



## **ANORO ELLIPTA**

### **Umeclidinium/Vilanterol**

#### **1. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each delivered dose (the dose leaving the mouthpiece of the inhaler) contains 55 micrograms umeclidinium (equivalent to 65 micrograms of umeclidinium bromide) and 22 micrograms vilanterol (as trifenate). This corresponds to a pre-dispensed dose of 62.5 micrograms of umeclidinium (equivalent to 74.2 micrograms umeclidinium bromide) and 25 micrograms vilanterol (as trifenate).

#### **2. PHARMACEUTICAL FORM**

Inhalation powder, pre-dispensed.

A light grey inhaler with a red mouthpiece cover and an integral dose counter. The *Ellipta* inhaler contains two blister strips, each of which contains a white powder.

#### **3. CLINICAL PARTICULARS**

##### **3.1 Indications**

*ANORO ELLIPTA* is indicated for maintenance bronchodilator treatment to relieve symptoms associated with chronic obstructive pulmonary disease (COPD).

##### **3.2 Dosage and Administration**

*ANORO ELLIPTA* is for oral inhalation only.

*ANORO ELLIPTA* should be administered once daily at the same time each day.

##### **Adults**

The recommended and maximum dose is one inhalation of *ANORO ELLIPTA* 62.5/25 micrograms once daily.

##### **Children**

Use in patients less than 18 years of age is not relevant given the indication for this product.

##### **Elderly**

No dosage adjustment is required in patients over 65 years (see *Pharmacokinetics – Special Patient Populations*).

##### **Renal impairment**

No dosage adjustment is required in patients with renal impairment (see *Pharmacokinetics – Special Patient Populations*).

##### **Hepatic impairment**

No dosage adjustment is required in patients with mild or moderate hepatic impairment. *ANORO ELLIPTA* has not been studied in patients with severe hepatic impairment (see *Pharmacokinetics – Special Patient Populations*).

##### **3.3 Contraindications**

*ANORO ELLIPTA* is contraindicated in patients with severe milk-protein allergy.

Hypersensitivity to the active substances or to any of the excipients listed in section 5.1.

##### **3.4 Warnings and Precautions**

###### **Asthma**

Umeclidinium/vilanterol should not be used in patients with asthma since it has not been studied in this patient population.

#### **Paradoxical bronchospasm**

As with other inhalation therapies, administration of umeclidinium/vilanterol may produce paradoxical bronchospasm that may be life-threatening. Treatment with umeclidinium/vilanterol should be discontinued immediately if paradoxical bronchospasm occurs and alternative therapy instituted if necessary.

#### **Not for acute use**

Umeclidinium/vilanterol is not indicated for the treatment of acute episodes of bronchospasm.

#### **Deterioration of disease**

Increasing use of short-acting bronchodilators to relieve symptoms indicates deterioration of control. In the event of deterioration of COPD during treatment with umeclidinium/vilanterol, a re-evaluation of the patient and of the COPD treatment regimen should be undertaken.

#### **Cardiovascular effects**

Cardiovascular effects, such as cardiac arrhythmias e.g. atrial fibrillation and tachycardia, may be seen after the administration of muscarinic receptor antagonists and sympathomimetics, including Umeclidinium/vilanterol. Patients with clinically significant uncontrolled cardiovascular disease were excluded from clinical studies. Therefore, umeclidinium/vilanterol should be used with caution in patients with severe cardiovascular disease.

#### **Antimuscarinic activity**

Consistent with its antimuscarinic activity, umeclidinium/vilanterol should be used with caution in patients with urinary retention or with narrow-angle glaucoma.

#### **Hypokalaemia**

Beta<sub>2</sub>-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation.

No clinically relevant effects of hypokalaemia were observed in clinical studies with umeclidinium/vilanterol at the recommended therapeutic dose. Caution should be exercised when umeclidinium/vilanterol is used with other medicinal products that also have the potential to cause hypokalaemia.

#### **Hyperglycaemia**

Beta<sub>2</sub>-adrenergic agonists may produce transient hyperglycaemia in some patients.

No clinically relevant effects on plasma glucose were observed in clinical studies with umeclidinium/vilanterol at the recommended therapeutic dose. Upon initiation of treatment with umeclidinium/vilanterol plasma glucose should be monitored more closely in diabetic patients.

#### **Coexisting conditions**

Umeclidinium/vilanterol should be used with caution in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta<sub>2</sub>-adrenergic agonists.

#### **Excipients**

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

### 3.5 Interactions

#### Interaction with beta-blockers

Beta-adrenergic blockers may weaken or antagonise the effect of beta<sub>2</sub>-agonists, such as vilanterol. Concurrent use of either non-selective or selective beta-adrenergic blockers should be avoided unless there are compelling reasons for their use.

#### Interaction with CYP3A4 inhibitors/Metabolic and transporter based interactions

Vilanterol, a component of *ANORO ELLIPTA*, is a substrate of cytochrome P450 3A4 (CYP3A4) and cleared by CYP3A4 mediated extensive first-pass metabolism in the gastrointestinal tract and in the liver. Concomitant administration of strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir, telithromycin) may inhibit the metabolism of, and increase the systemic exposure to, vilanterol. Co-administration with ketoconazole (400 mg) in healthy volunteers increased mean vilanterol AUC<sub>(0-t)</sub> and C<sub>max</sub>, 65% and 22% respectively. The increase in vilanterol exposure was not associated with an increase in beta-adrenergic agonist related systemic effects on heart rate, blood potassium or QT interval (corrected using the Fridericia method).

Care is advised when co-administering umeclidinium/vilanterol with ketoconazole and other known strong CYP3A4 inhibitors as there is potential for an increased systemic exposure to Vilanterol, which could lead to an increase in the potential for adverse reactions (see *Pharmacokinetics*). Verapamil, a moderate CYP3A4 inhibitor, did not significantly affect the pharmacokinetics of Vilanterol.

Umeclidinium is a substrate of cytochrome P450 2D6 (CYP2D6). The steady-state pharmacokinetics of umeclidinium was assessed in healthy volunteers lacking CYP2D6 (poor metabolisers). No effect on umeclidinium AUC or C<sub>max</sub> was observed at a 8-fold higher dose. An approximately 1.3-fold increase in umeclidinium AUC was observed at 16-fold higher dose with no effect on umeclidinium C<sub>max</sub>. Based on the magnitude of these changes, no clinically relevant drug interaction is expected when umeclidinium/vilanterol is co-administered with CYP2D6 inhibitors or when administered to patients genetically deficient in CYP2D6 activity (poor metabolisers).

Both umeclidinium and vilanterol are substrates of the P-glycoprotein transporter (P-gp). The effect of the moderate P-gp inhibitor verapamil (240 mg once daily) on the steady-state pharmacokinetics of umeclidinium and vilanterol was assessed in healthy volunteers. No effect of verapamil was observed on umeclidinium or vilanterol C<sub>max</sub>. An approximately 1.4-fold increase in umeclidinium AUC was observed with no effect on vilanterol AUC. Based on the magnitude of these changes, no clinically relevant drug interaction is expected when umeclidinium/vilanterol is co-administered with P-gp inhibitors.

#### Other antimuscarinics and sympathomimetics

Co-administration of umeclidinium/vilanterol with other long-acting muscarinic antagonists, long-acting beta<sub>2</sub>-adrenergic agonists or medicinal products containing either of these agents has not been studied and is not recommended as it may potentiate known inhaled muscarinic antagonist or beta<sub>2</sub>-adrenergic agonist adverse reactions.

#### Hypokalaemia

Concomitant hypokalaemic treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta<sub>2</sub>-adrenergic agonists, therefore use with caution.

#### Other medicinal products for COPD

Although no formal *in vivo* drug interaction studies have been performed, inhaled umeclidinium/vilanterol has been used concomitantly with other COPD medicinal products including short acting sympathomimetic bronchodilators and inhaled corticosteroids without clinical evidence of drug interactions.

### 3.6 Fertility, Pregnancy, and Lactation

#### Fertility

There are no data on the effects of *ANORO ELLIPTA* on human fertility. Animal studies indicate no effects of umeclidinium or vilanterol on fertility (see *Pre-clinical Safety Data*).

### Pregnancy

There are no or limited amount of data from the use of *ANORO ELLIPTA* in pregnant women. Studies in animals have shown reproductive toxicity after inhaled administration of vilanterol (see *Pre-clinical Safety Data*). *ANORO ELLIPTA* should be used during pregnancy only if the expected benefit to the mother justifies the potential risk to the foetus.

### Lactation

It is unknown whether umeclidinium or vilanterol are excreted in human milk. However, other beta<sub>2</sub>-agonists are detected in human milk. A risk to breastfed newborns/infants cannot be excluded.

A decision must be made whether to discontinue breastfeeding or to discontinue *ANORO ELLIPTA* therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

### 3.7 Effects on Ability to Drive and Use Machines

There have been no studies to investigate the effect of *ANORO ELLIPTA* on the ability to perform tasks that require judgement, motor or cognitive skills.

### 3.8 Adverse Reactions

#### Clinical trial data

The safety profile of *ANORO ELLIPTA* is based on approximately 3000 patients with COPD who received doses of umeclidinium/vilanterol 62.5/25 micrograms or greater for up to one year during clinical studies. This includes approximately 1600 patients who received 62.5/25 micrograms and approximately 1300 patients who received 125/25 micrograms, both once daily.

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  and  $< 1/10$ ), uncommon ( $\geq 1/1,000$  and  $< 1/100$ ), rare ( $\geq 1/10,000$  and  $< 1/1,000$ ) and very rare ( $< 1/10,000$ ).

<b>MedDRA System organ class</b>	<b>Adverse reaction(s)</b>	<b>Frequency</b>
Infections and Infestations	Urinary tract infection	Common
	Sinusitis	Common
	Nasopharyngitis	Common
	Pharyngitis	Common
	Upper respiratory tract infection	Common
Immune System Disorders	Hypersensitivity reactions including: Rash	Uncommon
	Anaphylaxis, angioedema, and urticaria	Rare
Nervous System Disorders	Headache	Common
	Tremor	Uncommon
	Dysgeusia	Uncommon
Eye Disorders	Vision blurred	Rare
	Glaucoma	Rare
	Intraocular pressure increased	Rare
Cardiac Disorders	Atrial fibrillation	Uncommon
	Supraventricular tachycardia	Uncommon
	Rhythm idioventricular	Uncommon
	Tachycardia	Uncommon
	Supraventricular extrasystoles	Uncommon
	Palpitations	Uncommon
Respiratory, Thoracic and Mediastinal Disorders	Cough	Common
	Oropharyngeal pain	Common
	Dysphonia	Uncommon
	Paradoxical bronchospasm	Rare

<b>MedDRA System organ class</b>	<b>Adverse reaction(s)</b>	<b>Frequency</b>
Gastrointestinal Disorders	Constipation Dry mouth	Common Common
Skin and Subcutaneous Tissue Disorders	Rash	Uncommon
Renal and Urinary Disorders	Urinary retention Dysuria Bladder outlet obstruction	Rare Rare Rare

### Reporting of suspected adverse reaction

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to GlaxoSmithKline Indonesia by phone +628118438228 or email to [yqq68540@gsk.com](mailto:yqq68540@gsk.com).

### 3.9 Overdose

#### Symptoms and signs

An overdose of *ANORO ELLIPTA* will likely produce signs and symptoms due to the individual components' actions, consistent with the known inhaled muscarinic antagonist adverse effects (e.g. dry mouth, visual accommodation disturbances and tachycardia) and those seen with overdose of other beta<sub>2</sub>-agonists (e.g. tremor, headache and tachycardia).

#### Treatment

There is no specific treatment for an overdose of *ANORO ELLIPTA*. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

## 4. PHARMACOLOGICAL PROPERTIES

### 4.1 Pharmacodynamics

Pharmacotherapeutic group: Drugs for obstructive airway diseases, adrenergics in combination with anticholinergics, ATC code: R03AL03.

#### Mechanism of action

Umeclidinium/vilanterol is a combination inhaled long-acting muscarinic receptor antagonist/long-acting beta<sub>2</sub>-adrenergic agonist (LAMA/LABA). Following inhalation both compounds act locally on airways to produce bronchodilation by separate mechanisms.

#### *Umeclidinium*

Umeclidinium is a long acting muscarinic receptor antagonist (also referred to as an anticholinergic). It is a quinuclidine derivative that is a muscarinic receptor antagonist with activity across multiple muscarinic cholinergic receptor subtypes. Umeclidinium exerts its bronchodilatory activity by competitively inhibiting the binding of acetylcholine with muscarinic acetylcholine receptors on airway smooth muscle. It demonstrates slow reversibility at the human M3 muscarinic receptor subtype *in vitro* and a long duration of action *in vivo* when administered directly to the lungs in pre-clinical models.

#### *Vilanterol*

Vilanterol is a selective long-acting, beta<sub>2</sub>-adrenergic receptor agonist (beta<sub>2</sub>-agonist).

The pharmacologic effects of beta<sub>2</sub>-agonists, including vilanterol, are at least in part attributable to stimulation of intracellular adenylate cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) 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 from mast cells.

## 4.2 Pharmacodynamic effects

In one placebo controlled clinical efficacy study *ANORO ELLIPTA* increased FEV<sub>1</sub> after the first dose on Day 1 with an improvement compared with placebo of 0.11 L (p<0.001) at 15 minutes following administration. The change from baseline to peak FEV<sub>1</sub> during 0-6 hours post-dose at Day 1 and Week 24 was 0.27 L and 0.32 L respectively for *ANORO ELLIPTA*, compared with 0.11 L (Day 1) and 0.10 L (Week 24) for placebo.

### Cardiovascular effects

The effect of umeclidinium/vilanterol on the QT interval was evaluated in a placebo and moxifloxacin controlled QT study involving once daily administration of umeclidinium/vilanterol 125/25 micrograms or 500/100 micrograms for 10 days in 103 healthy volunteers. The maximum mean difference in prolongations of QT interval (corrected using the Fridericia method, QTcF) from placebo after baseline-correction was 4.3 (90% CI=2.2 to 6.4) milliseconds seen 10 minutes after administration with umeclidinium/vilanterol 125/25 micrograms and 8.2 (90% CI=6.2 to 10.2) milliseconds seen 30 minutes after administration with umeclidinium/vilanterol 500/100 micrograms. No clinically relevant effect on prolongation of QT interval (corrected using the Fridericia method) was observed.

A dose-dependent increase in heart rate was also observed. The maximum mean difference in heart rate from placebo after baseline-correction was 8.4 (90% CI=7.0 to 9.8) beats/minute and 20.3 (90% CI=18.9 to 21.7) beats/minute seen 10 minutes after administration of umeclidinium/vilanterol 113/22 micrograms and 500/100 micrograms respectively.

In addition, no clinically significant effects of umeclidinium/vilanterol on cardiac rhythm were observed on 24-hour Holter monitoring in 281 patients who received umeclidinium/vilanterol 125/25 micrograms once daily for up to 12 months.

## 4.3 Pharmacokinetics

When umeclidinium and vilanterol were administered in combination by the inhaled route, the pharmacokinetics of each component was similar to those observed when each active substance was administered separately (see *Metabolism; Drug-drug interactions*). For pharmacokinetic purposes each component can therefore be considered separately.

### Absorption

#### Umeclidinium

Following inhaled administration of umeclidinium in healthy volunteers, C<sub>max</sub> occurred at 5 to 15 minutes. The absolute bioavailability of inhaled umeclidinium was on average 13% of the dose, with negligible contribution from oral absorption. Following repeat dosing of inhaled umeclidinium, steady state was achieved within 7 to 10 days with 1.5 to 2-fold accumulation.

#### Vilanterol

Following inhaled administration of vilanterol in healthy volunteers, C<sub>max</sub> occurred at 5 to 15 minutes. The absolute bioavailability of inhaled vilanterol was 27%, with negligible contribution from oral absorption. Following repeat dosing of inhaled vilanterol, steady state was achieved within 6 days with up to 2.4-fold accumulation.

### Distribution

#### Umeclidinium

Following intravenous administration to healthy subjects, the mean volume of distribution was 86 litres. *In vitro* plasma protein binding in human plasma was on average 89%.

#### Vilanterol

Following intravenous administration to healthy volunteers, the mean volume of distribution at steady state was 165 litres. *In vitro* plasma protein binding in human plasma was on average 94%.

## **Metabolism**

### ***Umeclidinium***

*In vitro* studies showed that umeclidinium is metabolised principally via cytochrome P450 2D6 (CYP2D6) and is a substrate for the P-glycoprotein (P-gp) transporter.

The primary metabolic routes for umeclidinium are oxidative (hydroxylation, O-dealkylation) followed by conjugation (glucuronidation, etc), resulting in a range of metabolites with either reduced pharmacological activity or for which the pharmacological activity has not been established. Systemic exposure to the metabolites is low.

### ***Vilanterol***

*In vitro* studies showed that vilanterol is metabolised principally via cytochrome P450 3A4 (CYP3A4) and is a substrate for the P-gp transporter. The primary metabolic routes are O-dealkylation to a range of metabolites with significantly reduced beta<sub>1</sub>- and beta<sub>2</sub>- agonist activity. Plasma metabolic profiles following oral administration of vilanterol in a human radiolabel study were consistent with high first-pass metabolism. Systemic exposure to the metabolites is low.

## ***Drug-drug interactions***

Available pharmacokinetic data in healthy volunteers and patients with COPD show that the systemic exposure ( $C_{max}$  and AUC) and population pharmacokinetic predicted exposures to umeclidinium and vilanterol is unaffected by administration with the umeclidinium/vilanterol combination compared to the components administered separately. Co-administration with the strong CYP3A4 inhibitor ketoconazole (400 mg) increased mean vilanterol AUC<sub>(0-t)</sub> and  $C_{max}$ , 65% and 22% respectively. The increase in vilanterol exposure was not associated with an increase in beta-agonist related systemic effects on heart rate, blood potassium or QT interval (corrected using the Fridericia method).

Both umeclidinium and vilanterol are substrates of P-glycoprotein (P-gp). The effect of the moderate P-gp transporter inhibitor verapamil (240 mg once daily) on the steady-state pharmacokinetics of umeclidinium and vilanterol was assessed in healthy volunteers. No effect of verapamil was observed on umeclidinium or vilanterol  $C_{max}$ . An approximately 1.4-fold increase in umeclidinium AUC was observed with no effect on vilanterol AUC.

## **Elimination**

### ***Umeclidinium***

Plasma clearance following intravenous administration was 151 litres/hour. Following intravenous administration, approximately 58% of the administered radiolabelled dose (or 73% of the recovered radioactivity) was excreted in faeces by 192 hours post-dose. Urinary elimination accounted for 22% of the administered radiolabelled dose by 168 hours (27% of recovered radioactivity). The excretion of the drug-related material in the faeces following intravenous dosing indicated secretion into the bile. Following oral administration to healthy male subjects, total radioactivity was excreted primarily in faeces (92% of the administered radiolabelled dose or 99% of the recovered radioactivity) by 168 hours post-dose. Less than 1% of the orally administered dose (1% of recovered radioactivity) was excreted in urine, suggesting negligible absorption following oral administration. Umeclidinium plasma elimination half-life following inhaled dosing for 10 days averaged 19 hours, with 3% to 4% drug excreted unchanged in urine at steady-state.

### ***Vilanterol***

Plasma clearance of vilanterol following intravenous administration was 108 litres/hour. Following oral administration of radiolabelled vilanterol, mass balance showed 70% of the radiolabel in urine and 30% in faeces. Primary elimination of vilanterol was by metabolism followed by excretion of metabolites in urine and faeces. Vilanterol plasma elimination half-life following inhaled dosing for 10 days averaged 11 hours.

## **Special patient populations**

### **Elderly**

A population pharmacokinetic analysis showed that pharmacokinetics of umeclidinium and vilanterol were similar between COPD patients 65 years and older and those younger than 65 years of age.

### **Renal impairment**

Subjects with severe renal impairment showed no evidence of an increase in systemic exposure to either umeclidinium or vilanterol ( $C_{max}$  and AUC), and no evidence of altered protein binding between subjects with severe renal impairment and healthy volunteers.

### **Hepatic impairment**

Subjects with moderate hepatic impairment showed no evidence of an increase in systemic exposure to either umeclidinium or vilanterol ( $C_{max}$  and AUC), and no evidence of altered protein binding between subjects with moderate hepatic impairment and healthy volunteers. umeclidinium/vilanterol has not been evaluated in subjects with severe hepatic impairment.

### **Other patient characteristics**

A population pharmacokinetic analysis showed that no dose adjustment is required for umeclidinium or vilanterol based on the effect of age, race, gender, inhaled corticosteroid use, or weight. A study in CYP2D6 poor metabolisers showed no evidence of a clinically significant effect of CYP2D6 genetic polymorphism on systemic exposure to umeclidinium.

## **4.4 Clinical Studies**

The safety and efficacy of *ANORO ELLIPTA* administered once daily were evaluated in eight Phase III clinical studies in adult patients with a clinical diagnosis of COPD; five were 6-month efficacy studies (DB2113361, DB2113373, DB2113360, DB2113374 and ZEP117115), two were 12-week exercise endurance studies (DB2114417 and DB2114418) and one study (DB2113359) evaluated the safety of umeclidinium/vilanterol administered over a 12-month treatment period. Studies included *ANORO ELLIPTA* 62.5/25 micrograms and/or umeclidinium/vilanterol 125/25 micrograms, all once daily. Efficacy results for *ANORO ELLIPTA* 62.5/25 micrograms are presented below.

### **Placebo Controlled Studies**

In a 6-month study, DB2113373, *ANORO ELLIPTA* 62.5/25 micrograms demonstrated a statistically significant improvement in lung function (as defined by change from baseline trough FEV<sub>1</sub> at Week 24) compared with placebo (see *Table 1*). Bronchodilatory effects with *ANORO ELLIPTA* compared with placebo were evident after the first day of treatment and were maintained over the 24 week treatment period.

**Table 1. Primary efficacy endpoint at Week 24 (Study DB2113373)**

	Trough FEV <sub>1</sub> (L)		
			Difference from Placebo
	Baseline (SD)	Change from Baseline (SE)	Treatment Difference (95% CI) p-value
<b>Study DB2113373</b>			
<i>ANORO ELLIPTA</i> 62.5/25 mcg OD (n=413)	1.28 (0.56)	0.17 (0.01)	0.17 (0.13, 0.21) <0.001
Placebo (n=280)	1.20 (0.47)	0.00 (0.02)	-

Abbreviations: CI=confidence interval; FEV<sub>1</sub>=forced expiratory volume in 1 second; L=litres; mcg=micrograms; n=number receiving treatment; OD=once daily; SD=standard deviation; SE=standard error.

*ANORO ELLIPTA* demonstrated a statistically significant greater improvement from baseline in weighted mean FEV<sub>1</sub> over 0-6 hours post-dose at Week 24 compared with placebo (0.24 L; p<0.001).

A statistically significant improvement from placebo in the Transitional Dyspnoea Index (TDI) focal score at Week 24 was demonstrated for *ANORO ELLIPTA* (1.2 units; p<0.001). The percentage of patients receiving *ANORO ELLIPTA* that responded with a minimum clinically important difference (MCID) of ≥1 unit TDI focal score at Week 24 was 58% (226/389) compared with 41% (106/260) for placebo.

A statistically significant improvement from placebo in the change from baseline in total score at Week 24 for the St. George's Respiratory Questionnaire (SGRQ), a disease-specific health status measure, was also demonstrated for *ANORO ELLIPTA* (-5.51 units; p≤0.001). The percentage of patients receiving *ANORO ELLIPTA* that responded with a reduction from baseline of ≥4 units (MCID) in SGRQ total score was 49% (188/381) compared with 34% (86/254) for placebo.

In addition, patients treated with *ANORO ELLIPTA* required less rescue salbutamol than those treated with placebo (on average a statistically significant reduction of 0.8 puffs per day; p=0.001). Throughout the 24-week study, patients treated with *ANORO ELLIPTA* had more days when no rescue medication was needed (on average 36.1%) compared with placebo (on average 21.7%; no formal statistical analysis was performed on this endpoint).

Treatment with *ANORO ELLIPTA* 62.5/25 micrograms resulted in a lower risk of COPD exacerbation compared with placebo (analysis of time to first exacerbation: Hazard Ratio (HR) 0.5, 95% CI 0.3 to 0.8, risk reduction 50%, p=0.004).

#### **Tiotropium Comparator Studies**

In studies ZEP117115 and DB2113360, treatment with *ANORO ELLIPTA* 62.5/25 micrograms provided statistically significant and clinically meaningful improvements in change from baseline in trough FEV<sub>1</sub> compared with tiotropium at Week 24 (see *Table 2*). In study DB2113374, *ANORO ELLIPTA* 62.5/25 micrograms showed a clinically meaningful improvement in change from baseline in trough FEV<sub>1</sub> compared with tiotropium at Week 24 (see *Table 2*).

**Table 2. Primary efficacy endpoint at Week 24 (Studies ZEP117115, DB2113360 and DB2113374)**

	Trough FEV <sub>1</sub> (L)		
			Difference from Tiotropium
	Baseline (SD)	Change from Baseline (SE)	Treatment Difference (95% CI) p-value
<b>Study ZEP117115</b>			
<i>ANORO ELLIPTA</i> 62.5/25 mcg OD (n=454)	1.25 (0.49)	0.21 (0.01)	0.11 (0.08, 0.14) <0.001
Tiotropium 18 mcg OD (n=451)	1.25 (0.49)	0.09 (0.01)	-
<b>Study DB2113360</b>			
<i>ANORO ELLIPTA</i> 62.5/25 mcg OD (n=207)	1.32 (0.53)	0.21 (0.02)	0.09 (0.04, 0.14) <0.001
Tiotropium 18 mcg OD (n=203)	1.29 (0.53)	0.12 (0.02)	-
<b>Study DB2113374</b>			
<i>ANORO ELLIPTA</i> 62.5/25 mcg OD (n=216)	1.16 (0.48)	0.21 (0.02)	0.06 (0.01, 0.11) 0.018*
Tiotropium 18 mcg OD (n=215)	1.16 (0.45)	0.15 (0.02)	

Abbreviations: CI=confidence interval; FEV<sub>1</sub>=forced expiratory volume in 1 second; L=litres; mcg=micrograms; n=number receiving treatment; OD=once daily; SD=standard deviation; SE=standard error; \*As a result of a prior test in the predefined testing hierarchy not achieving statistical significance, statistical significance cannot be inferred for this comparison.

In studies ZEP117115 and DB2113360 *ANORO ELLIPTA* showed statistically significant greater improvements of 0.11 L and 0.07 L respectively in change from baseline in weighted mean FEV<sub>1</sub> over 0-6 hours at Week 24 compared with tiotropium (both p<0.005). In study DB2113374 *ANORO ELLIPTA* showed a clinically meaningful improvement of 0.10 L in change from baseline in weighted mean FEV<sub>1</sub> over 0-6 hours at Week 24 compared with tiotropium.

In studies DB2113360 and DB2113374, *ANORO ELLIPTA* and tiotropium both improved measures of dyspnoea (TDI focal score) and health-related quality of life (SGRQ) compared with baseline. In the third active-comparator study (ZEP117115), a statistically significant improvement compared with tiotropium in the change from baseline in SGRQ total score at Week 24 was demonstrated for *ANORO ELLIPTA* (-2.10 units; p=0.006). The percentage of patients receiving *ANORO ELLIPTA* that responded with a reduction from baseline of ≥4 units (MCID) in SGRQ total score from this study was 53% (237/445) compared with 46% (196/430) for tiotropium.

Statistically significant improvements in rescue salbutamol use over weeks 1-24 were observed for *ANORO ELLIPTA* over tiotropium in studies ZEP117115 (-0.5 puffs per day; p<0.001) and DB2113360 (-0.7 puffs per day; p=0.022).

Throughout studies ZEP117115, DB2113360 and DB2113374, patients treated with *ANORO ELLIPTA* had, on average, a greater reduction from baseline in the proportion of days when no rescue medication was needed (21.5%, 18.6% and 17.6% respectively) compared with tiotropium (13.3%, 11.7% and 13.4% respectively; no formal statistical analysis was performed on this endpoint).

In study ZEP117115, treatment with *ANORO ELLIPTA* 62.5/25 micrograms resulted in a lower risk of COPD exacerbation compared with tiotropium (analysis of time to first exacerbation: Hazard Ratio (HR)

0.5, 95% CI 0.3 to 1.0, risk reduction 50%, p=0.044).

### **Supportive 3-month exercise endurance studies**

Exercise endurance was evaluated with the endurance shuttle walk test (ESWT) in adult COPD patients with hyperinflation (functional residual capacity [FRC] >120%) in two replicate, 12-week clinical studies.

In one study (DB2114418), treatment with *ANORO ELLIPTA* 62.5/25 micrograms demonstrated a statistically significant improvement over placebo in exercise endurance time (EET) obtained 3 hours after dosing at Week 12 of 69.4 seconds (p=0.003). Improvement in EET compared with placebo was seen at Day 2 and was sustained at Week 6 and Week 12. In the second study (DB2114417), treatment with *ANORO ELLIPTA* 62.5/25 micrograms did not show a statistically significant improvement over placebo in EET (21.9 seconds; p>0.05).

In study DB2114418, *ANORO ELLIPTA* showed a statistically significant improvement compared to placebo in change from baseline in trough FEV<sub>1</sub> at Week 12 of 0.24 L (p<0.001), and statistically significant improvements compared to placebo in change from baseline in lung volume measures at trough and at 3 hours post dose at Week 12 (inspiratory capacity: 0.24 L and 0.32 L respectively, residual volume: -0.47 L and -0.64 L respectively and functional residual capacity: -0.35 L and -0.52 L respectively; all p<0.001). In Study DB2114417, *ANORO ELLIPTA* showed a clinically meaningful improvement compared to placebo in change from baseline in trough FEV<sub>1</sub> at Week 12 of 0.21 L, and improvements compared to placebo in change from baseline in lung volume measures at trough and at 3 hours post dose at Week 12 (inspiratory capacity: 0.20 L and 0.24 L respectively, residual volume: -0.29 L and -0.35 L respectively and functional residual capacity: -0.24 L and -0.30 L respectively).

### **4.5 Pre-clinical Safety Data**

In nonclinical studies with umeclidinium and vilanterol, findings were those typically associated with the primary pharmacology of either muscarinic receptor antagonists or beta<sub>2</sub>-agonists respectively and/or local irritancy. Administration of umeclidinium and vilanterol in combination did not result in any new toxicity. The following statements reflect studies conducted on the individual components.

#### **Carcinogenesis/mutagenesis**

Umeclidinium was not genotoxic in a standard battery of studies and was not carcinogenic in lifetime inhalation studies in mice or rats at exposures  $\geq 26$  or  $\geq 22$ -fold, times the human clinical exposure of umeclidinium 62.5 micrograms, based on AUC, respectively.

Genetic toxicity studies indicate vilanterol does not represent a genotoxic hazard to humans. Consistent with findings for other beta<sub>2</sub>-agonists, in lifetime inhalation studies vilanterol caused proliferative effects in the female rat and mouse reproductive tract and in the rat pituitary gland. There was no increase in tumour incidence in rats or mice at exposures 0.5- or 13-fold, times the human clinical exposure of vilanterol 25 micrograms based on AUC, respectively.

#### **Reproductive Toxicology**

Neither umeclidinium nor vilanterol had any adverse effects on male or female fertility in rats.

Umeclidinium was not teratogenic in rats or rabbits. In a pre- and post-natal study, subcutaneous administration of umeclidinium to rats resulted in lower maternal body weight gain and food consumption and slightly decreased pre-weaning pup body weights in dams given 180 micrograms/kg/day dose (approximately 80-times the human clinical exposure of 62.5 micrograms umeclidinium, based on AUC).

Vilanterol was not teratogenic in rats. In inhalation studies in rabbits, vilanterol caused effects similar to those seen with other beta<sub>2</sub>-agonists (cleft palate, open eyelids, sternal fusion and limb flexure/malrotation) at 6-times the human clinical exposure based on AUC. When given subcutaneously there were no effects at 36-times the human clinical exposure of 25 micrograms vilanterol based on AUC.

## **5. PHARMACEUTICAL PARTICULARS**

### **5.1 List of Excipients**

Lactose monohydrate (which contains milk protein).  
(25 milligrams Lactose monohydrate per dose).

Magnesium stearate

### **5.2 Incompatibilities**

No incompatibilities have been identified.

### **5.3 Shelf Life**

The expiry date is indicated on the packaging.

In-use shelf-life:

Following removal from the tray, the product may be stored for a maximum period of 6 weeks.

Write the date the inhaler should be discarded on the label in the space provided. The date should be added as soon as the inhaler has been removed from the tray.

### **5.4 Special Precautions for Storage**

Do not store above 30°C. If stored in the refrigerator, allow the inhaler to return to room temperature for at least an hour before use.

Keep the inhaler inside the sealed tray to protect from moisture and only remove immediately before first use.

### **5.5 Nature and Contents of Container**

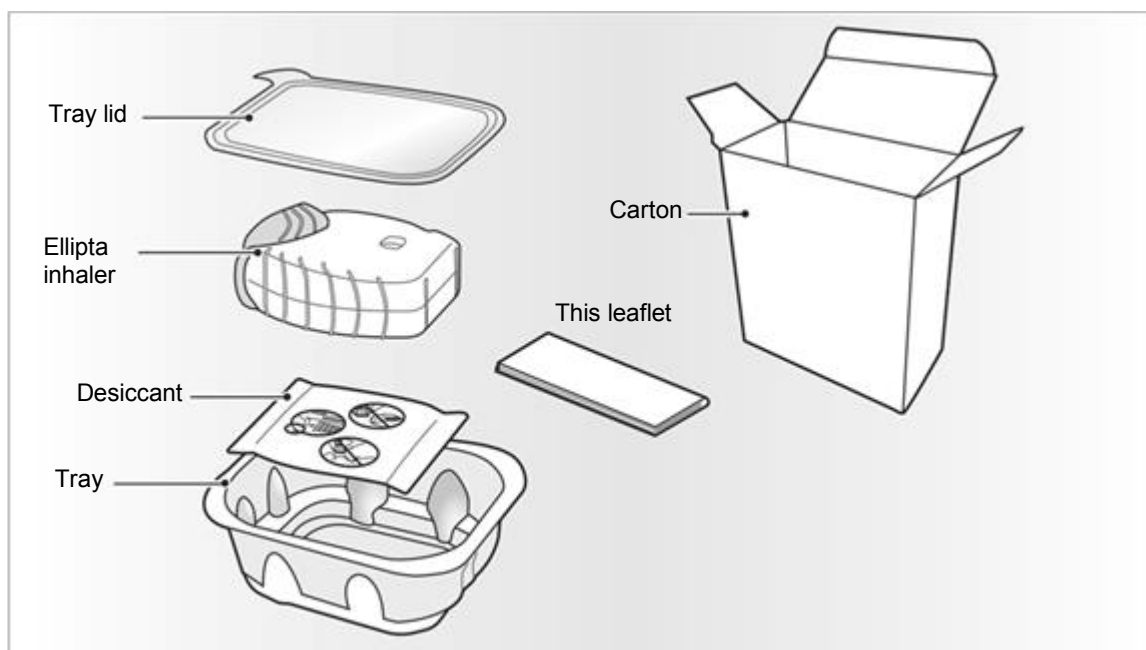
The plastic Ellipta inhaler consists of a light grey body, a red mouthpiece cover and a dose counter, packed into a foil laminate tray containing a desiccant sachet. The tray is sealed with a peelable foil lid.

The inhaler contains two strips of 30 regularly distributed blisters, with one strip containing 62.5 micrograms of Umeclidinium and the other strip containing 25 micrograms of Vilanterol.

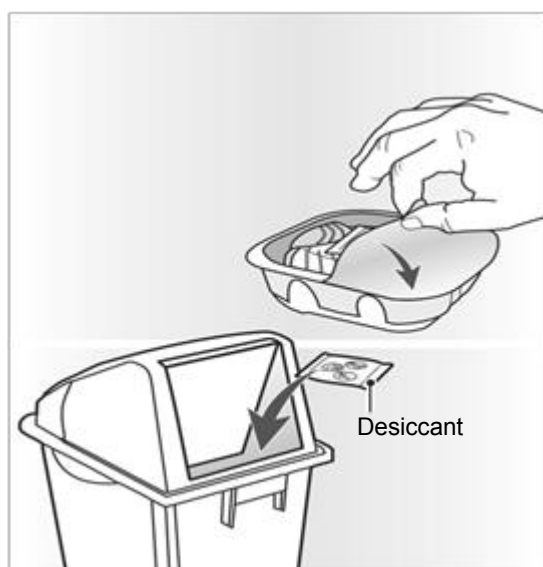
### **5.6 Instructions for Use**

When you first use the Ellipta inhaler you do not need to check that it is working properly, and you do not need to prepare it for use in any special way. Just follow the instructions below.

**Your Ellipta inhaler carton contains**



The inhaler is packaged in a tray. **Do not open the tray until you are ready to inhale a dose of your medicine.** When you are ready to use your inhaler, peel back the lid to open the tray. The tray contains a **desiccant** sachet, to reduce moisture. Throw this desiccant sachet away – **don't** eat or inhale it.



When you take the inhaler out of the sealed tray, it will be in the 'closed' position. **Don't open until you are ready to inhale a dose of medicine.** Write the "Discard by" date on the inhaler label in the space provided. The "Discard by" date is 6 weeks from the date you open the tray. **After this date, the inhaler should no longer be used.**

**a) Read this before you start**

**If you open and close the cover without inhaling the medicine, you will lose the dose.**

The lost dose will be securely held inside the inhaler, but it will no longer be available.

It is not possible to accidentally take extra medicine or a double dose in one inhalation.

### Dose counter

This shows how many doses of medicine are left in the inhaler.

**Before the inhaler has been used, it shows exactly 30 doses.**

It counts down by **1** each time you open the cover.

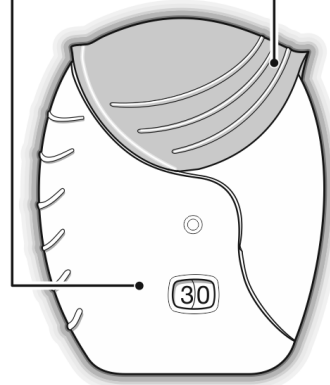
**When fewer than 10 doses are left, half of the dose counter shows red.**

After you have used the last dose, **half of the dose counter shows red and the number 0 is displayed.** Your inhaler is now empty.

If you open the cover after this, the dose counter will change from half red to completely red.

### Cover

Each time you open this, you prepare one dose of medicine.

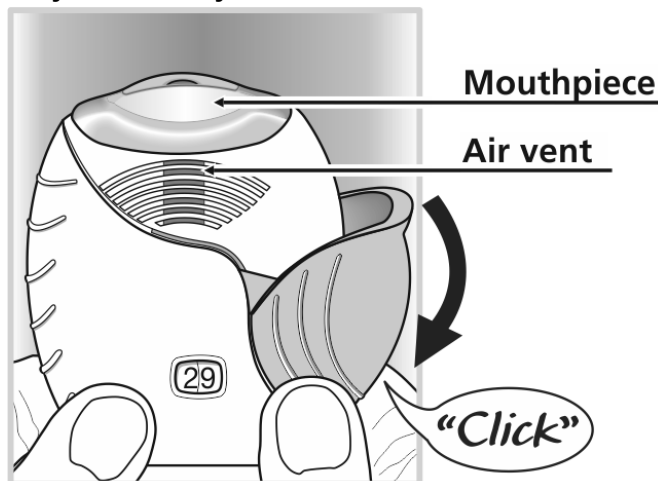


### b) Prepare a dose

**Wait to open the cover until you are ready to take your dose.**

**Do not shake the inhaler.**

- **Slide the cover fully down until you hear a “click”.**



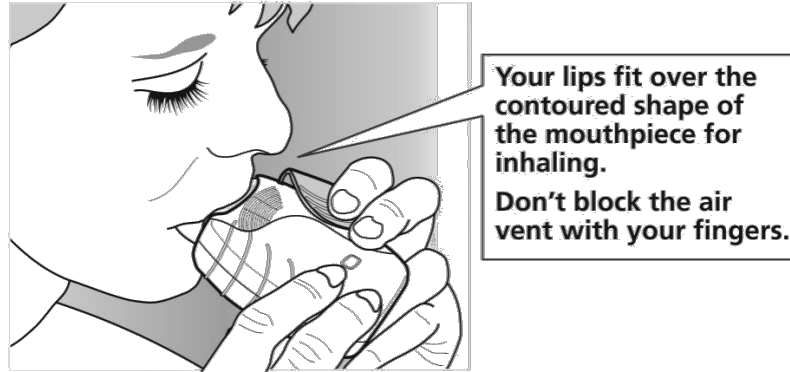
Your medicine is now ready to be inhaled.

The dose counter counts down by 1 to confirm.

- **If the dose counter does not count down as you hear the “click”, the inhaler will not deliver medicine. Take it back to your pharmacist for advice.**
- **Do not shake the inhaler at any time.**

### c) Inhale your medication

- **While holding the inhaler away from your mouth, breathe out as far as is comfortable. Don't breathe out into the inhaler.**
- **Put the mouthpiece between your lips, and close your lips firmly around it. Don't block the air vent with your fingers.**

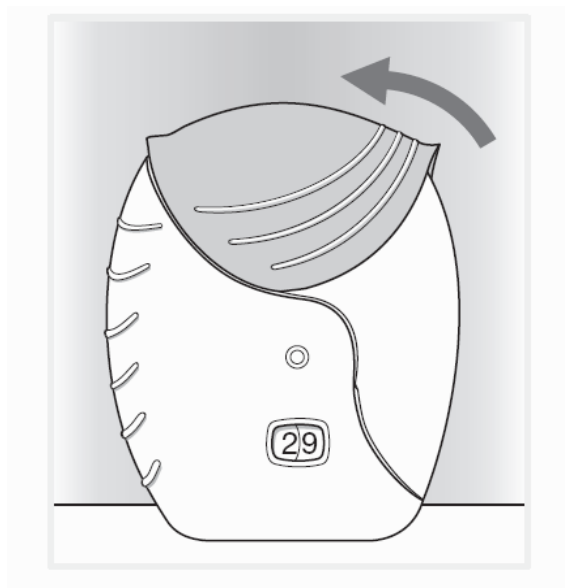


- Take one long, steady, deep breath in. Hold this breath for as long as possible (at least 3-4 seconds).
- Remove the inhaler from your mouth.
- Breathe out slowly and gently.

You may not be able to taste or feel the medicine, even when you are using the inhaler correctly.

If you want to clean the mouthpiece, use a **dry tissue**, **before** you close the cover.

**d) Close the inhaler**



- Slide the cover upwards as far as it will go, to cover the mouthpiece.

**HARUS DENGAN RESEP DOKTER**

ANORO ELLIPTA, Box, 1 Ellipta inhaler @30 doses

Reg. No. XXXXXXXXXXXXXXXXX

Manufactured by  
GlaxoSmithKline LLC  
Zebulon, USA

Imported by  
PT Glaxo Wellcome Indonesia  
Jakarta, Indonesia

Version number : GDS03/IP104 – transfer to Zebulon + new GSK logo  
Date of issue : 11 April 2014

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## ANORO ELLIPTA

### Umeclidinium/Vilanterol

Penggunaan obat ini tunduk terhadap pengawasan tambahan. Hal ini memungkinkan identifikasi cepat untuk informasi keamanan baru. Anda dapat membantu dengan melaporkan efek samping apapun yang mungkin Anda dapatkan. Lihat *Bagian 4* untuk melaporkan efek samping.

**Baca keseluruhan brosur ini secara teliti sebelum Anda mulai menggunakan ANORO Ellipta karena brosur ini mengandung informasi penting untuk Anda.**

- Simpan petunjuk ini. Anda mungkin membutuhkannya untuk dibaca kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat.
- ANORO Ellipta ini hanya diresepkan kepada Anda. Jangan diberikan kepada orang lain. Hal tersebut dapat membahayakan mereka, meskipun gejala penyakit mereka sama dengan gejala Anda.
- Jika Anda merasakan efek samping, bicarakan dengan dokter, apoteker, atau perawat. Termasuk kemungkinan efek samping lain yang tidak tertulis dalam petunjuk ini. Lihat *Bagian 4*.

#### Apa Saja yang Ada dalam Petunjuk Ini:

1. Apa itu ANORO dan digunakan untuk apa
2. Apa yang perlu Anda ketahui sebelum menggunakan ANORO
3. Bagaimana cara menggunakan ANORO
4. Efek samping yang mungkin terjadi
5. Bagaimana cara penyimpanan ANORO
6. Isi dari kemasan dan informasi lain
7. Cara pakai

#### 1 Apa itu ANORO dan digunakan untuk apa

##### Apa Itu ANORO

ANORO mengandung 2 zat aktif yaitu umeclidinium dan vilanterol. Kedua zat tersebut masuk ke dalam kelompok obat bronkodilator.

##### Digunakan Untuk Apa ANORO

ANORO digunakan untuk terapi Penyakit Paru Obstruktif Kronis (PPOK) pada pasien dewasa. PPOK adalah kondisi jangka panjang ditandai dengan kesulitan bernapas yang secara perlahan akan memburuk.

Pada pasien PPOK, terjadi pengencangan otot di sekitar saluran napas. Obat ini menghambat pengencangan otot tersebut, mempermudah udara keluar masuk paru-paru. Pada penggunaan rutin, ANORO dapat membantu mengontrol kesulitan bernapas Anda dan mengurangi efek PPOK.

**ANORO tidak digunakan untuk mengatasi serangan mendadak dari sesak napas atau mengi.**

Jika Anda terkena serangan ini, Anda harus segera menggunakan inhaler pelega kerja cepat (seperti salbutamol).

#### 2 Apa yang perlu Anda ketahui sebelum menggunakan ANORO

##### Jangan Gunakan ANORO:

Jika Anda **alergi** terhadap umeclidinium, vilanterol, atau bahan lain dari ANORO (terdaftar di *Bagian 6*).

Jika Anda merasa hal tersebut di atas berlaku untuk Anda, **jangan gunakan ANORO** hingga Anda berkonsultasi ke dokter.

##### Perhatian dan Pencegahan

Bicarakan dengan dokter Anda sebelum menggunakan ANORO:

- Jika Anda memiliki **asma** (jangan gunakan ANORO untuk mengobati asma).
- Jika Anda memiliki **gangguan jantung** atau **tekanan darah tinggi**.
- Jika Anda memiliki **glaukoma** (penyakit pada mata).

- Jika Anda memiliki **pembesaran prostat, kesulitan berkemih** atau **penyumbatan di kandung kemih**.
  - Jika Anda menderita **epilepsi**.
  - Jika Anda memiliki **masalah kelenjar tiroid**.
  - Jika Anda memiliki **diabetes**.
  - Jika Anda memiliki **penyakit hati yang berat**.
- Pastikan dengan dokter** jika Anda merasa hal tersebut di atas berlaku terhadap Anda.

### **Kesulitan Bernapas Mendadak**

Jika Anda merasa dada tertekan, batuk, mengi atau sesak napas yang muncul segera setelah menggunakan ANORO:

**Hentikan penggunaan obat dan segera cari pertolongan medis karena Anda mungkin mengalami kondisi serius yang disebut bronkospasme paradoksal.**

### **Masalah pada Mata Selama Perawatan dengan ANORO**

Jika Anda mengalami sakit mata atau rasa tidak nyaman, penglihatan kabur sementara, terlihat lingkaran cahaya atau gambar berwarna yang berhubungan dengan mata merah selama perawatan dengan ANORO:

**Hentikan penggunaan obat dan segera cari pertolongan medis**, hal ini dapat merupakan tanda serangan akut dari glaukoma.

### **Anak-anak dan Remaja**

ANORO seharusnya tidak diberikan kepada **anak-anak atau remaja di bawah usia 18 tahun**.

### **Obat Lain dan ANORO**

Beri tahu dokter atau apoteker jika Anda sedang, baru saja, atau akan menggunakan obat lain.

Beberapa obat dapat mempengaruhi cara kerja ANORO, atau membuat Anda lebih mungkin akan terkena efek samping. Obat tersebut meliputi:

- Obat beta bloker (seperti propranolol), untuk terapi **tekanan darah tinggi** atau **gangguan jantung** lainnya.
- Ketokonazole atau itraconazole, untuk terapi **infeksi yang disebabkan jamur**.
- Clarithromycin atau telithromycin, untuk terapi **infeksi yang disebabkan bakteri**.
- Ritonavir, untuk terapi **infeksi HIV**.
- Obat yang menurunkan kadar potassium dalam darah, seperti obat-obatan diuretik.
- Obat kinerja cepat lain untuk terapi gangguan pernapasan yang serupa, seperti tiotropium dan indicaterol. Jangan gunakan ANORO jika Anda sedang menggunakan obat tersebut.

**Beritahukan dokter atau apoteker** jika Anda sedang menggunakan obat-obatan di atas.

### **Kehamilan, Menyusui, dan Kesuburan**

Jika Anda hamil atau sedang menyusui, merasa mungkin hamil, atau berencana untuk memiliki anak, **tanyakan saran ke dokter Anda** sebelum menggunakan ANORO. Anda sebaiknya tidak menggunakan ANORO jika Anda hamil kecuali atas saran dokter.

Tidak diketahui apakah bahan-bahan ANORO dapat melalui ASI. **Jika Anda sedang menyusui, Anda harus berkonsultasi ke dokter** sebelum Anda menggunakan ANORO. Anda sebaiknya tidak menggunakan ANORO jika Anda sedang menyusui kecuali atas saran dokter.

### **Berkendara dan Menjalankan Mesin**

ANORO tidak mempengaruhi kemampuan Anda mengemudi atau menjalankan mesin.

### **ANORO Mengandung Laktosa**

Jika Anda sudah diberitahu oleh dokter bahwa Anda intoleran terhadap gula, hubungi dokter Anda sebelum menggunakan ANORO.

## **3 Bagaimana menggunakan ANORO**

Selalu gunakan obat sesuai petunjuk dokter. Pastikan dengan dokter atau apoteker apabila Anda tidak yakin.

**Dosis yang direkomendasikan** adalah satu kali hirupan satu kali sehari pada waktu yang sama. Anda hanya butuh menghirup satu kali sehari karena efek kerja ANORO bertahan sampai 24 jam.

**Jangan gunakan melebihi dosis anjuran dokter.**

#### **Gunakan ANORO Secara Teratur**

Sangat penting untuk Anda menggunakan ANORO setiap hari, seperti yang dianjurkan oleh dokter. Hal ini akan membantu Anda bebas dari munculnya gejala selama sehari semalam.

**ANORO tidak** digunakan untuk mengatasi **serangan mendadak dari sesak napas atau mengi**. Jika Anda terkena serangan ini, Anda harus segera menggunakan inhaler pelega kerja cepat (seperti salbutamol).

#### **Bagaimana Cara Menggunakan Inhaler Elipta**

Lihat *Bagian 7* dalam brosur ini untuk informasi lengkapnya.

Untuk menggunakan ANORO, bernapaslah ke dalam paru-paru melalui mulut menggunakan inhaler Elipta.

#### **Jika Gejala Anda Tidak Membaik**

Jika gejala PPOK (sesak napas, mengi, batuk) tidak membaik atau menjadi semakin memburuk, atau jika Anda juga sedang menggunakan inhaler aksi cepat lebih sering:

**Hubungi dokter Anda secepat mungkin.**

#### **Jika Anda Menggunakan ANORO Lebih dari yang Seharusnya**

Jika Anda secara tidak sengaja menggunakan ANORO lebih banyak, **segera hubungi dokter atau apoteker untuk meminta saran** apakah Anda butuh perhatian medis. Jika memungkinkan, tunjukkan kepada mereka inhaler Elipta, kemasan, atau brosur ini. Anda mungkin merasakan bahwa jantung Anda berdetak lebih kencang dari biasanya, tubuh Anda menggigil, Anda merasakan gangguan penglihatan, mulut kering, atau sakit kepala.

#### **Jika Anda Lupa untuk Menggunakan ANORO**

**Jangan menggunakan dosis tambahan untuk mengganti dosis yang terlewatkan.** Cukup gunakan dosis selanjutnya di waktu yang sama. Jika Anda menjadi mengi atau sesak napas, gunakan inhaler aksi cepat Anda (seperti salbutamol), kemudian carilah saran medis.

#### **Jika Anda Menghentikan Penggunaan ANORO**

Gunakan ANORO sesuai dengan jangka waktu yang direkomendasikan dokter. ANORO hanya akan efektif selama Anda menggunakannya. Jangan menghentikan penggunaan kecuali disarankan oleh dokter, bahkan meski Anda merasa sehat, karena gejala Anda mungkin dapat memburuk.

Jika Anda memiliki pertanyaan lebih jauh pada penggunaan obat ini, tanyakan dokter, apoteker, atau perawat.

#### **4 Efek samping yang mungkin terjadi**

Seperti obat lainnya, obat ini dapat menyebabkan efek samping, meski tidak semua pasien mengalaminya.

Tidak umum terjadi reaksi alergi terhadap ANORO (terjadi kurang dari 1 dalam 100 pasien).

Jika Anda merasakan gejala di bawah ini setelah menggunakan ANORO, **hentikan penggunaan dan segera hubungi dokter.**

- Ruam pada kulit (gatal dan bintik-bintik) atau kemerahan.
- Bengkak, kadang pada wajah atau mulut (angioedema).
- Suara menjadi serak, batuk, atau kesulitan bernapas.
- Mendadak merasa lemah atau kepala terasa ringan (yang dapat mengakibatkan roboh atau hilang kesadaran).

#### **Kesulitan Bernapas Mendadak**

Jarang terjadi kesulitan bernapas mendadak setelah menggunakan ANORO (terjadi kurang dari 1 dalam 1.000 pasien). Jika Anda merasa dada tertekan, batuk, mengi atau sesak napas yang muncul segera setelah menggunakan ANORO:

**Hentikan penggunaan obat dan segera cari pertolongan medis karena Anda mungkin mengalami kondisi serius yang disebut bronkospasme paradoksal.**

#### **Efek Samping yang Umum Terjadi**

Hal ini mungkin dapat terjadi pada  $\geq 1/100$  dan  $< 1/10$  pasien:

- infeksi saluran kemih
- sinusitis
- nasofaringitis
- radang tenggorokan
- infeksi saluran pernapasan atas
- sakit kepala
- batuk
- nyeri orofaringeal
- konstipasi
- mulut kering.

#### **Efek Samping yang Tidak Umum Terjadi**

Hal ini mungkin dapat terjadi pada  $\geq 1/1.000$  dan  $< 1/100$  pasien:

- ruam pada kulit atau kemerahan
- tremor
- *dysgeusia* (mulut terasa asam atau tidak enak)
- fibrilasi atrial
- takikardi supraventrikular
- *rhythm idioventricular*
- takikardi
- ekstrasistol supraventricular
- palpitasi
- *dysphonia* (gangguan pada suara).

#### **Efek Samping yang Jarang Terjadi**

Hal ini mungkin dapat terjadi pada  $\geq 1/10,000$  dan  $< 1/1,000$  pasien:

- anafilaksis, angioedema, dan urtikaria
- penglihatan kabur
- glaukoma
- peningkatan tekanan dalam bola mata
- bronkospasme paradoksal
- retensi kemih
- nyeri saat berkemih
- obstruksi kandung kemih.

#### **Pelaporan Efek Samping**

Jika Anda merasakan efek samping, laporkan ke dokter, apoteker, atau perawat. Termasuk kemungkinan efek samping lain yang tidak tertulis dalam informasi ini. Anda juga dapat melaporkan efek samping secara langsung lewat telepon ke +628118438228 atau email ke [yqq68540@gsk.com](mailto:yqq68540@gsk.com). Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih terhadap keamanan obat ini.

### **5 Bagaimana cara penyimpanan ANORO**

Simpan obat ini jauh dari jangkauan anak-anak.

Jangan menggunakan obat setelah tanggal kedaluwarsa, yang ditulis pada label dan karton setelah kata 'EXP'. Tanggal kedaluwarsa merujuk pada hari terakhir bulan tersebut.

Simpan di dalam wadah tertutup supaya terjaga dari kelembaban dan jangan membuka *foil* penutup hingga siap untuk penggunaan pertama. Setelah *foil* penutup terbuka, inhaler Ellipta dapat digunakan hingga 6 minggu ke depan, dimulai dari tanggal pembukaan bungkus kemasan. Tulis tanggal kapan

inhaler Ellipta harus dimusnahkan pada bagian label yang tersedia. Tanggal harus ditambahkan segera setelah inhaler dibuka dari bungkus kemasannya.

Jangan menyimpan di atas suhu 30°C.

Jika Anda menyimpan dalam lemari es, biarkan inhaler Ellipta kembali ke suhu ruangan minimal satu jam sebelum penggunaan.

Jangan membuang obat apapun di air limbah atau limbah rumah tangga. Tanyakan pada apoteker bagaimana membuang obat yang tidak digunakan lagi. Langkah ini membantu dalam menjaga lingkungan.

## 6 Isi dari kemasan dan informasi lain

### Apa Kandungan ANORO

Zat aktif ANORO adalah umeclidinium bromide dan vilanterol.

Setiap satu hirupan memberikan dosis terlepas (dosis yang meninggalkan *mouthpiece*) sebanyak 55 mikrogram umeclidinium (setara dengan 65 mikrogram umeclidinium bromide) dan 22 mikrogram vilanterol (dalam bentuk trifenate).

Dosis di atas setara dengan dosis *pre-dispensed* 62.5 mikrogram umeclidinium (setara dengan 74.2 mikrogram umeclidinium bromide) dan 25 mikrogram vilanterol (dalam bentuk trifenate).

Bahan lainnya adalah lactose monohidrate dan magnesium stearate.

### Seperti Apa Bentuk ANORO dan Isi dari Kemasan

Inhaler Ellipta sendiri terdiri dari komponen plastik abu-abu, tutup *mouthpiece* berwarna merah, dan penghitung dosis. ANORO dikemas dalam *tray* berlaminasi *foil* dengan tutup *foil* yang mudah dikelupas. Di dalam *tray* terdapat penyerap lembab untuk mengurangi kelembaban di dalam kemasan.

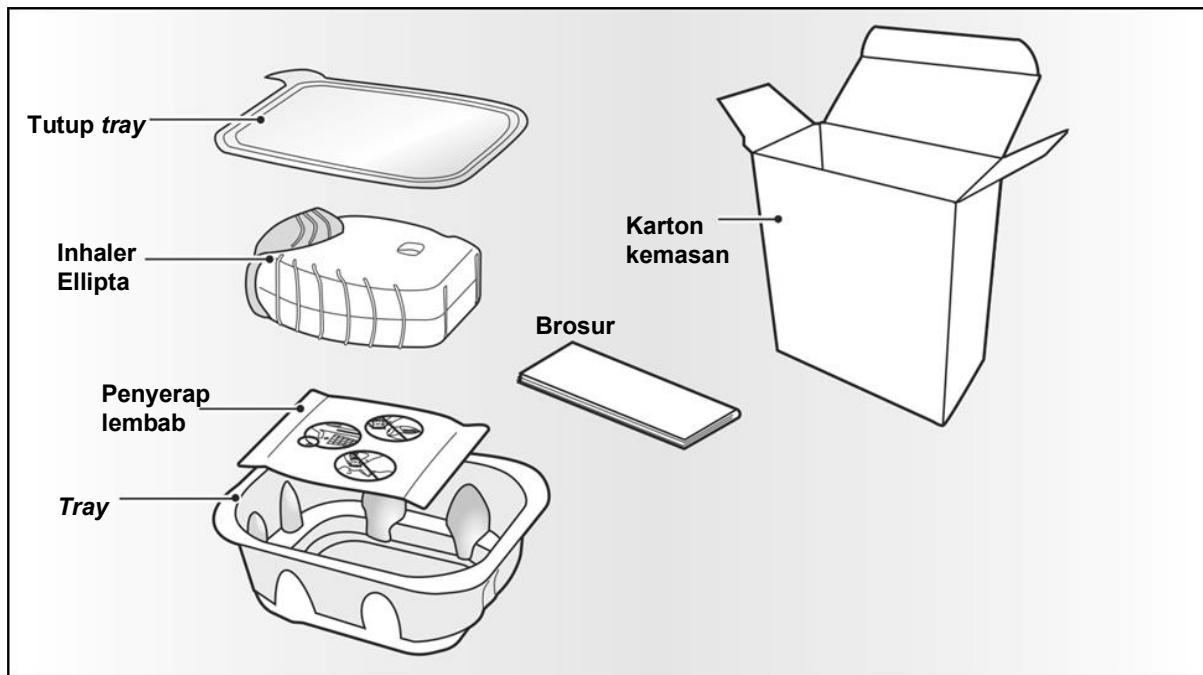
Zat aktif berupa serbuk putih pada strip blister di dalam inhaler Ellipta. Tiap inhaler mengandung 30 dosis.

## 7 Cara Pakai

### Apa Itu Inhaler Ellipta?

Saat pertama kali Anda menggunakan ANORO, Anda tidak perlu mencoba apakah inhaler Ellipta bekerja dengan baik; inhaler Ellipta dari awal mengandung dosis terukur yang siap untuk langsung digunakan.

### Kandungan dalam Karton Kemasan ANORO



Inhaler dikemas dalam *tray*. **Jangan membukanya hingga Anda siap untuk menghirup dosis obat.** Saat Anda siap untuk menggunakan inhaler Ellipta, kupas tutup *tray*. *Tray* mengandung sebungkus penyerap lembab untuk mengurangi kelembaban. Buanglah bungkus penyerap lembab tersebut, **jangan** dibuka, dimakan, atau menghirupnya.



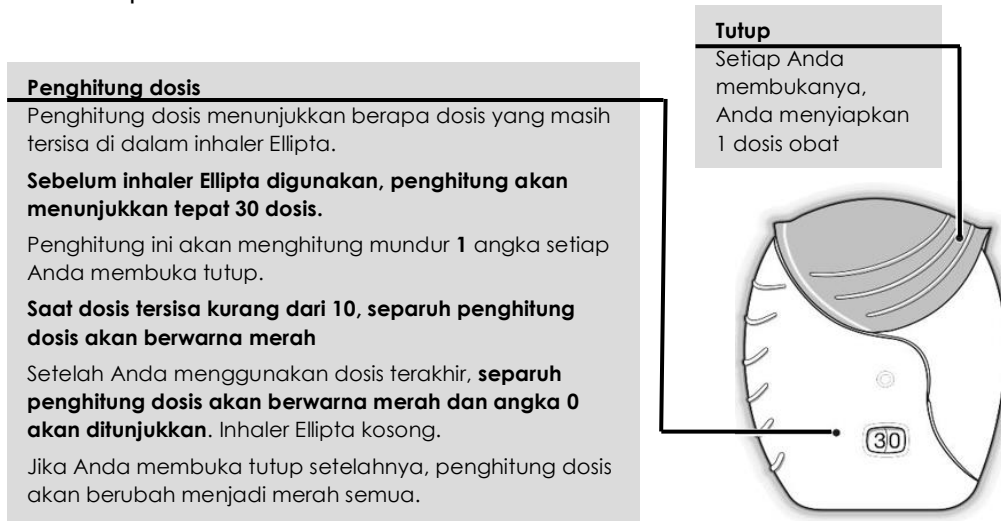
Ketika Anda mengambil inhaler Ellipta keluar dari kemasannya, inhaler Ellipta akan dalam keadaan 'tertutup'. **Jangan membukanya hingga Anda siap untuk menghirup dosis obat.** Ketika *tray* dibuka, tulis tanggal 'Pemusnahan' pada bagian label inhaler yang tersedia. Tanggal 'Pemusnahan' adalah 6 minggu dari tanggal *tray* dibuka. Setelah tanggal 'Pemusnahan' tersebut sebaiknya inhaler Ellipta tidak digunakan lagi. *Tray* dapat dimusnahkan setelah dibuka pertama kali.

**Baca Langkah Berikut Sebelum Anda Memulai**

**Jika Anda membuka dan menutup tutup tanpa menghirup obat, Anda akan kehilangan dosis.**

Dosis yang hilang akan aman tertahan di dalam inhaler, namun tidak lagi tersedia.

Tidak memungkinkan untuk secara tidak sengaja menggunakan kelebihan dosis atau dosis ganda dalam satu hirupan.

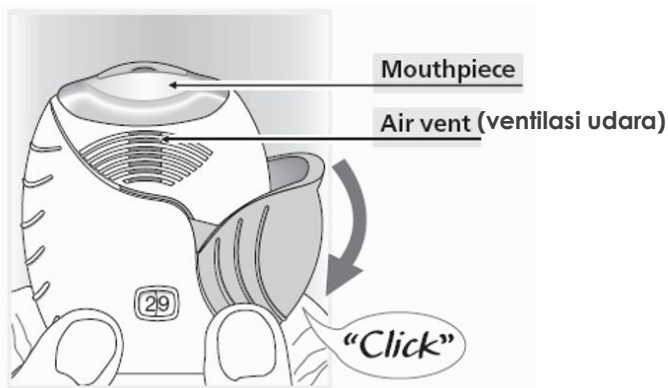


### 1) Menyiapkan dosis

Buka tutup saat Anda sudah siap menggunakan dosis Anda.

Jangan kocok inhaler Ellipta.

- Geser tutup ke bawah hingga terdengar bunyi 'klik'.



Sekarang, obat Anda siap untuk dihirup.

Penghitung dosis berkurang 1 untuk memastikannya.

- **Jika penghitung dosis Anda tidak berkurang ketika terdengar bunyi 'klik', inhaler Ellipta tidak akan menghantarkan obat.**  
Kembalikan produk obat ini ke apoteker untuk meminta saran.

### 2) Hirup obat Anda

- Saat inhaler Anda pegang jauh dari mulut, hembuskan napas sebanyak dan senyaman Anda. **Jangan** hembuskan napas ke dalam inhaler.
- **Letakkan *mouthpiece* di antara bibir Anda, dan tutup rapat menyelubungi *mouthpiece*.** **Jangan** tutup ventilasi udara dengan jari Anda.



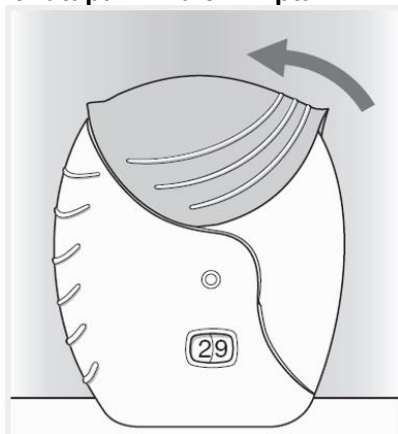
Bibir Anda menyesuaikan sekeliling bentuk *mouthpiece* untuk penghirupan.  
Jangan menutup ventilasi udara dengan jari Anda.

- Tarik napas kuat dan panjang melalui mulut. Tahan napas tersebut selama Anda mampu (minimal 3-4 detik).
- Lepas inhaler Ellipta dari mulut Anda.
- Hembuskan napas perlahan.

Kemungkinan Anda tidak dapat merasakan obatnya, meski Anda menggunakan inhaler dengan benar.

Jika Anda ingin membersihkan *mouthpiece*, gunakan tisu kering sebelum menutupnya.

### 3) Penutupan inhaler Ellipta



Geser tutup ke atas sejauh dapat tergeser untuk menutup *mouthpiece*.

### HARUS DENGAN RESEP DOKTER

ANORO ELLIPTA, Dus, 1 inhaler Ellipta @ 30 dosis

No. Reg. XXXXXXXXXXXXXXXXX

Diproduksi oleh  
GlaxoSmithKline LLC  
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Diimpor oleh  
PT Glaxo Wellcome Indonesia  
Jakarta, Indonesia

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