

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

202450Orig1s000

LABELING

1 **HIGHLIGHTS OF PRESCRIBING INFORMATION**

2
3 **These highlights do not include all the**
4 **information needed to use TUDORZA PRESSAIR**
5 **safely and effectively. See full prescribing**
6 **information for TUDORZA PRESSAIR.**

7
8 **TUDORZA™ PRESSAIR™ (aclidinium bromide**
9 **inhalation powder)**

10
11 **FOR ORAL INHALATION ONLY**

12
13 **Initial U.S. Approval: 2012**

14
15 -----**INDICATIONS AND USAGE**-----

16 TUDORZA PRESSAIR is an anticholinergic indicated for
17 the long-term maintenance treatment of bronchospasm
18 associated with chronic obstructive pulmonary disease
19 (COPD), including chronic bronchitis and emphysema.
20 (1)

21
22 -----**DOSAGE AND ADMINISTRATION**-----

23 For oral inhalation only
24 • One inhalation of TUDORZA PRESSAIR 400 mcg
25 twice daily. (2)

26
27 -----**DOSAGE FORMS AND STRENGTHS**-----

28 • Inhalation powder; The multi-dose device is a dry
29 powder inhaler metering 400 mcg of aclidinium
30 bromide per actuation. (3)

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32 -----**CONTRAINDICATIONS**-----

33 None.

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35 -----**WARNINGS AND PRECAUTIONS**-----

36 • Not for acute use: Not for use as a rescue
37 medication. (5.1)

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- 38 • Paradoxical bronchospasm: Discontinue TUDORZA
39 PRESSAIR and consider other treatments if
40 paradoxical bronchospasm occurs. (5.2)
41 • Worsening of narrow-angle glaucoma may occur.
42 Use with caution in patients with narrow-angle
43 glaucoma and instruct patients to consult a
44 physician immediately if this occurs. (5.3)
45 • Worsening of urinary retention may occur. Use
46 with caution in patients with prostatic hyperplasia
47 or bladder-neck obstruction and instruct patients to
48 consult a physician immediately if this occurs.
49 (5.4)
50 • Immediate hypersensitivity reactions: Use with
51 caution in patients with severe hypersensitivity to
52 milk proteins. (5.5)

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

55 Most common adverse reactions (≥3% incidence and
56 greater than placebo) are headache, nasopharyngitis
57 and cough. (6.1)

58
59 **To report SUSPECTED ADVERSE REACTIONS,**
60 **Contact Forest Laboratories, Inc. at 1-800-678-**
61 **1605 or FDA at 1-800-FDA-1088 or**
62 **www.fda.gov/medwatch.**

63
64 -----**DRUG INTERACTIONS**-----

65 Anticholinergics: May interact additively with
66 concomitantly used anticholinergic medications. Avoid
67 administrations of TUDORZA PRESSAIR with other
68 anticholinergic-containing drugs. (7.2)

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70 **See 17 for PATIENT COUNSELING INFORMATION**
71 **AND FDA-approved patient labeling**

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REVISED: 07/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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77 **FULL PRESCRIBING INFORMATION**

78
79 **1 INDICATIONS AND USAGE**

80 TUDORZA™ PRESSAIR™ (aclidinium bromide inhalation powder) is indicated for the long-term, maintenance
81 treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic
82 bronchitis and emphysema.

83
84 **2 DOSAGE AND ADMINISTRATION**

85 The recommended dose of TUDORZA PRESSAIR is one oral inhalation of 400 mcg, twice daily.

86
87 **3 DOSAGE FORMS AND STRENGTHS**

88 Inhalation Powder. TUDORZA PRESSAIR is a breath-actuated multi-dose dry powder inhaler metering 400 mcg of
89 aclidinium bromide per actuation. Each actuation delivers 375 mcg of aclidinium bromide from the mouthpiece.

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91 **4 CONTRAINDICATIONS**

92 None.

93
94 **5 WARNINGS AND PRECAUTIONS**

95
96 **5.1 Not for Acute Use**

97 TUDORZA PRESSAIR is intended as a twice-daily maintenance treatment for COPD and is not indicated for the
98 initial treatment of acute episodes of bronchospasm (i.e., rescue therapy).

99
100 **5.2 Paradoxical Bronchospasm**

101 Inhaled medicines, including TUDORZA PRESSAIR, may cause paradoxical bronchospasm. If this occurs, treatment
102 with TUDORZA PRESSAIR should be stopped and other treatments considered.

103
104 **5.3 Worsening of Narrow-Angle Glaucoma**

105 TUDORZA PRESSAIR should be used with caution in patients with narrow-angle glaucoma. Prescribers and patients
106 should be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., eye pain or discomfort, blurred
107 vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal
108 edema). Instruct patients to consult a physician immediately should any of these signs or symptoms develop.

109
110 **5.4 Worsening of Urinary Retention**

111 TUDORZA PRESSAIR should be used with caution in patients with urinary retention. Prescribers and patients
112 should be alert for signs and symptoms of prostatic hyperplasia or bladder-neck obstruction (e.g., difficulty passing
113 urine, painful urination). Instruct patients to consult a physician immediately should any of these signs or
114 symptoms develop.

115
116 **5.5 Immediate Hypersensitivity Reactions**

117 Immediate hypersensitivity reactions may occur after administration of TUDORZA PRESSAIR. If such a reaction
118 occurs, therapy with TUDORZA PRESSAIR should be stopped at once and alternative treatments should be
119 considered. Given the similar structural formula of atropine to aclidinium, patients with a history of
120 hypersensitivity reactions to atropine should be closely monitored for similar hypersensitivity reactions to TUDORZA
121 PRESSAIR. In addition, TUDORZA PRESSAIR should be used with caution in patients with severe hypersensitivity
122 to milk proteins.

123
124 **6 ADVERSE REACTIONS**

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

- 126 • Paradoxical bronchospasm [see Warnings and Precautions (5.2)]
- 127 • Worsening of narrow-angle glaucoma [see Warnings and Precautions (5.3)]
- 128 • Worsening of urinary retention [see Warnings and Precautions (5.4)]

129
130 **6.1 Clinical Trials Experience**

131 Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical
132 trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the
133 rates observed in practice.

134
135 *3-Month and 6-Month Trials*

136 TUDORZA PRESSAIR was studied in two 3-month (Trials B and C) and one 6-month (Trial D) placebo-controlled
137 trials in patients with COPD. In these trials, 636 patients were treated with TUDORZA PRESSAIR at the
138 recommended dose of 400 mcg twice daily.

139
140 The population had a mean age of 64 years (ranging from 40 to 89 years), with 58% males, 94% Caucasian, and
141 had COPD with a mean pre-bronchodilator forced expiratory volume in one second (FEV₁) percent predicted of

48%. Patients with unstable cardiac disease, narrow-angle glaucoma, or symptomatic prostatic hypertrophy or bladder outlet obstruction were excluded from these trials.

Table 1 shows all adverse reactions that occurred with a frequency of greater than or equal to 1% in the TUDORZA PRESSAIR group in the two 3-month and one 6-month placebo-controlled trials where the rates in the TUDORZA PRESSAIR group exceeded placebo.

Table 1: Adverse Reactions (% Patients) in Placebo-Controlled Clinical Trials

Adverse Reactions Preferred Term	Treatment	
	TUDORZA PRESSAIR	Placebo
	(N=636) n (%)	(N=640) n (%)
Headache	42 (6.6)	32 (5.0)
Nasopharyngitis	35 (5.5)	25 (3.9)
Cough	19 (3.0)	14 (2.2)
Diarrhea	17 (2.7)	9 (1.4)
Sinusitis	11 (1.7)	5 (0.8)
Rhinitis	10 (1.6)	8 (1.2)
Toothache	7 (1.1)	5 (0.8)
Fall	7 (1.1)	3 (0.5)
Vomiting	7 (1.1)	3 (0.5)

In addition, among the adverse reactions observed in the clinical trials with an incidence of less than 1% were diabetes mellitus, dry mouth, 1st degree AV block, osteoarthritis, cardiac failure, and cardio-respiratory arrest.

Long-term Safety Trials

TUDORZA PRESSAIR was studied in three long term safety trials, two double blind and one open label, ranging from 40 to 52 weeks in patients with moderate to severe COPD. Two of these trials were extensions of the 3-month trials, and one was a dedicated long term safety trial. In these trials, 891 patients were treated with TUDORZA PRESSAIR at the recommended dose of 400 mcg twice daily. The demographic and baseline characteristics of the long term safety trials were similar to those of the placebo-controlled trials. The adverse events reported in the long term safety trials were similar to those occurring in the placebo-controlled trials of 3 to 6 months. No new safety findings were reported compared to the placebo controlled trials.

7 DRUG INTERACTIONS

In vitro studies suggest limited potential for CYP450-related metabolic drug interactions, thus no formal drug interaction studies have been performed with TUDORZA PRESSAIR [see *Clinical Pharmacology (12.3)*].

7.1 Sympathomimetics, Methylxanthines, Steroids

In clinical studies, concurrent administration of acclidinium bromide and other drugs commonly used in the treatment of COPD including sympathomimetics (short-acting beta₂ agonists), methylxanthines, and oral and inhaled steroids showed no increases in adverse drug reactions.

7.2 Anticholinergics

There is a potential for an additive interaction with concomitantly used anticholinergic medications. Therefore, avoid coadministration of TUDORZA PRESSAIR with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic effects.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C: There are no adequate and well controlled studies in pregnant women. Adverse development effects were observed in rats and rabbits exposed to acclidinium bromide. TUDORZA PRESSAIR should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Effects of acclidinium bromide on embryo-fetal development were examined in rats and rabbits. No evidence of structural alterations was observed in rats exposed during the period of organogenesis at approximately 15 times the recommended human daily dose (RHDD) [based on summed AUCs of acclidinium bromide and its metabolites at inhaled doses less than or equal to 5.0 mg/kg/day]. However, decreased pup weights were observed from dams exposed during the lactation period at approximately 5 times the RHDD [based on summed AUCs of acclidinium

190 bromide and its metabolites at inhaled doses greater than or equal to 0.2 mg/kg/day]. Maternal toxicity was also
191 observed at inhaled doses greater than or equal to 0.2 mg/kg/day.

193 No evidence of structural alterations was observed in Himalayan rabbits exposed during the period of
194 organogenesis at approximately 20 times the RHDD [based on summed AUCs of acclidinium bromide and its
195 metabolites at inhaled doses less than or equal to 3.6 mg/kg/day]. However, increased incidences of additional
196 liver lobes (3-5%), as compared to 0% in the control group, were observed at approximately 1,400 times the
197 RHDD [based on summed AUCs of acclidinium bromide and its metabolites at oral doses greater than or equal to
198 150 mg/kg/day], and decreased fetal body weights were observed at approximately 2,300 times the RHDD [based
199 on summed AUCs of acclidinium bromide and its metabolites at oral doses greater than or equal to 300 mg/kg/day].
200 These fetal findings were observed in the presence of maternal toxicity.

201 **8.2 Labor and Delivery**

202 The effect of TUDORZA PRESSAIR on labor and delivery is unknown. TUDORZA PRESSAIR should be used during
203 labor and delivery only if the potential benefit to the patient justifies the potential risk to the fetus.

204 **8.3 Nursing Mothers**

205 Acclidinium bromide is excreted into the milk of lactating female rats, and decreased pup weights were observed.
206 Excretion of acclidinium into human milk is probable. There are no human studies that have investigated the effects
207 of TUDORZA PRESSAIR on breast-fed infants. Caution should be exercised when TUDORZA PRESSAIR is
208 administered to nursing women.

209 **8.4 Pediatric Use**

210 TUDORZA PRESSAIR is approved for use in the maintenance treatment of bronchospasm associated with COPD.
211 COPD does not normally occur in children. The safety and effectiveness of TUDORZA PRESSAIR in pediatric
212 patients have not been established.

213 **8.5 Geriatric Use**

214 Of the 636 COPD patients exposed to TUDORZA PRESSAIR 400 mcg twice daily for up to 24 weeks in three
215 placebo-controlled clinical trials, 197 were less than 60 years, 272 were greater than or equal to 60 to less than 70
216 years, and 167 were greater than or equal to 70 years of age. No overall differences in safety or effectiveness
217 were observed between these subjects and younger subjects. Other reported clinical experience has not identified
218 differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals
219 cannot be ruled out. Based on available data for TUDORZA PRESSAIR, no adjustment of dosage in geriatric patients
220 is warranted [see *Clinical Pharmacology* (12.3)].

221 **8.6 Renal Impairment**

222 The pharmacokinetics of TUDORZA PRESSAIR were investigated in subjects with normal renal function and in
223 subjects with mild, moderate and severe renal impairment [see *Clinical Pharmacology* (12.3)]. No clinically
224 significant differences in acclidinium pharmacokinetics were noted between these populations. Based on available
225 data for TUDORZA PRESSAIR, no adjustment of dosage in renally impaired subjects is warranted.

226 **8.7 Hepatic Impairment**

227 The effects of hepatic impairment on the pharmacokinetics of TUDORZA PRESSAIR were not studied [see *Clinical*
228 *Pharmacology* (12.3)].

229 **10 OVERDOSAGE**

230 **10.1 Human Experience**

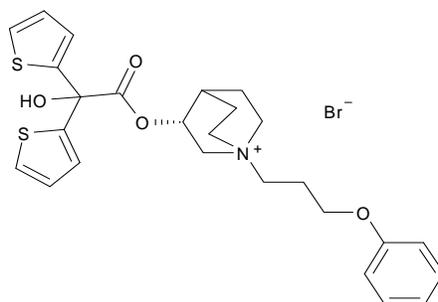
231 No case of overdose has been reported in clinical studies with TUDORZA PRESSAIR. There were no systemic
232 anticholinergic or other adverse effects following a single inhaled dose of up to 6,000 mcg acclidinium bromide (7.5
233 times the RHDD) in 16 healthy volunteers.

234 **11 DESCRIPTION**

235 TUDORZA PRESSAIR consists of a dry powder formulation of acclidinium bromide for oral inhalation only.

236 Acclidinium bromide, the active component of TUDORZA PRESSAIR is an anticholinergic with specificity for
237 muscarinic receptors. Acclidinium bromide is a synthetic, quaternary ammonium compound, chemically described
238 as 1-Azoniabicyclo[2.2.2]octane, 3-[(hydroxydi-2-thienylacetyl)oxy]-1-(3-phenoxypropyl)-, bromide, (3R)-. The
239 structural formula is:

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Acclidinium bromide is a white powder with a molecular formula of $C_{26}H_{30}NO_4S_2Br$ and a molecular mass of 564.56. It is very slightly soluble in water and ethanol and sparingly soluble in methanol.

TUDORZA PRESSAIR is a breath-actuated multi-dose dry powder inhaler. Each actuation of TUDORZA PRESSAIR provides a metered dose of 13 mg of the formulation which contains lactose monohydrate (which may contain milk proteins) as the carrier and 400 mcg of acclidinium bromide. This results in delivery of 375 mcg acclidinium bromide from the mouthpiece, based on *in vitro* testing at an average flow rate of 63 L/min with constant volume of 2 L. The amount of drug delivered to the lungs will vary depending on patient factors such as inspiratory flow rate and inspiratory time. The PRESSAIR inhaler delivers the target dose at flow rates as low as 35 L/min. Based on a study in adult patients with moderate (N=24) and severe (N=24) COPD the mean peak inspiratory flow (PIF) was 95.3 L/min (range: 54.6 to 129.4 L/min) and 88.7 L/min (range: 72.0 to 106.4 L/min) respectively.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Acclidinium bromide is a long-acting antimuscarinic agent, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M_1 to M_5 . In the airways, it exhibits pharmacological effects through inhibition of M_3 receptor at the smooth muscle leading to bronchodilation. The competitive and reversible nature of antagonism was shown with human and animal origin receptors and isolated organ preparations. In preclinical *in vitro* as well as *in vivo* studies, prevention of acetylcholine-induced bronchoconstriction effects was dose-dependent and lasted longer than 24 hours. The clinical relevance of these findings is unknown. The bronchodilation following inhalation of acclidinium bromide is predominantly a site-specific effect.

12.2 Pharmacodynamics

Cardiovascular Effects

In a thorough QT Study, 200 mcg and 800 mcg TUDORZA PRESSAIR was administered to healthy volunteers once daily for 3 days; no effects on prolongation of QT interval were observed using QTcF heart-rate correction methods.

Additionally, the effect of TUDORZA PRESSAIR on cardiac rhythm was assessed in 336 COPD patients, 164 patients received acclidinium bromide 400 mcg twice daily and 172 patients received placebo, using 24-hr Holter monitoring. No clinically significant effects on cardiac rhythm were observed.

12.3 Pharmacokinetics

Absorption

The absolute bioavailability of acclidinium bromide is approximately 6% in healthy volunteers. Following twice-daily oral inhalation administration of 400 mcg acclidinium bromide in healthy subjects, peak steady state plasma levels were observed within 10 minutes after inhalation.

Distribution

Acclidinium bromide shows a volume of distribution of approximately 300 L following intravenous administration of 400 mcg in humans.

Metabolism

Clinical pharmacokinetics studies, including a mass balance study, indicate that the major route of metabolism of acclidinium bromide is hydrolysis, which occurs both chemically and enzymatically by esterases. Acclidinium bromide is rapidly and extensively hydrolyzed to its alcohol and dithienylglycolic acid derivatives, neither of which binds to muscarinic receptors and are devoid of pharmacologic activity.

Therefore, due to the low plasma levels achieved at the clinically relevant doses, acclidinium bromide and its metabolites are not expected to alter the disposition of drugs metabolized by the human CYP450 enzymes.

306 *Elimination*

307 Total clearance was approximately 170 L/h after an intravenous dose of acridinium bromide in young healthy
308 volunteers with an inter-individual variability of 36%. Intravenously administered radiolabelled acridinium bromide
309 was administered to healthy volunteers and was extensively metabolized with 1% excreted as unchanged
310 acridinium. Approximately 54% to 65% of the radioactivity was excreted in urine and 20% to 33% of the dose was
311 excreted in feces. The combined results indicated that almost the entire acridinium bromide dose was eliminated
312 by hydrolysis. After dry powder inhalation, urinary excretion of acridinium is about 0.09% of the dose and the
313 estimated effective half-life is 5 to 8 hours.

314
315 *Drug Interactions*

316 Formal drug interaction studies were not performed. *In vitro* studies using human liver microsomes indicated that
317 acridinium bromide and its major metabolites do not inhibit CYP450, 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1,
318 3A4/5 or 4A9/11 at concentrations up to 1,000-fold higher than the maximum plasma concentration that would be
319 expected to be achieved at the therapeutic dose. Therefore, it is unlikely that acridinium bromide causes CYP450
320 related drug interactions [see *Drug Interactions (7)*].

321
322 *Specific Populations*

323
324 Elderly Patients

325 The pharmacokinetic profile of acridinium bromide and its main metabolites was assessed in 12 elderly COPD
326 patients (aged 70 years or older) compared to a younger cohort of 12 COPD patients (40-59 years) that were
327 administered 400 mcg acridinium bromide once daily for 3 days via inhalation. No clinically significant differences
328 in systemic exposure (AUC and C_{max}) were observed when the two groups were compared. No dosage adjustment
329 is necessary in elderly patients [Use in *Specific Populations (8.5)*].

330
331 Renal Impairment

332 The impact of renal disease upon the pharmacokinetics of acridinium bromide was studied in 18 subjects with mild,
333 moderate, or severe renal impairment. Systemic exposure (AUC and C_{max}) to acridinium bromide and its main
334 metabolites following single doses of 400 mcg acridinium bromide was similar in renally impaired patients
335 compared with 6 matched healthy control subjects. No dose adjustment is necessary in renally impaired patients
336 [see Use in *Specific Populations (8.6)*].

337
338 Hepatic Impairment

339 The effects of hepatic impairment on the pharmacokinetics of acridinium bromide were not studied. However,
340 hepatic insufficiency is not expected to have relevant influence on acridinium bromide pharmacokinetics, since it is
341 predominantly metabolized by chemical and enzymatic hydrolysis to products that do not bind to muscarinic
342 receptors [see Use in *Specific Populations (8.7)*].

343
344 **13 NONCLINICAL TOXICOLOGY**

345
346 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

347 Two-year inhalation studies were conducted in mice and rats to assess the carcinogenic potential of acridinium
348 bromide. No evidence of tumorigenicity was observed in rats and mice at acridinium doses up to 0.20 and 2.4
349 mg/kg/day, respectively [approximately 10 and 80 times the Recommended Human Daily Dose (RHDD)],
350 respectively, based on summed AUCs of acridinium bromide and its metabolites].

351
352 Acridinium bromide was positive in the *in vitro* bacterial gene mutation assay and the *in vitro* thymidine locus
353 mouse lymphoma assay. However, acridinium bromide was negative in the *in vivo* mouse micronucleus assay and
354 the *in vivo/in vitro* unscheduled DNA synthesis assay with rat liver.

355
356 Acridinium bromide impaired several fertility and reproductive performance indices (increased number of days to
357 mate, decreased conception rate, decreased number of corpora lutea, increased pre-implantation loss with
358 consequent decreased number of implantations and live embryos) in both male and female rats administered
359 inhaled doses greater than or equal to 0.8 mg/kg/day [approximately 15 times the RHDD based on summed AUCs
360 of acridinium bromide and its metabolites]. These adverse fertility effects were observed in the presence of
361 paternal toxicity as evidenced by mortality and decreased body weight gain. However, there were no effects on
362 mating index and sperm number and morphology. In the separate fertility assessments (treated males mated with
363 untreated females; treated females mated with untreated males), no effect was observed in male and female rats
364 at inhaled dose of 1.9 and 0.8 mg/kg/day, respectively [approximately 30 and 15 times the RHDD, respectively,
365 based on summed AUCs of acridinium bromide and its metabolites].

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373 **14 CLINICAL STUDIES**
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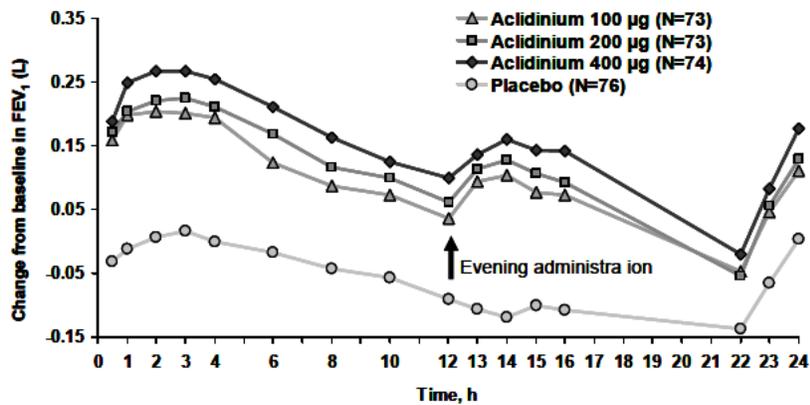
375 **14.1 Chronic Obstructive Pulmonary Disease (COPD)**

376 The TUDORZA PRESSAIR clinical development program included a dose-ranging trial (Trial A) for nominal dose
377 selection and three confirmatory trials (Trials B, C, and D).
378

379 *Dose-ranging trial*

380 Trial A was a randomized, double-blind, placebo-controlled, active-controlled, cross-over trial with 7-day treatment
381 periods separated by 5-day washout periods. Trial A enrolled 79 patients who had a clinical diagnosis of COPD,
382 were 40 years of age or older, had a history of smoking at least 10 pack-years, had a forced expiratory volume in
383 one second (FEV₁) of at least 30% and less than 80% of predicted normal value, and a ratio of FEV₁ over forced
384 vital capacity (FEV₁/FVC) of less than 0.7. Trial A included TUDORZA PRESSAIR doses of 400 mcg, 200 mcg and
385 100 mcg twice daily, formoterol active control, and placebo. Trial A demonstrated that the effect on trough FEV₁
386 and serial FEV₁ in patients treated with the TUDORZA PRESSAIR 100 mcg twice daily and 200 mcg twice daily doses
387 was lower compared to patients treated with the TUDORZA PRESSAIR 400 mcg twice daily dose (Figure 1).
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389
390 **Figure 1. Change from baseline in FEV₁ Over Time**
391 **(prior to and after administration of study drug) at Week 1 in Trial A**
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412
413 *Confirmatory trials*

414 Trials B, C, and D were three randomized, double-blind, placebo-controlled trials in patients with COPD. Trials B
415 and C were 3 months in duration, and Trial D was 6 months in duration. These trials enrolled 1,276 patients who
416 had a clinical diagnosis of COPD, were 40 years of age or older, had a history of smoking at least 10 pack-years,
417 had an FEV₁ of at least 30% and less than 80% of predicted normal value, and a ratio of FEV₁/FVC of less than 0.7;
418 59% were male, and 93% were Caucasian.
419

420
421 These clinical trials evaluated TUDORZA PRESSAIR 400 mcg twice daily (636 patients) and placebo (640 patients).
422 TUDORZA PRESSAIR 400 mcg resulted in statistically significantly greater bronchodilation as measured by change
423 from baseline in morning pre-dose FEV₁ at 12 weeks (the primary efficacy endpoint) compared to placebo in all
424 three trials (Table 2).
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Table 2: Change from Baseline in Trough FEV₁ (L) at Week 12

Treatment Arm	Baseline	Change from Baseline LS Mean (SE)	Treatment Difference LS Mean (95% CI)
Trial B (N=375)			
Acidinium 400 mcg	1.33	0.10 (0.01)	0.12 (0.08, 0.16)
Placebo	1.38	-0.02 (0.02)	
Trial C (N=359)			
Acidinium 400 mcg	1.25	0.06 (0.02)	0.07 (0.03, 0.12)
Placebo	1.46	-0.01 (0.02)	
Trial D* (N=542)			
Acidinium 400 mcg	1.51	0.06 (0.02)	0.11 (0.07, 0.14)
Placebo	1.50	-0.05 (0.02)	

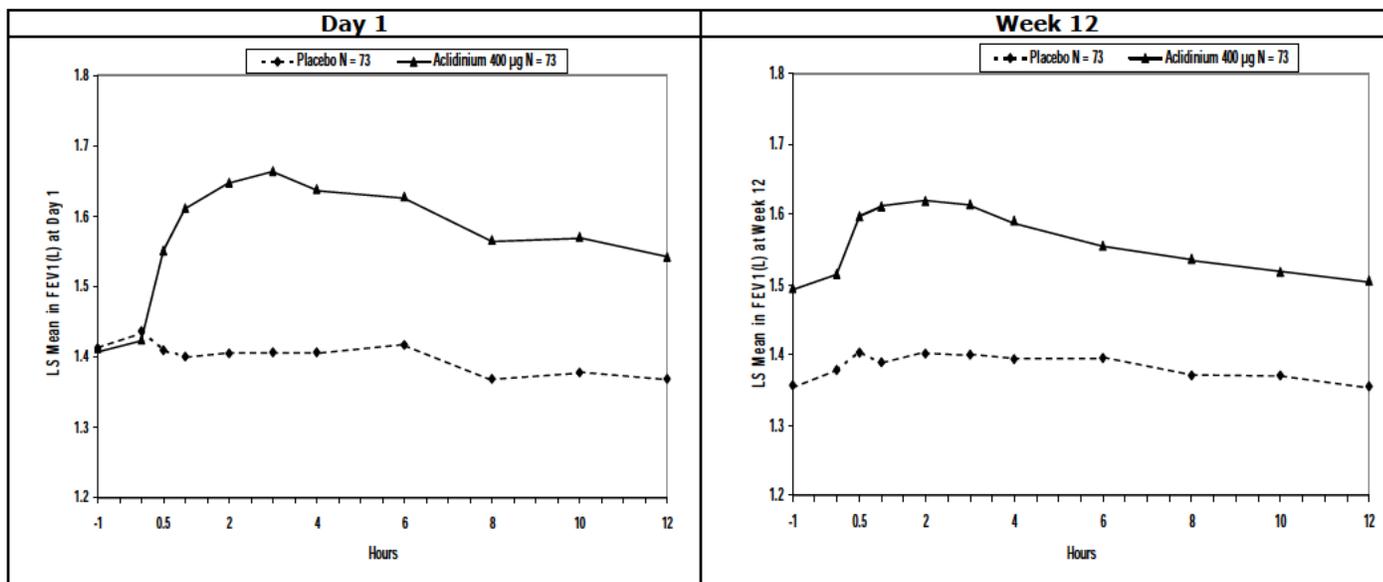
SE=standard error, and LS mean=least square mean. LS mean, and 95% confidence interval were obtained from an ANCOVA model with change from baseline in trough FEV₁ as response, with treatment group and sex as factors and baseline trough FEV₁ and age as covariates.

*In the 6-month Trial D, placebo adjusted change from baseline in Trough FEV₁ at 24 weeks was 0.13 (0.09, 0.17).

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Serial spirometric evaluations were performed throughout daytime hours in a subset of patients in the three trials. The serial FEV₁ values over 12 hours for one of the 3-month trials (Trial B) are displayed in Figure 2. Results for the other two placebo-controlled trials were similar to the results for Trial B. Improvement of lung function was maintained for 12 hours after a single dose and was consistent over the 3- or 6-month treatment period.

Figure 2. Mean FEV₁ Over Time (prior to and after administration of study drug) on Day 1 and Week 12 in Subset of Patients Participating in the 12 hours Serial Spirometry Substudy for Trial B (a 3-month Placebo-Controlled Study)



462
463

464 Mean peak improvements in FEV₁ for TUDORZA PRESSAIR relative to baseline were assessed in all patients in trials
465 B, C and D after the first dose on day 1 and were similar at week 12. In Trials B and D but not in Trial C, patients
466 treated with TUDORZA PRESSAIR used less daily rescue albuterol during the trial compared to patients treated with
467 placebo.
468

469 **16 HOW SUPPLIED/STORAGE AND HANDLING**

470 **16.1 How Supplied**

471 TUDORZA™ PRESSAIR™ (aclidinium bromide inhalation powder) 400 mcg is supplied in a sealed labeled aluminum
472 pouch and is available in 60 metered doses (NDC 0456-0800-60).
473

474 The active ingredient is administered using a multi-dose dry powder inhaler, PRESSAIR™, which delivers 60 doses
475 of aclidinium bromide powder for oral inhalation. The PRESSAIR inhaler is a white and green colored device and is
476 comprised of an assembled plastic dosing mechanism with a dose indicator, a drug-product storage unit containing
477 the drug-product formulation, and a mouthpiece covered by a green protective cap. The inhaler should be
478 discarded when the marking "0" with a red background shows in the middle of the dose indicator or when the
479 device locks out, whichever comes first.
480
481

482 **16.2 Storage and Handling**

483 Store TUDORZA PRESSAIR in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [*see USP*
484 *Controlled Room Temperature*].
485

486 The PRESSAIR inhaler should be stored inside the sealed pouch and only be opened immediately before use.
487

488 Discard the PRESSAIR inhaler 45 days after opening the pouch, after the marking "0" with a red background shows
489 in the middle of the dose indicator, or when the device locks out, whichever comes first.
490

491 Keep out of reach of children.
492

493 **17 PATIENT COUNSELING INFORMATION**

494 *See FDA-approved Patient Labeling (Patient Information and Instructions for Use)*
495

496 **17.1 Instructions for Administering TUDORZA PRESSAIR**

497 It is important for patients to understand how to correctly use TUDORZA PRESSAIR.
498

499 **Inform patients that if they miss a dose, they should take their next dose at the usual time; they should
500 not take 2 doses at one time.**
501

502 **17.2 Acute Bronchospasm**

503 Instruct patients that TUDORZA PRESSAIR is a twice daily maintenance bronchodilator and should not be used for
504 immediate relief of breathing problems (i.e., as a rescue medication) [*see Warnings and Precautions (5.1)*].
505

506 **17.3 Paradoxical Bronchospasm**

507 Inform patients that TUDORZA PRESSAIR can cause paradoxical bronchospasm. Advise patients that if paradoxical
508 bronchospasm occurs, patients should discontinue TUDORZA PRESSAIR [*see Warnings and Precautions (5.2)*].
509

510 **17.4 Visual Effects**

511 Eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival
512 congestion and corneal edema may be signs of acute narrow-angle glaucoma. Inform patients to consult a
513 physician immediately should any of these signs and symptoms develop. Advise patients that miotic eye drops
514 alone are not considered to be effective treatment [*see Warnings and Precautions (5.3)*].
515

516 Inform patients that care must be taken not to allow the powder to enter into the eyes as this may cause blurring
517 of vision and pupil dilation.
518

519 **17.5 Urinary Retention**

520 Difficulty passing urine and dysuria may be symptoms of new or worsening prostatic hyperplasia or bladder outlet
521 obstruction. Patients should be instructed to consult a physician immediately should any of these signs or
522 symptoms develop [*see Warnings and Precautions (5.4)*].
523

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525
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541 RMC XXXX

542

Patient Information

TUDORZA™ PRESSAIR™ (TU-door-za PRESS-air) (acclidinium bromide inhalation powder)

FOR ORAL INHALATION ONLY

Read the Patient Information that comes with TUDORZA PRESSAIR before you start using it and each time you get a refill. There may be new information. This Patient Information does not take the place of talking to your doctor about your medical condition or your treatment.

What is TUDORZA PRESSAIR?

TUDORZA PRESSAIR is a prescription medicine used long term, 2 times each day to treat symptoms of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. You may start to feel like it is easier to breathe on the first day, but it may take longer for you to feel the full effects of the medicine. TUDORZA PRESSAIR works best and may help make it easier to breathe when you use it every day.

TUDORZA PRESSAIR is **not** a rescue medicine and should not be used for treating sudden breathing problems. Your doctor may give you other medicine to use for sudden breathing problems.

It is not known if TUDORZA PRESSAIR is safe and effective in children.

What should I tell my doctor before using TUDORZA PRESSAIR?

Before you use TUDORZA PRESSAIR, tell your doctor about all your medical conditions, including if you:

- have eye problems, especially glaucoma. TUDORZA PRESSAIR may make your glaucoma worse.
- have prostate or bladder problems, or problems passing urine. TUDORZA PRESSAIR may make these problems worse.
- have a severe allergy to milk proteins. Ask your doctor if you are not sure.
- are pregnant or plan to become pregnant. It is not known if TUDORZA PRESSAIR can harm your unborn baby.
- are breastfeeding or plan to breastfeed. TUDORZA PRESSAIR may pass into your breast milk. You and your doctor should decide if you will take TUDORZA PRESSAIR.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines and eye drops, vitamins, and herbal supplements.

TUDORZA PRESSAIR and certain other medicines may interact with each other. This may cause serious side effects.

Especially tell your doctor if you take:

- anticholinergics (including Tiotropium, Ipratropium)
- atropine

Ask your doctor or pharmacist for a list of these medicines if you are not sure.

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

How should I use TUDORZA PRESSAIR?

See the step-by-step instructions for using TUDORZA PRESSAIR at the end of this Patient Information.

- Use TUDORZA PRESSAIR exactly as prescribed.
- The usual dose of TUDORZA PRESSAIR is one oral inhalation 2 times a day. Each dose should be about 12 hours apart.
- If you miss a dose, just skip the dose. Take your next dose at your usual time. Do not take 2 doses at one time.

TUDORZA PRESSAIR does not relieve sudden symptoms of COPD. Always have a rescue inhaler medicine with you to treat sudden symptoms. If you do not have a rescue inhaler medicine, call your doctor to have one prescribed for you.

Do not use TUDORZA PRESSAIR more often than prescribed or take more medicine than prescribed for you.

- **Call your doctor or get emergency medical care right away if:**
 - your breathing problems worsen with TUDORZA PRESSAIR
 - you need to use your rescue inhaler medicine more often than usual
 - your rescue inhaler medicine does not work as well for you at relieving symptoms

What are the possible side effects of TUDORZA PRESSAIR?

TUDORZA PRESSAIR can cause serious side effects including:

- **sudden shortness of breath immediately after use of TUDORZA PRESSAIR.** If you have this symptom, stop taking TUDORZA PRESSAIR and call your doctor right away or go to the nearest hospital emergency room.

- **new or worsened increased pressure in your eyes (acute narrow-angle glaucoma).** Acute narrow-angle glaucoma can lead to permanent loss of vision if not treated. Symptoms of acute narrow-angle glaucoma may include:
 - eye pain or discomfort
 - nausea or vomiting
 - blurred vision
 - seeing halos or bright colors around lights
 - red eyes

Using only eye drops to treat these symptoms may not work. If you have these symptoms, stop taking TUDORZA PRESSAIR and call your doctor right away.

- **new or worsened urinary retention.** Urinary retention can be caused by blockage in your bladder or, if you are a male, a larger than normal prostate. Symptoms of urinary retention may include:
 - difficulty urinating
 - painful urination
 - urinating frequently
 - urination in a weak stream or drips

If you have these symptoms of urinary retention, stop taking TUDORZA PRESSAIR and call your doctor right away.

- **serious allergic reactions including rash, hives, swelling of the face, mouth, and tongue, and breathing problems.** Call your doctor or get emergency medical care if you get any symptoms of a serious allergic reaction.

The most common side effects of TUDORZA PRESSAIR include:

- headache
- common cold symptoms
- cough

If your COPD symptoms worsen over time do not increase your dose of TUDORZA PRESSAIR, instead call your doctor.

Tell your doctor if you get any side effect that bothers you or does not go away.

These are not all the possible side effects with TUDORZA PRESSAIR. Ask your doctor or pharmacist for more information.

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

How should I store TUDORZA PRESSAIR?

Store TUDORZA PRESSAIR at room temperature between 68°F to 77°F (20° to 25°C) in the protective pouch. **Do not open the sealed pouch until you are ready to use a dose of TUDORZA PRESSAIR. Once a sealed pouch is opened, start using**

your TUDORZA PRESSAIR. Discard the PRESSAIR inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator, or when the device locks out, whichever comes first.

- Keep TUDORZA PRESSAIR in a dry place.
- Do not store the inhaler on a vibrating surface.

Keep TUDORZA PRESSAIR and all medicines out of the reach of children.

General information about the safe and effective use of TUDORZA PRESSAIR

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

This patient leaflet summarizes the most important information about TUDORZA PRESSAIR. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about TUDORZA PRESSAIR that is written for health professionals.

For more information, go to www.tudorza.com, or a call 1-800-678-1605.

What are the ingredients in TUDORZA PRESSAIR?

Active ingredient: aclidinium bromide

Inactive ingredient: lactose monohydrate

Instructions for Use

TUDORZA™ PRESSAIR™ (TU-door-za PRESS-air) (aclidinium bromide inhalation powder)

FOR ORAL INHALATION ONLY

Read this Instructions for Use before you start using TUDORZA PRESSAIR and each time you get a refill. There may be new information. This information does not take the place of talking to your doctor about your medical condition or your treatment.

Your TUDORZA PRESSAIR INHALER:

When you are ready to use TUDORZA PRESSAIR for the first time, remove the TUDORZA PRESSAIR inhaler from the pouch. To remove the inhaler from the pouch, tear along the “notch.” The pouch may then be discarded.

Look at the parts of the inhaler so you become familiar with them. (See Figure A)

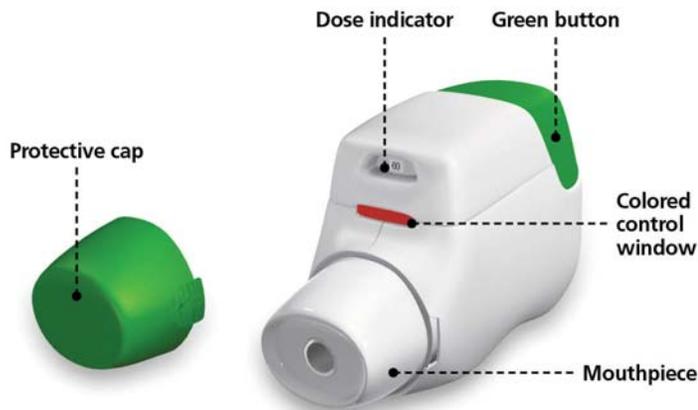


Figure A

Taking a dose from the TUDORZA PRESSAIR Inhaler requires you to press, release, and inhale. See the step-by-step instructions for using TUDORZA PRESSAIR below.

How to prepare and use your TUDORZA PRESSAIR Inhaler

Step 1. Remove the protective cap by **lightly squeezing the arrows** marked on each side of the cap and pulling outwards. (See Figure B)

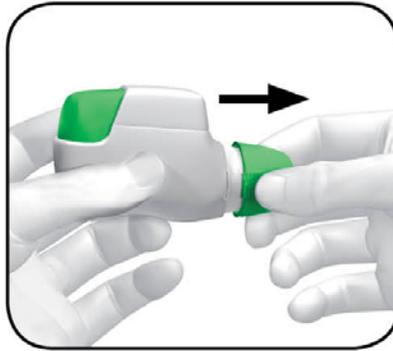


Figure B

- Look to see that nothing is blocking the mouthpiece.

Step 2. Hold the TUDORZA PRESSAIR inhaler with the mouthpiece facing you, but not inside your mouth. The green button should be facing straight up. **(See Figure C)**

Hold with the green button facing straight up. Do not tilt.

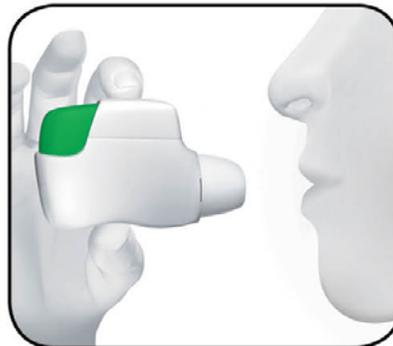
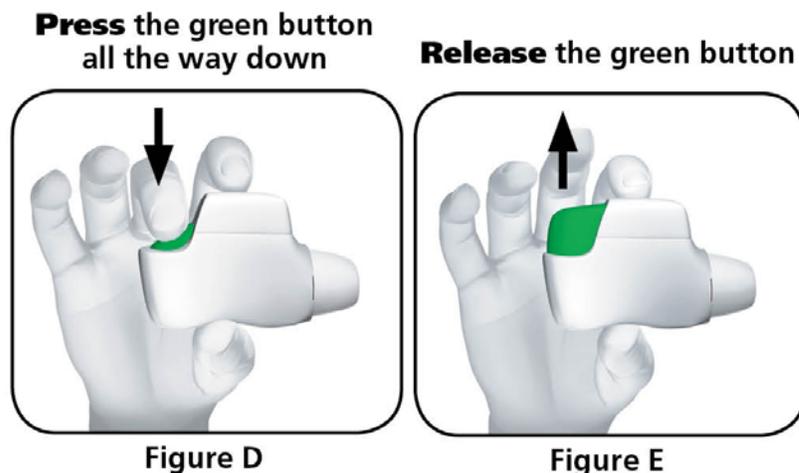


Figure C

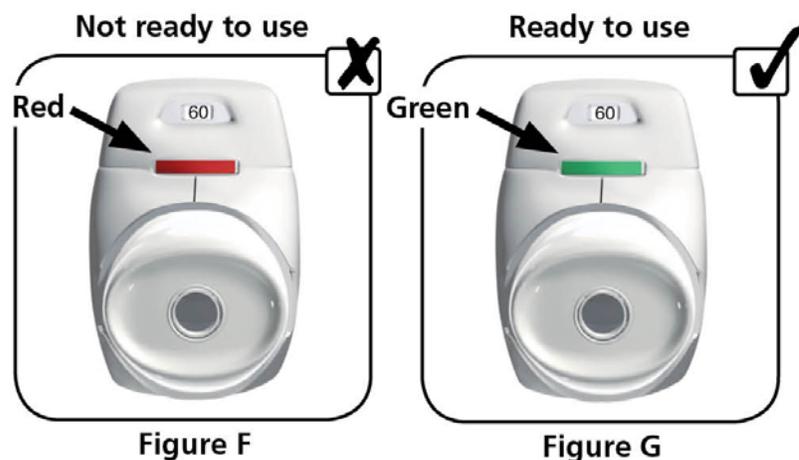
Step 3. Before you put the inhaler into your mouth, **press** the green button all the way down. **(See Figure D)**

- Then **release** the green button. **(See Figure E)**
- **Do not continue to hold the green button down.**



Step 4. Stop and Check the Control Window to make sure your dose is ready for inhalation. Look to see if the colored control window has changed from red (See Figure F), to green (See Figure G)

- The green control window tells you that your medicine is ready for inhalation. (See Figure G)



- If the control window stays red (See Figure F), repeat the Press and Release actions in Step 3 until the control window is green.

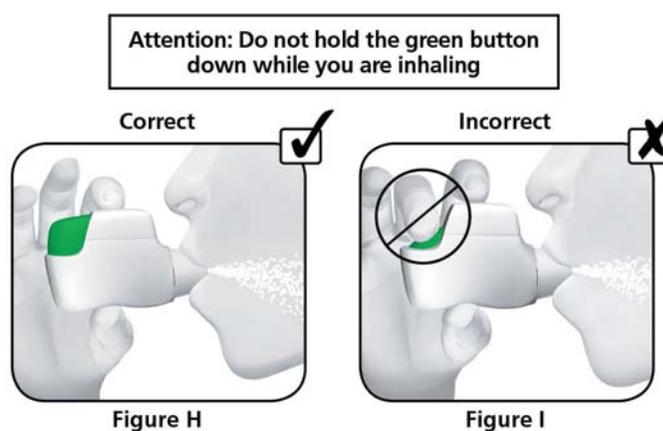
Now the dose is ready to be inhaled.

Step 5. Before you put the inhaler into your mouth, breathe out completely. Do not breathe out into the inhaler.

- Put your lips tightly around the mouthpiece of the TUDORZA PRESSAIR inhaler. Breathe in **quickly** and **deeply** through your mouth. (See Figure H). This quick,

deep breath makes sure that you get enough of the medication from the inhaler into your lungs.

- Breathe in until you hear a “**click**” sound. Keep breathing in, even after you have heard the inhaler “**click**” to be sure you get the full dose.



- **Do not hold down the green button while you are breathing in.**
(See Figure I)

Step 6. Remove the TUDORZA PRESSAIR inhaler from your mouth and hold your breath for as long as is comfortable (See Figure J), then breathe out slowly through your nose.

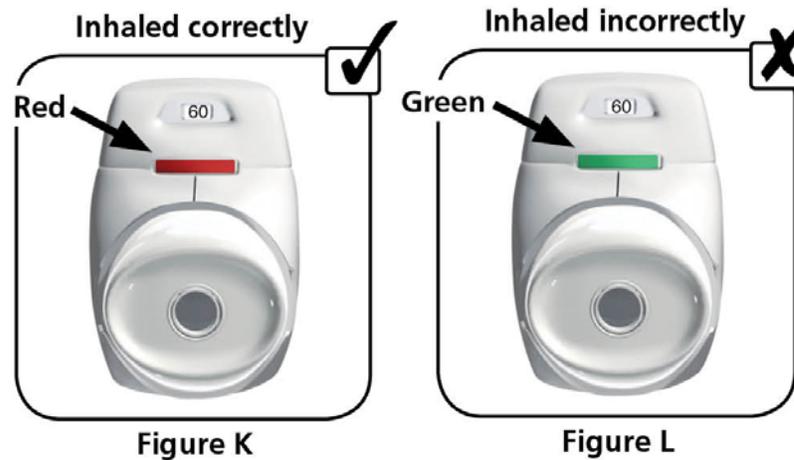


Figure J

Some people may taste the medicine during their inhalation. Do not take an extra dose even if you do not taste anything after inhaling.

Step 7. Stop and Check the Control Window. Make sure you have used your TUDORZA PRESSAIR inhaler correctly.

- Look at the control window to see if it has turned to **red** (See **Figure K**) from **green** (See **Figure L**). If the window is **red** you have inhaled your full dose of medicine correctly.



If the colored control window is still green, repeat **Step 5**.

- If the window still does not change to **red**, you may have forgotten to release the **green** button before inhaling or may not have inhaled correctly. If that happens repeat **Step 5** again.
- Make sure you have released the green button and take a **quick** and **deep** breath in through the mouthpiece.
- If you are unable to inhale correctly after several attempts, call your doctor.

Step 8. Once the window has turned **red**, place the protective cap back onto the inhaler by pressing it back onto the mouthpiece. (See **Figure M**)

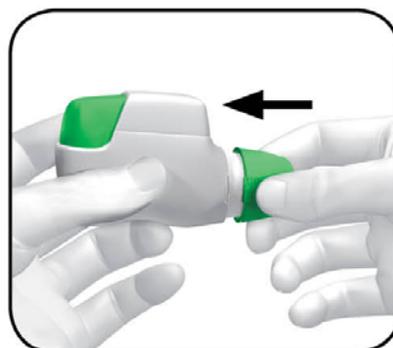


Figure M

Additional information about the safe and effective use of TUDORZA PRESSAIR inhaler

The “click” sound and colored control window:

- The “**click**” that you hear while inhaling tells you that you are using the TUDORZA PRESSAIR inhaler correctly.
- When you use the inhaler correctly the colored control window changes from **green** to **red**.
- Each time you are ready to use the TUDORZA PRESSAIR inhaler again, you will need to make sure the inhaler is ready by pressing and releasing the green button as seen in **Step 3**. When you press and release the green button the colored control window will change from **red** to **green**.

When should you get a new TUDORZA PRESSAIR inhaler?

- The TUDORZA PRESSAIR inhaler has a dose indicator to show you how many doses are left in your inhaler. Each TUDORZA PRESSAIR inhaler has 60 doses of medicine.
 - When you start using the inhaler for the first time you will see the number **60** in the dose indicator.
 - You will see the number of doses count down in the dose indicator as you use the inhaler. The dose indicator moves down slowly, displaying intervals of 10 (60, 50, 40, 30, 20, 10, 0).
 - When a red band begins to appear in the dose indicator (**See Figure N**), this means you are nearing your last dose and should obtain a new PRESSAIR inhaler.

Dose indicator goes down by intervals of 10: 60, 50, 40, 30, 20, 10, 0.

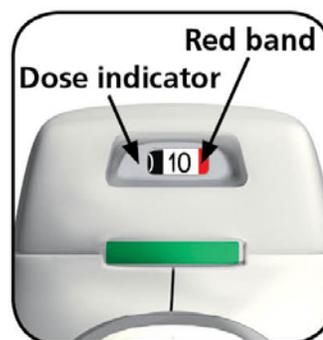


Figure N

- You should discard the inhaler and start a new one when
 - the marking “0” with the red background shows in the middle of the dose indicator (**See Figure O**), or
 - the device locks out (**See Figure P**), or
 - 45 days after you took the inhaler out of the sealed pouch, whichever comes first.



Figure O



Figure P

- If your TUDORZA PRESSAIR inhaler appears to be damaged or if you lose the cap, your inhaler should be replaced.
- You **do not need** to clean your TUDORZA PRESSAIR inhaler. If you wish to clean it, wipe the outside of the mouthpiece with a dry tissue or paper towel. **Do not** use water to clean your TUDORZA PRESSAIR inhaler, as this may damage your medicine.

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

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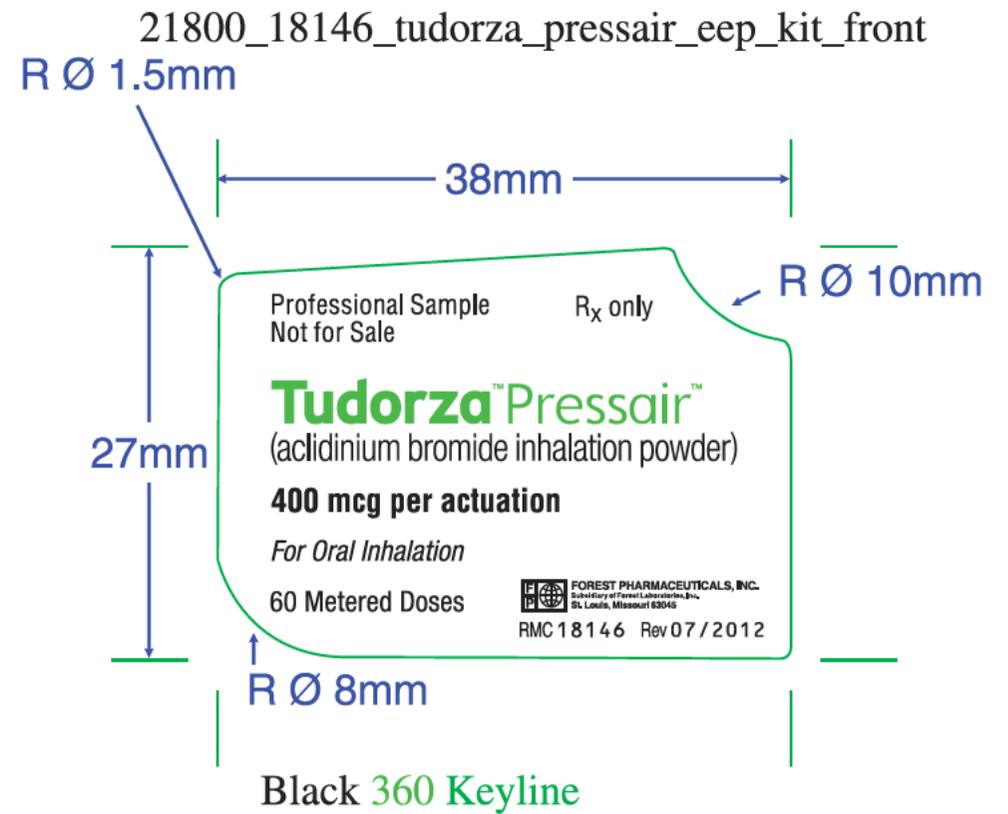
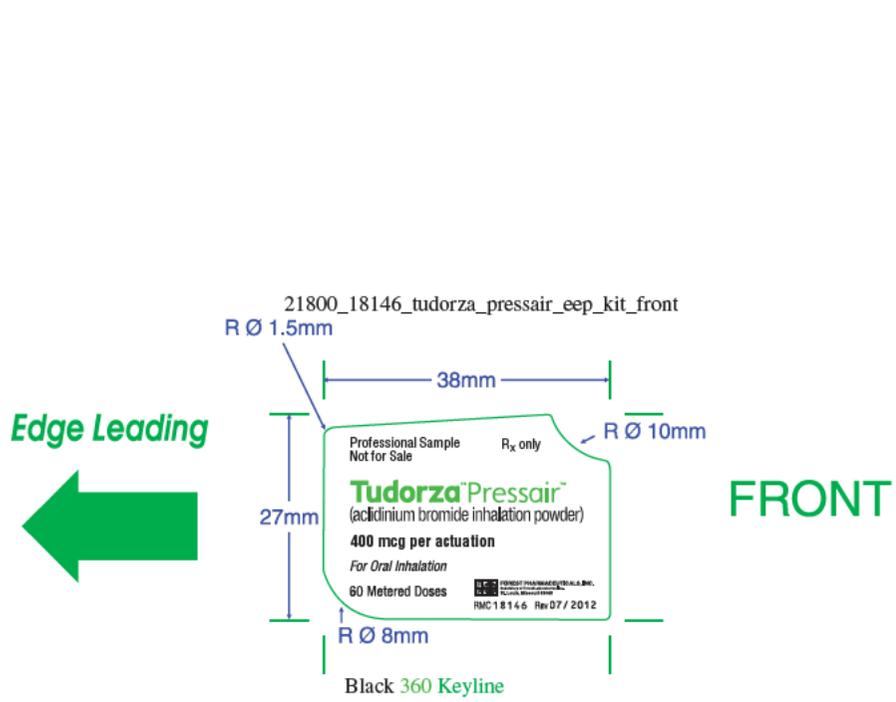


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Approved July 2012



Customer:	FOREST LABORATORIES IRE. LTD.	Colours Label:	Colours Leaflet Front:
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Material / Adhesive:			
Size:			
Roll Quantity:	(b) (4)		
Labels to View:			
Comments:			
Originated By:	(b) (4)	Date: 03 / 07 / 2012	Checked By:
			Colours Leaflet Back:

215. mm

150. mm

Professional Sample
Not for Sale

R_x only

Tudorza™ Pressair™

(aclidinium bromide inhalation powder)

400 mcg per actuation

For Oral Inhalation

60 Metered Doses

Each metered dose of Tudorza™ Pressair™ contains 400 mcg of aclidinium bromide with lactose monohydrate, delivering 375 mcg aclidinium bromide from the mouthpiece.

Keep Tudorza Pressair inhaler inside the sealed pouch until the administration period starts.

Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first. Fill in the dates on the Pressair inhaler appropriately.

Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].
Keep out of reach of children.

See Package Insert for Full Prescribing Information and Patient's Instructions for Use.

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RMC 18145

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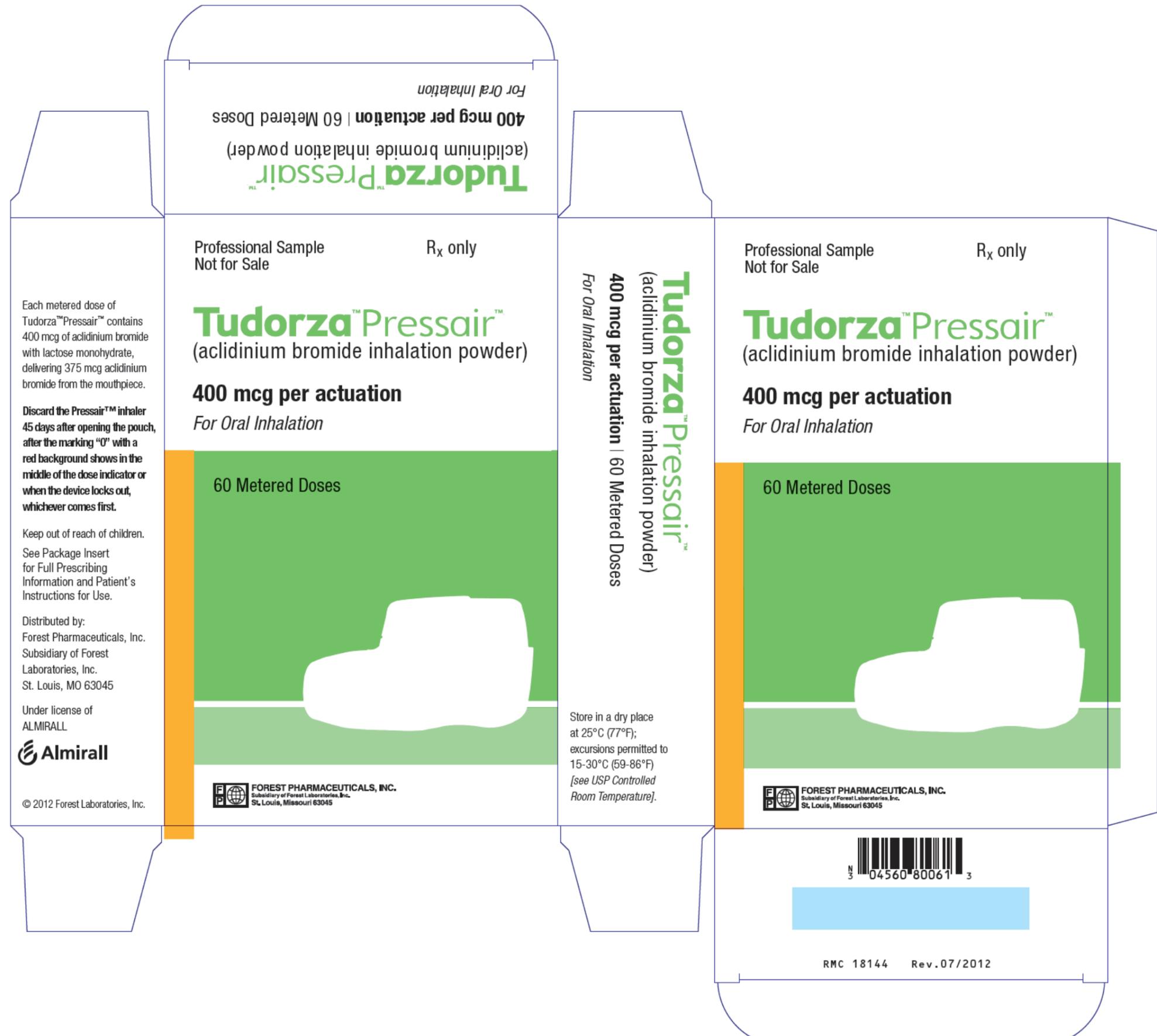
6 x 15 mm

66.5 mm

Unwind sense / Sentido de salida

(b) (4)

Reference



Each metered dose of Tudorza™ Pressair™ contains 400 mcg of acclidinium bromide with lactose monohydrate, delivering 375 mcg acclidinium bromide from the mouthpiece.

Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first.

Keep out of reach of children. See Package Insert for Full Prescribing Information and Patient's Instructions for Use.

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Professional Sample Not for Sale Rx only

Tudorza™ Pressair™
(acclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation

60 Metered Doses

FOREST PHARMACEUTICALS, INC.
Subsidiary of Forest Laboratories, Inc.
St. Louis, Missouri 63045

Tudorza™ Pressair™
(acclidinium bromide inhalation powder)
400 mcg per actuation | 60 Metered Doses
For Oral Inhalation

Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

Professional Sample Not for Sale Rx only

Tudorza™ Pressair™
(acclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation

60 Metered Doses

FOREST PHARMACEUTICALS, INC.
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St. Louis, Missouri 63045



RMC 18144 Rev. 07/2012

GRAIN

28¹⁹/₃₂

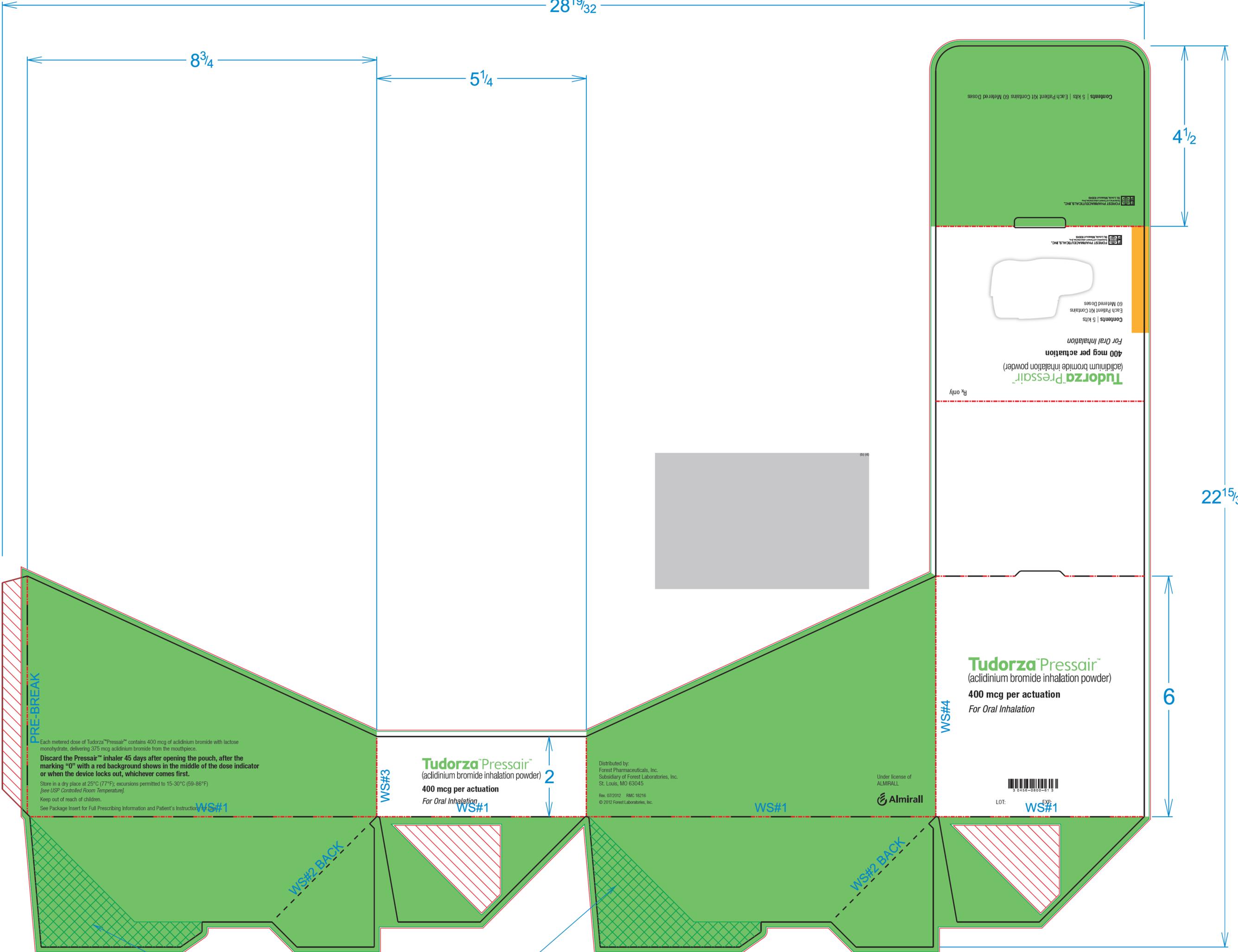
8³/₄

5¹/₄

4¹/₂

22¹⁵/₃₂

6



PRE-BREAK

Each metered dose of Tudorza™ Pressair™ contains 400 mcg of aclidinium bromide with lactose monohydrate, delivering 375 mcg aclidinium bromide from the mouthpiece.

Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first.

Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

Keep out of reach of children.

See Package Insert for Full Prescribing Information and Patient's Instructions for Use.

Tudorza™ Pressair™
(aclidinium bromide inhalation powder)
400 mcg per actuation
For Oral Inhalation

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Tudorza™ Pressair™
(aclidinium bromide inhalation powder)
400 mcg per actuation
For Oral Inhalation



LOT: _____ EXP: _____

WS#1

WS#3

WS#1

WS#1

WS#4

WS#2 BACK

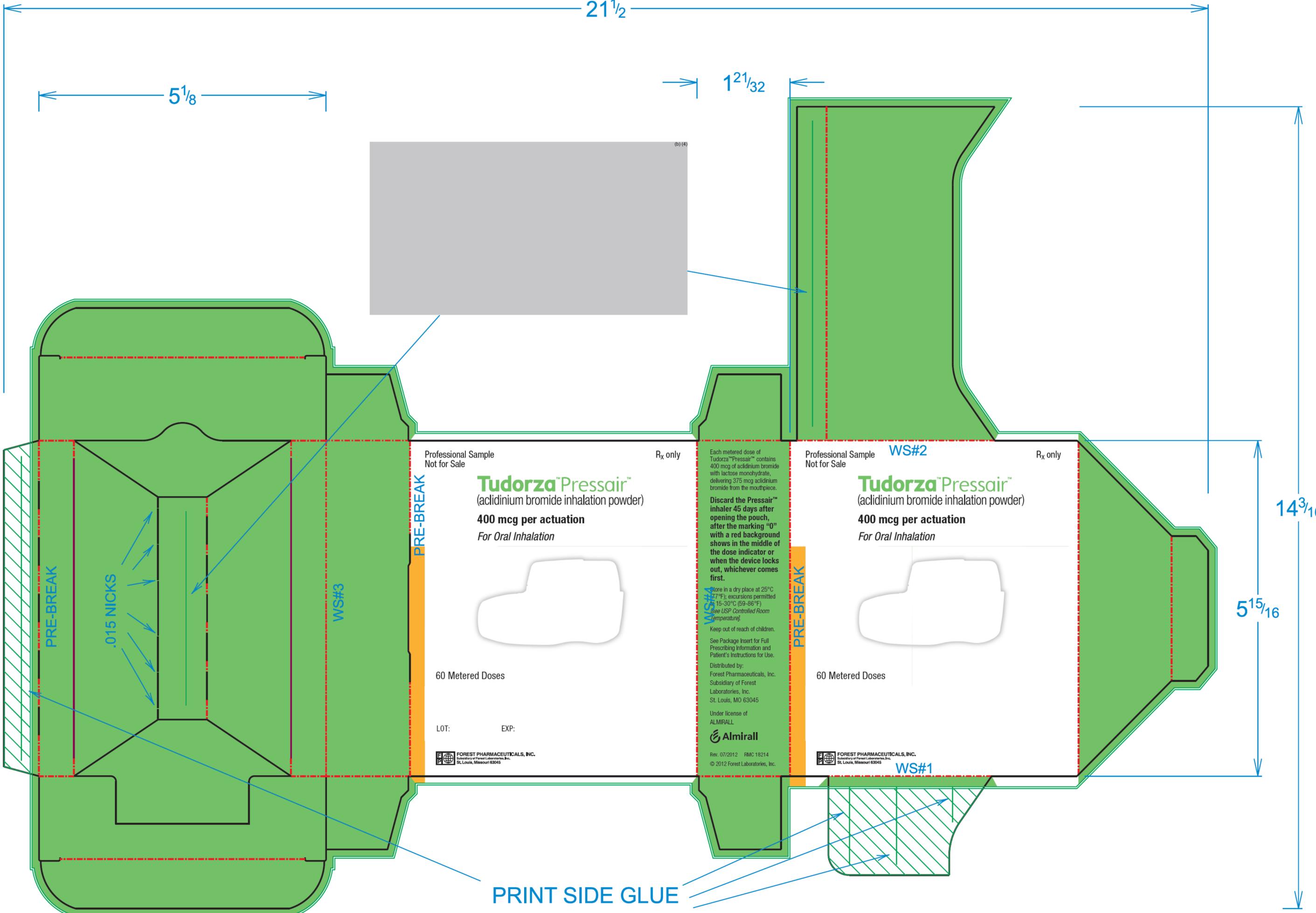
WS#2 BACK

GRAIN →

21 1/2

5 1/8

1 21/32



Professional Sample Not for Sale Rx only

Tudorza™ Pressair™ (acclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation



60 Metered Doses

LOT: EXP:

FOREST PHARMACEUTICALS, INC.
St. Louis, Missouri 63045

Professional Sample Not for Sale Rx only

Tudorza™ Pressair™ (acclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation



60 Metered Doses

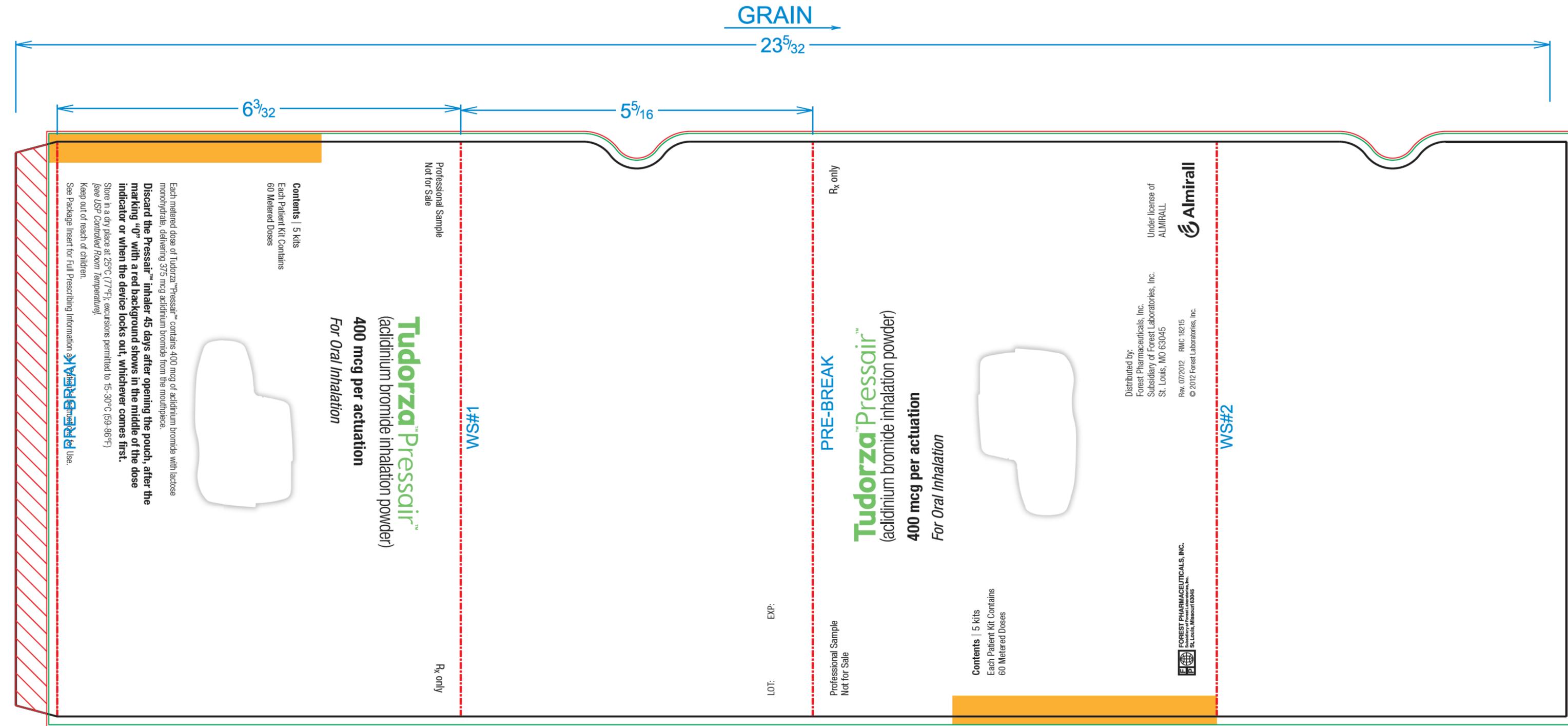
WS#4
Each metered dose of Tudorza™ Pressair™ contains 400 mcg of acclidinium bromide with lactose monohydrate, delivering 375 mcg acclidinium bromide from the mouthpiece.
Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first.
Store in a dry place at 25°C (77°F); excursions permitted 15-30°C (59-86°F).
See USP Controlled Room Temperature.
Keep out of reach of children.
See Package Insert for Full Prescribing Information and Patient's Instructions for Use.
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St. Louis, Missouri 63045

WS#1

PRINT SIDE GLUE

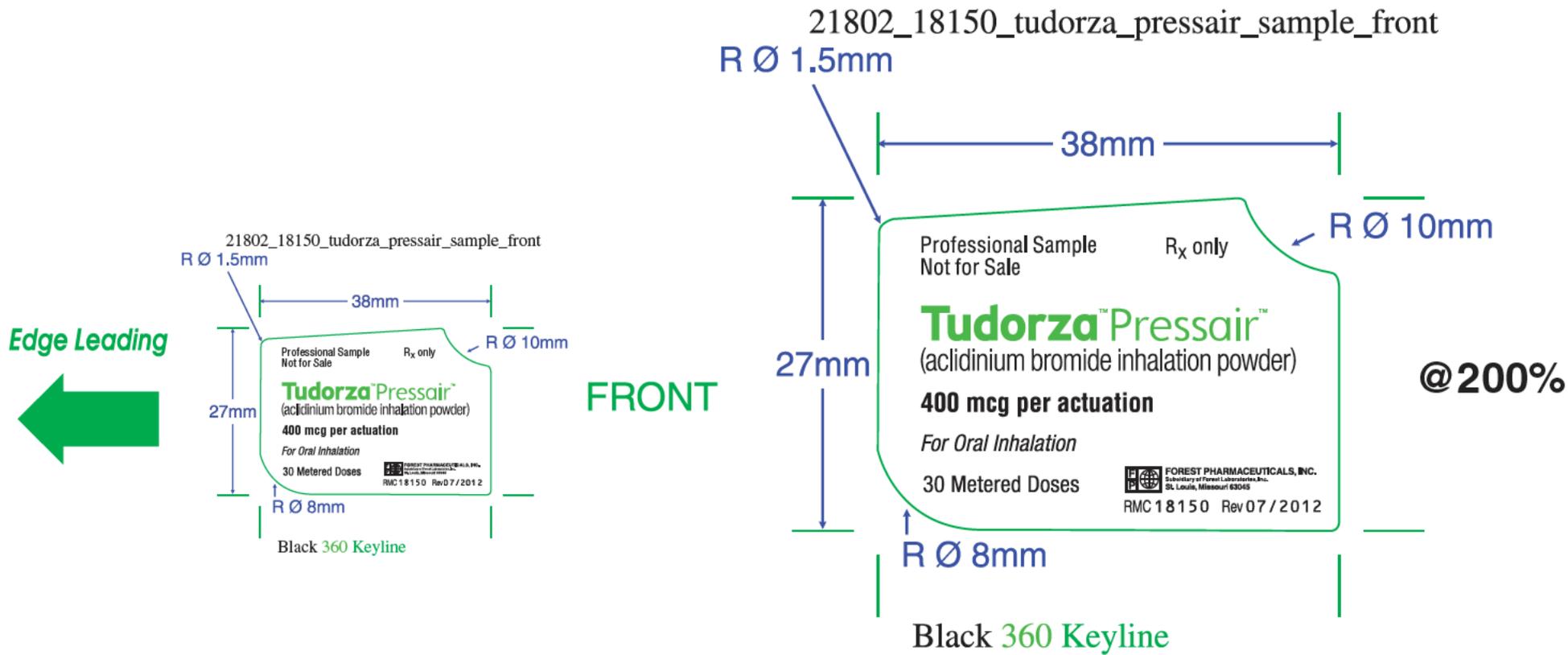


FORE18505.2_A
PRINT SIDE
Acridinium 1 X 5 Display (Vertical) Sleeve
5-6-11

Notes:

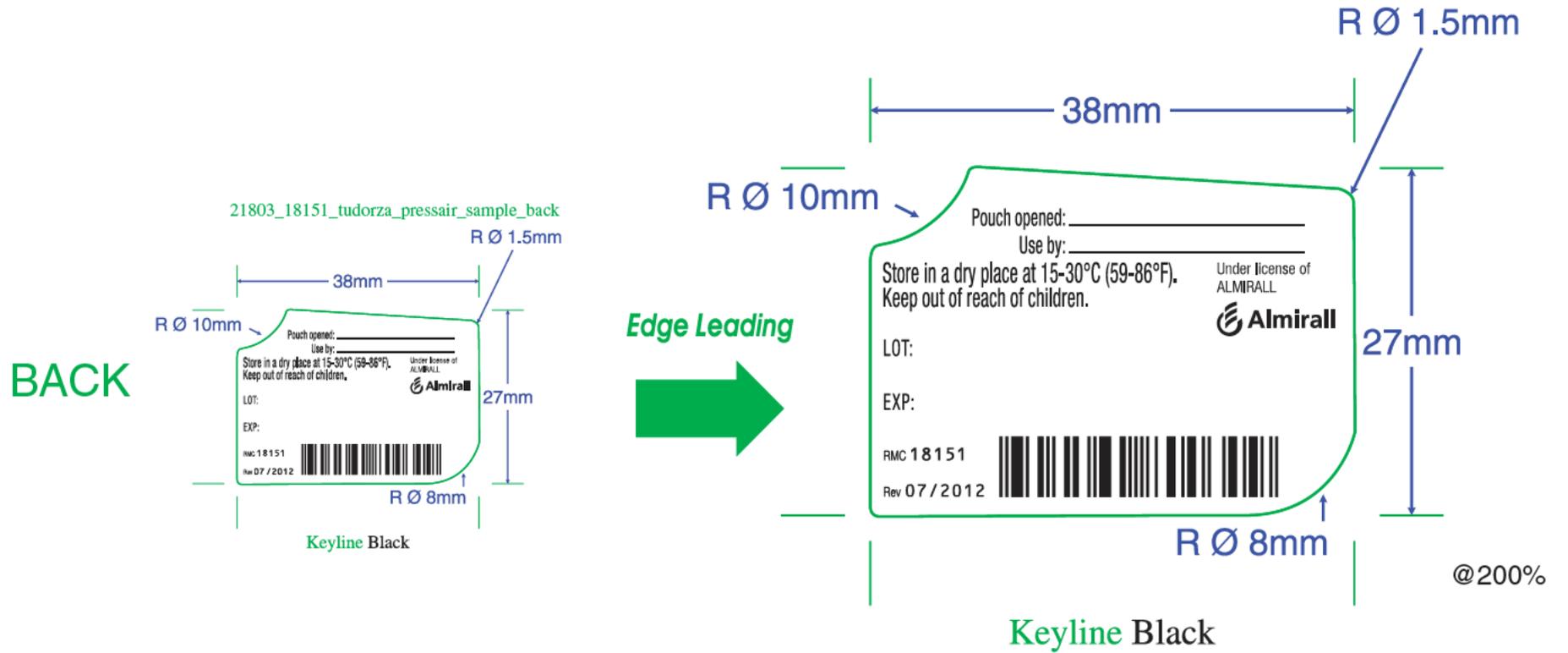
- This "coating free area" symbol, indicates manufacturing specifications for drop outs. Any additional drop outs required by your machinery or graphics, must be marked on the die drawing for Zumbiel's structural department to adjust.

Zumbiel is not held responsible for any additional drop outs not conveyed to our structural department.



Customer:	FOREST LABORATORIES IRE. LTD.	Colours Label:	Colours Leaflet Front:
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Size:			
Roll Quantity:			
Labels to View:			
Comments:			
Originated By:	(b) (4)	Date: 03 / 07 / 2012	Checked By:
			Colours Leaflet Back:

21803_18151_tudorza_pressair_sample_back



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Originated By: (b) (4)	Date: 13 / 06 / 2012	Checked By:	<input type="checkbox"/>	

215. mm

150. mm

Professional Sample
Not for Sale

R_x only

Tudorza™ Pressair™

(aclidinium bromide inhalation powder)

400 mcg per actuation

For Oral Inhalation

30 Metered Doses

Each metered dose of Tudorza™ Pressair™ contains 400 mcg of aclidinium bromide with lactose monohydrate, delivering 375 mcg aclidinium bromide from the mouthpiece.

Keep Tudorza Pressair inhaler inside the sealed pouch until the administration period starts.

Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first. Fill in the dates on the Pressair inhaler appropriately.

Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Keep out of reach of children.

See Package Insert for Full Prescribing Information and Patient's Instructions for Use.

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St. Louis, Missouri 63045

 Almirall



RMC 18149

Rev. 07/2012

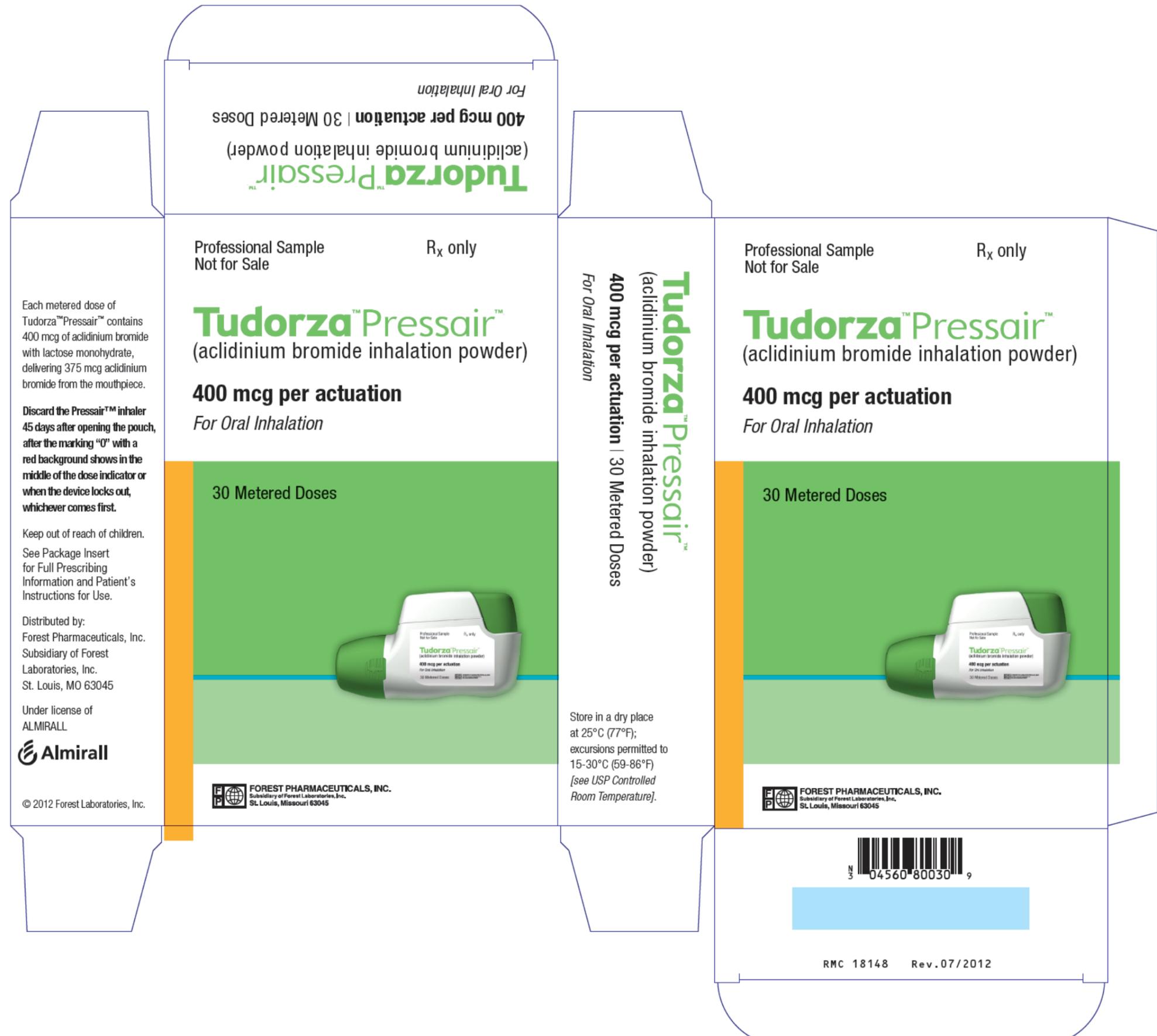
6 x 15 mm

66.5 mm

(b) (4)

Reference

Unwind sense / Sentido de salida



For Oral Inhalation
400 mcg per actuation | 30 Metered Doses
Tudorza Pressair™
(aclidinium bromide inhalation powder)

Professional Sample Not for Sale Rx only

Tudorza Pressair™
(aclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation

30 Metered Doses



Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

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Professional Sample Not for Sale Rx only

Tudorza Pressair™
(aclidinium bromide inhalation powder)

400 mcg per actuation
For Oral Inhalation

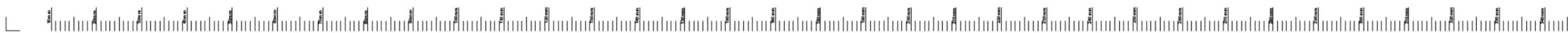
30 Metered Doses



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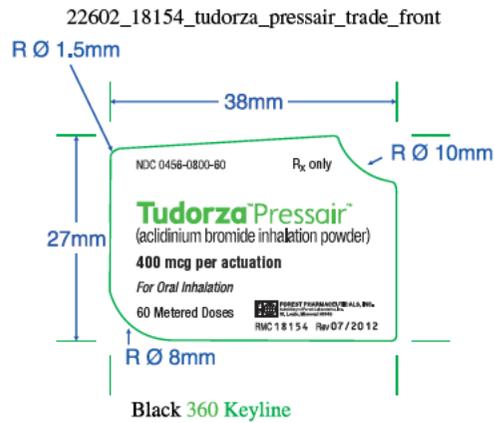


RMC 18148 Rev. 07/2012



22602_18154_tudorza_pressair_trade_front

Edge Leading



R Ø 1.5mm

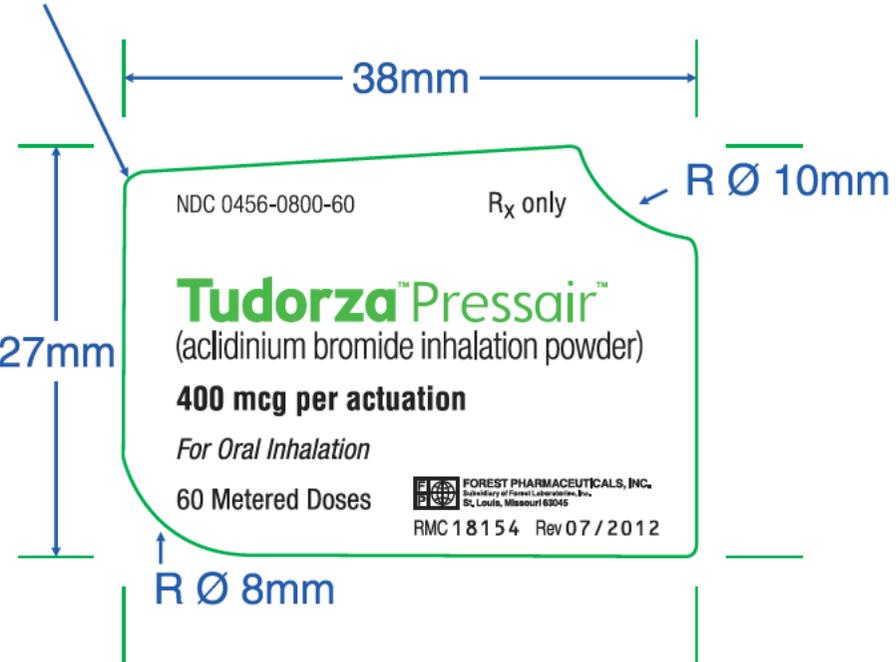
38mm

27mm

R Ø 10mm

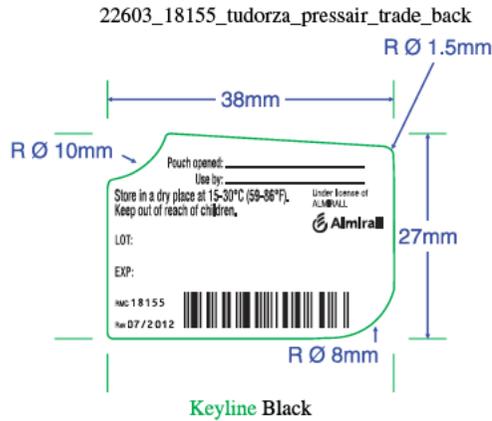
R Ø 8mm

Black 360 Keyline

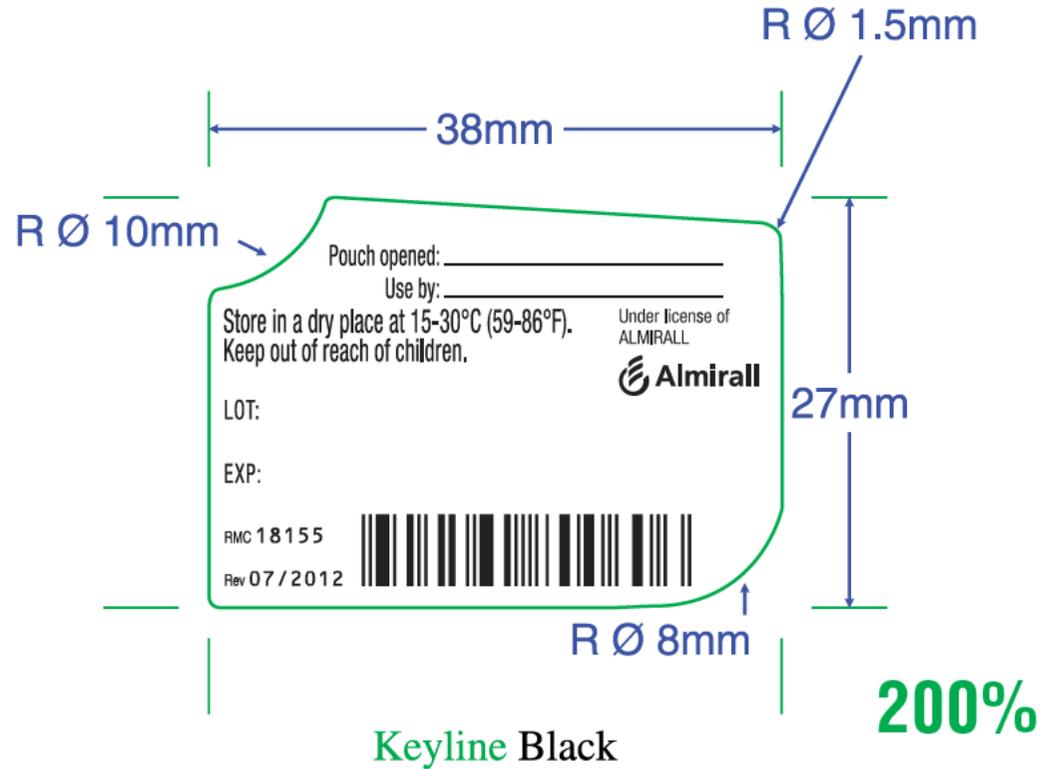


Customer:	FOREST LABORATORIES IRE. LTD.	Colours Label:	Colours Leaflet Front:	(b) (4)
Part Number:	(b) (4)	(b) (4)		
Material / Adhesive:	(b) (4)			
Size:	(b) (4)			
Roll Quantity:				
Labels to View:				
Comments:	1 2 3 4 5 6 7 8			
Originated By:	(b) (4)	Date: 03 / 07 / 2012	Checked By:	
			Colours Leaflet Back:	

22603_18155_tudorza_pressair_trade_back



Edge Leading



Customer:		FOREST LABORATORIES IRE. LTD.		Colours Label:		Colours Leaflet Front:	
Part Number:		(b) (4)		BLACK			
Material / Adhesive:		(b) (4)					
Size:		(b) (4)					
Roll Quantity:							
Labels to View:							
Comments:							
NDC barcode reads: 304560800606						Colours Leaflet Back:	
Originated By: (b) (4)		Date: 13 / 06 / 2012		Checked By:			

+215 mm

+150 mm

NDC 0456-0800-60

R_x only

Tudorza™ Pressair™

(aclidinium bromide inhalation powder)

400 mcg per actuation

For Oral Inhalation

60 Metered Doses

Each metered dose of Tudorza™ Pressair™ contains 400 mcg of aclidinium bromide with lactose monohydrate, delivering 375 mcg aclidinium bromide from the mouthpiece.

Keep Tudorza Pressair inhaler inside the sealed pouch until the administration period starts.

Discard the Pressair™ inhaler 45 days after opening the pouch, after the marking "0" with a red background shows in the middle of the dose indicator or when the device locks out, whichever comes first. Fill in the dates on the Pressair inhaler appropriately.

Store in a dry place at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Keep out of reach of children.

See Package Insert for Full Prescribing Information and Patient's Instructions for Use.

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 Almirall



RMC 18153

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6 x 15 mm

66.5 mm

Unwind sense / Sentido de salida

(b) (4)

Reference

Tudorza[™]Pressair[™]
(acclidinium bromide inhalation powder)
400 mcg per actuation | 60 Metered Doses
For Oral Inhalation

NDC 0456-0800-60

R_x only

Tudorza[™]Pressair[™]
(acclidinium bromide inhalation powder)

400 mcg per actuation

For Oral Inhalation

60 Metered Doses



Store in a dry place
at 25°C (77°F);
excursions permitted to
15-30°C (59-86°F)
[see USP Controlled
Room Temperature].

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St. Louis, Missouri 63045

Each metered dose of
Tudorza[™]Pressair[™] contains
400 mcg of acclidinium bromide
with lactose monohydrate,
delivering 375 mcg acclidinium
bromide from the mouthpiece.

Discard the Pressair[™] inhaler
45 days after opening the pouch,
after the marking "0" with a
red background shows in the
middle of the dose indicator or
when the device locks out,
whichever comes first.

Keep out of reach of children.
See Package Insert
for Full Prescribing
Information and Patient's
Instructions for Use.

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NDC 0456-0800-60

R_x only

Tudorza[™]Pressair[™]
(acclidinium bromide inhalation powder)

400 mcg per actuation

For Oral Inhalation

60 Metered Doses



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RMC 18152 Rev. 07/2012



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/s/

CURTIS J ROSEBRAUGH
07/23/2012