PDL NEW DRUG REVIEW

Proprietary Name: Anoro Ellipta®
Common Name: umeclidinium & vilanterol
PDL Category: Antiasthmatic Adrenergic Combos

Comparable Products	Preferred Drug List Status
Ipratropium	Preferred
Spiriva	Preferred
Tudorza	Non-Preferred

Summary

Indications and Usage: 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. It is NOT indicated for the relief of acute bronchospasm or for the treatment of asthma. This is a pregnancy category C medication. The safety and efficacy of use in children under the age of 18 years have not been established.

Drug Interactions: Vilanterol is a substrate of CYP3A4; use with caution if administer concomitantly with ketoconazole or other known strong CYP3A4 inhibitors (e.g. ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, or voriconazole).

Vilanterol should be used with extreme caution in patients being treated with MAO Inhibitors, TCAs, or other medications known to prolong the QTc interval, or within 2 weeks of discontinuation of such agents.

Patients with COPD should typically not be treated with beta-blockers. They block the pulmonary effects of vilanterol; however, if they are needed and no other alternatives are available, the cardioselective beta-blockers could be considered. Use with caution.

While the clinical significance of the interaction is not known, it is recommended that the coadministration of Anoro Ellipta® with non-potassium-sparing diuretics be used with caution.

The concomitant use of Anoro Ellipta® with other anticholinergic-containing medications should be avoided.

Dosage Forms: Powder for inhalation, with 2 double-foil blister strips, each with 30 doses per inhaler; one strip contains 62.5mcg umeclidinium, and the other strip contains 25mcg vilanterol

Recommended Dosage: The daily dosing is one inhalation once daily by the orally inhaled route. Every time the cover of the inhaler is moved to expose the mouthpiece, a 'click' sound should be heard and then the inhaler is ready to use. No shaking of the inhaler is necessary. If the cover of the inhaler is opened and then closed without inhaling the medicine, the dose will be lost and will no longer be available to be inhaled. The lost dose with be

securely held inside the inhaler. Therefore, do not close the cover of the inhaler until after the medicine has been inhaled.

Once the tray has been opened, the 'tray opened' and 'discard' date should be written on the inhaler label. The discard date is 6 weeks from the date that the tray was opened.

Dosage adjustments are not required in those with renal or mild to moderate hepatic impairment. Use in those with severe hepatic impairment has not been studied.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug* (*Anoro Ellipta®*) *minus reported % incidence for placebo.* The most commonly reported adverse events included pharyngitis (>1%), sinusitis (<1%), lower respiratory tract infection (<1%), constipation (<1%), diarrhea (1%), pain in extremity (1%), muscle spasm (<1%), neck pain (<1%), and chest pain (<1%).

Anoro Ellipta® should be used with caution in those with narrow-angle glaucoma and with urinary retention. Signs and symptoms for worsening of the condition should be monitored.

Contraindications: In those with severe hypersensitivity to milk proteins, or who have shown hypersensitivity to umeclidinium, vilanterol, or any component of the compound

Manufacturer: GlaxoSmithKline

Analysis: Anoro Ellipta® is a combination product that contains umeclidinium, which is an anticholinergic, and vilanterol, which is a long-acting beta2-adrenergic agonist (LABA). This product allows for a dual mechanism of action to help target associated symptoms of COPD. Umeclidinium is a long-acting, antimuscarinic agent with similar affinity to muscarinic receptors M1 to M5. Vilanterol is a LABA, causing relaxation of bronchial smooth muscle and inhibition of the release of mediators of immediate hypersensitivity from cells, especially mast cells.

As with all LABA-containing products, Anoro Ellipta® carries a box warning regarding the risk of asthma-related death due to the LABA. In a clinical trial with salmeterol, another LABA, patients treated with salmeterol were found to have an associated increase in asthma-related deaths as compared to those receiving placebo. This finding is considered a class effect of all LABAs, including vilanterol. Furthermore, the box warning indicates that the safety and efficacy of Anoro Ellipta® in patients with asthma have not been established; thus, Anoro Ellipta® is not indicated for the treatment of asthma.

Numerous clinical trials were performed to demonstrate the safety and efficacy of Anoro Ellipta®, including 6 dose-ranging trials, 4 lung function trials that were 6 months in duration (2 were placebo-controlled and 2 were active-controlled), 2 crossover trials that were 12 weeks in duration, and a 12-month long-term safety study.

In the confirmatory trials, all patients (N=4733) had COPD, were ≥40 years of age, had a history of smoking >10 pack-years, and a post-albuterol FEV1 ≤70% of predicted normal values. The first 6 month trial compared Anoro Ellipta® with umeclidinium 62.5mcg, vilanterol 25mcg, and placebo. The primary endpoint was the change from baseline in trough (predose) FEV1 at day 169. Results suggested that Anoro Ellipta® had a larger increase in mean change from baseline vs all comparators. The least squares mean change from baseline in trough FEV1 was 167ml vs placebo; 52ml vs umeclidinium; and 95ml vs vilanterol. Trial 2 had a comparable study design; however, it evaluated umeclidinium/vilanterol 125/25mcg, umeclidinium 125mcg, vilanterol 25mcg, and placebo. Results from this trial were similar to trial 2. Furthermore, results from the 2 active-controlled trials and the 2 crossover trials provided additional support for the efficacy of Anoro Ellipta®.

There are currently several trials that compare umeclidinium/vilanterol combination (in various strengths) with tiotropium. Information accessed and utilized in this review was obtained from the manufacturer as data on file.

All studies were randomized, double-blind, double-dummy studies, with the primary endpoint being the trough FEV1 on day 169.

In the first study, significant improvements in trough FEV1 at day 169 were seen with Anoro Ellipta® 62.5/25mcg vs tiotropium 18mcg (by 90ml; p<0.001). In a second study, umeclidinium/vilanterol 125/25mcg significantly improved trough FEV1 at day 169 by 74ml as compared with tiotropium (p=0.003); however, please note that the dose of umeclidinium/vilanterol is not an FDA approved dose. As not all primary endpoints were met in this study, the comparison of Anoro Ellipta® with tiotropium as a further analysis was considered 'descriptive only'. In a third study, Anoro Ellipta® 62.5/25mcg significantly improved trough FEV1 at day 169 as compared with tiotropium by 112ml (p<0.001).[2]

It is recommended that Anoro Ellipta® remain non-preferred, as more cost effective alternatives are available, and be available to the few who are unable to tolerate any preferred medications.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred**
- ☐ **Preferred with Conditions**

References

[1] Anoro Ellipta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2013.

[2] Comparison of Anoro Ellipta® with tiotropium in the treatment of chronic obstructive pulmonary disease. Information requested from GlaxoSmithKline. Available as Data on file at GlaxoSmithKline.

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