PDL NEW DRUG REVIEW

Proprietary Name: Striverdi® Respimat
Common Name: olodaterol
PDL Category: Antiasthmatic- Beta-Adrenergics

Comparable Products	Preferred Drug List Status
Foradil	Preferred
Serevent	Preferred

Summary

Indications and Usage: For the long-term, maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. This is not indicated to treat acute deteriorations of COPD and is not indicated to treatment asthma. The safety and efficacy of use in asthma have not been established. This is a pregnancy category C medication. The safety and efficacy of use in children have not been established.

Dosage Forms: Respimat inhaler with cartridge containing olodaterol (as HCl); 1 actuation=2.7mcg olodaterol HCl 2.7mcg=olodaterol 2.5mcg

Recommended Dosage: Use two inhalations once daily max; dosage adjustments are not required in those with renal impairment or in those with mild or moderate hepatic impairment. Use has not been studied in those with severe hepatic impairment.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Striverdi®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same or that the active drug was less than placebo.* The most frequently reported adverse events included nasopharyngitis (3.6%), upper respiratory tract infection (0.7%), bronchitis (1.1%), urinary tract infection (1.5%), cough (0.2%), dizziness (0.2%), rash (1.1%), diarrhea (0.4%), back pain (0.8%), and arthralgia (1.3%). In addition, lung cancers were reported in 0.7% of those taking Striverdi® 10mcg and 0.3% of those taking Striverdi® 5mcg as compared with 0.2% of placebo.

Contraindications: In patients with asthma without use of a long-term asthma control medication; it is not indicated for the treatment of asthma

Manufacturer: Boehringer Ingelheim

Analysis: Olodaterol, the active ingredient of Striverdi® Respimat, is a long-acting beta$_2$-agonist (LABA). It works by binding and activating the beta2-adrenoreceptors in the airway smooth muscle after inhalation. Olodaterol carries a box warning regarding the increased risk of asthma-related deaths. Data from a large study that compared salmeterol with placebo showed an increase in asthma-related deaths in the salmeterol group. These results are considered to be a class effect. The box warning also includes that olodaterol is not indicated for the treatment of asthma.

For clinical assessment of Striverdi®, there were 3 dose-ranging studies performed in COPD patients, along with 8 confirmatory trials in patients with COPD. The 5mcg and 10mcg doses were further evaluated in the confirmatory trials, based upon results of the dose-ranging studies. There were 4 pairs of replicate, double-blind, placebo-controlled

confirmatory studies that included: 1.) 2 replicate, placebo-controlled, 48 weeks studies; 2.) 2 replicate, placebo- and active-controlled (formoterol 12mcg BID) 48 week studies; 3.) 2 replicate, placebo- and active-controlled (formoterol 12mcg BID), 6-week cross-over studies; and 4.) 2 replicate, placebo- and active-controlled (tiotropium 18mcg QD), 6-week cross-over studies. In all 48 week studies, the 5mcg dose demonstrated significant improvements in FEV1 ACU_{0-3h} as compared with placebo at week 12 and 24. In addition, the 5mcg dose showed significant improvements in trough FEV1 vs placebo at week 12 (3 of 4 trials) and at week 24 (4 trials). The 10mcg dose did not have an additional benefit over the 5mcg dose. In addition, less rescue albuterol was used with the 5mcg dose vs placebo.

In the 2 replicate 48 week studies comparing olodaterol with placebo and active comparator formoterol[2], olodaterol significantly improved FEV1 AUC_{0-3h} ($p<0.0001$) and FEV1 trough responses vs placebo ($p<0.01$). Formoterol was also significantly better than placebo for these endpoints. Significant differences between placebo vs olodaterol 5mcg (-2.8 difference vs placebo; $p<0.005$) and vs olodaterol 10mcg (-3.4 difference vs placebo; $p<0.0005$) were seen with the St. George's Respiratory Questionnaire (SGRQ) endpoint; however, significant differences were not seen with formoterol vs placebo (-1.2 difference vs placebo; p=NS). Statistically significant reductions in weekly mean daytime and nighttime rescue medications were seen with all active treatments vs placebo.

In the 2 replicate 6-week crossover studies comparing olodaterol with placebo and active comparator formoterol[3], the co-primary endpoints included the FEV1 AUC_{0-12} response and FEV1 AUC_{12-24h} response. Results suggested that all active treatments significantly improved the primary endpoints as compared with placebo ($p<0.0001$). In addition, the pooled data did not show differences between olodaterol 5 and 10mcg QD as compared to formoterol 12mcg BID for the FEV1 AUC_{0-12} response; however, the adjusted mean FEV1 AUC_{12-24} response was significantly greater with formoterol than olodaterol 5 and 10mcg. Nevertheless, statistically significant differences in FEV1 AUC_{0-24} responses were not seen between the 3 active comparators. The incidence of adverse events was comparable between active treatment groups.

Data from the phase 3 studies vs tiotropium was not found. Nevertheless, an indirect treatment comparison by Roskell et al[4] was found that included 10 studies with indacaterol and 8 with olodaterol in the meta-analysis. The authors concluded that olodaterol 5mcg and indacaterol 75-150mcg had comparable efficacy for treatment of patients with COPD, in regards to changes in trough FEV1. Head-to-head studies are needed.

There is no data found to suggest that Striverdi® is safer or more effective than other more cost-effective medications available within the class. It is recommended that Striverdi® remain non-preferred and require prior authorization and be available to the few who are unable to tolerate or who have failed on preferred medications.

PDL Placement:

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

References

[1] Striverdi [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2014.

[2] Koch A, Pizzichini E, Hamilton A, et al. Lung function efficacy and symptomatic benefit of olodaterol once daily delivered via Respimat® versus placebo and formoterol twice daily in patients with GOLD 2-4 COPD: results from 2 replicate 48-week studies. *Int J COPD*. 2014; 9: 697-714.

[3] Feldman GJ, Bernstein JA, Hamilton A, et al. The 24-h FEV1 time profile of olodaterol once daily via Respimat® and formoterol twice daily via Aerolizer® in patients with GOLD 2-4 COPD: results from two 6-week crossover studies. *Springerplus*. 2014; 3: 419.

[4] Roskell NS, Anzueto A, Hamilton A, et al. Once-daily long-acting beta-agonists for chronic obstructive pulmonary disease: an indirect comparison of olodaterol and indacaterol. *Int J Chron Obstruct Pulmon Dis*. 2014; 9:813-24.