Drug Monograph

Drug/Drug Class:	**Tudorza™ Pressair™ (aclidinium bromide) inhalation, powder/ anticholinergic**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Each actuation of the inhalation powder of Tudorza™ Pressair™ contains 400 micrograms of aclidinium bromide. Forest Pharmaceuticals, 13600 Shoreline Drive**,** St. Louis, MO 63045
Summary of Findings:	Tudorza™ Pressair™ is an inhaled powder that has shown efficacy for long-term maintenance treatment of chronic obstructive pulmonary disease (COPD) associated bronchospasms. COPD diseases include emphysema and chronic bronchitis. Tudorza™ Pressair™ is a long-acting anticholinergic drug, specifically an antimuscarinic agent.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL Product
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Non-preferred agent ☐ Appropriate Indications ☒ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction

Chronic obstructive pulmonary disorder (COPD) is a concerning pulmonary condition that makes it difficult for patients to breathe. The foremost cause of COPD is smoking cigarettes. Signs and symptoms of COPD include excessive sputum, chronic cough, and tightness in the chest. In the United States, COPD is the fourth leading cause of death.

Dosage Form(s) [1]

Each actuation of the inhalation powder of Tudorza™ Pressair™ contains 400 micrograms aclidinium bromide.

Manufacturer

Forest Pharmaceuticals, 13600 Shoreline Drive**,** St. Louis, MO 63045

Indication(s) [1]

Indicated for long-term maintenance treatment of chronic obstructive pulmonary disease (COPD) associated bronchospasms. COPD includes the disease states emphysema and chronic bronchitis.

Clinical Efficacy[1-12] (mechanism of action/pharmacology, comparative efficacy)

Tudorza™ Pressair™ is a long-acting anticholinergic medication, specifically an antimuscarinic drug. It inhibits muscarinic receptors M1 through M5, however, its inhibition of the M3 receptor is what leads to its bronchodilation effect via smooth muscle relaxation in the airways.

PHARMACOKINETICS

	Tudorza™ Pressair™
Volume of distribution	300 Liters (specific to intravenous administration)
Half-life	5 to 8 hours (specific to inhalation administration)
Metabolism	Esterases hydrolyze Tudorza™ Pressair™ extensively and quickly to inactive metabolites (dithienylglycolic acid derivatives and alcohol)
Excretion	The following excretion data is specific to intravenous administration: Feces: 20% to 33% Urine: 54% to 65%

The approval of Tudorza™ Pressair™ inhaler was based primarily upon 3 randomized, placebo-controlled confirmatory clinical trials that involved 1276 patients with stable, moderate to severe COPD and a smoking history of at least 1 pack a day for 10 years. In all 3 trials, Tudorza™ Pressair™ (400 mcg twice daily) resulted in a statistically significant increase from baseline morning trough forced expiratory volume in 1 second (FEV1) compared with placebo at week 12. Clinical head-to-head comparisons are limited between Tudorza™ Pressair™ inhaler and other agents used in treating COPD.

STUDY Chronic Obstructive Pulmonary Disease (COPD) – 3 DOUBLE-BLIND TRIALS USING TUDORZA™ PRESSAIR™

STUDY DESIGN:	Three randomized, double-blind, placebo-controlled confirmatory clinical trials (Trials B, C, and D; n=1276).
INCLUSION CRITERIA:	Patients with a clinical diagnosis of COPD, had a history of at least 10 pack-years smoking, were 40 years of age or older, 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; 93% were Caucasian and 59% were male.
EXCLUSION CRITERIA:	None specified.
TREATMENT REGIMEN:	Patients were randomized to receive Tudorza™ Pressair™ inhaler (400 mcg twice daily, n=636) or placebo (n=640).
RESULTS	Treatment with Tudorza™ Pressair™ 400 mcg twice daily resulted in statistically significantly greater bronchodilation as measured by change from baseline in morning pre-dose FEV1 at 12 weeks compared with placebo in all 3 trials. This was the primary efficacy endpoint. The least square mean treatment difference from baseline compared to placebo in trough FEV1 at week 12 in Trial B, C, and D, respectively was 0.12 (95% CI, 0.08 to 0.16), 0.07 (95% CI, 0.03 to 0.12) and 0.11 (95% CI, 0.07 to 0.14). Mean peak FEV1 improvements, for Tudorza™ Pressair™ relative to baseline, were assessed in all patients in trials B, C, and D after the first dose on day 1 and were similar at week 12. In Trials B and D only, patients treated with Tudorza™ Pressair™ used less daily rescue albuterol throughout the trial compared with the placebo groups.
SAFETY	The most common adverse reactions (>= 3% and occurring more than in the placebo) were headache, nasopharyngitis, and cough.

Contraindications[1]

- None.

Warnings and Precautions[1]

- Cannot use Tudorza™ Pressair™ for acute problems or as a rescue medication.
- Paradoxical bronchospasm: If paradoxical bronchospasm occurs, discontinue use and consider alternative treatments.
- Worsening of narrow-angle glaucoma may occur. Caution should be used in patients with narrow-angle glaucoma; if vision changes do occur, instruct patients to consult a physician immediately.
- Worsening of urinary retention may occur. Use with caution in patients with bladder-neck obstruction or prostatic hyperplasia; if urination becomes difficult or painful instruct patients to consult a physician immediately

- Hypersensitivity reactions: Caution should be used in patients with severe hypersensitivity to milk proteins.

Adverse Effects[1]

Most common, ≥ 1%	Placebo (n=640)	Tudorza™ Pressair™ (n=636)
▪ Headache	5.0%	6.6%
▪ Nasopharyngitis	3.9%	5.5%
▪ Cough	2.2%	3.0%
▪ Diarrhea	1.4%	2.7%
▪ Sinusitis	0.8%	1.7%
▪ Rhinitis	1.2%	1.6%
▪ Toothache	0.8%	1.1%
▪ Fall	0.5%	1.1%
▪ Vomiting	0.5%	1.1%

Drug Interactions[1]

- Anticholinergics

Dosage and Administration[1]

The recommended dose of Tudorza™ Pressair™ is 400 micrograms inhaled by mouth twice daily. One actuation/inhalation is 400 micrograms of aclidinium bromide.

Cost Comparisons (at commonly used dosages)

COST (WAC)*

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/ MONTH
Aclidinium bromide inhalation	Tudorza Pressair	Forest	400 mcg/actuation, 60 metered doses	400 mcg twice daily	$ 217.15 (WAC)**
Tiotropium bromide inhalation	Spiriva	Boehringer Ingelheim	18 mcg capsules, 30 doses/package	18 mcg once daily	$ 240.90

*WAC – Wholesale Acquisition Cost (WAC)

Conclusion

Tudorza™ Pressair™ is an inhaled powder that has shown efficacy for long-term maintenance treatment of chronic obstructive pulmonary disease (COPD) associated bronchospasms. COPD diseases include emphysema and chronic bronchitis. Tudorza™ Pressair™ is a long-acting anticholinergic drug, specifically an antimuscarinic drug. There is not much head-to-head data regarding its efficacy compared to the other long-acting anticholinergic drug currently on the market, tiotropium bromide. Additionally, the FDA has ordered the manufacturer to continue ongoing post market studies to evaluate the risk of cardiovascular adverse effects due to Tudorza™ Pressair™.

Recommendation

This product is being considered for inclusion into the state specific Preferred Drug List and is currently under solicitation.

References

1. Product Information: Tudorza™ Pressair™, aclidinium bromide inhaler. Forest Pharmaceuticals, St. Louis, MO 07/2012.
2. Gavalda A, Miralpeix M, Ramos I, et al: Characterization of aclidinium bromide, a novel inhaled muscarinic antagonist, with long duration of action and a favorable pharmacological profile. J Pharmacol Exp Ther 2009; 331(2):740-751.
3. Sims MW & Panettieri RA Jr: Profile of aclidinium bromide in the treatment of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2011; 6:457-466.
4. Alagha K, Bourdin A, Tummino C, et al: An update on the efficacy and safety of aclidinium bromide in patients with COPD. Ther Adv Respir Dis 2011; 5(1):19-28.
5. Kerwin EM, D'Urzo AD, Gelb AF, et al; ACCORD I study investigators: Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). COPD 2012; 9(2):90-101.
6. Maltais F, Celli B, Casaburi R, et al: Aclidinium bromide improves exercise endurance and lung hyperinflation in patients with moderate to severe COPD. Respir Med 2011; 105(4):580-587.
7. Jones PW, Rennard SI, Agusti A, et al: Efficacy and safety of once-daily aclidinium in chronic obstructive pulmonary disease. Respir Res 2011; 12:55.
8. Fuhr R, Magnussen H, Sarem K, et al: Efficacy of aclidinium bromide 400 {micro}g twice daily compared with placebo and tiotropium in patients with moderate to severe COPD. Chest 2012; 141(3):745-752.
9. Chanez P, Burge PS, Dahl R, et al: Aclidinium bromide provides long-acting bronchodilation in patients with COPD. Pulm Pharmacol Ther 2010; 23(1):15-21.
10. Vestbo J, Vogelmeier C, Creemers J, et al: Onset of effect of aclidinium, a novel, long-acting muscarinic antagonist, in patients with COPD. COPD 2010; 7(5):331-336.
11. 11. Joos GF, Schelfhout VJ, Pauwels RA, et al: Bronchodilatory effects of aclidinium bromide, a long-acting muscarinic antagonist, in COPD patients. Respir Med 2010; 104(6):865-872.
12. Cazzola M: Aclidinium bromide, a novel long-acting muscarinic M3 antagonist for the treatment of COPD. Curr Opin Investig Drugs 2009; 10(5):482-490.

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