

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

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 foil blister strip of powder formulation for oral inhalation. Each blister contains 62.5 mcg of umeclidinium. (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 healthcare provider 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 healthcare provider immediately if symptoms occur. (5.5)

----- **ADVERSE REACTIONS** -----

Most common adverse reactions (incidence greater than or equal to 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: 2/2016

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1 FULL PRESCRIBING INFORMATION

2 1 INDICATIONS AND USAGE

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

3 2 DOSAGE AND ADMINISTRATION

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

9 INCRUSE ELLIPTA should be used 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 foil blister
15 strip of powder intended for oral inhalation only. Each blister contains umeclidinium 62.5 mcg.

16 **4 CONTRAINDICATIONS**

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

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

21 **5 WARNINGS AND PRECAUTIONS**

22 **5.1 Deterioration of Disease and Acute Episodes**

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

27 INCRUSE ELLIPTA should not be used for the relief of acute symptoms, i.e., as rescue therapy
28 for the treatment of acute episodes of bronchospasm. INCRUSE ELLIPTA has not been studied
29 in the relief of acute symptoms and extra doses should not be used for that purpose. Acute
30 symptoms should be treated with an inhaled, short-acting beta₂-agonist.

31 COPD may deteriorate acutely over a period of hours or chronically over several days or longer.
32 If INCRUSE ELLIPTA no longer controls symptoms of bronchoconstriction; the patient's
33 inhaled, short-acting beta₂-agonist becomes less effective; or the patient needs more short-acting
34 beta₂-agonist than usual, these may be markers of deterioration of disease. In this setting a
35 reevaluation of the patient and the COPD treatment regimen should be undertaken at once.
36 Increasing the daily dose of INCRUSE ELLIPTA beyond the recommended dose is not
37 appropriate in this situation.

38 **5.2 Paradoxical Bronchospasm**

39 As with other inhaled medicines, INCRUSE ELLIPTA can produce paradoxical bronchospasm,
40 which may be life threatening. If paradoxical bronchospasm occurs following dosing with
41 INCRUSE ELLIPTA, it should be treated immediately with an inhaled, short-acting

42 bronchodilator; INCRUSE ELLIPTA should be discontinued immediately; and alternative
43 therapy should be instituted.

44 **5.3 Hypersensitivity Reactions**

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

49 **5.4 Worsening of Narrow-Angle Glaucoma**

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

55 **5.5 Worsening of Urinary Retention**

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

61 **6 ADVERSE REACTIONS**

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

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

66 **6.1 Clinical Trials Experience**

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

70 In the 8 clinical trials conducted to support initial approval of INCRUSE ELLIPTA, a total of
71 1,663 subjects with COPD (mean age: 62.7 years; 89% white; 65% male across all treatments,
72 including placebo) received at least 1 inhalation dose of umeclidinium at doses of 62.5 or
73 125 mcg. In the 4 randomized, double-blind, placebo- or active-controlled, efficacy clinical
74 trials, 1,185 subjects received umeclidinium for up to 24 weeks, of which 487 subjects received
75 the recommended dose of umeclidinium 62.5 mcg. In a 12-month, randomized, double-blind,

76 placebo-controlled, long-term safety trial, 227 subjects received umeclidinium 125 mcg for up to
 77 52 weeks [see *Clinical Studies (14)*].

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

80 **Table 1. Adverse Reactions with INCRUSE ELLIPTA with $\geq 1\%$ Incidence and More**
 81 **Common than Placebo in Subjects with Chronic Obstructive Pulmonary Disease**

Adverse Reaction	INCRUSE ELLIPTA (n = 487) %	Placebo (n = 348) %
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%

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

84 In a long-term safety trial, 336 subjects (n = 227 umeclidinium 125 mcg, n = 109 placebo) were
 85 treated for up to 52 weeks with umeclidinium 125 mcg or placebo. The demographic and
 86 baseline characteristics of the long-term safety trial were similar to those of the efficacy trials
 87 described above. Adverse reactions that occurred with a frequency greater than or equal to 1% in
 88 subjects receiving umeclidinium 125 mcg that exceeded that in placebo in this trial were:
 89 nasopharyngitis, upper respiratory tract infection, urinary tract infection, pharyngitis, pneumonia,
 90 lower respiratory tract infection, rhinitis, supraventricular tachycardia, supraventricular

91 extrasystoles, sinus tachycardia, idioventricular rhythm, headache, dizziness, sinus headache,
92 cough, back pain, arthralgia, pain in extremity, neck pain, myalgia, nausea, dyspepsia, diarrhea,
93 rash, depression, and vertigo.

94 The safety and efficacy of INCRUSE ELLIPTA in combination with an inhaled
95 corticosteroid/long-acting beta₂-adrenergic agonist (ICS/LABA) were also evaluated in four
96 12-week clinical trials. A total of 1,637 subjects with COPD across four 12-week, randomized,
97 double-blind clinical trials received at least 1 dose of INCRUSE ELLIPTA (62.5 mcg) or
98 placebo administered once daily in addition to background ICS/LABA (mean age: 64 years, 88%
99 white, 65% male across all treatments). Two trials (Trials 1 and 2) evaluated INCRUSE
100 ELLIPTA in combination with fluticasone furoate/vilanterol (FF/VI) 100 mcg/25 mcg
101 administered once daily, and 2 trials (Trials 3 and 4) evaluated INCRUSE ELLIPTA
102 administered once daily in combination with fluticasone propionate/salmeterol (FP/SAL) 250
103 mcg/50 mcg administered twice daily [*see Clinical Studies (14.2)*]. Adverse reactions that
104 occurred with INCRUSE ELLIPTA in combination with an ICS/LABA were similar to those
105 reported with INCRUSE ELLIPTA as monotherapy. In addition to the umeclidinium
106 monotherapy adverse reactions reported above, adverse reactions occurring with INCRUSE
107 ELLIPTA in combination with an ICS/LABA, at an incidence of greater than or equal to 1% and
108 exceeding ICS/LABA alone, were oropharyngeal pain and dysgeusia.

109 **7 DRUG INTERACTIONS**

110 **7.1 Anticholinergics**

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

115 **8 USE IN SPECIFIC POPULATIONS**

116 **8.1 Pregnancy**

117 Teratogenic Effects

118 Pregnancy Category C. There are no adequate and well-controlled trials with INCRUSE
119 ELLIPTA in pregnant women. Because animal reproduction studies are not always predictive of
120 human response, INCRUSE ELLIPTA should be used during pregnancy only if the potential
121 benefit justifies the potential risk to the fetus. Women should be advised to contact their
122 healthcare providers if they become pregnant while taking INCRUSE ELLIPTA.

123 There were no teratogenic effects in rats and rabbits at approximately 50 and 200 times,
124 respectively, the maximum recommended human daily inhaled dose (MRHDID) in adults (on an
125 AUC basis at maternal inhaled doses up to 278 mcg/kg/day in rats and maternal subcutaneous
126 doses up to 180 mcg/kg/day in rabbits).

127 Nonteratogenic Effects

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

130 **8.2 Labor and Delivery**

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

134 **8.3 Nursing Mothers**

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

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

144 **8.4 Pediatric Use**

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

147 **8.5 Geriatric Use**

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

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

155 **8.6 Hepatic Impairment**

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

160 **8.7 Renal Impairment**

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

165 **10 OVERDOSAGE**

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

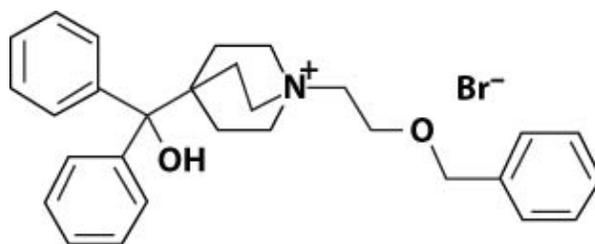
167 High doses of umeclidinium may lead to anticholinergic signs and symptoms. However, there
168 were no systemic anticholinergic adverse effects following a once-daily inhaled dose of up to
169 1,000 mcg umeclidinium (16 times the maximum recommended daily dose) for 14 days in
170 subjects with COPD.

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

173 **11 DESCRIPTION**

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

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



178
179 Umeclidinium bromide is a white powder with a molecular weight of 508.5, and the empirical
180 formula is $C_{29}H_{34}NO_2 \cdot Br$ (as a quaternary ammonium bromide compound). It is slightly soluble
181 in water.

182 INCRUSE ELLIPTA is a light grey and light green plastic inhaler containing a foil blister strip.
183 Each blister on the strip contains a white powder mix of micronized umeclidinium bromide
184 (74.2 mcg equivalent to 62.5 mcg of umeclidinium), magnesium stearate (75 mcg), and lactose
185 monohydrate (to 12.5 mg). The lactose monohydrate contains milk proteins. After the inhaler is
186 activated, the powder within the blister is exposed and ready for dispersion into the airstream
187 created by the patient inhaling through the mouthpiece.

188 Under standardized in vitro test conditions, INCRUSE ELLIPTA delivers 55 mcg of
189 umeclidinium per blister when tested at a flow rate of 60 L/min for 4 seconds.

190 In adult subjects with obstructive lung disease and severely compromised lung function (COPD
191 with forced expiratory volume in 1 second/forced vital capacity [FEV₁/FVC] less than 70% and
192 FEV₁ less than 30% predicted or FEV₁ less than 50% predicted plus chronic respiratory failure),
193 mean peak inspiratory flow through the ELLIPTA inhaler was 67.5 L/min (range: 41.6 to
194 83.3 L/min).

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

197 **12 CLINICAL PHARMACOLOGY**

198 **12.1 Mechanism of Action**

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

208 **12.2 Pharmacodynamics**

209 Cardiac Electrophysiology

210 QTc interval prolongation was studied in a double-blind, multiple dose, placebo- and positive-
211 controlled, crossover trial in 86 healthy subjects. Following repeat doses of umeclidinium
212 500 mcg once daily (8 times the recommended dosage) for 10 days, umeclidinium does not
213 prolong QTc to any clinically relevant extent.

214 **12.3 Pharmacokinetics**

215 Linear pharmacokinetics were observed for umeclidinium (62.5 to 500 mcg).

216 Absorption

217 Umeclidinium plasma levels may not predict therapeutic effect. Following inhaled
218 administration of umeclidinium in healthy subjects, C_{max} occurred at 5 to 15 minutes.
219 Umeclidinium is mostly absorbed from the lung after inhaled doses with minimum contribution
220 from oral absorption. Following repeat dosing of inhaled INCRUSE ELLIPTA, steady state was
221 achieved within 14 days with 1.8-fold accumulation.

222 Distribution

223 Following intravenous administration to healthy subjects, the mean volume of distribution was
224 86 L. In vitro plasma protein binding in human plasma was on average 89%.

225 Metabolism

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

232 Elimination

233 Following intravenous dosing with radiolabeled umeclidinium, mass balance showed 58% of the
234 radiolabel in the feces and 22% in the urine. The excretion of the drug-related material in the
235 feces following intravenous dosing indicated elimination in the bile. Following oral dosing to
236 healthy male subjects, radiolabel recovered in feces was 92% of the total dose and that in urine
237 was less than 1% of the total dose, suggesting negligible oral absorption. The effective half-life
238 after once-daily dosing is 11 hours.

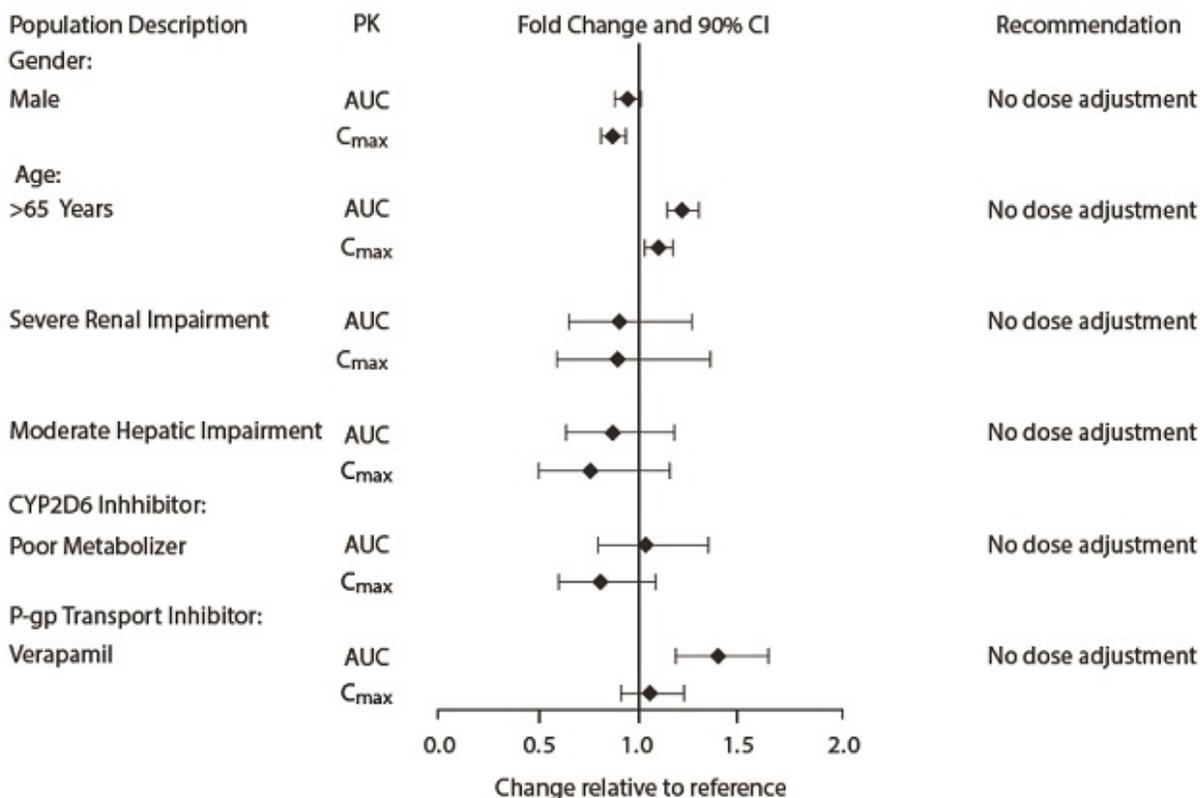
239 Special Populations

240 Population pharmacokinetic analysis showed no evidence of a clinically significant effect of age
241 (40 to 93 years) (see Figure 1), gender (69% male) (see Figure 1), inhaled corticosteroid use
242 (48%), or weight (34 to 161 kg) on systemic exposure of umeclidinium. In addition, there was no
243 evidence of a clinically significant effect of race.

244 *Hepatic Impairment:* The impact of hepatic impairment on the pharmacokinetics of INCRUSE
245 ELLIPTA has been evaluated in subjects with moderate hepatic impairment (Child-Pugh score of
246 7-9). There was no evidence of an increase in systemic exposure to umeclidinium (C_{max} and
247 AUC) (see Figure 1). There was no evidence of altered protein binding in subjects with moderate
248 hepatic impairment compared with healthy subjects. INCRUSE ELLIPTA has not been
249 evaluated in subjects with severe hepatic impairment.

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

255 **Figure 1. Impact of Intrinsic and Extrinsic Factors on the Systemic Exposure of**
 256 **Umeclidinium**



257

258 Drug Interactions

259 *Umeclidinium and P-glycoprotein Transporter:* Umeclidinium is a substrate of P-gp. The effect
 260 of the moderate P-gp transporter inhibitor verapamil (240 mg once daily) on the steady-state
 261 pharmacokinetics of umeclidinium was assessed in healthy subjects. No effect on umeclidinium
 262 C_{max} was observed; however, an approximately 1.4-fold increase in umeclidinium AUC was
 263 observed (see Figure 1).

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

269 **13 NONCLINICAL TOXICOLOGY**

270 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

271 Umeclidinium produced no treatment-related increases in the incidence of tumors in 2-year
 272 inhalation studies in rats and mice at inhaled doses up to 137 and 295/200 mcg/kg/day

273 (male/female), respectively (approximately 20 and 25/20 times the MRHDID in adults on an
274 AUC basis, respectively).

275 Umeclidinium tested negative in the following genotoxicity assays: the in vitro Ames assay, in
276 vitro mouse lymphoma assay, and in vivo rat bone marrow micronucleus assay.

277 No evidence of impairment of fertility was observed in male and female rats at subcutaneous
278 doses up to 180 mcg/kg/day and inhaled doses up to 294 mcg/kg/day, respectively
279 (approximately 100 and 50 times, respectively, the MRHDID in adults on an AUC basis).

280 **14 CLINICAL STUDIES**

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

286 The safety and efficacy of INCRUSE ELLIPTA in combination with an ICS/LABA were also
287 evaluated in four 12-week clinical trials. The efficacy of INCRUSE ELLIPTA in combination
288 with an ICS/LABA is based on 1,637 subjects with COPD.

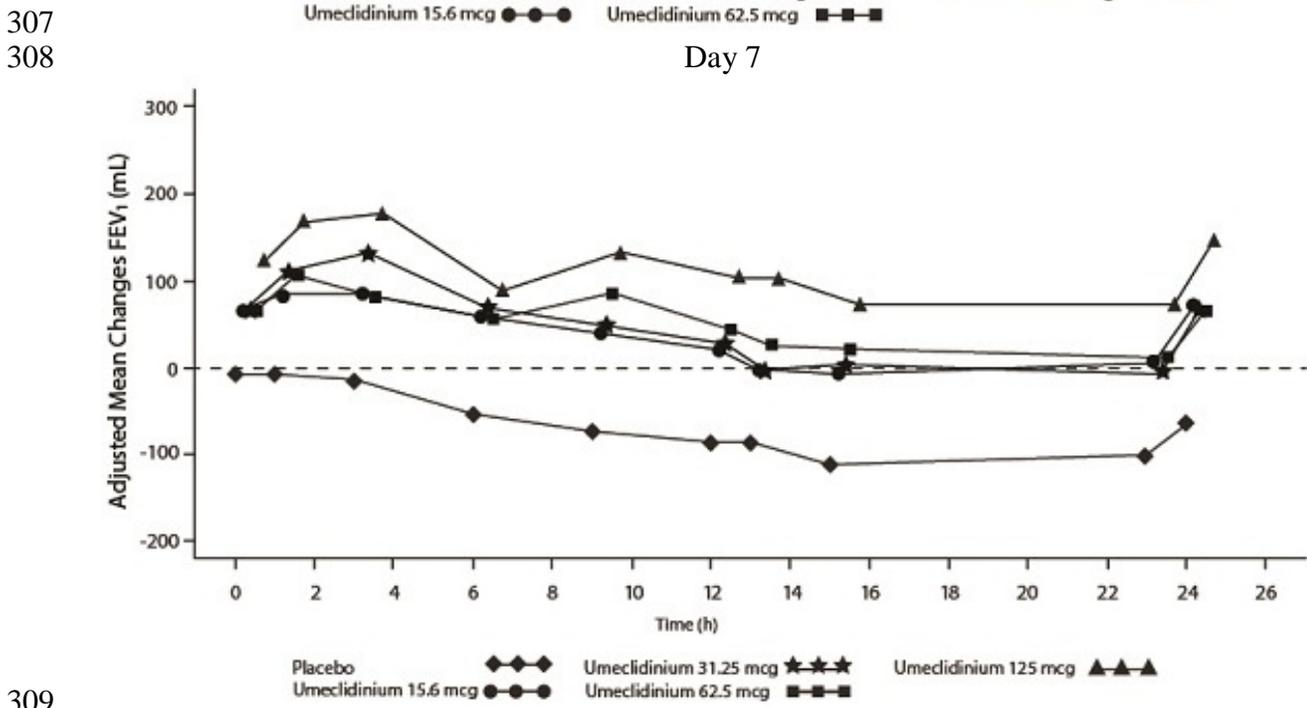
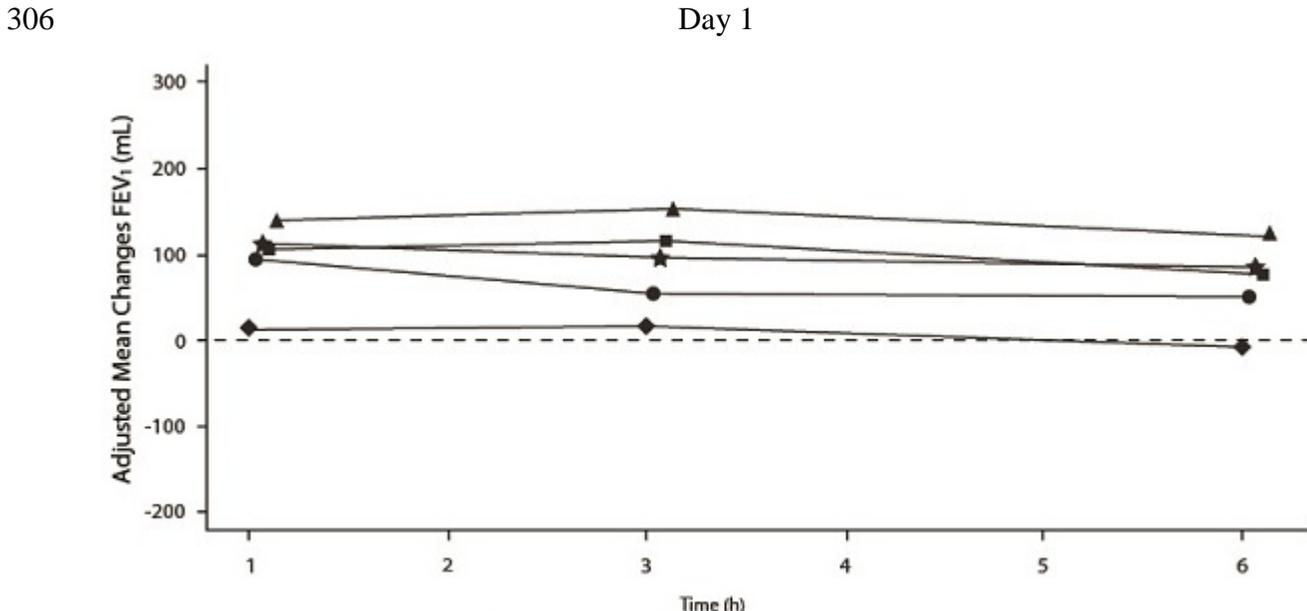
289 **14.1 Dose-Ranging Trials**

290 Dose selection for umeclidinium in COPD was supported by a 7-day, randomized, double-blind,
291 placebo-controlled, crossover trial evaluating 4 doses of umeclidinium (15.6 to 125 mcg) or
292 placebo dosed once daily in the morning in 163 subjects with COPD. A dose ordering was
293 observed, with the 62.5- and 125-mcg doses demonstrating larger improvements in FEV₁ over 24
294 hours compared with the lower doses of 15.6 and 31.25 mcg (Figure 2).

295 The differences in trough FEV₁ from baseline after 7 days for placebo and the 15.6-, 31.25-,
296 62.5-, and 125-mcg doses were -74 mL (95% CI: -118, -31), 38 mL (95% CI: -6, 83), 27 mL
297 (95% CI: -18, 72), 49 mL (95% CI: 6, 93), and 109 mL (95% CI: 65, 152), respectively. Two
298 additional dose-ranging trials in subjects with COPD demonstrated minimal additional benefit at
299 doses above 125 mcg. The dose-ranging results supported the evaluation of 2 doses of
300 umeclidinium, 62.5 and 125 mcg, in the confirmatory COPD trials to further assess dose
301 response.

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

304 **Figure 2. Adjusted Mean Change from Baseline in Postdose Serial FEV₁ (mL) on Days 1**
 305 **and 7**



309

310 **14.2 Maintenance Treatment: Confirmatory Trials**

311 The clinical development program for INCRUSE ELLIPTA included 2 randomized, double-
 312 blind, placebo-controlled, parallel-group trials in subjects with COPD designed to evaluate the
 313 efficacy of INCRUSE ELLIPTA on lung function. Trial 1 was a 24-week placebo-controlled

314 trial, and Trial 2 was a 12-week placebo-controlled trial. These trials treated subjects that had a
 315 clinical diagnosis of COPD, were 40 years of age or older, had a history of smoking greater than
 316 or equal to 10 pack-years, had a post-albuterol FEV₁ less than or equal to 70% of predicted
 317 normal values, had a ratio of FEV₁/FVC of less than 0.7, and had a Modified Medical Research
 318 Council (mMRC) score greater than or equal to 2. Subjects in Trial 1 had a mean age of 63 years
 319 and an average smoking history of 46 pack-years, with 50% identified as current smokers. At
 320 screening, the mean post-bronchodilator percent predicted FEV₁ was 47% (range: 13% to 74%),
 321 the mean post-bronchodilator FEV₁/FVC ratio was 0.47 (range: 0.20 to 0.74), and the mean
 322 percent reversibility was 15% (range: -35% to 109%). Baseline demographics and lung function
 323 for subjects in Trial 2 were similar to those in Trial 1.

324 Trial 1 evaluated umeclidinium 62.5 mcg and placebo. The primary endpoint was change from
 325 baseline in trough (predose) FEV₁ at Day 169 (defined as the mean of the FEV₁ values obtained
 326 at 23 and 24 hours after the previous dose on Day 168) compared with placebo. INCRUSE
 327 ELLIPTA 62.5 mcg demonstrated a larger increase in mean change from baseline in trough
 328 (predose) FEV₁ relative to placebo (Table 2). Similar results were obtained from Trial 2.

329 **Table 2. Least Squares Mean Change from Baseline in Trough FEV₁ (mL) at Day**
 330 **169 in the Intent-to-Treat Population (Trial 1)**

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

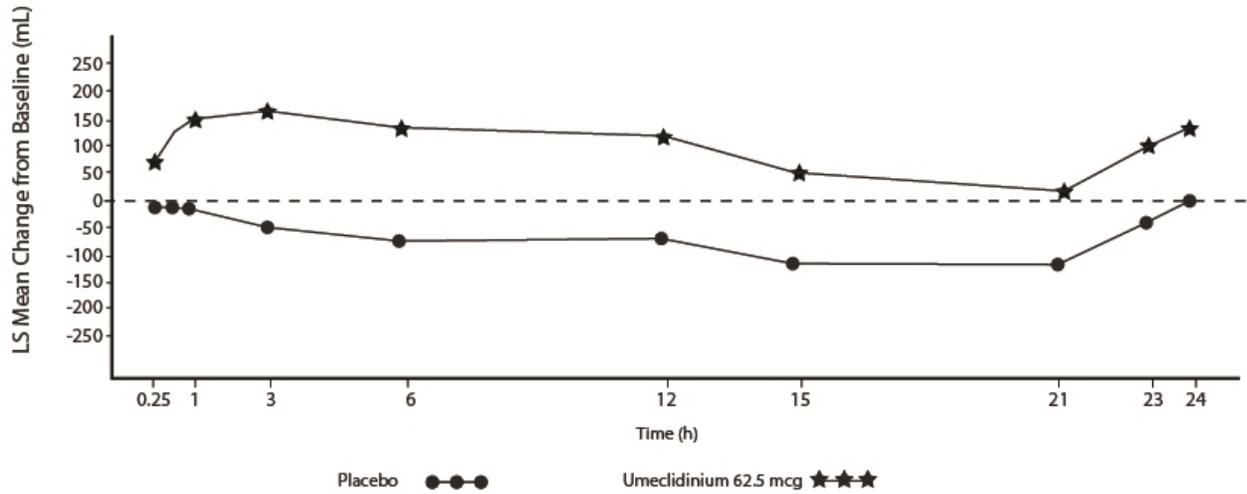
331 n = Number in intent-to-treat population.

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

336 **Figure 3. Least Squares (LS) Mean Change from Baseline in FEV₁ (mL) over Time (0-24 h)**
 337 **on Days 1 and 168 (Trial 1 Subset Population)**

338

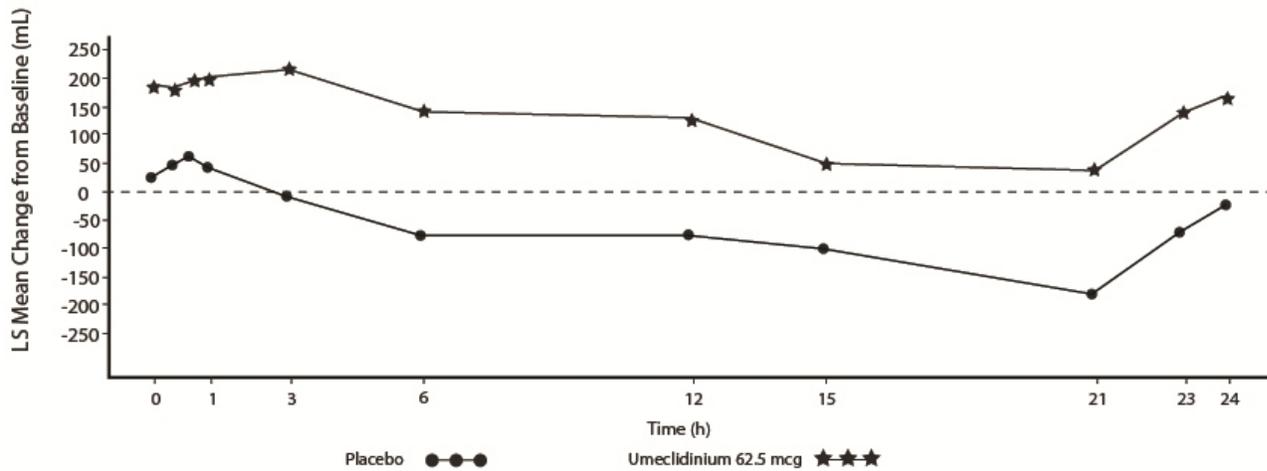
Day 1



339

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Day 168



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342 In Trial 1, the mean peak FEV₁ (over the first 6 hours relative to baseline) at Day 1 and at Day
 343 168 for the group receiving umeclidinium 62.5 mcg compared with placebo was 126 and
 344 130 mL, respectively.

345 Health-related quality of life was measured using St. George's Respiratory Questionnaire
 346 (SGRQ). Umeclidinium demonstrated an improvement in mean SGRQ total score compared with
 347 placebo treatment at Day 168: -4.69 (95% CI: -7.07,-2.31). The proportion of patients with a
 348 clinically meaningful decrease (defined as a decrease of at least 4 units from baseline) at Week
 349 24 was greater for INCRUSE ELLIPTA 62.5 mcg (42%; 172/410) compared with placebo (31%;
 350 86/274).

351 **14.3 Maintenance Treatment: Combination with an ICS/LABA Trials**

352 The efficacy of INCRUSE ELLIPTA in combination with an ICS/LABA was evaluated in 4
353 randomized, double-blind, parallel-group trials in subjects with COPD. These trials, all of similar
354 study design, were of 12-weeks' treatment duration. Subjects were randomized to INCRUSE
355 ELLIPTA 62.5 mcg + ICS/LABA or placebo + ICS/LABA. Entry criteria for subjects enrolled in
356 these trials were similar to those described above in Section 14.2. The primary endpoint for these
357 trials was change from baseline in trough (predose) FEV₁ at Day 85 (defined as the mean of the
358 FEV₁ values obtained at 23 and 24 hours after the previous dose on Day 84). Baseline FEV₁ was
359 measured while subjects were on background ICS/LABA.

360 Combination with Fluticasone Furoate + Vilanterol

361 Trials 1 and 2 randomized subjects to INCRUSE ELLIPTA 62.5 mcg + FF/VI 100 mcg/25 mcg
362 administered once daily or placebo + FF/VI 100 mcg/25 mcg administered once daily. Trial
363 population demographics and results for Trials 1 and 2 were similar; therefore, only Trial 1
364 results are presented below.

365 Subjects in Trial 1 across all treatment arms had a mean age of 64 years and an average smoking
366 history of 50 pack-years, with 42% identified as current smokers. At screening, the mean
367 postbronchodilator percent predicted FEV₁ was 45% (range: 13% to 76%), the mean
368 postbronchodilator FEV₁/FVC ratio was 0.48 (range: 0.22 to 0.70), and the mean percent
369 reversibility was 14% (range: -20% to 71%).

370 The primary endpoint was change from baseline in trough (predose) FEV₁ at Day 85 (defined as
371 the mean of the FEV₁ values obtained at 23 and 24 hours after the previous dose on Day 84)
372 compared with placebo (INCRUSE ELLIPTA + FF/VI vs. placebo + FF/VI). INCRUSE
373 ELLIPTA + FF/VI demonstrated a larger mean change from baseline in trough (predose) FEV₁
374 relative to placebo + FF/VI (Table 3).

375 **Table 3. Least Squares Mean Change from Baseline in Trough FEV₁ (mL) at**
376 **Day 85 in the Intent-to-Treat Population (Trial 1)**

Treatment	n	Trough FEV ₁ (mL) at Day 85
		Difference from Placebo + FF/VI (95% CI) n = 206
INCRUSE ELLIPTA + FF/VI	n = 206	124 (93, 154)

377 FF/VI = Fluticasone furoate/vilanterol.

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

379 Combination with Fluticasone Propionate + Salmeterol

380 Trials 3 and 4 randomized subjects to INCRUSE ELLIPTA 62.5 mcg + FP/SAL
381 250 mcg/50 mcg or placebo + FP/SAL 250 mcg/50 mcg. The treatments with INCRUSE

382 ELLIPTA and placebo were administered once daily, while the FP/SAL treatment was
383 administered twice daily. Trial population demographics and results for Trials 3 and 4 were
384 similar; therefore, only Trial 3 results are presented below.

385 Subjects in Trial 3 across all treatment arms had a mean age of 63 years and an average smoking
386 history of 50 pack-years, with 54% identified as current smokers. At screening, the mean
387 postbronchodilator percent predicted FEV₁ was 47% (range: 12% to 70%), the mean
388 postbronchodilator FEV₁/FVC ratio was 0.47 (range: 0.22 to 0.69), and the mean percent
389 reversibility was 16% (range: -36% to 79%).

390 The primary endpoint was change from baseline in trough (predose) FEV₁ at Day 85 (defined as
391 the mean of the FEV₁ values obtained at 23 and 24 hours after the previous dose on Day 84)
392 compared with placebo (INCRUSE ELLIPTA + FP/SAL vs. placebo + FP/SAL). INCRUSE
393 ELLIPTA + FP/SAL demonstrated a larger mean change from baseline in trough (predose) FEV₁
394 relative to placebo + FP/SAL (Table 4).

395 **Table 4. Least Squares Mean Change from Baseline in Trough FEV₁ (mL) at**
396 **Day 85 in the Intent-to-Treat Population (Trial 3)**

Treatment	n	Trough FEV ₁ (mL) at Day 85
		Difference from Placebo + FP/SAL (95% CI) n = 205
INCRUSE ELLIPTA+FP/SAL	n = 204	147 (107, 187)

397 FP/SAL = Fluticasone propionate/salmeterol.

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

399 **16 HOW SUPPLIED/STORAGE AND HANDLING**

400 INCRUSE ELLIPTA is supplied as a disposable light grey and light green plastic inhaler
401 containing a foil strip with 30 blisters (NDC 0173-0873-10) or 7 blisters (institutional pack)
402 (NDC 0173-0873-06).

403 The inhaler is packaged in a moisture-protective foil tray with a desiccant and a peelable lid.

404 Store at room temperature between 68°F and 77°F (20°C and 25°C); excursions permitted from
405 59°F to 86°F (15°C to 30°C) [See USP Controlled Room Temperature]. Store in a dry place
406 away from direct heat or sunlight. Keep out of reach of children.

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

411 **17 PATIENT COUNSELING INFORMATION**

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

414 Not for Acute Symptoms

415 Inform patients that INCRUSE ELLIPTA is not meant to relieve acute symptoms of COPD and
416 extra doses should not be used for that purpose. Advise patients to treat acute symptoms with an
417 inhaled, short-acting beta₂-agonist such as albuterol. Provide patients with such medicine and
418 instruct them in how it should be used.

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

- 420 • Decreasing effectiveness of inhaled, short-acting beta₂-agonists
- 421 • Need for more inhalations than usual of inhaled, short-acting beta₂-agonists
- 422 • Significant decrease in lung function as outlined by the physician

423 Tell patients they should not stop therapy with INCRUSE ELLIPTA without healthcare provider
424 guidance since symptoms may recur after discontinuation.

425 Paradoxical Bronchospasm

426 As with other inhaled medicines, INCRUSE ELLIPTA can cause paradoxical bronchospasm. If
427 paradoxical bronchospasm occurs, instruct patients to discontinue INCRUSE ELLIPTA.

428 Worsening of Narrow-Angle Glaucoma

429 Instruct patients to be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., eye
430 pain or discomfort, blurred vision, visual halos or colored images in association with red eyes
431 from conjunctival congestion and corneal edema). Instruct patients to consult a healthcare
432 provider immediately if any of these signs or symptoms develops.

433 Worsening of Urinary Retention

434 Instruct patients to be alert for signs and symptoms of urinary retention (e.g., difficulty passing
435 urine, painful urination). Instruct patients to consult a healthcare provider immediately if any of
436 these signs or symptoms develops.

437

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439

440



441

442 GlaxoSmithKline

443 Research Triangle Park, NC 27709

444
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446
447 INC:xPI

448
449 **Patient Information**

450 **INCRUSE[®] ELLIPTA[®] [IN-cruise e-LIP-ta]**
451 **(umeclidinium inhalation powder)**

452
453 **What is INCRUSE ELLIPTA?**

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

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

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

466
467 **Who should not use INCRUSE ELLIPTA?**

468 Do not use INCRUSE ELLIPTA if you:

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

472
473 **What should I tell my healthcare provider before using INCRUSE ELLIPTA?**

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

- 475 • have heart problems.
476 • have eye problems such as glaucoma. INCRUSE ELLIPTA may make your glaucoma worse.
477 • have prostate or bladder problems, or problems passing urine. INCRUSE ELLIPTA may make these
478 problems worse.
479 • are allergic to any of the ingredients in INCRUSE ELLIPTA, any other medicines, or food products.
480 See “What are the ingredients in INCRUSE ELLIPTA?” below for a complete list of ingredients.
481 • have any other medical conditions.

- 482 • are pregnant or planning to become pregnant. It is not known if INCRUSE ELLIPTA may harm your
483 unborn baby.
- 484 • are breastfeeding. It is not known if the medicine in INCRUSE ELLIPTA passes into your milk and if it
485 can harm your baby.

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

489 Especially tell your healthcare provider if you take:

- 490 • anticholinergics (including tiotropium, ipratropium, aclidinium)
491 • atropine

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

494

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

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

- 498 • **Do not** use INCRUSE ELLIPTA unless your healthcare provider has taught you how to use the
499 inhaler and you understand how to use it correctly.
- 500 • Use INCRUSE ELLIPTA exactly as your healthcare provider tells you to use it. **Do not** use INCRUSE
501 ELLIPTA more often than prescribed.
- 502 • Use 1 inhalation of INCRUSE ELLIPTA 1 time each day. Use INCRUSE ELLIPTA at the same time
503 each day.
- 504 • If you miss a dose of INCRUSE ELLIPTA, take it as soon as you remember. Do not take more than 1
505 inhalation each day. Take your next dose at your usual time. Do not take 2 doses at 1 time.
- 506 • If you take too much INCRUSE ELLIPTA, call your healthcare provider or go to the nearest hospital
507 emergency room right away if you have any unusual symptoms, such as worsening shortness of
508 breath, chest pain, increased heart rate, or shakiness.
- 509 • **Do not use other medicines that contain an anticholinergic for any reason.** Ask your healthcare
510 provider or pharmacist if any of your other medicines are anticholinergic medicines.
- 511 • Do not stop using INCRUSE ELLIPTA unless told to do so by your healthcare provider because your
512 symptoms might get worse. Your healthcare provider will change your medicines as needed.
- 513 • **INCRUSE ELLIPTA does not relieve sudden breathing problems.** Always have a rescue inhaler
514 with you to treat sudden symptoms. If you do not have a rescue inhaler, call your healthcare provider
515 to have one prescribed for you.
- 516 • Call your healthcare provider or get medical care right away if:

- 517 • your breathing problems get worse.
- 518 • you need to use your rescue inhaler more often than usual.
- 519 • your rescue inhaler does not work as well to relieve your symptoms.

520

521 **What are the possible side effects with INCRUSE ELLIPTA?**

522 **INCRUSE ELLIPTA can cause serious side effects, including:**

- 523 • **sudden breathing problems immediately after inhaling your medicine.** If you have sudden
524 breathing problems immediately after inhaling your medicine, stop taking INCRUSE ELLIPTA and call
525 your healthcare provider right away.

- 526 • **serious allergic reactions.** Call your healthcare provider or get emergency medical care if you get
527 any of the following symptoms of a serious allergic reaction:

- 528 • rash
- 529 • hives
- 530 • swelling of your face, mouth, and tongue
- 531 • breathing problems

- 532 • **new or worsened eye problems including acute narrow-angle glaucoma.** Acute narrow-angle
533 glaucoma can cause permanent loss of vision if not treated. Symptoms of acute narrow-angle
534 glaucoma may include:

- 535 • eye pain or discomfort
- 536 • nausea or vomiting
- 537 • blurred vision
- 538 • seeing halos or bright colors around lights
- 539 • red eyes

540 If you have these symptoms, call your healthcare provider right away before taking another dose.

- 541 • **urinary retention.** People who take INCRUSE ELLIPTA may develop new or worse urinary retention.
542 Symptoms of urinary retention may include:

- 543 • difficulty urinating
- 544 • painful urination
- 545 • urinating frequently
- 546 • urination in a weak stream or drips

547 If you have these symptoms of urinary retention, stop taking INCRUSE ELLIPTA, and call your
548 healthcare provider right away before taking another dose.

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

- 550 • upper respiratory infection
- 551 • stuffy or runny nose
- 552 • cough
- 553 • sore throat

- 554 • joint pain
- 555 • muscle pain
- 556 • tooth pain
- 557 • stomach pain
- 558 • bruising or dark areas of skin
- 559 • fast or irregular heartbeat

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

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

563 Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-
564 1088.

565

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

567 • Store INCRUSE ELLIPTA at room temperature between 68°F and 77°F (20°C and 25°C). Keep in a
568 dry place away from heat and sunlight.

569 • Store INCRUSE ELLIPTA in the unopened foil tray and only open when ready for use.

570 • Safely throw away INCRUSE ELLIPTA in the trash 6 weeks after you open the foil tray or when the
571 counter reads “0”, whichever comes first. Write the date you open the tray on the label on the inhaler.

572 • **Keep INCRUSE ELLIPTA and all medicines out of the reach of children.**

573

574 **General information about the safe and effective use of INCRUSE ELLIPTA**

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

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

582 For more information about INCRUSE ELLIPTA, call 1-888-825-5249 or visit our website at
583 www.INCRUSE.com.

584

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

586 Active ingredients: umeclidinium

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

588

589

Instructions for Use

590 **For Oral Inhalation Only.**

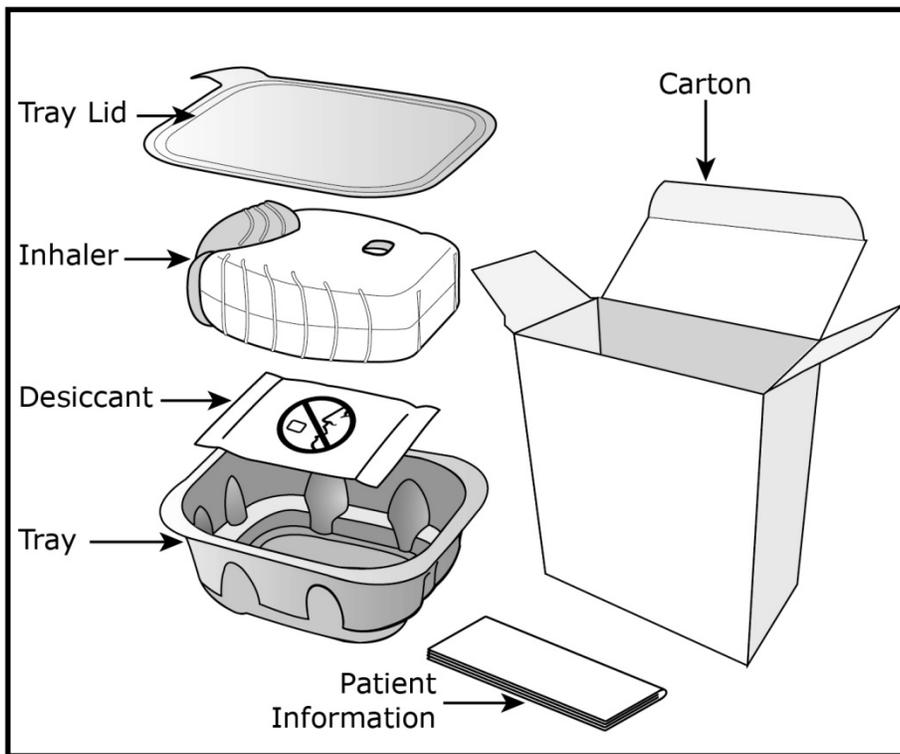
591

592 **Read this before you start:**

- 593 • **If you open and close the cover without inhaling the medicine, you will lose the dose.**
- 594 • **The lost dose will be securely held inside the inhaler, but it will no longer be available to be**
- 595 **inhaled.**
- 596 • **It is not possible to accidentally take a double dose or an extra dose in 1 inhalation.**

597

598 **Your INCRUSE ELLIPTA inhaler**



599

600

601 **How to use your inhaler**

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

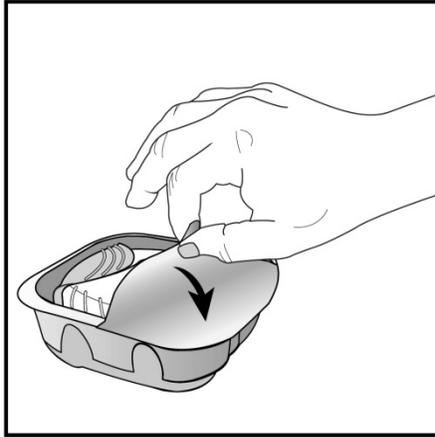


Figure A

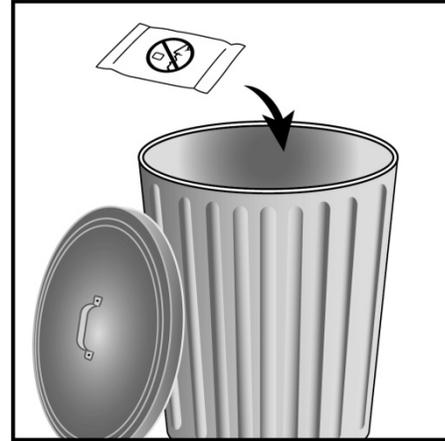


Figure B

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612 **Important Notes:**

- 613 • Your inhaler contains 30 doses (7 doses if you have a sample or institutional pack).
- 614 • Each time you fully open the cover of the inhaler (you will hear a clicking sound), a dose is ready to be inhaled. This is shown by a decrease in the number on the counter.
- 616 • If you open and close the cover without inhaling the medicine, you will lose the dose. The lost dose will be held in the inhaler, but it will no longer be available to be inhaled. It is not possible to accidentally take a double dose or an extra dose in 1 inhalation.
- 619 • **Do not** open the cover of the inhaler until you are ready to use it. To avoid wasting doses after the inhaler is ready, **do not** close the cover until after you have inhaled the medicine.
- 621 • Write the “Tray opened” and “Discard” dates on the inhaler label. The “Discard” date is 6 weeks from the date you open the tray.

623

624 **Check the counter. See Figure C.**

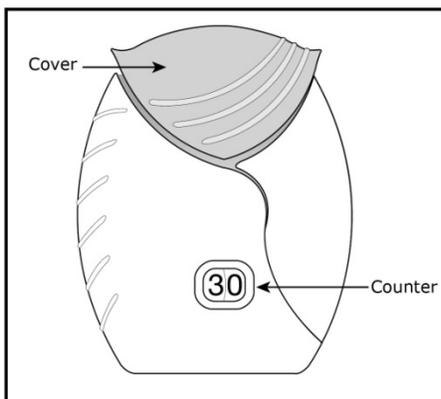


Figure C

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- 628 • 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.
- 632 • Each time you open the cover, you prepare 1 dose of medicine.
- 634 • The counter counts down by 1 each time you open the cover.

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

639

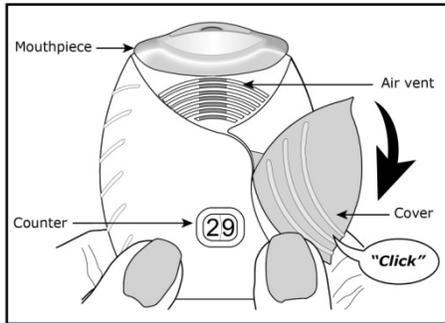


Figure D

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.

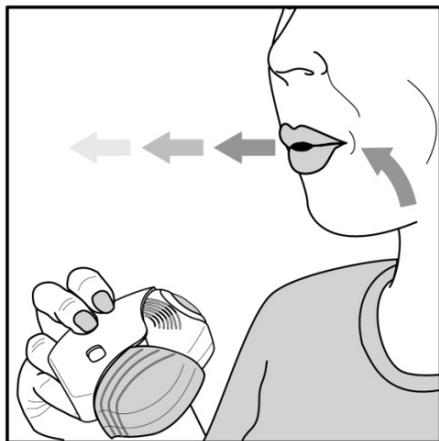


Figure E

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.

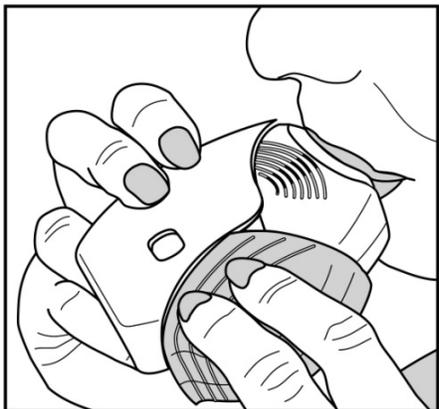


Figure F

Step 3. Inhale your medicine. See Figure F.

- Put the mouthpiece between your lips, and close your lips firmly around it. Your lips should fit over the curved shape of the mouthpiece.
- Take 1 long, steady, deep breath in through your mouth. **Do not** breathe in through your nose.

Do not block the air vent with your fingers.

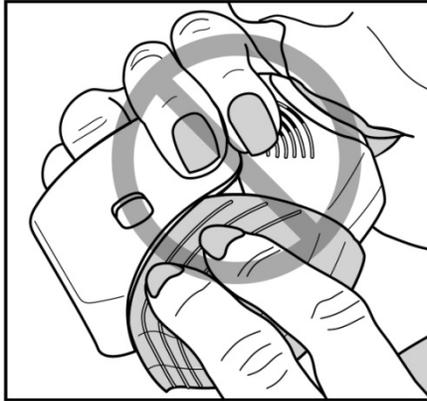


Figure G

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

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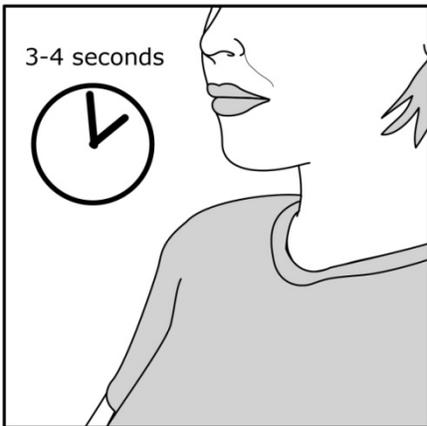


Figure H

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

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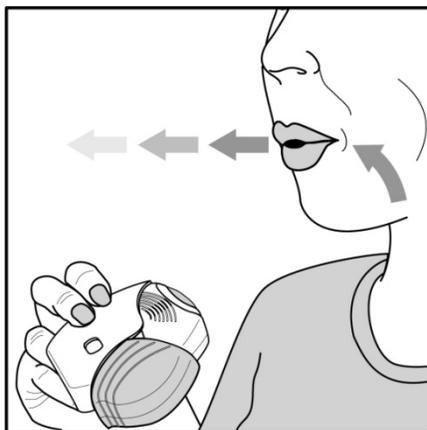


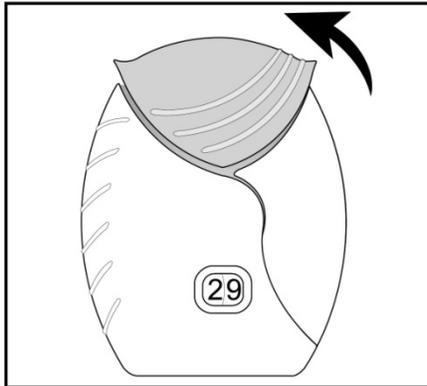
Figure I

Step 4. Breathe out slowly and gently. See Figure I.

- You may not taste or feel the medicine, even when you are using the inhaler correctly.
- **Do not** take another dose from the inhaler even if you do not feel or taste the medicine.

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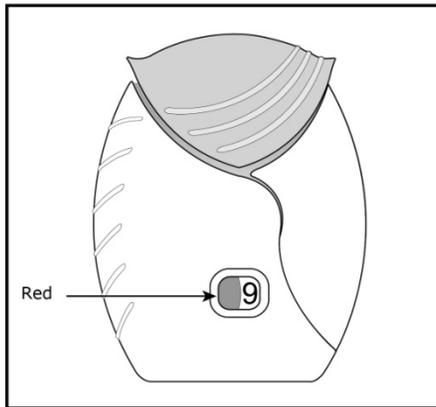


714
715 **Figure J**
716

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

- 719 • You can clean the mouthpiece if needed, using a dry
720 tissue, before you close the cover. Routine cleaning is
721 not required.
- 722 • Slide the cover up and over the mouthpiece as far as
723 it will go.

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



725
726 **Figure K**

- 727 • **When you have less than 10 doses remaining** in
728 your inhaler, the left half of the counter shows red as a
729 reminder to get a refill. **See Figure K.**
- 730 • After you have inhaled the last dose, the counter will
731 show “0” and will be empty.
- 732 • Throw the empty inhaler away in your household trash
733 out of reach of children and pets.

734

735 If you have questions about INCRUSE ELLIPTA or how to use your inhaler, call GlaxoSmithKline (GSK)
736 at 1-888-825-5249 or visit www.INCRUSE.com.

737

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

740

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745 GlaxoSmithKline

746 Research Triangle Park, NC 27709

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749 Month Year

750 INC:xPIL