Drug Monograph

Drug/Drug Class:	**Anoro™ Ellipta (umeclidinium bromide and vilanterol trifenatate) inhalation powder/ anticholinergic/ long-acting beta2-adrenergic agonist**
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:	Anoro™ Ellipta is an inhalation powder. Each inhaler contains 2 double-foil blister strips of powder formulation for oral inhalation. One strip contains umeclidinium 62.5 mcg per blister and the other contains vilanterol 25 mcg per blister. GlaxoSmithKline Research Triangle Park, NC 27709
Summary of Findings:	Anoro™ Ellipta is a combination of umeclidinium, an anticholinergic, and vilanterol, a long-acting beta2-adrenergic agonist, indicated for the long-term, once-daily, maintenance treatment of chronic obstructive pulmonary disease (COPD).
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Fiscal Edit ☒ PDL Edit
Type of PA Criteria:	☐ Increased Risk of ADE ☐ 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[1]

COPD is a debilitating condition that causes its sufferers to have significant difficulty breathing. It leads to a decreased quality of life as well as increased health care costs. Long-term, maintenance treatment is shown to decrease exacerbations as well as overall cost.

Dosage Form(s) [1]

Anoro™ Ellipta is an inhalation powder. The inhaler contains 2 double-foil blister strips of powder formulation for oral inhalation. One strip contains umeclidinium 62.5 mcg per blister and the other contains vilanterol 25 mcg per blister.

Manufacturer [1]

GlaxoSmithKline
Research Triangle Park, NC 27709

Indication(s) [1]

Anoro™ Ellipta is FDA approved for long-term, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

Clinical Efficacy [1-2] (mechanism of action/pharmacology, comparative efficacy)

Umeclidinium is a long-acting anticholinergic agent that reversibly inhibits the M3 receptor at the smooth muscle, leading to bronchodilation. Vilanterol is a LABA that increases cyclic adenosine monophosphate (cAMP) levels, resulting in relaxation of bronchial smooth muscle and inhibition of mast cell release of immediate hypersensitivity mediators.

Pharmacokinetics

	Umeclidinium	**Vilanterol**
Protein binding	89%	94%
Volume of distribution	86 L	165 L
Metabolism	Hepatic, via CYP2D6	Hepatic, via CYP3A4
Excretion	Feces, 92% (oral) Urine, < 1% (oral)	Feces, 30% (oral) Urine, 70% (oral)
Half-life	11 hours	11 hours

The effect of Anoro™ Ellipta on lung function in the treatment of COPD was studied in a large, multicenter, randomized, double-blind, placebo-controlled clinical trial (n=1532). The trough FEV1 at 6 months was significantly improved in patients treated with umeclidinium/vilanterol when compared with umeclidinium monotherapy, vilanterol monotherapy, or placebo. Results were similar in a smaller randomized, placebo-controlled clinical trial of 413 patients.

COPD

STUDY DESIGN	Randomized, double-blind, placebo-controlled, 24-week, multicenter clinical trial (n=1532).
INCLUSION CRITERIA	Patients 40 years or older with a smoking history of at least 10 pack-years and COPD with airflow limitation that was not fully reversible.
EXCLUSION CRITERIA	Any concomitant non-COPD respiratory disorder.
TREATMENT REGIMEN	Patients were randomized to receive umeclidinium 62.5 mcg/vilanterol 25 mcg (n=413), umeclidinium 62.5 mcg (n=418), vilanterol 25 mcg (n=421), or placebo (n=280) inhaled once daily via dry powder inhaler. Concomitant rescue doses of salbutamol and stable doses of inhaled corticosteroids were allowed.
RESULTS	Mean age ranged from 62.2 to 64 years and mean baseline percent predicted FEV1 ranged from 46.8% to 48.2%. At day 169, umeclidinium 62.5 mcg/vilanterol 25 mcg improved trough FEV1 by 52 mL more than umeclidinium 62.5 mcg (p=0.004), by 95 mL more than vilanterol 25 mcg (p < 0.001), and by 167 mL more than placebo (p < 0.001). Quality of life was measured using the Transition Dyspnoea Index, Shortness of Breath with Daily Activities score, and St George's Respiratory Questionnaire. The scores improved significantly more in the 3 treatment groups compared with placebo, but there was no significant difference in score improvement between the 3 treatment groups. Umeclidinium 62.5 mcg/vilanterol 25 mcg was associated with a lower risk of COPD exacerbations compared with placebo (hazard ratio, 0.5; 95% CI, 0.3 to 0.8; p <= 0.01).
SAFETY	The incidence of adverse effects was similar across all treatment and placebo groups.

Contraindications [(1)]

- Hypersensitivity to milk proteins, severe
- Hypersensitivity to umeclidinium, vilanterol, or any component of the product

Warnings and Precautions [1]

- Asthma (unapproved use); increased risk of asthma-related death may occur with long-acting beta(2)-adrenergic agonists, including umeclidinium/vilanterol.
- Acute symptom relief (ie, rescue therapy for acute bronchospasm); use not recommended; not studied.
- Cardiovascular disorders (eg, coronary insufficiency, cardiac arrhythmias, hypertension); increased risk for cardiovascular effects and ECG changes.
- Cardiovascular effects, clinically significant (eg, increased pulse rate, systolic or diastolic blood pressure, or symptoms), may occur; discontinue use if occurs.
- Concomitant, regular (eg, 4 times/day) use of short-acting beta(2) agonists; avoid use.
- Concomitant use of anticholinergic-containing drugs; avoid use.
- Concomitant use of beta blockers; avoid use if possible; consider cardioselective beta blockers if no alternatives exist.
- Concomitant use of other long-acting beta(2) agonists (eg, salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol); avoid use.
- Convulsive disorders, thyrotoxicosis, or patients with unusual responsiveness to sympathomimetic amines; contains sympathomimetic amines.
- Deteriorating COPD, acute, or potentially life-threatening; use not recommended; not studied.
- Diabetes mellitus and ketoacidosis; exacerbations have been reported with IV doses of albuterol.
- ECG changes (eg, QTc prolongation, flattening of T wave, ST depression) have been reported with beta agonists.
- Higher than recommended doses or use more frequently than recommended (once per 24 hours); avoid use.
- Hyperglycemia, transient, may occur.
- Hypersensitivity reactions, including anaphylaxis, may occur.
- Hypokalemia, significant, may occur and result in cardiovascular adverse effects.
- Narrow-angle glaucoma; worsening may occur; monitoring recommended.
- Paradoxical bronchospasm, potentially life-threatening, may occur; discontinue use immediately if occurs.
- Urinary retention, especially in patients with prostatic hyperplasia or bladder neck obstruction); exacerbation of symptoms may occur; monitoring recommended.

Adverse Effects [1]

Most common, >= 1%	Umeclidinium/Vilanterol (n=842)	Placebo (n=555)
▪ Diarrhea	2%	1%
▪ Extremity pain	2%	1%
▪ Pharyngitis	2%	< 1%
▪ Chest pain	1%	< 1%
▪ Constipation	1%	< 1%
▪ Lower respiratory tract infection	1%	< 1%

▪ Muscle spasms	1%	< 1%
▪ Neck pain	1%	< 1%
▪ Sinusitis	1%	< 1%

Drug Interactions [1]

- Anticholinergic agents
- Beta blockers
- CYP3A4 inhibitors, strong: clarithromycin, ketoconazole
- Diuretics, loop or thiazide
- Monoamine oxidase inhibitors
- Tricyclic antidepressants

Dosage and Administration [1]

The recommended dose is one oral inhalation once daily at the same time each day.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST*/ MONTH
Umeclidinium bromide/ Vilanterol trifenatate	Anoro Ellipta	GlaxoSmithKline	62.5 mcg/ 25 mcg, 30 doses/inhaler	1 inhalation once daily	$ 280.80
Salmeterol xinafoate	Serevent Diskus	GlaxoSmithKline	50 mcg disk, 60 doses/ inhaler	1 inhalation twice daily	$ 257.40
Tiotropium bromide	Spiriva	Boehringer Ingelheim	18 mcg capsule	1 capsule inhaled once daily	$ 281.10

*WholesaleAcquisitionCost

Conclusion

Anoro™ Ellipta is the first combination bronchodilator approved for the long-term maintenance treatment of COPD. It is a combination of a long-acting anticholinergic agent and a LABA agent that is administered as a once daily inhalation. It has demonstrated efficacy in improving lung function when compared with placebo, umeclidinium monotherapy, and vilanterol monotherapy, but its efficacy has not been evaluated in comparison with other FDA-approved long-acting anticholinergic agents or LABA. The most common adverse effects include diarrhea, pharyngitis, and extremity pain.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL).

References

1. Product Information: Anoro™ Ellipta™, umeclidinium/vilanterol oral inhalation powder. GlaxoSmithKline, Research Triangle Park, NC, 12/2013.
2. Donohue JF, Maleki-Yazdi MR, Kilbride S et al: Efficacy and safety of once-daily umeclidinium/vilanterol 62.5/25 mcg in COPD. Respir Med 2013; 107(10):1538-1546.

Prepared by: Katie Wilbers, PharmD

Date: June 6, 2014

