

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**205382Orig1s000**

**LABELING**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use INCRUSE ELLIPTA safely and effectively. See full prescribing information for INCRUSE ELLIPTA.

**INCRUSE ELLIPTA (umeclidinium inhalation powder)  
FOR ORAL INHALATION USE  
Initial U.S. Approval: 2013**

**INDICATIONS AND USAGE**

INCRUSE ELLIPTA is an anticholinergic indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD). (1)

**DOSAGE AND ADMINISTRATION**

- For oral inhalation only. (2)
- Maintenance treatment of COPD: 1 inhalation of INCRUSE ELLIPTA once daily. (2)

**DOSAGE FORMS AND STRENGTHS**

Inhalation Powder. Inhaler containing a double-foil blister strip of powder formulation for oral inhalation. Each blister contains umeclidinium 62.5 mcg. (3)

**CONTRAINDICATIONS**

- Severe hypersensitivity to milk proteins. (4)
- Hypersensitivity to any ingredient. (4)

**WARNINGS AND PRECAUTIONS**

- Do not initiate in acutely deteriorating COPD or to treat acute symptoms. (5.1)
- If paradoxical bronchospasm occurs, discontinue INCRUSE ELLIPTA and institute alternative therapy. (5.2)
- Worsening of narrow-angle glaucoma may occur. Use with caution in patients with narrow-angle glaucoma and instruct patients to contact a physician immediately if symptoms occur. (5.4)
- Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and instruct patients to contact a physician immediately if symptoms occur. (5.5)

**ADVERSE REACTIONS**

Most common adverse reactions (incidence ≥2% and more common than placebo) include nasopharyngitis, upper respiratory tract infection, cough, arthralgia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

Anticholinergics: May interact additively with concomitantly used anticholinergic medications. Avoid administration of INCRUSE ELLIPTA with other anticholinergic-containing drugs. (7.1)

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

Revised: XX/20XX

**FULL PRESCRIBING INFORMATION: CONTENTS\***

- 1 INDICATIONS AND USAGE**
- 2 DOSAGE AND ADMINISTRATION**
- 3 DOSAGE FORMS AND STRENGTHS**
- 4 CONTRAINDICATIONS**
- 5 WARNINGS AND PRECAUTIONS**
  - 5.1 Deterioration of Disease and Acute Episodes
  - 5.2 Paradoxical Bronchospasm
  - 5.3 Hypersensitivity Reactions
  - 5.4 Worsening of Narrow-Angle Glaucoma
  - 5.5 Worsening of Urinary Retention
- 6 ADVERSE REACTIONS**
  - 6.1 Clinical Trials Experience
- 7 DRUG INTERACTIONS**
  - 7.1 Anticholinergics
- 8 USE IN SPECIFIC POPULATIONS**
  - 8.1 Pregnancy
  - 8.2 Labor and Delivery
  - 8.3 Nursing Mothers

- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment
- 8.7 Renal Impairment
- 10 OVERDOSAGE**
- 11 DESCRIPTION**
- 12 CLINICAL PHARMACOLOGY**
  - 12.1 Mechanism of Action
  - 12.2 Pharmacodynamics
  - 12.3 Pharmacokinetics
- 13 NONCLINICAL TOXICOLOGY**
  - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 14 CLINICAL STUDIES**
  - 14.1 Dose-Ranging Trials
  - 14.2 Confirmatory Trials
- 16 HOW SUPPLIED/STORAGE AND HANDLING**
- 17 PATIENT COUNSELING INFORMATION**

\*Sections or subsections omitted from the full prescribing information are not listed.

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 INCRUSE™ ELLIPTA® is an anticholinergic indicated for the long-term, once-daily,  
4 maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary  
5 disease (COPD), including chronic bronchitis and/or emphysema.

6 **2 DOSAGE AND ADMINISTRATION**

7 INCRUSE ELLIPTA (umeclidinium 62.5 mcg) should be administered as 1 inhalation  
8 once daily by the orally inhaled route only.

9 INCRUSE ELLIPTA should be taken at the same time every day. Do not use INCRUSE  
10 ELLIPTA more than 1 time every 24 hours.

11 No dosage adjustment is required for geriatric patients, patients with renal impairment, or  
12 patients with moderate hepatic impairment [*see Clinical Pharmacology (12.3)*].

13 **3 DOSAGE FORMS AND STRENGTHS**

14 Inhalation Powder. Disposable light grey and light green plastic inhaler containing a  
15 double-foil blister strip with 30 blisters containing powder intended for oral inhalation only.  
16 Each blister contains umeclidinium 62.5 mcg. An institutional pack containing a blister strip with  
17 7 blisters is also available.

18 **4 CONTRAINDICATIONS**

19 The use of INCRUSE ELLIPTA is contraindicated in the following conditions:

- 20 • Severe hypersensitivity to milk proteins [*see Warnings and Precautions (5.3)*]  
21 • Hypersensitivity to umeclidinium or any of the excipients [*see Warnings and Precautions*  
22 (*5.3*), *Description (11)*]

23 **5 WARNINGS AND PRECAUTIONS**

24 **5.1 Deterioration of Disease and Acute Episodes**

25 INCRUSE ELLIPTA should not be initiated in patients during rapidly deteriorating or  
26 potentially life-threatening episodes of COPD. INCRUSE ELLIPTA has not been studied in  
27 subjects with acutely deteriorating COPD. The initiation of INCRUSE ELLIPTA in this setting  
28 is not appropriate.

29 INCRUSE ELLIPTA should not be used for the relief of acute symptoms, i.e., as rescue  
30 therapy for the treatment of acute episodes of bronchospasm. INCRUSE ELLIPTA has not been  
31 studied in the relief of acute symptoms and extra doses should not be used for that purpose.  
32 Acute symptoms should be treated with an inhaled, short-acting beta<sub>2</sub>-agonist.

33 COPD may deteriorate acutely over a period of hours or chronically over several days or  
34 longer. If INCRUSE ELLIPTA no longer controls symptoms of bronchoconstriction; the  
35 patient's inhaled, short-acting beta<sub>2</sub>-agonist becomes less effective; or the patient needs more  
36 short-acting beta<sub>2</sub>-agonist than usual, these may be markers of deterioration of disease. In this

37 setting a re-evaluation of the patient and the COPD treatment regimen should be undertaken at  
38 once. Increasing the daily dose of INCRUSE ELLIPTA beyond the recommended dose is not  
39 appropriate in this situation.

## 40 **5.2 Paradoxical Bronchospasm**

41 As with other inhaled medicines, INCRUSE ELLIPTA can produce paradoxical  
42 bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs following  
43 dosing with INCRUSE ELLIPTA, it should be treated immediately with an inhaled, short-acting  
44 bronchodilator; INCRUSE ELLIPTA should be discontinued immediately; and alternative  
45 therapy should be instituted.

## 46 **5.3 Hypersensitivity Reactions**

47 Hypersensitivity reactions may occur after administration of INCRUSE ELLIPTA. There  
48 have been reports of anaphylactic reactions in patients with severe milk protein allergy after  
49 inhalation of other powder products containing lactose; therefore, patients with severe milk  
50 protein allergy should not use INCRUSE ELLIPTA [see *Contraindications (4)*].

## 51 **5.4 Worsening of Narrow-Angle Glaucoma**

52 INCRUSE ELLIPTA should be used with caution in patients with narrow-angle  
53 glaucoma. Prescribers and patients should be alert for signs and symptoms of acute narrow-angle  
54 glaucoma (e.g., eye pain or discomfort, blurred vision, visual halos or colored images in  
55 association with red eyes from conjunctival congestion and corneal edema). Instruct patients to  
56 consult a physician immediately if any of these signs or symptoms develop.

## 57 **5.5 Worsening of Urinary Retention**

58 INCRUSE ELLIPTA should be used with caution in patients with urinary retention.  
59 Prescribers and patients should be alert for signs and symptoms of urinary retention (e.g.,  
60 difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or  
61 bladder-neck obstruction. Instruct patients to consult a physician immediately if any of these  
62 signs or symptoms develop.

## 63 **6 ADVERSE REACTIONS**

64 The following adverse reactions are described in greater detail in other sections:

- 65 • Paradoxical bronchospasm [see *Warnings and Precautions (5.2)*]
- 66 • Worsening of narrow-angle glaucoma [see *Warnings and Precautions (5.4)*]
- 67 • Worsening of urinary retention [see *Warnings and Precautions (5.5)*]

### 68 **6.1 Clinical Trials Experience**

69 Because clinical trials are conducted under widely varying conditions, adverse reaction  
70 rates observed in the clinical trials of a drug cannot be directly compared with rates in the  
71 clinical trials of another drug and may not reflect the rates observed in practice.

72 A total of 1,663 subjects with COPD across 8 clinical trials (mean age: 62.7 years; 89%  
73 white; 65% male across all treatments, including placebo) received at least 1 inhalation dose of  
74 umeclidinium at doses of 62.5 or 125 mcg. In the 4 randomized, double-blind, placebo- or  
75 active-controlled efficacy clinical trials, 1,185 subjects received umeclidinium for up to 24

76 weeks, of which 487 subjects received the recommended dose of umeclidinium 62.5 mcg. In a  
 77 12-month, randomized, double-blind, placebo-controlled, long-term safety trial, 227 subjects  
 78 received umeclidinium 125 mcg for up to 52 weeks [see *Clinical Studies (14)*].

79 The incidence of adverse reactions associated with INCRUSE ELLIPTA in Table 1 is  
 80 based upon 2 placebo-controlled efficacy trials: one 12-week trial and one 24-week trial.

81

82 **Table 1. Adverse Reactions With INCRUSE ELLIPTA With  $\geq 1\%$  Incidence and More**  
 83 **Common Than With Placebo in Subjects With Chronic Obstructive Pulmonary Disease**

<b>Adverse Reaction</b>	<b>INCRUSE ELLIPTA (n = 487) %</b>	<b>Placebo (n = 348) %</b>
Infections and infestations		
Nasopharyngitis	8%	7%
Upper respiratory tract infection	5%	4%
Pharyngitis	1%	<1%
Viral upper respiratory tract infection	1%	<1%
Respiratory, thoracic, and mediastinal disorders		
Cough	3%	2%
Musculoskeletal and connective tissue disorders		
Arthralgia	2%	1%
Myalgia	1%	<1%
Gastrointestinal disorders		
Abdominal pain upper	1%	<1%
Toothache	1%	<1%
Injury, poisoning, and procedural complications		
Contusion	1%	<1%
Cardiac disorders		
Tachycardia	1%	<1%

84

85 Other adverse reactions with INCRUSE ELLIPTA observed with an incidence less than  
 86 1% but more common than placebo included atrial fibrillation.

87 In a long-term safety trial, 336 subjects (n = 227 umeclidinium 125 mcg, n = 109  
 88 placebo) were treated for up to 52 weeks with umeclidinium 125 mcg or placebo. The  
 89 demographic and baseline characteristics of the long-term safety trial were similar to those of the  
 90 efficacy trials described above. Adverse reactions that occurred with a frequency greater than or  
 91 equal to 1% in subjects receiving umeclidinium 125 mcg that exceeded that in placebo in this

92 trial were: nasopharyngitis, upper respiratory tract infection, urinary tract infection, pharyngitis,  
93 pneumonia, lower respiratory tract infection, rhinitis, supraventricular tachycardia,  
94 supraventricular extrasystoles, sinus tachycardia, idioventricular rhythm, headache, dizziness,  
95 sinus headache, cough, back pain, arthralgia, pain in extremity, neck pain, myalgia, nausea,  
96 dyspepsia, diarrhea, rash, depression, and vertigo.

## 97 **7 DRUG INTERACTIONS**

### 98 **7.1 Anticholinergics**

99 There is potential for an additive interaction with concomitantly used anticholinergic  
100 medicines. Therefore, avoid coadministration of INCRUSE ELLIPTA with other  
101 anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects  
102 [see *Warnings and Precautions (5.4, 5.5), Adverse Reactions (6)*].

## 103 **8 USE IN SPECIFIC POPULATIONS**

### 104 **8.1 Pregnancy**

105 Teratogenic Effects: Pregnancy Category C. There are no adequate and well-controlled  
106 trials with INCRUSE ELLIPTA in pregnant women. Because animal reproduction studies are  
107 not always predictive of human response, INCRUSE ELLIPTA should be used during pregnancy  
108 only if the potential benefit justifies the potential risk to the fetus. Women should be advised to  
109 contact their physicians if they become pregnant while taking INCRUSE ELLIPTA.

110 There was no evidence of teratogenic effects in rats and rabbits at approximately 50 and  
111 200 times, respectively, the MRHDID (maximum recommended human daily inhaled dose) in  
112 adults (on an AUC basis at maternal inhaled doses up to 278 mcg/kg/day in rats and maternal  
113 subcutaneous doses up to 180 mcg/kg/day in rabbits).

114 Nonteratogenic Effects: There were no effects on perinatal and postnatal developments  
115 in rats at approximately 80 times the MRHDID in adults (on an AUC basis at maternal  
116 subcutaneous doses up to 180 mcg/kg/day).

### 117 **8.2 Labor and Delivery**

118 There are no adequate and well-controlled human trials that have investigated the effects  
119 of INCRUSE ELLIPTA during labor and delivery. INCRUSE ELLIPTA should be used during  
120 labor only if the potential benefit justifies the potential risk.

### 121 **8.3 Nursing Mothers**

122 It is not known whether INCRUSE ELLIPTA is excreted in human breast milk. Because  
123 many drugs are excreted in human milk, caution should be exercised when INCRUSE ELLIPTA  
124 is administered to a nursing woman. Since there are no data from well-controlled human studies  
125 on the use of INCRUSE ELLIPTA by nursing mothers, a decision should be made whether to  
126 discontinue nursing or to discontinue INCRUSE ELLIPTA, taking into account the importance  
127 of INCRUSE ELLIPTA to the mother.

128 Subcutaneous administration of umeclidinium to lactating rats at approximately 25 times  
129 the MRHDID in adults resulted in a quantifiable level of umeclidinium in 2 pups, which may  
130 indicate transfer of umeclidinium in milk.

131 **8.4 Pediatric Use**

132 INCRUSE ELLIPTA is not indicated for use in children. The safety and efficacy in  
133 pediatric patients have not been established.

134 **8.5 Geriatric Use**

135 Based on available data, no adjustment of the dosage of INCRUSE ELLIPTA in geriatric  
136 patients is necessary, but greater sensitivity in some older individuals cannot be ruled out.

137 Clinical trials of INCRUSE ELLIPTA included 810 subjects aged 65 years and older,  
138 and, of those, 183 subjects were aged 75 years and older. No overall differences in safety or  
139 effectiveness were observed between these subjects and younger subjects, and other reported  
140 clinical experience has not identified differences in responses between the elderly and younger  
141 subjects.

142 **8.6 Hepatic Impairment**

143 Patients with moderate hepatic impairment (Child-Pugh score of 7-9) showed no relevant  
144 increases in  $C_{max}$  or AUC, nor did protein binding differ between subjects with moderate hepatic  
145 impairment and their healthy controls. Studies in subjects with severe hepatic impairment have  
146 not been performed [see *Clinical Pharmacology (12.3)*].

147 **8.7 Renal Impairment**

148 Patients with severe renal impairment (creatinine clearance less than 30 mL/min) showed  
149 no relevant increases in  $C_{max}$  or AUC, nor did protein binding differ between subjects with  
150 severe renal impairment and their healthy controls. No dosage adjustment is required in patients  
151 with renal impairment [see *Clinical Pharmacology (12.3)*].

152 **10 OVERDOSAGE**

153 No case of overdose has been reported with INCRUSE ELLIPTA.

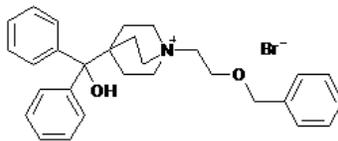
154 High doses of umeclidinium may lead to anticholinergic signs and symptoms. However,  
155 there were no systemic anticholinergic adverse effects following a once-daily inhaled dose of up  
156 to 1,000 mcg umeclidinium (16 times the maximum recommended daily dose) for 14 days in  
157 subjects with COPD.

158 Treatment of overdose consists of discontinuation of INCRUSE ELLIPTA together  
159 with institution of appropriate symptomatic and/or supportive therapy.

160 **11 DESCRIPTION**

161 INCRUSE ELLIPTA contains the active ingredient umeclidinium, an anticholinergic.

162 Umeclidinium bromide has the chemical name 1-[2-(benzyloxy)ethyl]-4-  
163 (hydroxydiphenylmethyl)-1-azoniabicyclo[2.2.2]octane bromide and the following chemical  
164 structure:



165

166 Umeclidinium bromide is a white powder with a molecular weight of 508.5, and the  
167 empirical formula is  $C_{29}H_{34}NO_2 \cdot Br$  (as a quaternary ammonium bromide compound). It is  
168 slightly soluble in water.

169 INCRUSE ELLIPTA is a light grey and light green plastic inhaler containing a double-  
170 foil blister strip. Each blister on the strip contains a white powder mix of micronized  
171 umeclidinium bromide (74.2 mcg equivalent to 62.5 mcg of umeclidinium), magnesium stearate  
172 (75 mcg), and lactose monohydrate (to 12.5 mg). The lactose monohydrate contains milk  
173 proteins. After the inhaler is activated, the powder within the blister is exposed and ready for  
174 dispersion into the airstream created by the patient inhaling through the mouthpiece.

175 Under standardized *in vitro* conditions, INCRUSE ELLIPTA delivers 55 mcg of  
176 umeclidinium per dose when tested at a flow rate of 60 L/min for 4 seconds.

177 In adult subjects with obstructive lung disease and severely compromised lung function  
178 (COPD with forced expiratory volume in 1 second/forced vital capacity [FEV<sub>1</sub>/FVC] less than  
179 70% and FEV<sub>1</sub> less than 30% predicted or FEV<sub>1</sub> less than 50% predicted plus chronic respiratory  
180 failure), mean peak inspiratory flow through the ELLIPTA inhaler was 66.5 L/min (range: 43.5  
181 to 81.0 L/min).

182 The actual amount of drug delivered to the lung will depend on patient factors, such as  
183 inspiratory flow profile.

## 184 **12 CLINICAL PHARMACOLOGY**

### 185 **12.1 Mechanism of Action**

186 Umeclidinium is a long-acting, antimuscarinic agent, which is often referred to as an  
187 anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the  
188 airways, it exhibits pharmacological effects through the inhibition of M3 receptor at the smooth  
189 muscle leading to bronchodilation. The competitive and reversible nature of antagonism was  
190 shown with human and animal origin receptors and isolated organ preparations. In preclinical *in*  
191 *vitro* as well as *in vivo* studies, prevention of methacholine and acetylcholine-induced  
192 bronchoconstrictive effects was dose-dependent and lasted longer than 24 hours. The clinical  
193 relevance of these findings is unknown. The bronchodilation following inhalation of  
194 umeclidinium is predominantly a site-specific effect.

### 195 **12.2 Pharmacodynamics**

196 Cardiac Electrophysiology: QTc interval prolongation was studied in a double-blind,  
197 multiple dose, placebo- and positive-controlled crossover trial in 86 healthy subjects. Following  
198 repeat doses of umeclidinium 500 mcg once daily (8 times the recommended dosage) for 10  
199 days, umeclidinium does not prolong QTc to any clinically relevant extent.

### 200 **12.3 Pharmacokinetics**

201 Linear pharmacokinetics was observed for umeclidinium (62.5 to 500 mcg).

202 Absorption: Umeclidinium plasma levels may not predict therapeutic effect. Following  
203 inhaled administration of umeclidinium in healthy subjects, C<sub>max</sub> occurred at 5 to 15 minutes.

204 Umeclidinium is mostly absorbed from the lung after inhaled doses with minimum contribution

205 from oral absorption. Following repeat dosing of inhaled INCRUSE ELLIPTA, steady state was  
206 achieved within 14 days with 1.8-fold accumulation.

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

209 **Metabolism:** *In vitro* data showed that umeclidinium is primarily metabolized by the  
210 enzyme cytochrome P450 2D6 (CYP2D6) and is a substrate for the P-glycoprotein (P-gp)  
211 transporter. The primary metabolic routes for umeclidinium are oxidative (hydroxylation, O-  
212 dealkylation) followed by conjugation (e.g., glucuronidation), resulting in a range of metabolites  
213 with either reduced pharmacological activity or for which the pharmacological activity has not  
214 been established. Systemic exposure to the metabolites is low.

215 **Elimination:** Following intravenous dosing with radio-labeled umeclidinium, mass  
216 balance showed 58% of the radio-label in the feces and 22% in the urine. The excretion of the  
217 drug-related material in the feces following intravenous dosing indicated elimination in the bile.  
218 Following oral dosing to healthy male subjects, radio-label recovered in feces was 92% of the  
219 total dose and that in urine was less than 1% of the total dose, suggesting negligible oral  
220 absorption. The effective half-life after once daily dosing is 11 hours.

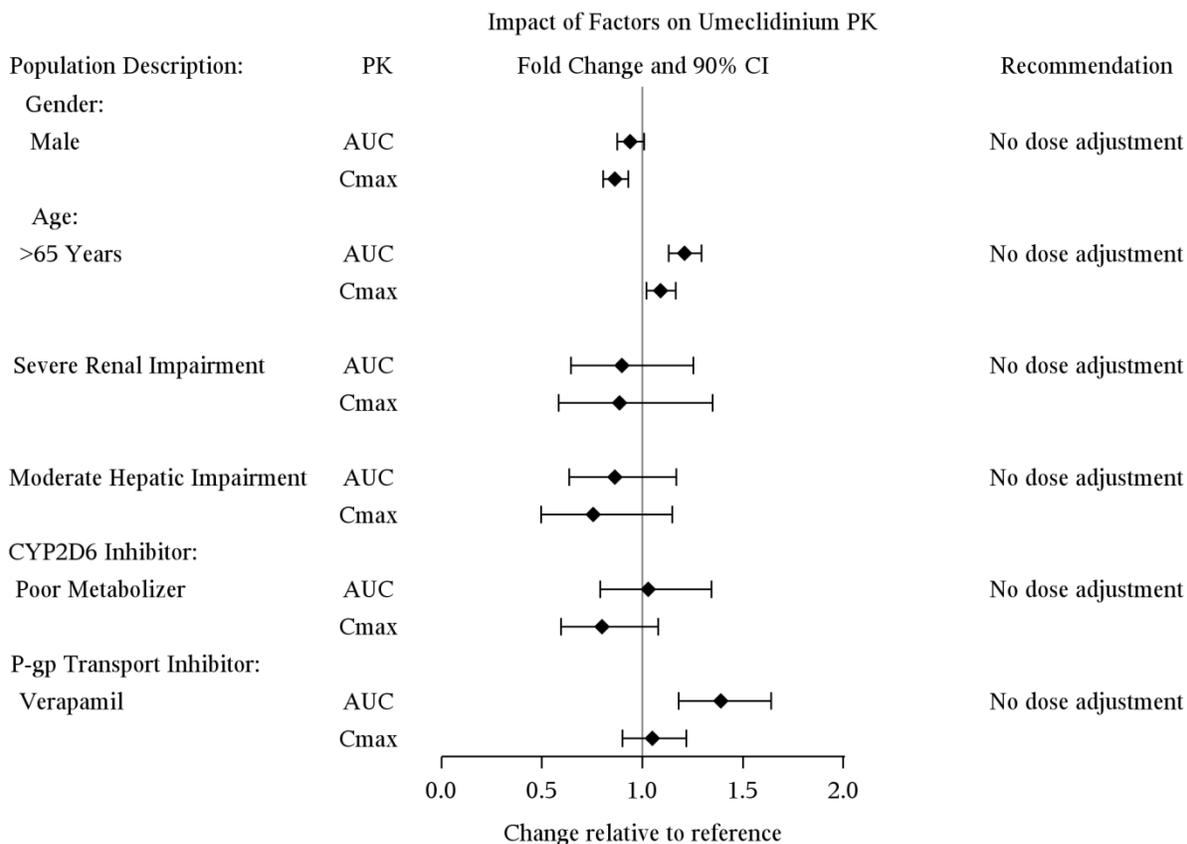
221 **Special Populations:** Population pharmacokinetic analysis showed no evidence of a  
222 clinically significant effect of age (40 to 93 years) (see Figure 1), gender (69% male) (see Figure  
223 1), inhaled corticosteroid use (48%), or weight (34 to 161 kg) on systemic exposure of  
224 umeclidinium. In addition, there was no evidence of a clinically significant effect of race.

225 ***Hepatic Impairment:*** The impact of hepatic impairment on the pharmacokinetics of  
226 INCRUSE ELLIPTA has been evaluated in subjects with moderate hepatic impairment (Child-  
227 Pugh score of 7-9). There was no evidence of an increase in systemic exposure to umeclidinium  
228 ( $C_{max}$  and AUC) (see Figure 1). There was no evidence of altered protein binding in subjects with  
229 moderate hepatic impairment compared with healthy subjects. INCRUSE ELLIPTA has not been  
230 evaluated in subjects with severe hepatic impairment.

231 ***Renal Impairment:*** The pharmacokinetics of INCRUSE ELLIPTA has been  
232 evaluated in subjects with severe renal impairment (creatinine clearance less than 30 mL/min).  
233 There was no evidence of an increase in systemic exposure to umeclidinium ( $C_{max}$  and AUC)  
234 (see Figure 1). There was no evidence of altered protein binding in subjects with severe renal  
235 impairment compared with healthy subjects.

236

237 **Figure 1. Impact of Intrinsic and Extrinsic Factors on the Systemic Exposure of**  
 238 **Umeclidinium**



239  
 240  
 241 **Drug Interactions: Umeclidinium and P-glycoprotein Transporter:** Umeclidinium is  
 242 a substrate of P-gp. The effect of the moderate P-gp transporter inhibitor verapamil (240 mg once  
 243 daily) on the steady-state pharmacokinetics of umeclidinium was assessed in healthy subjects.  
 244 No effect on umeclidinium C<sub>max</sub> was observed; however, an approximately 1.4-fold increase in  
 245 umeclidinium AUC was observed (see Figure 1).

246 **Umeclidinium and Cytochrome P450 2D6:** *In vitro* metabolism of umeclidinium is  
 247 mediated primarily by CYP2D6. However, no clinically meaningful difference in systemic  
 248 exposure to umeclidinium (500 mcg) (8 times the approved dose) was observed following repeat  
 249 daily inhaled dosing to normal (ultrarapid, extensive, and intermediate metabolizers) and  
 250 CYP2D6 poor metabolizer subjects (see Figure 1).

251 **13 NONCLINICAL TOXICOLOGY**

252 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

253 Umeclidinium produced no treatment-related increases in the incidence of tumors in 2-  
 254 year inhalation studies in rats and mice at inhaled doses up to 137 and 295/200 mcg/kg/day  
 255 (male/female), respectively (approximately 20 and 25/20 times the MRHDID in adults on an  
 256 AUC basis, respectively).

257 Umeclidinium tested negative in the following genotoxicity assays: the *in vitro* Ames  
258 assay, *in vitro* mouse lymphoma assay, and *in vivo* rat bone marrow micronucleus assay.  
259 No evidence of impairment of fertility was observed in male and female rats at  
260 subcutaneous doses up to 180 mcg/kg/day and inhaled doses up to 294 mcg/kg/day, respectively  
261 (approximately 100 and 50 times, respectively, the MRHDID in adults on an AUC basis).

## 262 **14 CLINICAL STUDIES**

263 The safety and efficacy of umeclidinium 62.5 mcg were evaluated in 3 dose-ranging  
264 trials, 2 placebo-controlled clinical trials (one 12-week trial and one 24-week trial), and a 12-  
265 month long-term safety trial. The efficacy of INCRUSE ELLIPTA is based primarily on the  
266 dose-ranging trials in 624 subjects with COPD and the 2 placebo-controlled confirmatory trials  
267 in 1,738 subjects with COPD.

### 268 **14.1 Dose-Ranging Trials**

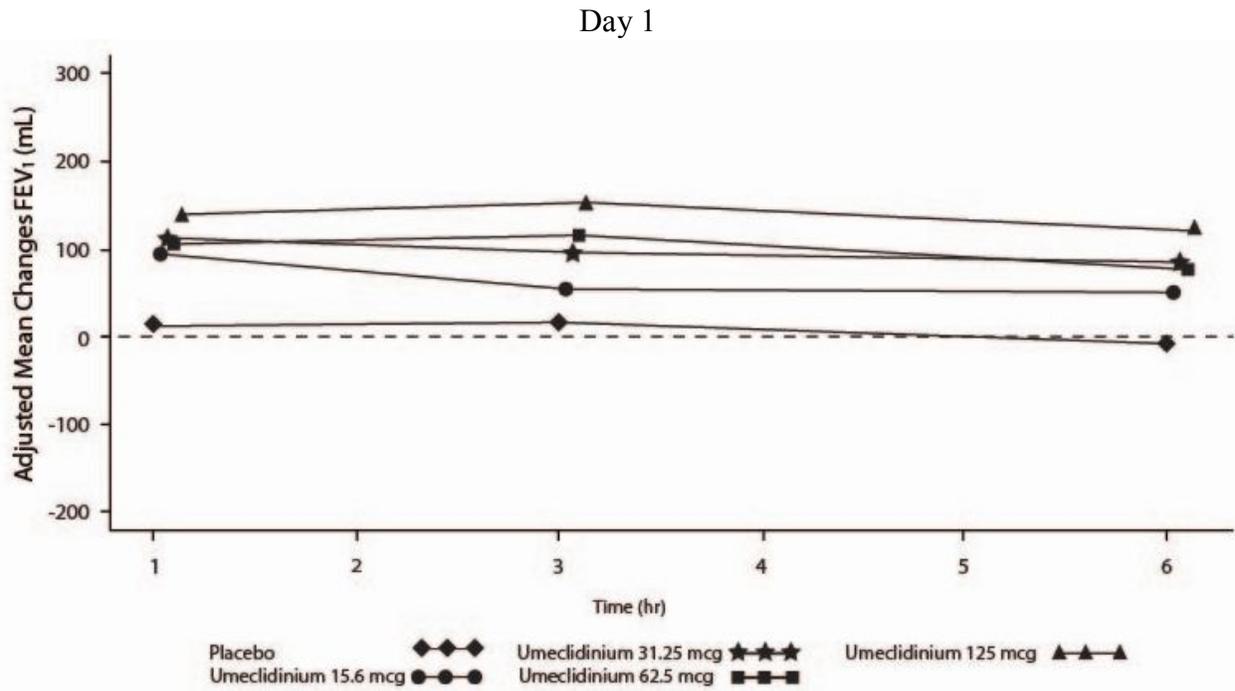
269 Dose selection for umeclidinium in COPD was supported by a 7-day, randomized,  
270 double-blind, placebo-controlled, crossover trial evaluating 4 doses of umeclidinium (15.6 to 125  
271 mcg) or placebo dosed once daily in the morning in 163 subjects with COPD. A dose ordering  
272 was observed, with the 62.5- and 125-mcg doses demonstrating larger improvements in FEV<sub>1</sub>  
273 over 24 hours compared with the lower doses of 15.6 and 31.25 mcg (Figure 2).

274 The differences in trough FEV<sub>1</sub> from baseline after 7 days for placebo and the 15.6-,  
275 31.25-, 62.5-, and 125-mcg doses were -74 mL (95% CI: -118, -31), 38 mL (95% CI: -6, 83), 27  
276 mL (95% CI: -18, 72), 49 mL (95% CI: 6, 93), and 109 mL (95% CI: 65, 152), respectively. Two  
277 additional dose-ranging trials in subjects with COPD demonstrated minimal additional benefit at  
278 doses above 125 mcg. The dose-ranging results supported the evaluation of 2 doses of  
279 umeclidinium, 62.5 and 125 mcg, in the confirmatory COPD trials to further assess dose  
280 response.

281 Evaluations of dosing interval by comparing once- and twice-daily dosing supported  
282 selection of a once-daily dosing interval for further evaluation in the confirmatory COPD trials.  
283

284 **Figure 2. Adjusted Mean Change From Baseline in Post-Dose Serial FEV<sub>1</sub> (mL) on Days 1**  
 285 **and 7**

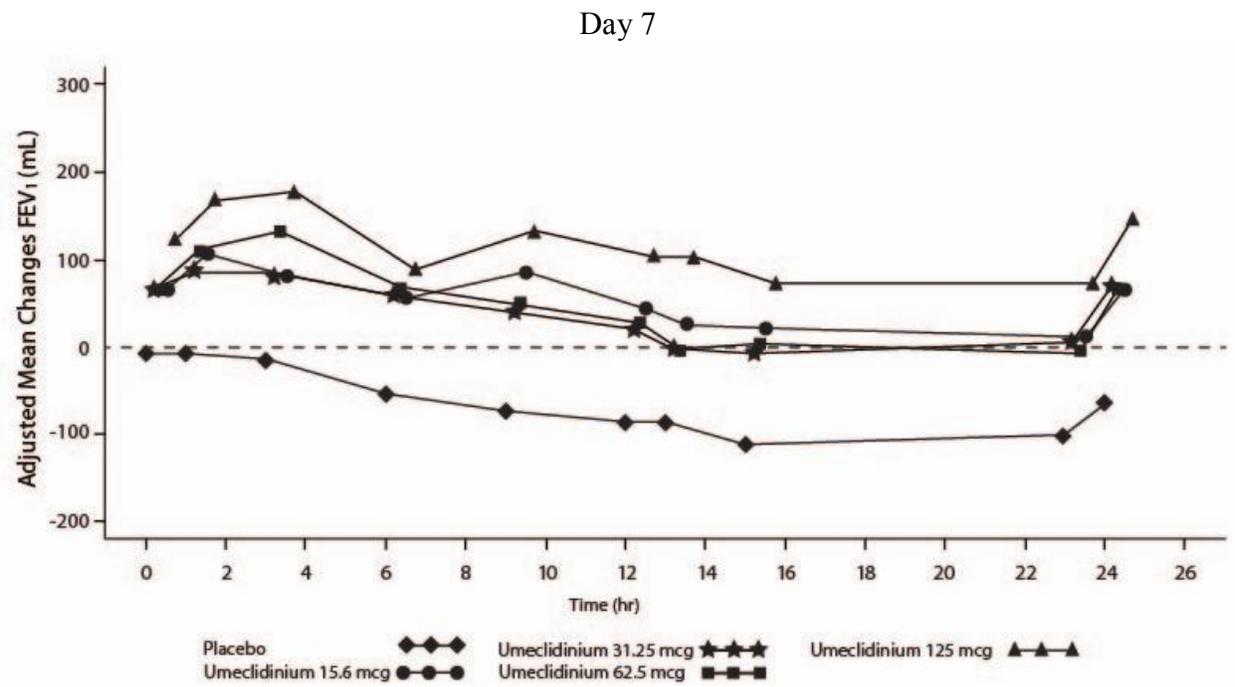
286



287

288

289



290

291

292 **14.2 Confirmatory Trials**

293 The clinical development program for INCRUSE ELLIPTA included 2 randomized,  
 294 double-blind, placebo-controlled, parallel-group trials in subjects with COPD designed to

295 evaluate the efficacy of INCRUSE ELLIPTA on lung function. Trial 1 was a 24-week placebo-  
 296 controlled trial, and Trial 2 was a 12-week placebo-controlled trial. These trials treated subjects  
 297 that had a clinical diagnosis of COPD, were 40 years of age or older, had a history of smoking  
 298 equal to or greater than 10 pack-years, had a post-albuterol FEV<sub>1</sub> less than or equal to 70% of  
 299 predicted normal values, had a ratio of FEV<sub>1</sub>/FVC of less than 0.7, and had a Modified Medical  
 300 Research Council (mMRC) score equal to or greater than 2. Subjects in Trial 1 had a mean age  
 301 of 63 years and an average smoking history of 46 pack-years, with 50% identified as current  
 302 smokers. At screening, the mean post-bronchodilator percent predicted FEV<sub>1</sub> was 47% (range:  
 303 13% to 74%), the mean post-bronchodilator FEV<sub>1</sub>/FVC ratio was 0.47 (range: 0.20 to 0.74), and  
 304 the mean percent reversibility was 15% (range: -35% to 109%). Baseline demographics and lung  
 305 function for subjects in Trial 2 were similar to those in Trial 1.

306 Trial 1 evaluated umeclidinium 62.5 mcg and placebo. The primary endpoint was change  
 307 from baseline in trough (predose) FEV<sub>1</sub> at Day 169 (defined as the mean of the FEV<sub>1</sub> values  
 308 obtained at 23 and 24 hours after the previous dose on Day 168) compared with placebo.  
 309 INCRUSE ELLIPTA 62.5 mcg demonstrated a larger increase in mean change from baseline in  
 310 trough (predose) FEV<sub>1</sub> relative to placebo (see Table 2). Similar results were obtained from Trial  
 311 2.

312

313 **Table 2. Least Squares (LS) Mean Change From Baseline in Trough FEV<sub>1</sub> (mL) at Day**  
 314 **169 in the Intent-to-Treat Population (Trial 1)**

Treatment	n	Trough FEV <sub>1</sub> (mL) at Day 169
		Difference From Placebo (95% CI) n = 280
INCRUSE ELLIPTA	n = 418	115 (76, 155)

315 n = Number in intent-to-treat population.

316

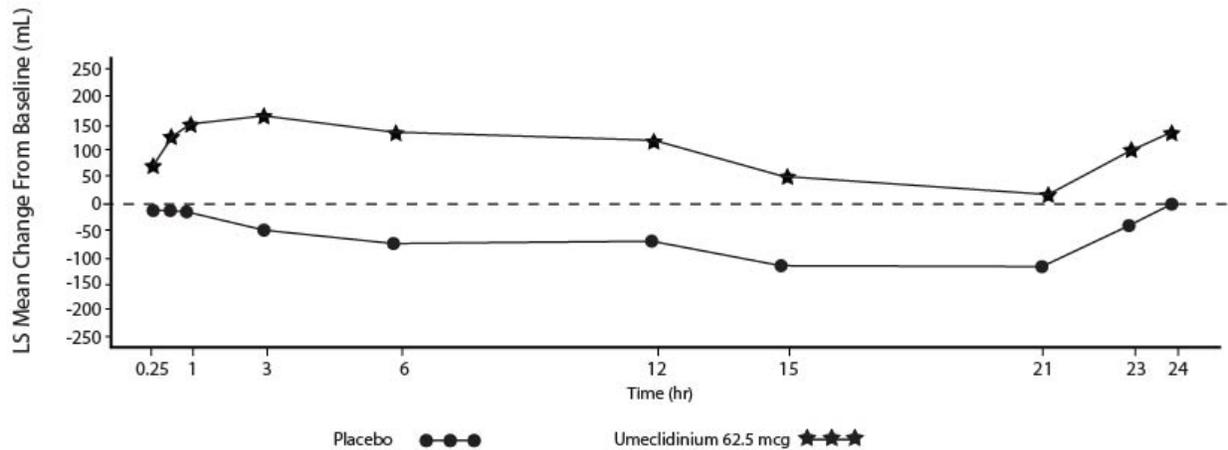
317 Serial spirometric evaluations throughout the 24-hour dosing interval were performed in  
 318 a subset of subjects (n = 54, umeclidinium 62.5 mcg; n = 36, placebo) at Days 1, 84, and 168 in  
 319 Trial 1, and for all patients at Days 1 and 84 in Trial 2. Results from Trial 1 at Day 1 and Day  
 320 168 are shown in Figure 3.

321

322 **Figure 3. Least Squares (LS) Mean Change From Baseline in FEV<sub>1</sub> (mL) Over Time (0-24**  
 323 **hr) on Days 1 and 168 (Trial 1 Subset Population)**

324

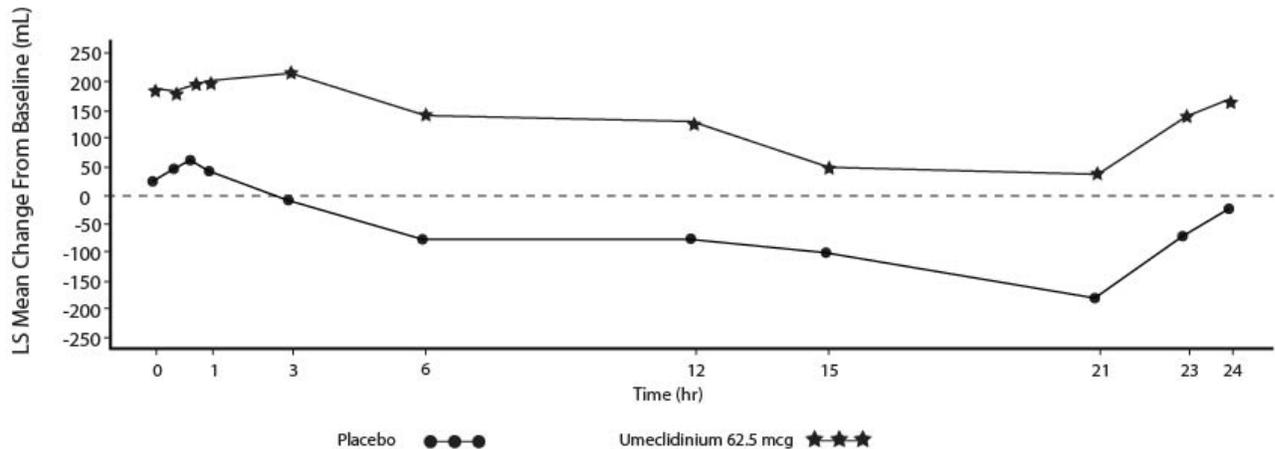
Day 1



325

326

Day 168



327

328 In Trial 1, the mean peak FEV<sub>1</sub> (over the first 6 hours relative to baseline) at Day 1 and at  
 329 Day 168 for the group receiving umeclidinium 62.5 mcg compared with placebo was 126 and  
 330 130 mL, respectively.

331 Health-related quality of life was measured using St. George's Respiratory Questionnaire  
 332 (SGRQ). Umeclidinium demonstrated an improvement in mean SGRQ total score compared with  
 333 placebo treatment at Day 168: -4.69 (95% CI: -7.07,-2.31). The proportion of patients with a  
 334 clinically meaningful decrease (defined as a decrease of at least 4 units from baseline) at Week  
 335 24 was greater for INCRUSE ELLIPTA 62.5 mcg (42%; 172/410) compared with placebo (31%;  
 336 86/274).

### 337 16 HOW SUPPLIED/STORAGE AND HANDLING

338 INCRUSE ELLIPTA is supplied as a disposable light grey and light green plastic inhaler  
 339 containing a double-foil blister strip with 30 blisters. The inhaler is packaged in a moisture-  
 340 protective foil tray with a desiccant and a peelable lid (NDC 0173-0873-10).

341 INCRUSE ELLIPTA is also supplied in an institutional pack of a disposable light grey  
 342 and light green plastic inhaler containing a double-foil blister strip with 7 blisters. The inhaler is

343 packaged in a moisture-protective foil tray with a desiccant and a peelable lid (NDC 0173-0873-  
344 06).

345 Store at room temperature between 68°F and 77°F (20°C and 25°C); excursions  
346 permitted from 59°F to 86°F (15°C to 30°C) [See USP Controlled Room Temperature]. Store in  
347 a dry place away from direct heat or sunlight. Keep out of reach of children.

348 INCRUSE ELLIPTA should be stored inside the unopened moisture-protective foil tray  
349 and only removed from the tray immediately before initial use. Discard INCRUSE ELLIPTA 6  
350 weeks after opening the foil tray or when the counter reads “0” (after all blisters have been used),  
351 whichever comes first. The inhaler is not reusable. Do not attempt to take the inhaler apart.

## 352 **17 PATIENT COUNSELING INFORMATION**

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

355 Not for Acute Symptoms: Inform patients that INCRUSE ELLIPTA is not meant to  
356 relieve acute symptoms of COPD and extra doses should not be used for that purpose. Advise  
357 them to treat acute symptoms with a rescue inhaler such as albuterol. Provide patients with such  
358 medicine and instruct them in how it should be used.

359 Instruct patients to seek medical attention immediately if they experience any of the  
360 following:

- 361 • Symptoms get worse
- 362 • Need for more inhalations than usual of their rescue inhaler

363 Patients should not stop therapy with INCRUSE ELLIPTA without physician/provider  
364 guidance since symptoms may recur after discontinuation.

365 Paradoxical Bronchospasm: As with other inhaled medicines, INCRUSE ELLIPTA  
366 can cause paradoxical bronchospasm. If paradoxical bronchospasm occurs, instruct patients to  
367 discontinue INCRUSE ELLIPTA.

368 Worsening of Narrow-Angle Glaucoma: Instruct patients to be alert for signs and  
369 symptoms of acute narrow-angle glaucoma (e.g., eye pain or discomfort, blurred vision, visual  
370 halos or colored images in association with red eyes from conjunctival congestion and corneal  
371 edema). Instruct patients to consult a physician immediately if any of these signs or symptoms  
372 develop.

373 Worsening of Urinary Retention: Instruct patients to be alert for signs and symptoms  
374 of urinary retention (e.g., difficulty passing urine, painful urination). Instruct patients to consult a  
375 physician immediately if any of these signs or symptoms develop.

376  
377 INCRUSE is a trademark and ELLIPTA is a registered trademark of the GSK group of  
378 companies.

379  
380



381  
382 GlaxoSmithKline  
383 Research Triangle Park, NC 27709

384  
385 ©Year, the GSK group of companies. All rights reserved.

386  
387 INC:xPI

## 389 Patient Information

### 390 **INCRUSE™ [IN-cruise] ELLIPTA® [e-LIP-ta]** 391 **(umeclidinium inhalation powder)**

392  
393 Read the Patient Information that comes with INCRUSE ELLIPTA before you start  
394 using it and each time you get a refill. There may be new information. This Patient  
395 Information does not take the place of talking to your healthcare provider about  
396 your medical condition or treatment.

#### 397 398 **What is INCRUSE ELLIPTA?**

399 INCRUSE ELLIPTA is an anticholinergic medicine. Anticholinergic medicines help the  
400 muscles around the airways in your lungs stay relaxed to prevent symptoms such  
401 as wheezing, cough, chest tightness, and shortness of breath. These symptoms can  
402 happen when the muscles around the airways tighten. This makes it hard to  
403 breathe.

404 INCRUSE ELLIPTA is a prescription medicine used to treat COPD. COPD is a chronic  
405 lung disease that includes chronic bronchitis, emphysema, or both. INCRUSE  
406 ELLIPTA is used long term as 1 inhalation, 1 time each day, to improve symptoms  
407 of COPD for better breathing.

- 408 • **INCRUSE ELLIPTA is not for use to treat sudden symptoms of COPD.**  
409 Always have a rescue inhaler (an inhaled, short-acting bronchodilator) with you  
410 to treat sudden symptoms. If you do not have a rescue inhaler, contact your  
411 healthcare provider to have one prescribed for you.
- 412 • INCRUSE ELLIPTA should not be used in children. It is not known if INCRUSE  
413 ELLIPTA is safe and effective in children.

#### 414 415 **Who should not use INCRUSE ELLIPTA?**

416 Do not use INCRUSE ELLIPTA if you:

- 417 • have a severe allergy to milk proteins. Ask your healthcare provider if you are  
418 not sure.
- 419 • are allergic to umeclidinium or any of the ingredients in INCRUSE ELLIPTA. See  
420 “What are the ingredients in INCRUSE ELLIPTA?” below for a complete list of  
421 ingredients.

422

423 **What should I tell my healthcare provider before using INCRUSE ELLIPTA?**

424 **Tell your healthcare provider about all of your health conditions, including**  
425 **if you:**

- 426 • have heart problems.
- 427 • have eye problems such as glaucoma. INCRUSE ELLIPTA may make your  
428 glaucoma worse.
- 429 • have prostate or bladder problems, or problems passing urine. INCRUSE  
430 ELLIPTA may make these problems worse.
- 431 • are allergic to any of the ingredients in INCRUSE ELLIPTA, any other medicines,  
432 or food products. See “What are the ingredients in INCRUSE ELLIPTA?” below for  
433 a complete list of ingredients.
- 434 • have any other medical conditions.
- 435 • are pregnant or planning to become pregnant. It is not known if INCRUSE  
436 ELLIPTA may harm your unborn baby.
- 437 • are breastfeeding. It is not known if the medicine in INCRUSE ELLIPTA passes  
438 into your milk and if it can harm your baby.

439 **Tell your healthcare provider about all the medicines you take**, including  
440 prescription and over-the-counter medicines, vitamins, and herbal supplements.  
441 INCRUSE ELLIPTA and certain other medicines may interact with each other. This  
442 may cause serious side effects.

443 Especially tell your healthcare provider if you take:

- 444 • anticholinergics (including tiotropium, ipratropium, acclidinium)  
445 • atropine

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

448

449 **How should I use INCRUSE ELLIPTA?**

450 **Read the step-by-step instructions for using INCRUSE ELLIPTA at the end**  
451 **of this Patient Information.**

- 452 • **Do not** use INCRUSE ELLIPTA unless your healthcare provider has taught you  
453 how to use the inhaler and you understand how to use it correctly.

- 454 • Use INCRUSE ELLIPTA exactly as your healthcare provider tells you to use it. **Do**  
455 **not** use INCRUSE ELLIPTA more often than prescribed.
- 456 • Use 1 inhalation of INCRUSE ELLIPTA 1 time each day. Use INCRUSE ELLIPTA at  
457 the same time each day.
- 458 • If you miss a dose of INCRUSE ELLIPTA, take it as soon as you remember. Do  
459 not take more than 1 inhalation each day. Take your next dose at your usual  
460 time. Do not take 2 doses at one time.
- 461 • If you take too much INCRUSE ELLIPTA, call your healthcare provider or go to  
462 the nearest hospital emergency room right away if you have any unusual  
463 symptoms, such as worsening shortness of breath, chest pain, increased heart  
464 rate, or shakiness.
- 465 • **Do not use other medicines that contain an anticholinergic for any**  
466 **reason.** Ask your healthcare provider or pharmacist if any of your other  
467 medicines are anticholinergic medicines.
- 468 • Do not stop using INCRUSE ELLIPTA unless told to do so by your healthcare  
469 provider because your symptoms might get worse. Your healthcare provider will  
470 change your medicines as needed.
- 471 • **INCRUSE ELLIPTA does not relieve sudden symptoms.** Always have a  
472 rescue inhaler with you to treat sudden symptoms. If you do not have a rescue  
473 inhaler, call your healthcare provider to have one prescribed for you.
- 474 • Call your healthcare provider or get medical care right away if:  
475 • your breathing problems get worse  
476 • you need to use your rescue inhaler more often than usual  
477 • your rescue inhaler does not work as well to relieve your symptoms  
478

#### 479 **What are the possible side effects with INCRUSE ELLIPTA?**

##### 480 **INCRUSE ELLIPTA can cause serious side effects, including:**

- 481 • **sudden breathing problems immediately after inhaling your medicine.** If  
482 you have sudden breathing problems immediately after inhaling your medicine,  
483 stop taking INCRUSE ELLIPTA and call your doctor right away.
- 484 • **serious allergic reactions.** Call your healthcare provider or get emergency  
485 medical care if you get any of the following symptoms of a serious allergic  
486 reaction:  
487 • rash  
488 • hives  
489 • swelling of the face, mouth, and tongue

- 490 • breathing problems
- 491 • **new or worsened eye problems including acute narrow-angle glaucoma.**
- 492 Acute narrow-angle glaucoma can cause permanent loss of vision if not treated.
- 493 Symptoms of acute narrow-angle glaucoma may include:
- 494 • eye pain or discomfort
- 495 • nausea or vomiting
- 496 • blurred vision
- 497 • seeing halos or bright colors around lights
- 498 • red eyes

499 If you have these symptoms, call your doctor right away before taking another  
500 dose.

- 501 • **urinary retention.** People who take INCRUSE ELLIPTA may develop new or  
502 worse urinary retention. Symptoms of urinary retention may include:
- 503 • difficulty urinating
- 504 • painful urination
- 505 • urinating frequently
- 506 • urination in a weak stream or drips

507 If you have these symptoms of urinary retention, stop taking INCRUSE ELLIPTA,  
508 and call your doctor right away before taking another dose.

509 **Common side effects of INCRUSE ELLIPTA include:**

- 510 • upper respiratory infection
- 511 • stuffy or runny nose
- 512 • cough
- 513 • sore throat
- 514 • joint pain
- 515 • muscle pain
- 516 • tooth pain
- 517 • stomach pain
- 518 • bruising or dark areas of skin
- 519 • fast or irregular heartbeat

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

522 These are not all the side effects with INCRUSE ELLIPTA. Ask your healthcare  
523 provider or pharmacist for more information.

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

526

527 **How do I store INCRUSE ELLIPTA?**

- 528 • Store INCRUSE ELLIPTA at room temperature between 68°F and 77°F (20°C and  
529 25°C). Keep in a dry place away from heat and sunlight.
- 530 • Store INCRUSE ELLIPTA in the unopened foil tray and only open when ready for  
531 use.
- 532 • Safely throw away INCRUSE ELLIPTA in the trash 6 weeks after you open the foil  
533 tray or when the counter reads “0”, whichever comes first. Write the date you  
534 open the tray on the label on the inhaler.
- 535 • **Keep INCRUSE ELLIPTA and all medicines out of the reach of children.**  
536

537 **General information about INCRUSE ELLIPTA**

538 Medicines are sometimes prescribed for purposes not mentioned in a Patient  
539 Information leaflet. Do not use INCRUSE ELLIPTA for a condition for which it was  
540 not prescribed. Do not give your INCRUSE ELLIPTA to other people, even if they  
541 have the same condition that you have. It may harm them.

542 This Patient Information leaflet summarizes the most important information about  
543 INCRUSE ELLIPTA. If you would like more information, talk with your healthcare  
544 provider or pharmacist. You can ask your healthcare provider or pharmacist for  
545 information about INCRUSE ELLIPTA that was written for healthcare professionals.

546 For more information about INCRUSE ELLIPTA, call 1-888-825-5249 or visit our  
547 website at [www.INCRUSE.com](http://www.INCRUSE.com).

548

549 **What are the ingredients in INCRUSE ELLIPTA?**

550 Active ingredients: umeclidinium

551 Inactive ingredients: lactose monohydrate (contains milk proteins), magnesium  
552 stearate

553

554 **Instructions for Use**

555 **For Oral Inhalation Only.**

556

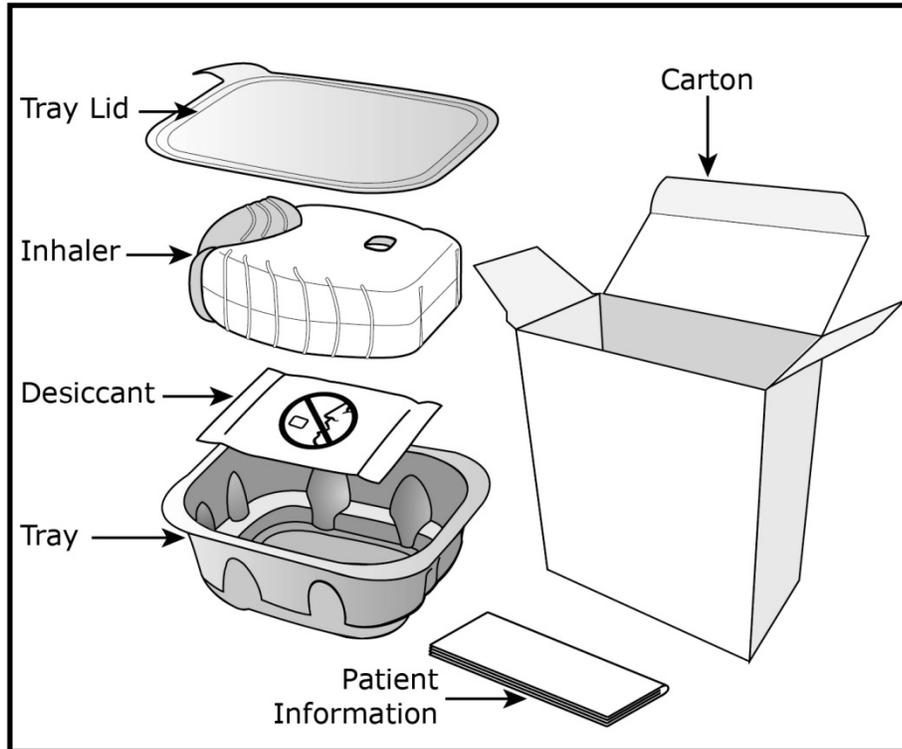
557 **Read this before you start:**

- 558 • **If you open and close the cover without inhaling the medicine, you will**  
559 **lose the dose.**
- 560 • **The lost dose will be securely held inside the inhaler, but it will no**  
561 **longer be available to be inhaled.**

- 562 • It is not possible to accidentally take a double dose or an extra dose in  
563 one inhalation.

564

565 **Your INCRUSE ELLIPTA inhaler**



566

567

568 **How to use your inhaler**

- 569 • INCRUSE ELLIPTA comes in a foil tray.
- 570 • Peel back the lid to open the tray. See Figure A.
- 571 • The tray contains a desiccant to reduce moisture. Do not eat or inhale. Throw it  
572 away in the household trash out of reach of children and pets. See Figure B.

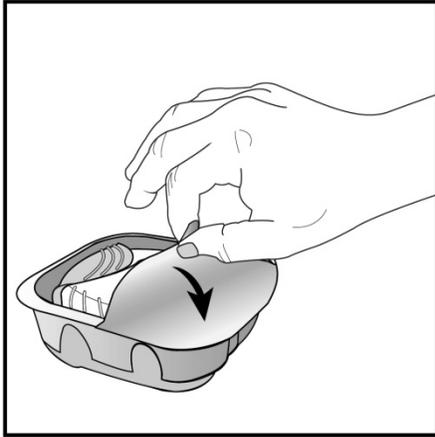


Figure A

573  
574  
575

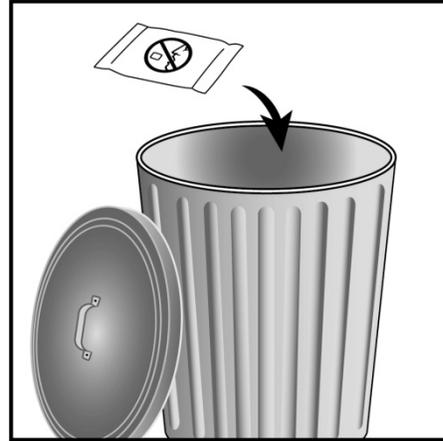


Figure B

576  
577  
578

579 **Important Notes:**

- 580 • Your inhaler contains 30 doses (7 doses if you have a sample or institutional  
581 pack).
- 582 • Each time you fully open the cover of the inhaler (you will hear a clicking  
583 sound), a dose is ready to be inhaled. This is shown by a decrease in the  
584 number on the counter.
- 585 • If you open and close the cover without inhaling the medicine, you will lose the  
586 dose. The lost dose will be held in the inhaler, but it will no longer be available  
587 to be inhaled. It is not possible to accidentally take a double dose or an extra  
588 dose in one inhalation.
- 589 • **Do not** open the cover of the inhaler until you are ready to use it. To avoid  
590 wasting doses after the inhaler is ready, **do not** close the cover until after you  
591 have inhaled the medicine.
- 592 • Write the "Tray opened" and "Discard" dates on the inhaler label. The "Discard"  
593 date is 6 weeks from the date you open the tray.

594  
595 **Check the counter. See Figure C.**

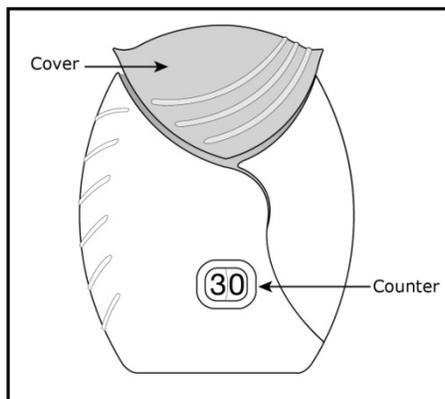


Figure C

- Before the inhaler is used for the first time, the counter should show the number 30 (7 if you have a sample or institutional pack). This is the number of doses in the inhaler.
- Each time you open the cover, you prepare 1 dose of medicine.
- The counter counts down by 1 each time you open the cover.

596  
597  
60798

**Prepare your dose:**

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

610

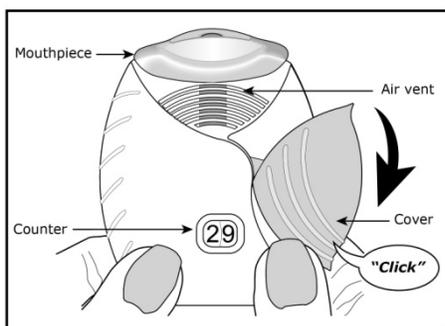


Figure D

**Step 1. Open the cover of the inhaler. See Figure D.**

- Slide the cover down to expose the mouthpiece. You should hear a "click." The counter will count down by 1 number. You do not need to shake this kind of inhaler. **Your inhaler is now ready to use.**

- If the counter does not count down as you hear the click, the inhaler will not deliver the medicine. Call your healthcare provider or pharmacist if this happens.

611  
612  
613  
614  
615  
616

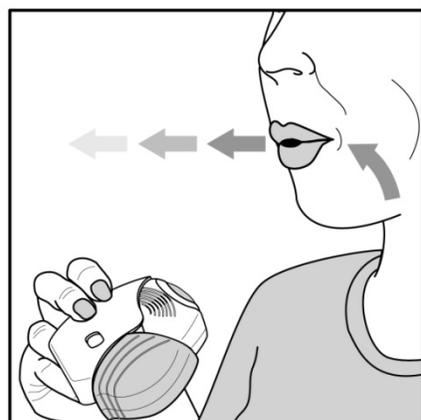


Figure E

**Step 2. Breathe out. See Figure E.**

- While holding the inhaler away from your mouth, breathe out (exhale) fully. Do not breathe out into the mouthpiece.

617  
618  
619  
620

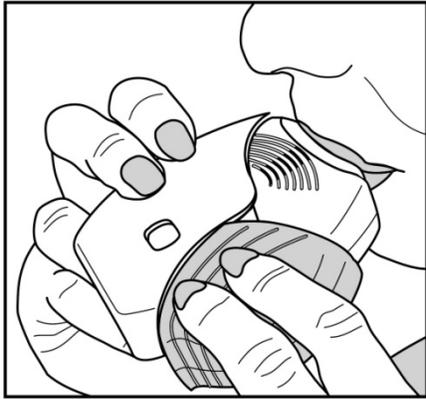


Figure F

646 **Step 3. Inhale your medicine. See Figure F.**

- 647 • Put the mouthpiece between your lips, and
- 648 close your lips firmly around it. Your lips
- 649 should fit over the curved shape of the
- 650 mouthpiece.
- 651 • Take one long, steady, deep breath in
- 652 through your mouth. **Do not** breathe in
- 653 through your nose.

638  
639  
640

654  
655  
656

Do not block the air vent with your fingers.



Figure G

- 657 • Do not block the air vent with your fingers.
- 658 **See Figure G.**

641  
642  
643

657  
658  
659  
660  
661  
662  
663  
664  
665  
666  
667  
668

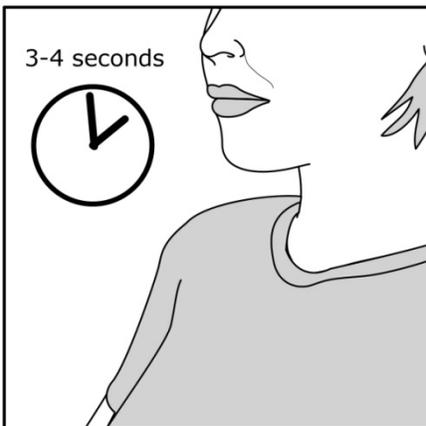


Figure H

- 669 • **Remove the inhaler from your mouth**
- 670 **and hold your breath for about 3 to 4**
- 671 **seconds** (or as long as comfortable for
- 672 you). **See Figure H.**

644  
645

669  
670  
671  
672  
673  
674

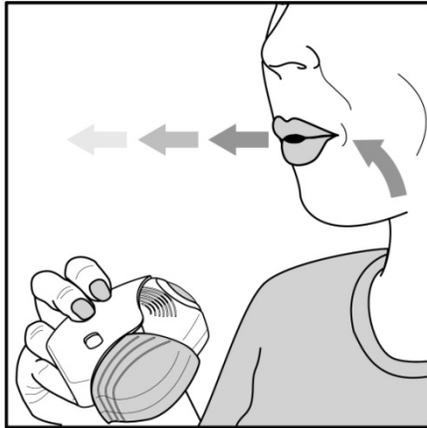


Figure I

682 **Step 4. Breathe out slowly and gently.**  
 683 **See Figure I.**

- 684 • You may not taste or feel the medicine,  
 685 even when you are using the inhaler  
 686 correctly.
- 687 • **Do not** take another dose from the inhaler  
 688 even if you do not feel or taste the  
 689 medicine.

675  
 676  
 677

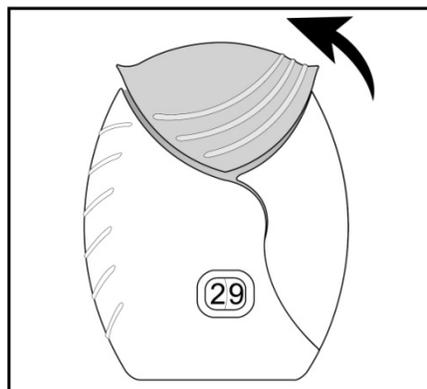


Figure J

693 **Step 5. Close the inhaler. See Figure J.**

- 694 • You can clean the mouthpiece if needed,  
 695 using a dry tissue, before you close the  
 696 cover. Routine cleaning is not required.
- 697 • Slide the cover up and over the  
 698 mouthpiece as far as it will go.

699

678  
 679  
 680

700 **Important Note: When should you get a refill?**

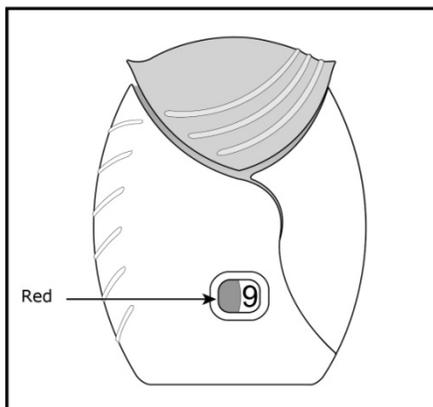


Figure K

703 • **When you have less than 10 doses**  
 704 **remaining** in your inhaler, the left half of  
 705 the counter shows red as a reminder to get  
 706 a refill. **See Figure K.**

707 • After you have inhaled the last dose, the  
 708 counter will show "0" and will be empty.

709 • Throw the empty inhaler away in your  
 710 household trash out of reach of children  
 711 and pets.

701  
 702

712  
 713 If you have questions about INCRUSE ELLIPTA or how to use your inhaler, call  
 714 GlaxoSmithKline (GSK) at 1-888-825-5249 or visit [www.INCRUSE.com](http://www.INCRUSE.com).

715

716 **This Patient Information and Instructions for Use have been approved by**  
717 **the U.S. Food and Drug Administration.**

718

719 INCRUSE is a trademark and ELLIPTA is a registered trademark of the GSK group of  
720 companies.

721

722



723

724 GlaxoSmithKline

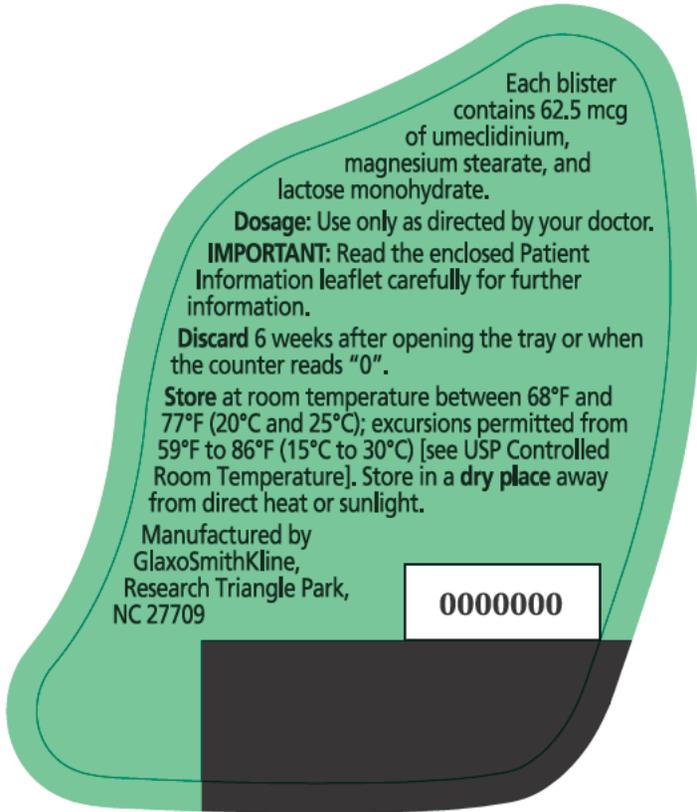
725 Research Triangle Park, NC 27709

726 ©Year, the GSK group of companies. All rights reserved.

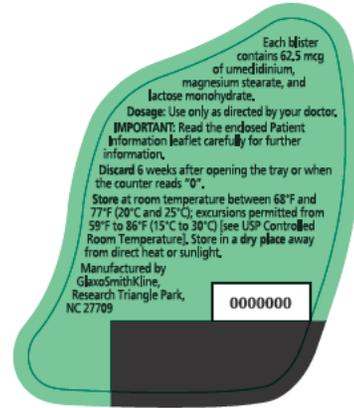
727

728 Month Year

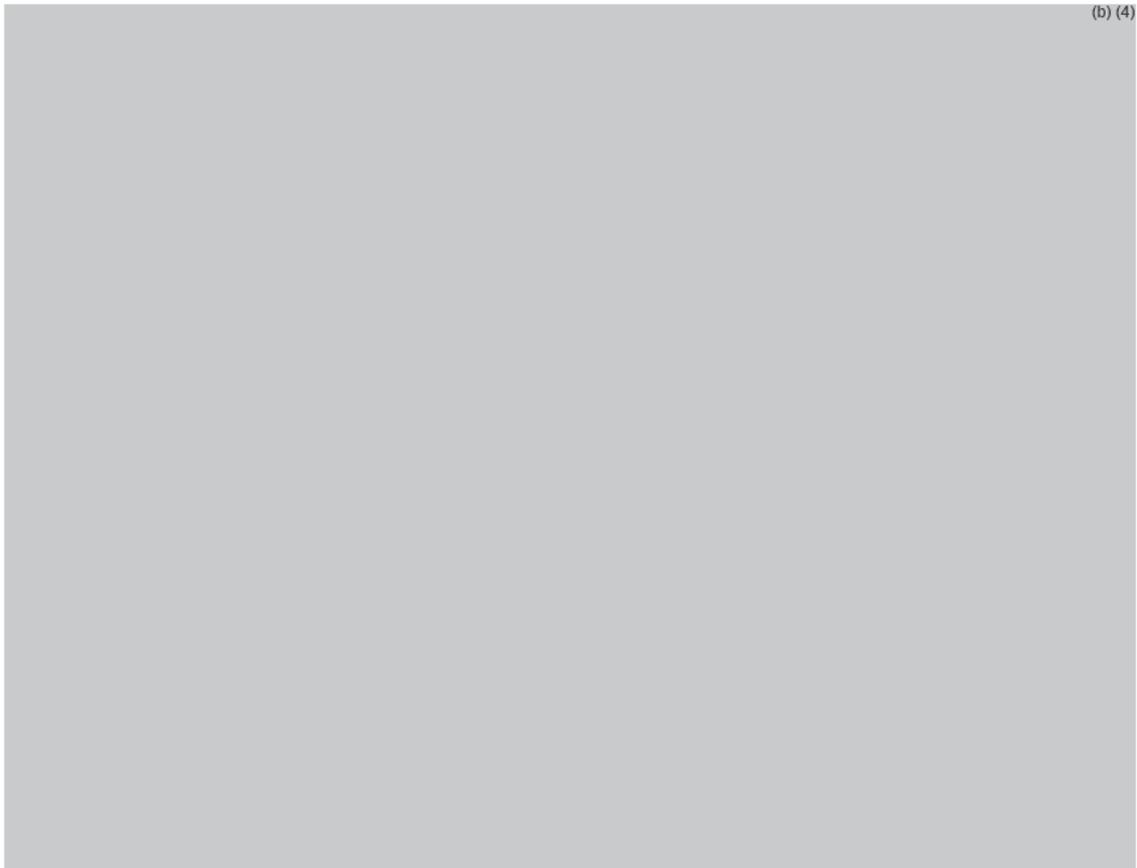
729 INC:xMG



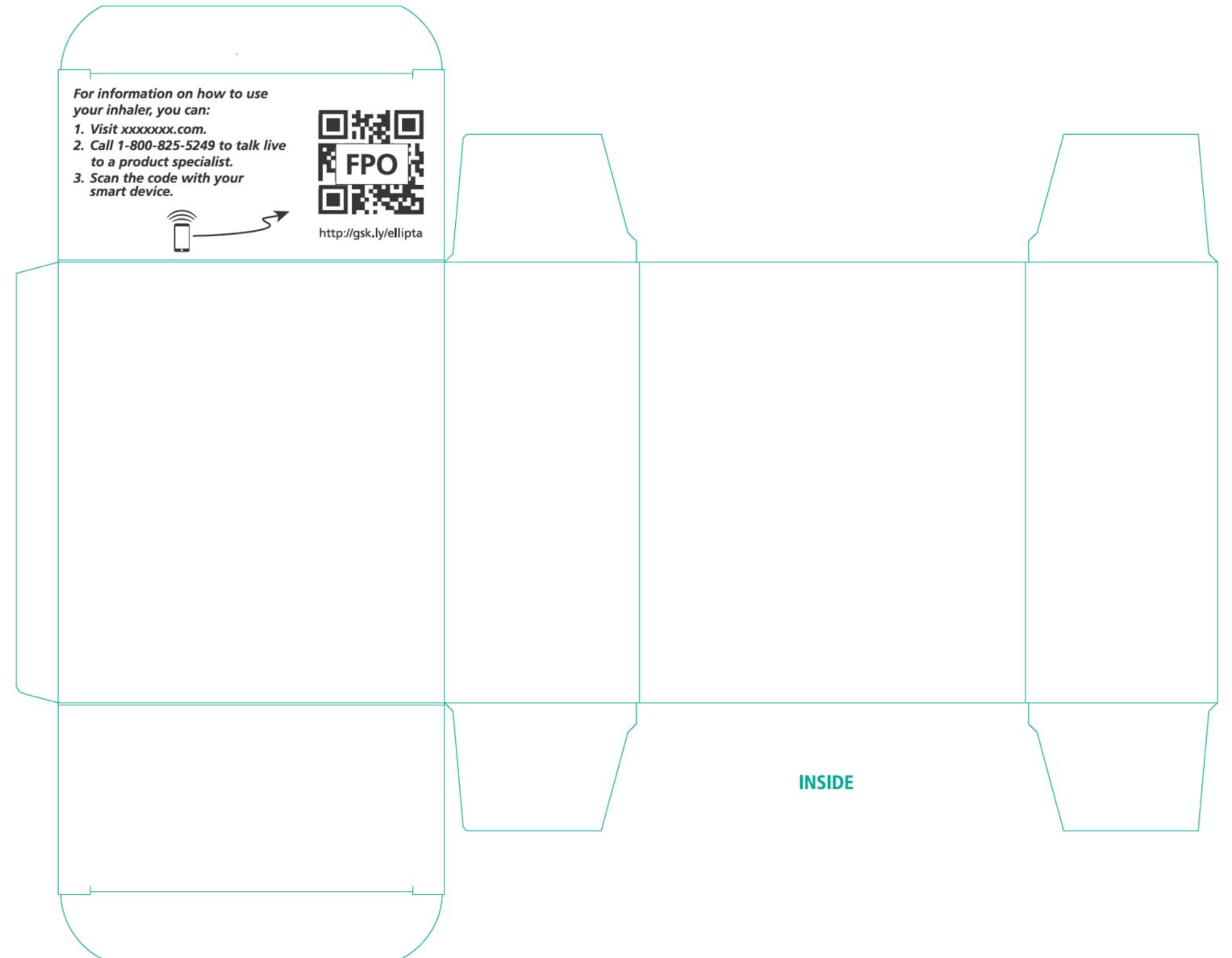
200%



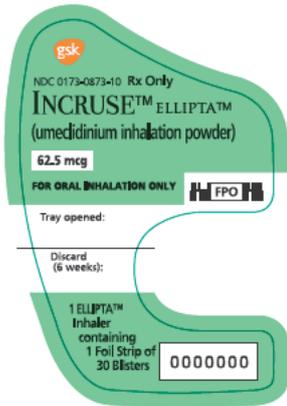
Actual Size (100%)



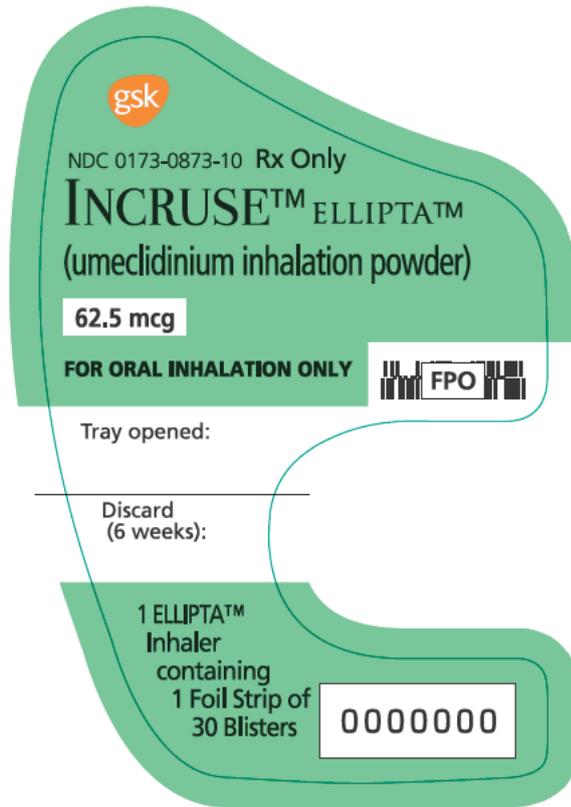
(b) (4)



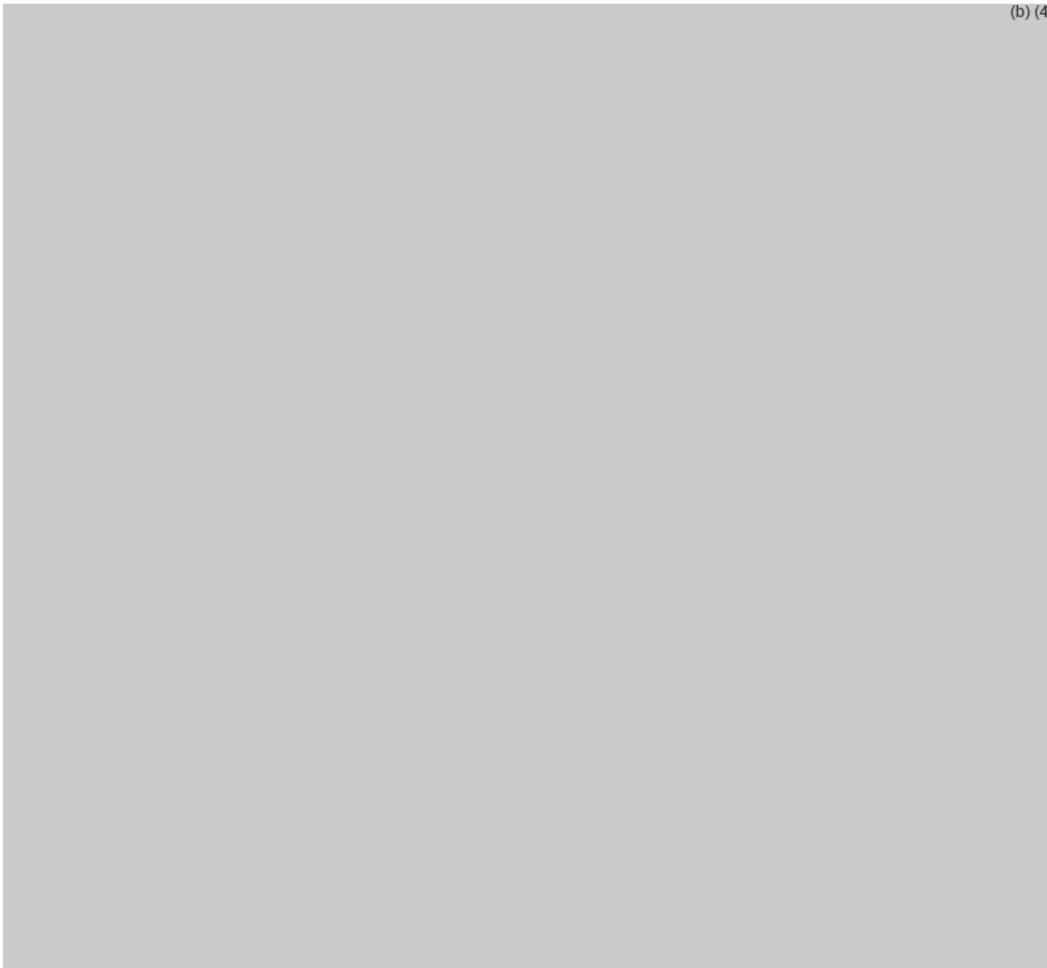
(b) (4)

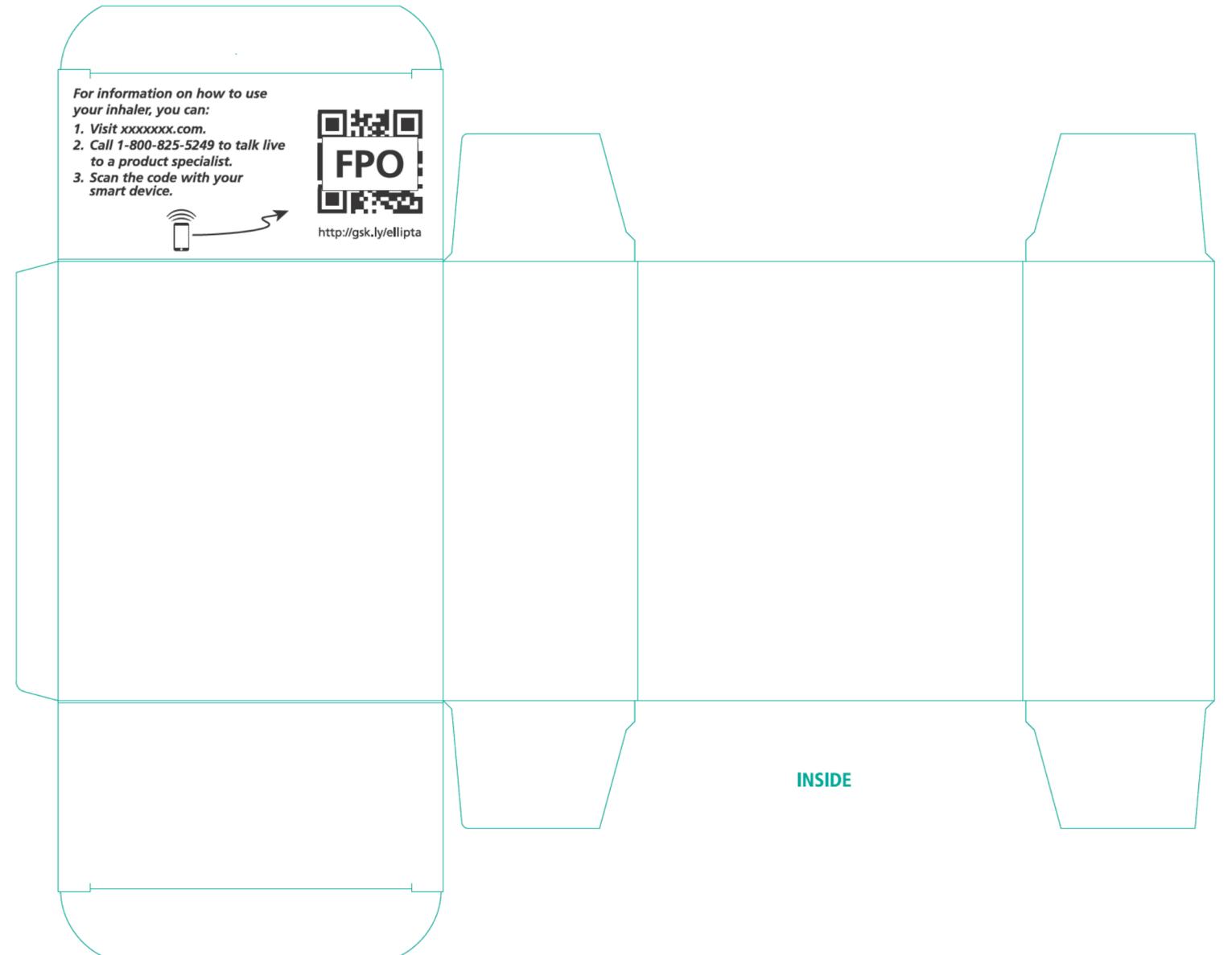
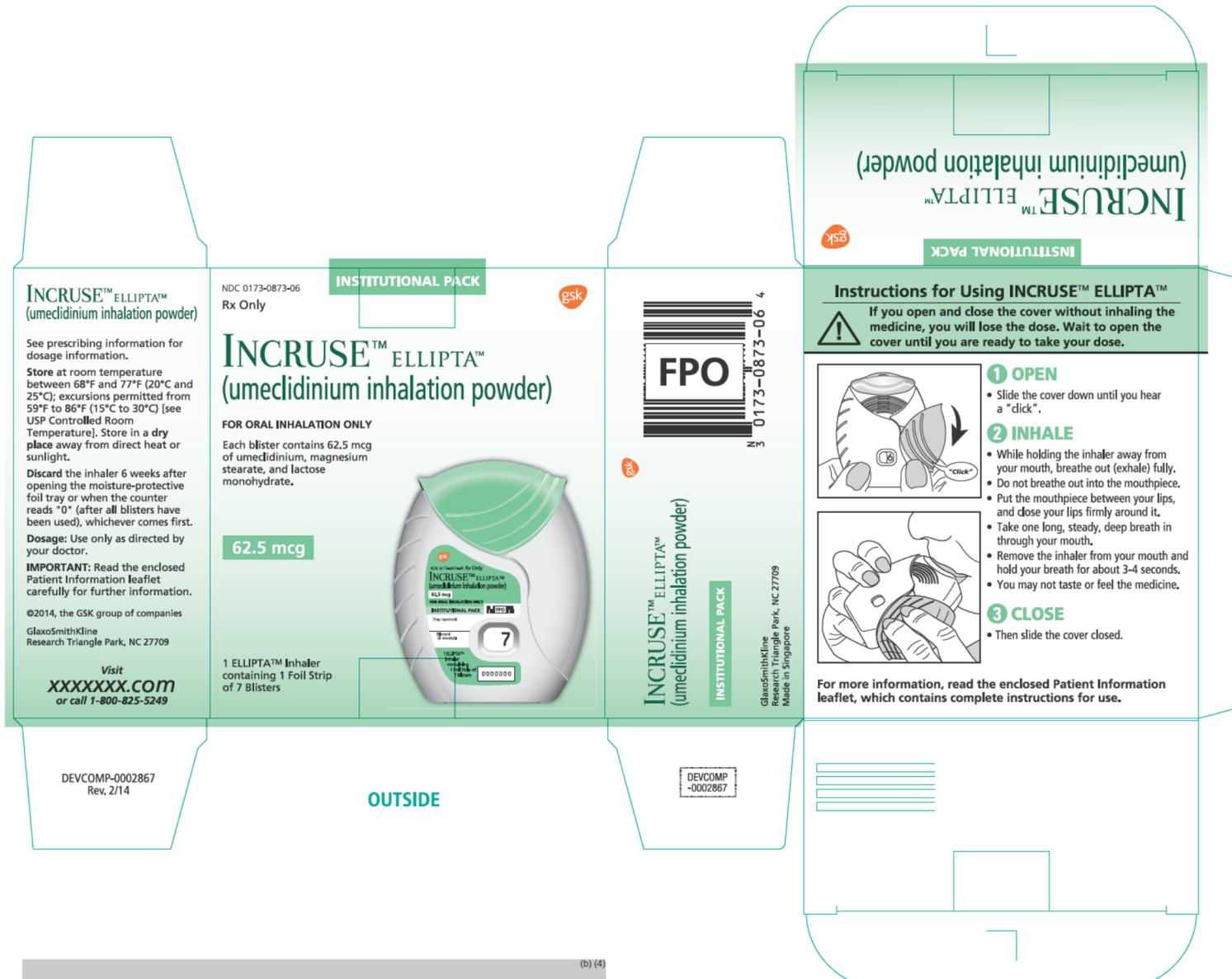


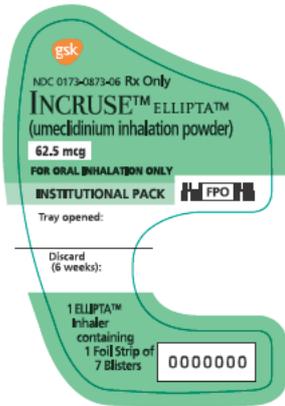
Actual Size



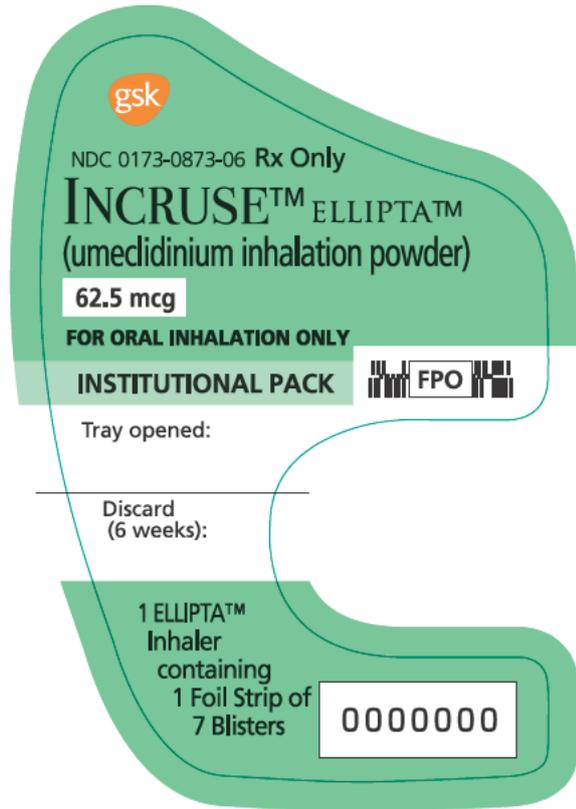
200%







Actual Size



200%

(b) (4)



INSTITUTIONAL PACK

NDC 0173-0873-06  Rx Only

# INCRUSE™ ELLIPTA™

## (umeclidinium inhalation powder)

**62.5 mcg** FOR ORAL INHALATION ONLY

Each blister contains 62.5 mcg of umeclidinium, magnesium stearate, and lactose monohydrate.  N 0 3 1 1 8 8 0 7 3

**Dosage:** Use only as directed by your doctor.

**IMPORTANT:** Read the enclosed Patient Information leaflet carefully for further information. **If you open and close the cover without inhaling the medicine, you will lose the dose.**

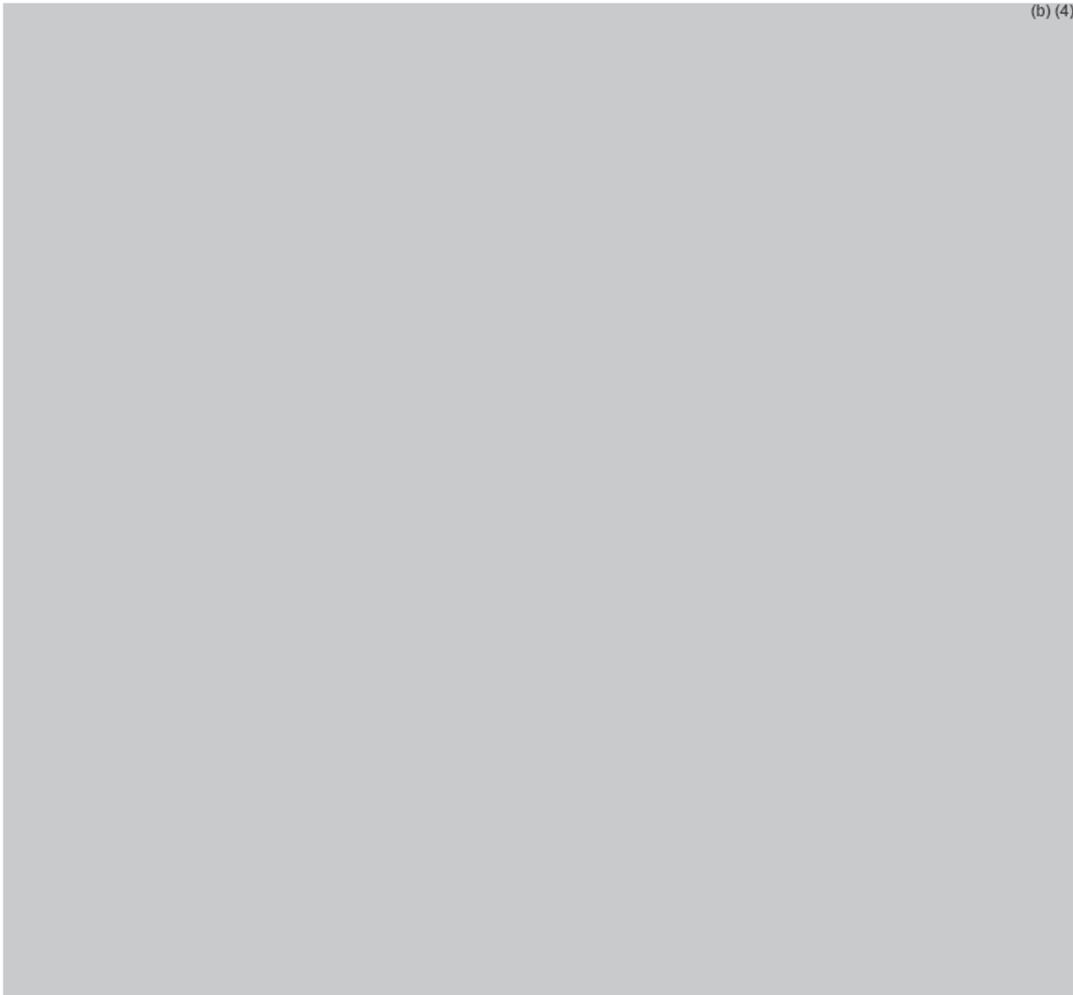
Discard the inhaler 6 weeks after opening the moisture-protective foil tray or when the counter reads "0" (after all blisters have been used), whichever comes first.

Store at room temperature between 68°F and 77°F (20°C and 25°C); excursions permitted from 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature]. Store in a dry place away from direct heat or sunlight.

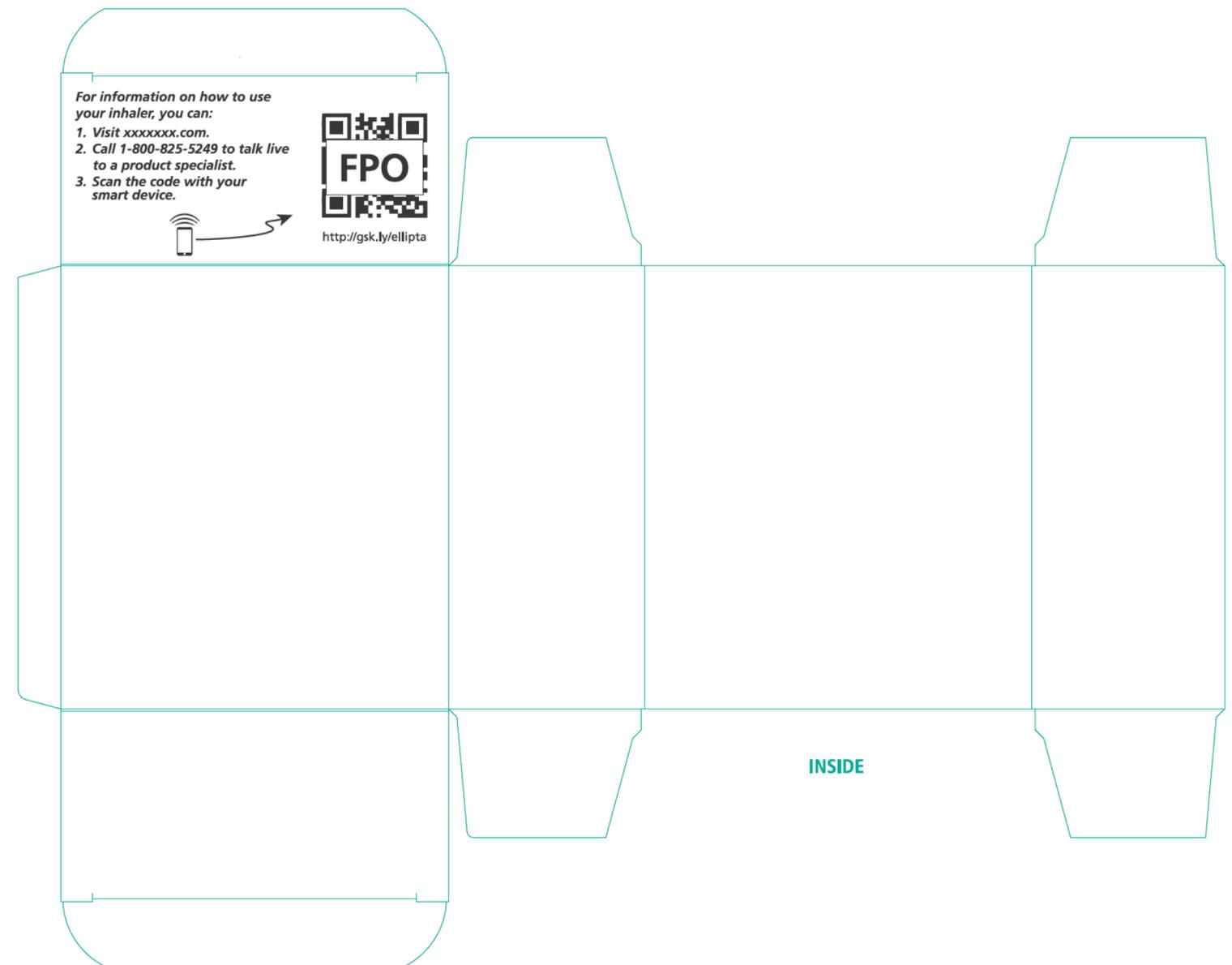
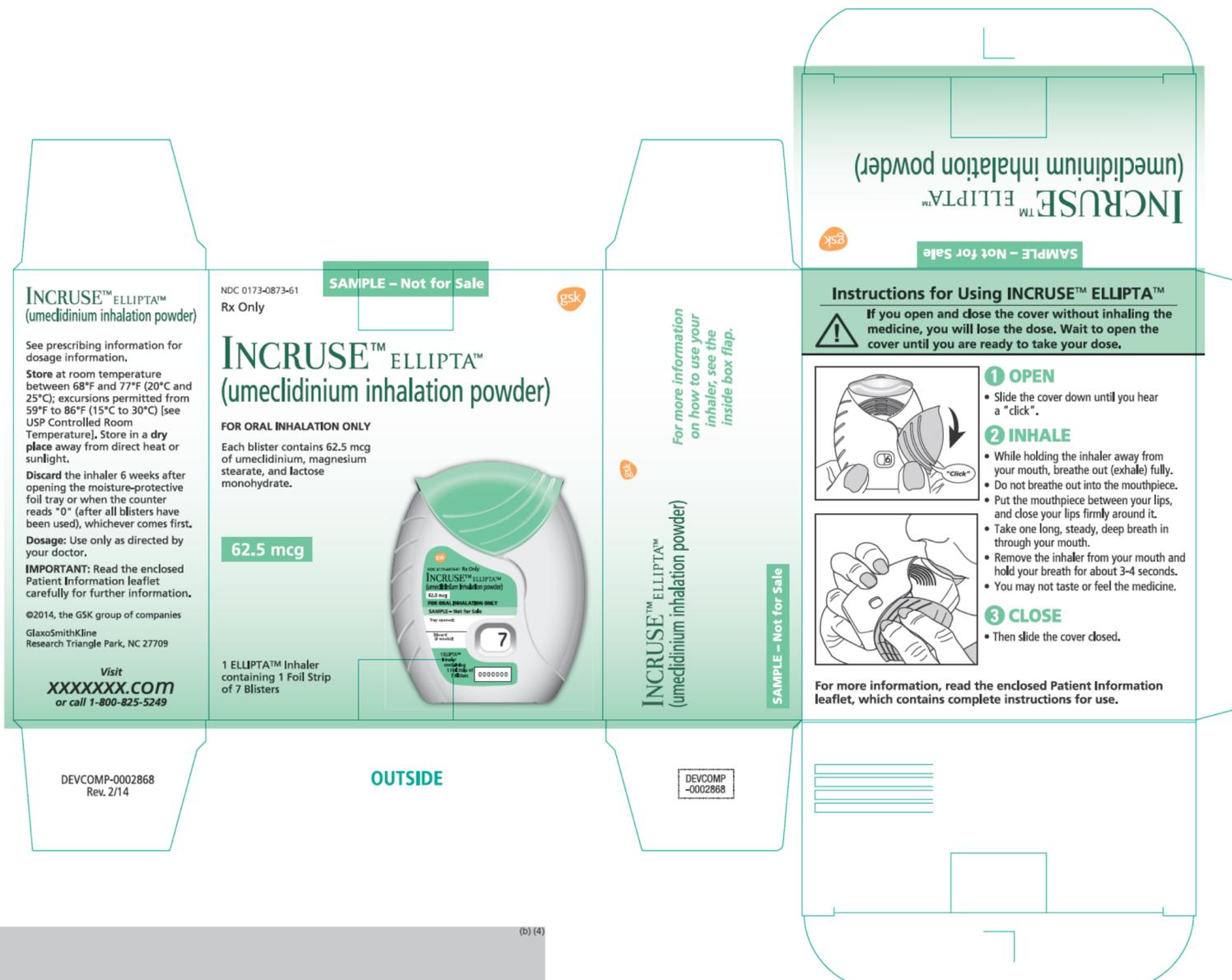
DEVCOM-002861 Rev. 2/14

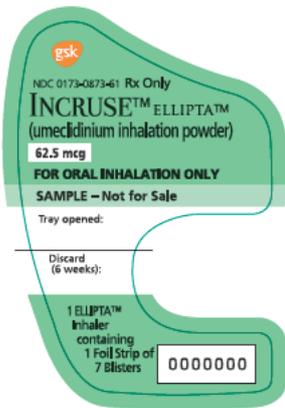
	Lot
	EXP

1 ELLIPTA™ Inhaler containing  
1 Foil Strip of 7 Blisters  
GlaxoSmithKline, Research Triangle Park, NC 27709

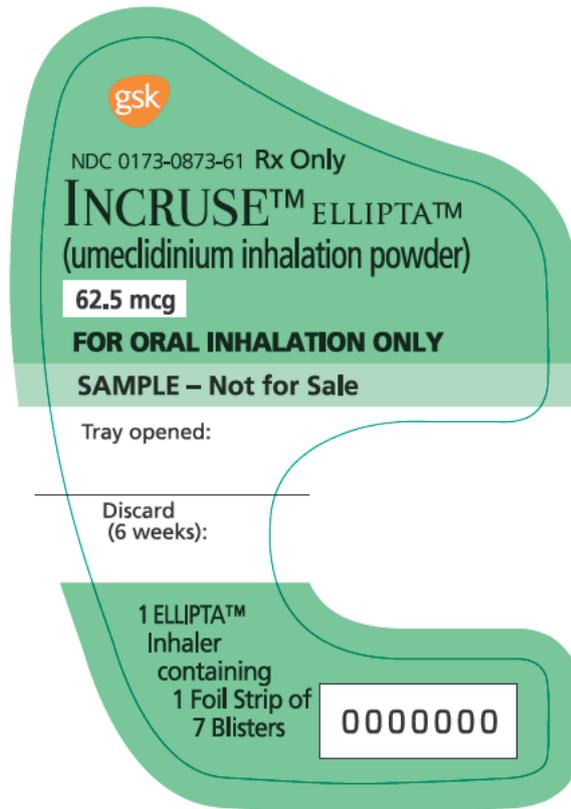


(b) (4)



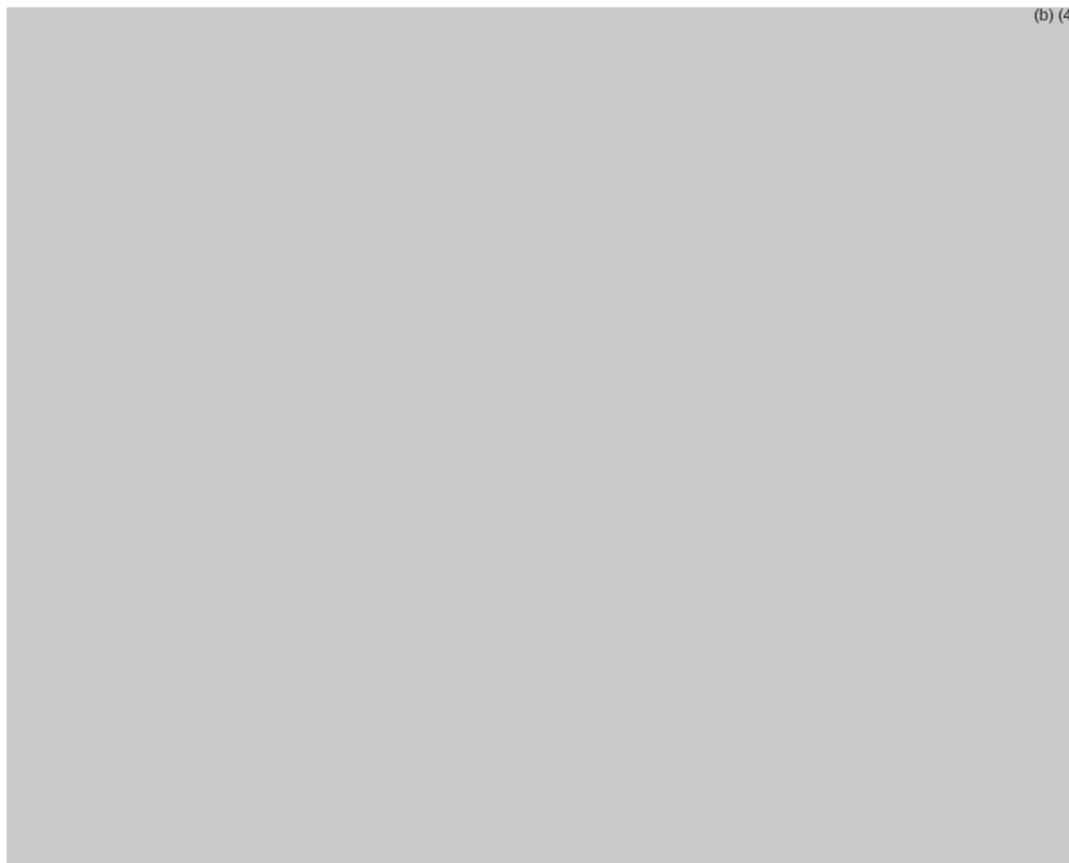


Actual Size



200%

(b) (4)



SAMPLE – Not for Sale

NDC 0173-0873-61  Rx Only

# INCRUSE™ ELLIPTA™

## (umeclidinium inhalation powder)

**62.5 mcg**      **FOR ORAL INHALATION ONLY**

Each blister contains 62.5 mcg of umeclidinium, magnesium stearate, and lactose monohydrate.  
**Dosage:** Use only as directed by your doctor.  
**IMPORTANT:** Read the enclosed Patient Information leaflet carefully for further information.  
**If you open and close the cover without inhaling the medicine, you will lose the dose.**  
**Discard the inhaler 6 weeks after opening the moisture-protective foil tray or when the counter reads "0" (after all blisters have been used), whichever comes first.**  
**Store** at room temperature between 68°F and 77°F (20°C and 25°C); excursions permitted from 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature].  
**Store in a dry place away from direct heat or sunlight.**

DEVCOM-002863 Rev. 2/14

	<p>Lot</p> <p>EXP</p> <p>1 ELLIPTA™ Inhaler containing            1 Foil Strip of 7 Blisters            GlaxoSmithKline, Research Triangle Park, NC 27709</p>
---	---



(b) (4)

NDC 0173-0873-10  Rx Only

# INCRUSE™ ELLIPTA™

## (umeclidinium inhalation powder)

**62.5 mcg** FOR ORAL INHALATION ONLY

Each blister contains 62.5 mcg of umeclidinium, magnesium stearate, and lactose monohydrate.  N 0 0 3 1 7 3 8 0 7 3

**Dosage:** Use only as directed by your doctor.

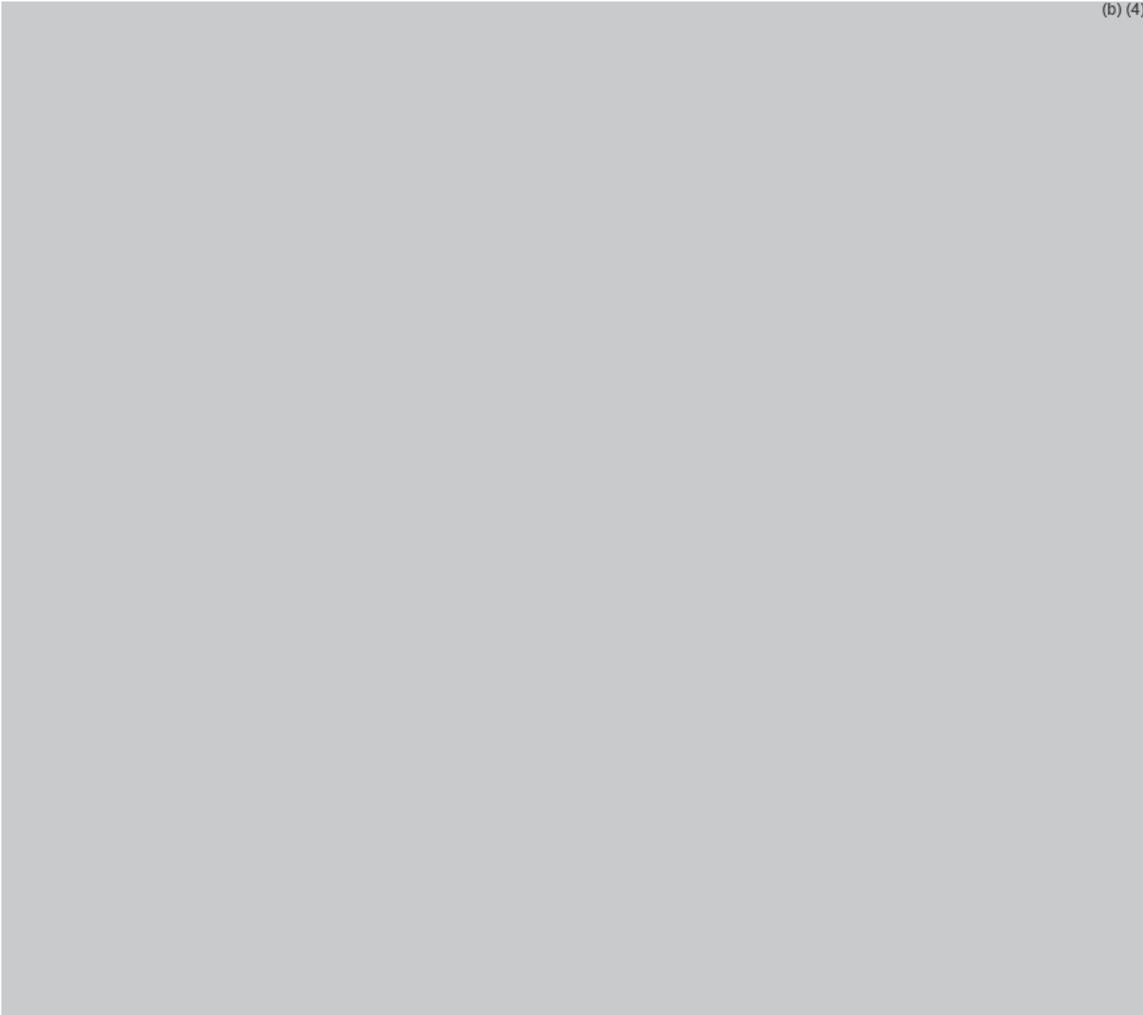
**IMPORTANT:** Read the enclosed Patient Information leaflet carefully for further information. **If you open and close the cover without inhaling the medicine, you will lose the dose.** Discard the inhaler 6 weeks after opening the moisture-protective foil tray or when the counter reads "0" (after all blisters have been used), whichever comes first.

Store at room temperature between 68°F and 77°F (20°C and 25°C); excursions permitted from 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature]. Store in a dry place away from direct heat or sunlight.

DEVCMM-002859 Rev. 2/14

	Lot
	EXP

1 ELLIPTA™ Inhaler containing  
1 Foil Strip of 30 Blisters  
GlaxoSmithKline, Research Triangle Park, NC 27709



(b) (4)

-----  
**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
-----

/s/  
-----

BADRUL A CHOWDHURY  
04/30/2014