralgia, nausea, vertigo, abdominal pain, pleuritic pain, viral respiratory tract infection, toothache, and diabetes mellitus.

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Please see accompanying full Prescribing Information, including Patient Information, for ANORO.

ANORO ELLIPTA
(umeclidinium 62.5 mcg and vilanterol 25 mcg inhalation powder)

Over half of patients had moderate or worse COPD at diagnosis.[1*]

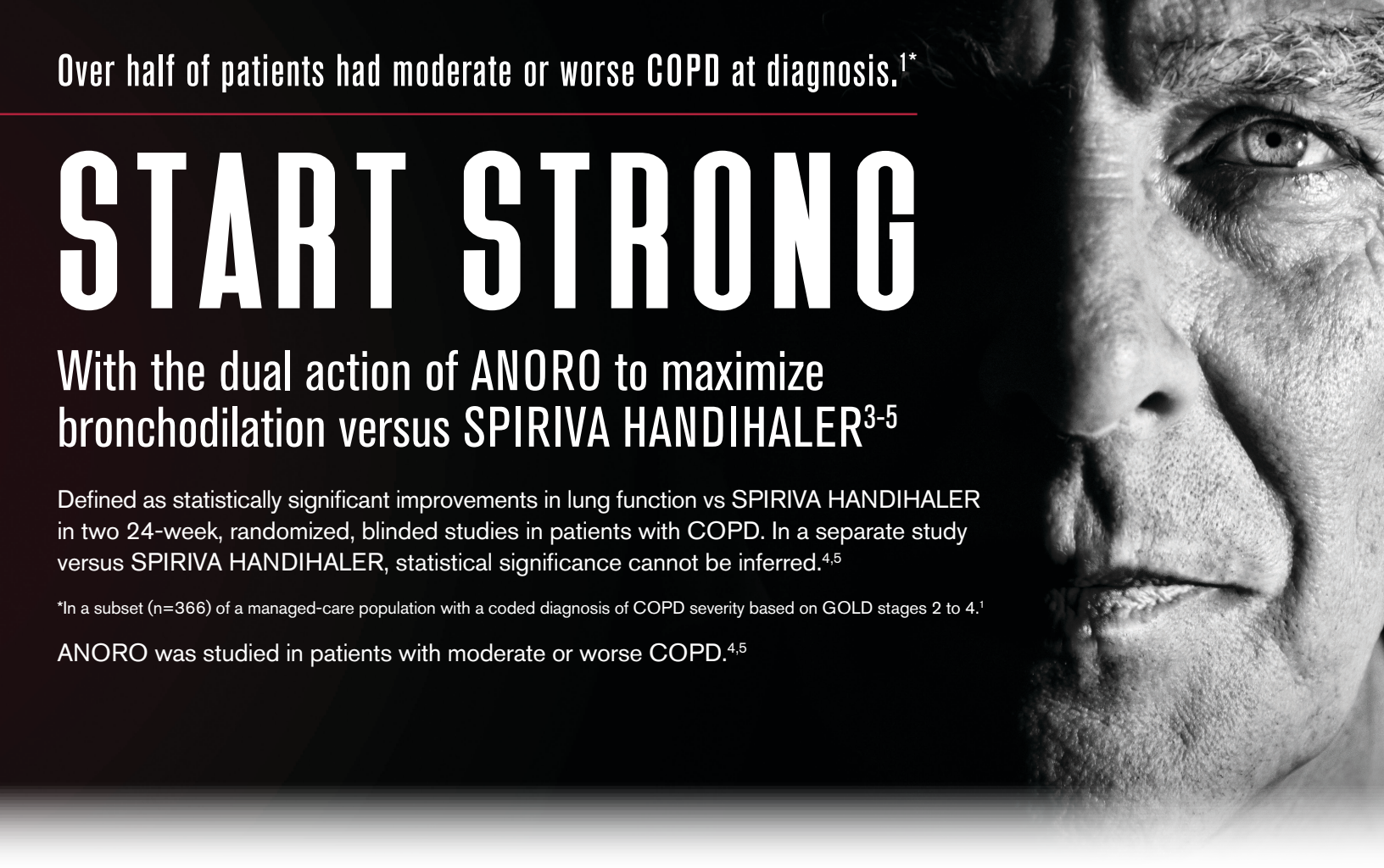
START STRONG

With the dual action of ANORO to maximize bronchodilation versus SPIRIVA HANDIHALER[3-5]

Defined as statistically significant improvements in lung function vs SPIRIVA HANDIHALER in two 24-week, randomized, blinded studies in patients with COPD. In a separate study versus SPIRIVA HANDIHALER, statistical significance cannot be inferred.[4,5]

*In a subset (n=366) of a managed-care population with a coded diagnosis of COPD severity based on GOLD stages 2 to 4.[1]

ANORO was studied in patients with moderate or worse COPD.[4,5]



IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS

- Caution should be exercised when considering the coadministration of ANORO with ketoconazole and other known strong CYP3A4 inhibitors as increased systemic exposure to vilanterol and cardiovascular adverse effects may occur. See prior Warning and Precaution regarding CYP3A4 inhibitors.
- ANORO should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QTc interval, or within 2 weeks of discontinuation of such agents, because they may potentiate the effect of vilanterol on the cardiovascular system.
- Use beta-blockers with caution as they not only block the pulmonary effect of beta-agonists, such as vilanterol, but may produce severe bronchospasm in patients with COPD.
- Use with caution in patients taking non–potassium-sparing diuretics, as ECG changes and/or hypokalemia associated with these diuretics may worsen with concomitant beta-agonists.
- Avoid coadministration of ANORO with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects.

Please see additional Important Safety Information for ANORO throughout this brochure.

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References: 1. Mapel DW, Dalal AA, Blanchette CM, et al. Severity of COPD at initial spirometry-confirmed diagnosis: data from medical charts and administrative claims. *Int J Chron Obstruct Pulmon Dis.* 2011;6:573-581. **2.** Nici L, Mammen MJ, Charbek E, et al. Pharmacologic management of chronic obstructive pulmonary disease. An official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med.* 2020;201(9):e56-e69. **3.** Cazzola M, Molimard M. The scientific rationale for combining long-acting β_2-agonists and muscarinic antagonists in COPD. *Pulm Pharmacol Ther.* 2010;23(4):257-267. **4.** Decramer M, Anzueto A, Kerwin E, et al. Efficacy and safety of umeclidinium plus vilanterol versus tiotropium, vilanterol, or umeclidinium monotherapies over 24 weeks in patients with chronic obstructive pulmonary disease: results from two multicentre, blinded, randomised controlled trials. *Lancet Respir Med.* 2014;2(6):472-486. **5.** Maleki-Yazdi MR, Kaelin T, Richard N, Zvarich M, Church A. Efficacy and safety of umeclidinium/vilanterol 62.5/25 mcg and tiotropium 18 mcg in chronic obstructive pulmonary disease: results of a 24-week, randomized, controlled trial. *Respir Med.* 2014;108(12):1752-1760. **6.** Data on file, GSK.

ANORO ELLIPTA was developed in collaboration with INNOVIVA

UCVLBND200015 October 2020
Produced in USA. 0002-0009-63

ANORO ELLIPTA
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