



Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: New Inhalers for Treatment of COPD
-August 2015-



Background:

Over the past three years, several new once daily, fixed-dose combination medications have been approved for the treatment of chronic obstructive pulmonary disease (COPD). Two of these agents combine a long-acting beta-agonist (LABA) and a long-acting muscarinic agent (LAMA); namely umeclidinium/vilanterol (Anoro Ellipta[®]) and tiotropium/olodaterol (Stiolto Respimat[®]). A third agent, fluticasone/vilanterol (Breo Ellipta[®]), offers the first combination of an inhaled corticosteroid (ICS) and long-acting beta-agonist approved for once daily use.

Evidence suggests improved adherence to combination LABA/LAMA therapy in the treatment of COPD based on the convenience of once daily dosing. Presently, there is insufficient evidence comparing these agents with existing, approved COPD treatments as well as insufficient long-term safety data to support addition of these agents to the National Core Formulary (NCF). It was determined that a short-acting muscarinic agent offers no additional advantage in the management of mild COPD over the short-acting beta-agonist albuterol presently on the NCF. Therefore, **ipratropium was removed from the NCF.**

Discussion:

Four major guidelines were reviewed including the 2015 Global Initiative for Chronic Obstructive Lung Disease (GOLD), the 2010 National Institute for Health and Care Excellence (NICE) guideline, the American Thoracic Society/European Respiratory Society's 2011 Clinical Practice Guideline, and the 2014 VA/DOD clinical practice guidelines¹⁻⁴. Each of these guidelines recommend diagnosing COPD based on results of spirometry, with a general consensus that a post-bronchodilator ratio of FEV1/FVC <0.70 is diagnostic. The guidelines recommend a treatment approach based on symptoms, rather than FEV1 measurements alone, as these can be misleading regarding the severity of disease. The GOLD guidelines include the risk of exacerbation in the assessment of disease severity. Notwithstanding a few minor differences, the treatment guidelines recommend initiating either a short-acting beta-agonist or a short-acting muscarinic agent before proceeding stepwise to a LABA or LAMA and ultimately the combination of LAMA, LABA and an inhaled ICS if indicated.

Findings:

Umeclidinium/vilanterol (Anoro Ellipta[®]): The 2014 NICE guideline and four other recent systematic reviews were analyzed. These focused mainly on four 24-week, pivotal, double-blind placebo-controlled or active comparator-controlled trials comparing umeclidinium/vilanterol to its individual components, tiotropium or placebo⁵. Reviews also cited a randomized 52-week, multinational safety trial that was conducted⁷. Umeclidinium/vilanterol showed modest, statistically significant improvements in FEV1 when compared against its individual components as monotherapy, tiotropium or placebo⁵. No significant safety differences were observed⁵⁻⁷. However, data is lacking regarding the frequency of COPD exacerbations, hospitalizations, and mortality. There were also insufficient head-to-head comparisons with other fixed-dose combinations^{5,7}.

Tiotropium/olodaterol (Stiolto Respimat[®]): Due to its recent approval in 2015, data from only two replicate, randomized, double-blind, parallel-group, multicenter phase III trials and a randomized, double-blind, placebo-controlled Phase III trial (with an incomplete crossover design) were available for review^{8,9}. These studies compared tiotropium/olodaterol against its individual components and placebo. Statistically significant improvement in FEV1 was seen with tiotropium/olodaterol when compared to placebo and its individual monotherapies⁸. No significant safety differences were noted^{8,9}. However, no data were available comparing tiotropium/olodaterol with other currently available treatments.

Fluticasone/vilanterol (Breo Ellipta®): The 2013 NICE guideline and two other systematic reviews were used for analysis. These focused mainly on 3 randomized controlled trials that provided the best published evidence for fluticasone/vilanterol for treating COPD and were published in full¹⁰. In these studies, fluticasone/vilanterol 100/25 micrograms reduced the mean yearly rate of moderate and severe exacerbations but not exacerbations requiring admission to the hospital, compared with vilanterol 25 micrograms alone¹⁰. Improved trough FEV₁ after 24 weeks' treatment compared with placebo was also shown but not compared with vilanterol alone¹⁰. There are limited data comparing fluticasone/vilanterol with other ICS/LABA combination inhalers in COPD. One systematic review noted a study comparing fluticasone/vilanterol and fluticasone/salmeterol (Advair®), concluding that fluticasone/vilanterol was at least as effective as twice-daily fluticasone/salmeterol¹¹. Long term safety data is currently lacking for fluticasone/vilanterol¹⁰.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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