Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Long-acting Asthma and COPD Drugs

Drug Effectiveness Review Project Summary Report

Date of Review: September 2016 **Date of Last Review:** September 2015

Current Status of PDL Class:
See **Appendix 1**.

Research Questions:

1. What is the comparative *within-class* and *across-class* efficacy and effectiveness of long-acting inhaled and long-acting oral medications used to treat outpatients with asthma or chronic obstructive pulmonary disease (COPD)?
2. What is the comparative *within-class* and *across-class* tolerability and frequency of adverse events of long-acting inhaled and long-acting oral medications used to treat outpatients with asthma or chronic obstructive pulmonary disease (COPD)?
3. Are there subgroups of patients [e.g. groups defined by demographics (age, racial groups, gender), asthma or COPD severity, comorbidities, other medications (drug-drug interactions), smoking status, genetics, or pregnancy] for which asthma or COPD controller medications differ in efficacy, effectiveness, or frequency of adverse events?

Conclusions:

- There is low to moderate quality evidence of no *within-class* differences in efficacy or harms for long-acting inhaled (i.e., beta-agonists (LABAs), muscarinic antagonists (LAMAs), or corticosteroids (ICS)) and long-acting oral medications (i.e., leukotriene modifiers [LM]) for patients with asthma or COPD.[1] There was insufficient evidence in subgroup populations with asthma or COPD to establish meaningful conclusions on efficacy or harms.[1]

Asthma

- There was low to high strength of evidence that ICS is associated with less exacerbations than LMs in patients with asthma.[1]
- Low to moderate evidence found ICS to have no difference in risk of exacerbations compared to LABAs.[1]
- ICS were found to be more effective than LABAs at decreasing exacerbations based on one comparison (moderate strength of evidence).[1]
- Risk of exacerbations were found to be similar between LABA and LAMA based on low strength of evidence.[1]
- Risk of adverse events were similar for most comparisons *between* the difference classes when used in patients with asthma.[1]

COPD

- Low to moderate strength of evidence found no difference in exacerbation rates when ICS were compared to LABA in COPD patients. One trial found ICS use to have an increased risk of mortality compared to LABA (low strength of evidence).[1]
- No difference in exacerbation rates were found when LAMA/LABA were compared to ICS/LABA based on low to moderate strength of evidence.[1]
- Moderate strength of evidence found patients treated with LABAs to have more exacerbations than LAMA treated patients.[1]

Author: Kathy Sentena, PharmD Date: September 2016

- ICS/LABA and LABA were found to have similar risk of exacerbations based on low strength of evidence.[1]
- Three comparisons found low strength of evidence that mortality rates were similar between ICS/LABA and LAMA.[1]
- For the outcomes of exacerbations, mortality, daily activities and quality of life there was low strength of evidence that LAMA/LABA was similar to LAMA.[1]
- An increased risk of serious pneumonia was associated with ICS use compared to LABA (OR 1.48; 95% CI 1.13 to 1.94) based on moderate strength of evidence.[1]

Recommendations:

- Current evidence for these agents does not support specific changes to the current Preferred Drug List (PDL).
- Recommend to continue current prior authorization (PA) criteria with minor clarification that patients with concomitant asthma and COPD may have access to a LAMA/LABA (Appendix 2).
- After review of comparative drug costs in the executive session, Combivent Respimat® (ipratropium/albuterol) was removed from the PDL and Ventolin HFA was added to the PDL. Grandfather current Combivent Respimat® users for 6 months.

Previous Conclusions:

- There is insufficient new comparative evidence for efficacy/effectiveness for the treatment of COPD. Evidence-based recommendations in new clinical practice guidelines from The Global Initiative for Chronic Obstructive Lung Disease (GOLD), The American College of Chest Physicians (ACCP) and Canadian Thoracic Society (CTS), and the Veterans Administration (VA)/Department of Defense (DoD) do not differentiate between drugs within a pharmacological class. Therefore, these guidelines cannot be used to support placement of specific therapies on Practitioner-Managed Prescription Drug Plan (PMPDP).
- There is insufficient new comparative evidence for efficacy/effectiveness for the treatment of asthma. New evidence primarily focuses on the use of omalizumab for severe asthma and continues to support the recommendation to reserve omalizumab to patients with allergic asthma who have failed other treatments.
- There is insufficient new comparative safety data for the treatment of COPD or asthma. New evidence primarily focuses on individual treatments and do not support a change to current placement of therapies for asthma or COPD on the Preferred Drug List (PDL).
- Two new formulations of drug products for COPD previously reviewed by the Pharmacy & Therapeutics Committee were identified. Both products were approved by the FDA based on short-term, 24-week studies that evaluated surrogate outcomes of lung function.
    - Tiotropium/olodaterol (Stiolto™ Respimat®) is indicated for long-term management of COPD. Tiotropium is a preferred inhaled anticholinergic for COPD and olodaterol is a non-preferred long-acting beta-agonist for COPD. Over 5,000 patients from two replicate studies with moderate to very severe COPD were studied for 52 weeks. Patients were randomized to one of 5 treatment arms: tiotropium 2.5 mcg, tiotropium 5 mcg, olodaterol 5 mcg, tiotropium 2.5 mcg/olodaterol 5 mcg and tiotropium 5 mcg/olodaterol 5 mcg. There is moderate level of evidence that tiotropium/olodaterol fixed-dose combination products are superior compared to its monotherapy components for the outcomes of change from baseline in FEV_1 $AUC_{0\text{-}3hr}$ ($p<0.0001$ for all comparisons) and trough FEV_1 ($p<0.05$ for all comparisons) at 24 weeks. There is insufficient evidence of comparative efficacy or safety between tiotropium/olodaterol and other drugs for the management of COPD.
    - Fluticasone furoate (Arnuity™ Ellipta®) is an ICS indicated for the maintenance treatment of asthma in patients 12 years and older. Fluticasone furoate demonstrated superiority over placebo with a mean difference in baseline evening trough FEV_1 of 146 mL (95% CI, 36 to 257 mL; p=0.009) at 24 weeks.
- A new indication for asthma in patients 18 years of age or older was identified for fluticasone furoate/vilanterol (Breo® Ellipta®). Approval for asthma by the FDA for the 100/25 mcg and 200/25 mcg dose of fluticasone furoate/vilanterol was based on short-term, 12 to 24-week studies.

- There is moderate quality evidence that the once-daily fixed dose combination products are more effective than their fluticasone furoate monotherapy counterparts in the ability to improve weighted mean FEV_1 (0-24 hours) from baseline. In addition, fluticasone furoate 100 mcg/vilanterol 25 mcg decreased time to first asthma exacerbation compared to fluticasone furoate 100 mcg alone (HR 0.80; 95% CI, 0.64 to 0.99; p=0.036).

Previous Recommendations:

- Make tiotropium/olodaterol, fluticasone furoate and fluticasone furoate/vilanterol products non-preferred at this time due to limited evidence.
- Create new PDL class for long-acting muscarinic antagonist/long-acting beta-agonist (LAMA/LABA) fixed-dose combination inhaler products.
- Re-organize and modify clinical PA criteria to promote step-therapy that is consistent with Oregon Asthma Guidelines and with medical evidence for COPD:
  - All non-preferred LABA inhalers must go through the LABA PA criteria for appropriate step therapy.
  - All non-preferred inhaled corticosteroids (ICS) must go through the ICS PA criteria for appropriate step therapy.
  - Remove clinical PA for "asthma controllers" and indacaterol. Drugs under these PAs will be incorporated into the ICS or LABA PA criteria.
  - Remove clinical PA for leukotriene inhibitors. Non-preferred leukotriene inhibitors will go through the generic non-preferred PDL PA.
  - Clerical changes to the roflumilast PA criteria.
  - Update LABA/ICS clinical PA and LABA/LAMA clinical PA to reflect best practices for initial COPD management. Bring back PAs to next P&T meeting.

Methods:

The June 2016 Drug Class Review on long-acting asthma and COPD drugs by the DERP at the Pacific Northwest Evidence-based Practice Center at the Oregon Health & Science University (OHSU) was used to inform recommendations for this drug class.

The final original report is available to Oregon Pharmacy and Therapeutics Committee members upon request. An executive summary report is publically available in the agenda packet and on the DURM website.

The purpose of the DERP reports is to make available information regarding the comparative clinical effectiveness and harms of different drugs. Reports are not usage guidelines, nor should they be read as an endorsement of or recommendation for any particular drug, use, or approach. OHSU does not recommend or endorse any guideline or recommendation developed by users of these reports.

Summary Findings:

Literature was searched through October 2015 and 35 new studies were identified for this class update.[1] Asthma patients 12 months of age and older and adult COPD patients were included in the studies. Drugs included in the search are listed in Table 1. There was low- to moderate-strength of evidence that there were no differences in efficacy of drugs *within* the same class. Evidence for available comparisons are presented below, separated by diagnosis of asthma or COPD. There was insufficient evidence on benefits and harms in subgroup populations.

Table 1. Drugs for Asthma and COPD.[1]

Generic Name	Trade Name	Formulation
Long-acting Beta-Agonists (LABA)		
Arformoterol tartrate	Brovana	Inhalation solution (nebulized)
Formoterol fumarate	Foradil Perforomist Aerolizer and Certihaler	Inhalation powder (DPI) Inhalation solution (nebulized) Inhalation powder (DPI)
Indacaterol maleate	Arcapta	Inhalation powder (DPI)
Olodaterol hydrochloride	Striverdi Respimat	Metered soft-mist spray (SMI)
Salmeterol xinafoate	Serevent	Inhalation powder (DPI)
Long-acting Muscarinic Antagonists (LAMA)		
Aclidinium	Tudorza Pressair	Inhalation powder (DPI)
Glycopyrrolate bromide	Seebri Breezhaler	Inhalation powder (DPI)
Tiotropium bromide	Spiriva Spiriva Respimat	Inhalation powder (DPI) Metered soft-mist spray (SMI)
Umeclidinium bromide	Incruse Ellipta	Inhalation powder (DPI)
Inhaled Corticosteroids (ICS)		
Beclomethasone dipropionate	QVAR	Inhalation aerosol (MDI)
Budesonide	Pulmicort Respules Pulmicort Flexhaler	Inhalation suspension (nebulized) Inhalation powder (DPI)
Ciclesonide	Alvesco	Inhalation aerosol (MDI)
Flunisolide hemihydrate	Aerospan	Inhalation aerosol (MDI)
Fluticasone furoate	Arnuity Ellipta	Inhalation powder (MDI)
Fluticasone propionate	Flovent DISKUS	Inhalation powder (MDI)
Mometasone furoate	Asmanex Twisthaler Asmanex HFA	Inhalation powder (DPI) Inhalation aerosol (MDI)
Fixed-dose Combination Products – ICS/LABA		
Formoterol/budesonide	Symbicort	Inhalation aerosol (MDI)
Formoterol/mometasone furoate	Dulera	Inhalation aerosol (MDI)
Slameterol xinafoate/fluticasone propionate	Advair Diskus Advair HFA	Inhalation powder (DPI) Inhalation aerosol (MDI)
Fixed-dose Combination Products – LABA/LAMA		
Indacaterol/glycopyrrolate	Utibron Neohaler	Inhalation powder (DPI)
Olodaterol hydrochloride/tiotropium bromide	Stiolto Respimat	Soft-mist spray (SMI)
Umeclidinium bromide/vilanterol trifenatate	Anoro Ellipta	Inhalation powder (DPI)
Vilanterol/fluticasone furoate	Breo Ellipta	Inhalation powder (DPI)
Leukotriene Modifiers (LM)		

Author: Sentena

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Montelukast sodium	Singulair	Chewable tablets
Zileuton	Zyflo Zyflo CR	Tablet Extended release tablet
Zafirlukast	Accolate	Tablet
Phosphodiesterase-4 inhibitor (PDE-4)		
Roflumilast	Daliresp	Tablet

ASTHMA

Within Class Comparisons:

ICS

- For the outcomes of asthma symptoms, exacerbations, rescue medications, quality of life, or adverse events there were no differences in ICSs at equivalent doses based on 47 trials (low to moderate strength).
- Low quality evidence of outcome differences between the ICSs are presented in Table 2.

Table 2. ICS Efficacy Comparisons in Patients with Asthma.[1]

Comparison	Findings	Strength of Evidence
Budesonide vs. mometasone	Mometasone associated with less rescue medication use compared to budesonide	Low
Beclomethasone vs. budesonide	Beclomethasone was found to have less risk of nocturnal awakenings compared to budesonide.	Low
Fluticasone propionate vs. beclomethasone	Fluticasone demonstrated lower risk of exacerbations compared to beclomethasone (RR 0.71; 95% CI, 0.51 to 0.99)	Low
Fluticasone propionate vs. budesonide	Fluticasone had better functional capacity results compared to budesonide.	Low
Abbreviations: RR – relative risk		

- Growth velocity in children was less affected by fluticasone propionate compared to beclomethasone. Height increases in children were less affected by ciclesonide versus budesonide.

LABA

- Three study comparisons of LABAs found no differences in the outcomes of asthma symptoms, exacerbation prevention, improved quality of life, hospitalizations and emergency room visits in patients not controlled on ICS alone (moderate strength of evidence). The one exception was a higher quality of life associated with olodaterol compared to formoterol.
- There were no differences found in tolerability or adverse events in a comparison of formoterol and salmeterol (with or without concomitant ICS use).

LM

- There was insufficient evidence to compare LMs.

ICS/LABA

- No difference between ICS/LABA formulations was found when 10 randomized controlled trials were compared. Two trials had insufficient evidence to compare efficacy. Comparative agents are detailed below in Table 3.

Table 3. ICS/LABA Efficacy Comparisons in Patients with Asthma.[1]

Comparison	Findings	Strength of Evidence
Beclomethasone/formoterol extrafine vs. fluticasone propionate/salmeterol	Comparative efficacy evidence was insufficient.	Insufficient
Budesonide/formoterol vs. fluticasone propionate/formoterol	Comparative efficacy evidence was insufficient.	Insufficient
Budesonide/formoterol vs. fluticasone propionate/salmeterol (+ medium-dose ICS in both groups)	No difference in exacerbations.	Moderate
Budesonide/formoterol vs. fluticasone propionate/salmeterol (+ high-dose ICS in both groups)	No difference in exacerbations.	Low
Fluticasone propionate/salmeterol vs. fluticasone furoate/vilanterol	No difference in quality of life.	Low

- Within class comparisons of ICS/LABA found no difference in adverse events or insufficient evidence to draw conclusions based on low to moderate strength of evidence. Specific comparisons are described in Table 4.

Table 4. ICS/LABA Harms Comparisons in Patients with Asthma.[1]

Comparison	Findings	Strength of Evidence
Beclomethasone/formoterol extrafine vs. fluticasone propionate/salmeterol	Comparative harms evidence was insufficient.	Insufficient
Budesonide/formoterol vs. fluticasone propionate/formoterol	Comparative harms evidence was insufficient.	Insufficient
Budesonide/formoterol vs. fluticasone propionate/salmeterol	Withdrawals due to adverse events were similar between groups.	Moderate
Mometasone/formoterol vs. fluticasone propionate/salmeterol	No difference in withdrawals due to adverse events or serious adverse events. Ocular toxicity was similar between groups.	Low -moderate Low
Fluticasone/salmeterol vs. fluticasone furoate/vilanterol	No difference in withdrawals due to adverse events or serious adverse events.	Low

Comparisons between Different Classes:

ICS vs. LM

- ICS use was associated with better outcomes compared to LM use with similar occurrence of adverse events. Table 5 below provides details on comparisons of specific ICSs to LMs.

Table 5. ICS vs. LM Efficacy Comparison in Patients with Asthma.[1]

Comparisons	Findings	Strength of Evidence
Fluticasone propionate vs. montelukast	Fluticasone was shown to have less exacerbations (OR 0.70; 95% CI 0.57 to 0.86) and improved quality of life compared to montelukast. Emergency department visits and missed school days were less with fluticasone compared to montelukast.	High Low
Beclomethasone vs. montelukast	Exacerbation rates were lower with beclomethasone compared to montelukast (SMD -0.15; 95% CI -0.30 to 0.00).	Low
Budesonide vs. montelukast	Two trials reported no significant difference in symptoms between groups. One trial found no difference in quality of life between the groups. One trial found budesonide to be associated with less daytime symptoms compared to montelukast.	Low to moderate
Fluticasone propionate vs. zafirlukast	Lower exacerbation rates were seen with fluticasone (SMD -0.21; 95% CI, -0.31 to -0.11)	High
Abbreviations: OR – odds ratio; SMD – standard mean difference		

- No difference in adverse events were shown between ICSs and LMs.

ICS vs. LABA

- Seventeen trials evaluated ICS to LABA comparisons. Four studies included pediatric patients while the majority included adults only. Specific comparisons are detailed below in Table 6.

Table 6. Efficacy Comparison of ICS to LABA in Patients with Asthma.[1]

Comparison	Findings	Strength of Evidence
Beclomethasone vs. salmeterol	No difference was demonstrated.	Moderate
Budesonide vs. formoterol	Trend favored budesonide for fewer symptoms, nocturnal awakenings, and exacerbations compared to formoterol.	Moderate
Fluticasone propionate vs. formoterol	No difference in exacerbations was found.	Low

Fluticasone propionate vs. salmeterol	No difference was found in outcomes.	Not provided
Mometasone vs. formoterol	Mometasone was favored over formoterol for less asthma deteriorations or clinically judged deteriorations.	Moderate

- Analysis of 16 trials found no difference in overall adverse events and withdrawals between ICSs and LABAs. LABA monotherapy is not recommended in patients with asthma.

LM vs. LABA
- There was insufficient evidence for conclusions to be made.

LABA vs. LAMA
- There was low strength of evidence from 3 trials comparing salmeterol to tiotropium that were no differences in exacerbation rate or quality of life.
- No difference was found between tiotropium and salmeterol in withdrawals due to adverse events or serious harms based on low strength of evidence.
- Overall adverse events, withdrawal due to adverse events or specific harms were similar between salmeterol and tiotropium.

ICS vs. PDE-4 Inhibitors
- Beclomethasone was found to be associated with fewer exacerbations compared to roflumilast (RR 3.6; 95% CI, 1.10 vs. 9.11). Wide confidence intervals led to the conclusion that roflumilast is noninferior to beclomethasone based on the results of one fair quality trial.
- There was insufficient evidence for harms comparisons between ICSs and PDE-4s.

ICS/LABA vs. ICS (different drug)
- Fluticasone furoate/vilanterol was found to have similar risk of exacerbation rates as fluticasone propionate based on the evaluation of 3 trials based on low strength of evidence.
- Low strength of evidence found ciclesonide to have more adverse events compared to fluticasone propionate/salmeterol (RR 1.15; 95% Cl, 1.01 to 1.30).
- No difference was found in serious adverse events or withdrawals between fluticasone furoate/vilanterol compared to fluticasone propionate based on low strength of evidence.

ICS/LABA vs. LM
- There is high strength of evidence from 5 randomized controlled trials of asthma patients that fluticasone propionate/salmeterol was associated with fewer exacerbations compared to montelukast (SMD 0.26; 95% CI, 0.16 to 0.35).
- Moderate strength of evidence showed no difference in adverse events or withdrawals due to adverse events between ICS/LABA and LM.

LABA/ICS vs. LM/ICS
- Exacerbations were decreased more with the addition of a LABA to ICS compared to adding a LM to ICS in adolescents and adults based on high-strength of evidence.
- High strength of evidence found no difference in withdrawals due to adverse events in comparisons of LABA/ICS and LM/LABA.

- The addition of LABA to ICS therapy was associated with more serious harms compared to adding LM to ICS (moderate strength of evidence).

LM/LABA vs. ICS/LABA
- There was insufficient evidence to make comparative efficacy conclusions.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Within Class Comparisons:

LAMA
- There was no difference in benefits or harms between the LAMA formulations based on low-strength of evidence (6 studies in patients with moderate to very severe COPD).

ICS/LABA
- No differences were found in studies comparing different ICS/LABA formulations. Specific comparisons are detailed in Table 7 below.

Table 7. ICS/LABA Efficacy Comparisons in Patients with COPD.[1]

Comparisons	Findings	Strength of Evidence
Beclomethasone/formoterol vs. fluticasone propionate/salmeterol	No difference was found in exacerbations, symptoms, 6-minute walk-test, or use of rescue medication. Quality of life evidence was insufficient.	Low Insufficient
Budesonide/formoterol vs. beclomethasone/formoterol	No difference in quality of life, total exacerbations or exacerbations leading to an ER visit, hospitalization or requiring corticosteroid treatment.	Low
Fluticasone 100 mcg/vilanterol 25 mcg vs. fluticasone propionate 500 mcg/salmeterol 100 mcg	No difference in exacerbations, rescue-free days or quality of life.	Moderate
Fluticasone furoate 100 mcg/vilanterol 25 mcg vs. fluticasone propionate 1000 mcg/salmeterol 100 mcg	No difference in rescue free days or quality of life.	Low

- ICS/LABA harms comparisons between different agents found insufficient evidence for comparison, low to high strength of evidence of no difference or imprecise data (Table 8).

Table 8. ICS/LABA Harms Comparisons in Patients with COPD.[1]

Comparisons	Findings	Strength of Evidence
Beclomethasone extra fine/formoterol vs. fluticasone propionate/salmeterol	Comparative harms evidence was insufficient.	Insufficient
Budesonide/formoterol vs. beclomethasone/formoterol	Comparative harms evidence was insufficient.	Insufficient
Fluticasone propionate/salmeterol vs. budesonide/formoterol	Imprecise evidence. Increased risk of pneumonia with fluticasone/salmeterol compared to budesonide/formoterol (RR 1.73; 95% CI, 1.57 to 1.90) and increased risk of mortality. No difference in pneumonia incidence was found in a second study.	Insufficient
Fluticasone furoate 100 mcg/vilanterol 25 mcg vs. fluticasone propionate 500 mcg/salmeterol 100 mcg	No difference in overall adverse events. No difference in pneumonia, withdrawals due to adverse events or serious adverse events.	High Moderate
Fluticasone furoate 100 mcg/vilanterol 25 mcg vs. fluticasone propionate 1000 mcg/salmeterol 100 mcg	No difference in overall adverse events or withdrawals due to adverse events.	Low

LABA

- Data from 7 studies was used to compare the efficacy of LABA therapies in patients with COPD. Specific therapy comparisons are detailed in Table 9.

Table 9. LABA Efficacy Comparisons in Patients with COPD.[1]

Comparison	Findings	Strength of Evidence
Arformoterol vs. formoterol	Exacerbation rates and quality of life similar between groups.	Low
Formoterol nebulized vs. formoterol via DPI	Exacerbation rates and quality of life similar between groups.	Low
Indacaterol vs. formoterol	Exacerbation rates and quality of life similar between groups.	Low
Indacaterol vs. salmeterol	Improvement in quality of life was higher for indacaterol compared to salmeterol (OR 1.59; 95% CI, 1.12 to 2.25).	Low
Olodaterol vs. formoterol	Exacerbation rates were similar. Olodaterol was found to increase quality of life scores more than formoterol.	Low Moderate

- An increased incidence of serious adverse events associated with indacaterol compared with salmeterol with no difference in withdrawals.
- A comparison between arformoterol and formoterol and between lower-dose indacaterol and formoterol found low strength of evidence that withdrawals and severe adverse events were similar for each comparison.

LAMA/LABA

- In LAMA/LABA comparisons exacerbations and quality of life outcomes were similar between glycopyrrolate/indacaterol and tiotropium/formoterol (low strength of evidence).
- Overall adverse events or withdrawals due to adverse events were similar between glycopyrrolate/indacaterol and tiotropium/formoterol based on low and moderate strength of evidence.

Comparisons between Different Classes:

ICS vs. LABA

- Majority of evidence shows similar results for efficacy outcomes in patients treated with either ICSs or LABAs. Comparisons of specific therapies are presented below in Table 10.

Table 10. Efficacy Comparisons of ICS to LABA in Patients with COPD.[1]

Comparison	Findings	Strength of Evidence
Budesonide vs. formoterol	No difference in mortality, exacerbations or exacerbations.	Low
Fluticasone propionate vs. salmeterol	Mortality was increased with fluticasone compared to salmeterol (OR 1.23; 95% CI, 1.01 to 1.51). SGRQ scores were significantly better with fluticasone compared with salmeterol (MD -0.77; 95% CI, -1.49 to -0.06). Exacerbation rates and hospitalizations were similar between groups.	Low Low Moderate
Mometasone vs. formoterol	SGRQ scores were similar between groups.	Low
Abbreviations: MD – mean difference; SGRQ – St. George's Respiratory Questionnaire		

- There was an increased incidence of pneumonia with ICS compared to LABA in COPD patients.
- Moderate strength of evidence found no difference in any adverse events between LABAs versus ICS in a meta-analysis of 5 studies (OR 1.12; 95% CI 0.96 to 1.30). The risk of serious pneumonia was higher for ICS compared to LABA (OR 1.48; 95% CI 1.13 to 1.94).
- Comparison of mometasone to formoterol found no difference in withdrawals due to adverse events, risk of experiencing an adverse event and risk of a serious adverse event (low strength of evidence).

LAMA/LABA vs. ICS/LABA

- Comparisons of vilanterol 25 mcg/umeclidinium 62.5 mcg and fluticasone propionate 500 mcg/salmeterol 100 mcg found no differences in exacerbations based on moderate strength of evidence. High quality evidence found no difference in quality of life between the two groups. No difference in rescue medication use was found.
- Low strength of evidence found no difference in exacerbation rates between vilanterol 25 mcg/umeclidinium 62.5 mcg and fluticasone propionate 1000 mcg/salmeterol 100 mcg. There was also moderate strength of evidence that there were differences in quality of life.
- High dose indacaterol 110 mcg/glycopyrrolate 50 mcg was found to have a lower risk of moderate to severe exacerbations than fluticasone propionate 100 mcg/salmeterol 1,000 mcg (RR 0.69, 95% CI, 0.48 to 1.00).

- A study between glycopyrrolate/indacaterol and fluticasone propionate/salmeterol found no difference in overall adverse events, withdrawals due to adverse events, pneumonia and adverse events leading to hospitalization.
- Moderate strength of evidence found no difference in vilanterol 25 mcg/umeclidinium 62.5 mcg and fluticasone propionate 500 mcg/salmeterol 100 mcg in overall adverse events, serious adverse events and withdrawals due to adverse events or pneumonia. There was also no difference in withdrawals due to adverse events or pneumonia or in overall adverse events between vilanterol 25 mcg/umeclidinium 62.5 mcg and fluticasone propionate 1000 mcg/salmeterol 100 mcg DPI daily.

LABA vs. LAMA

- Salmeterol was associated with more exacerbations than tiotropium (36% vs. 32%; OR 1.19; 95% CI, 1.09 to 1.30) based on moderate strength of evidence from one systematic review. Quality life and hospitalization rates were the same in both groups.
- In patients with severe COPD indacaterol was associated with more frequent exacerbations and similar effects on quality of life and mortality as tiotropium.
- Low strength of evidence found quality of life to improve in fewer patients using tiotropium compared to indacaterol with no difference in hospitalizations or exacerbations.
- Moderate strength of evidence found tiotropium to have less risk of nonfatal serious adverse events salmeterol. Tiotropium was also associated with less risk of withdrawal due to adverse events compared to salmeterol based on low strength of evidence.
- Tiotropium versus indacaterol and tiotropium compared to formoterol were found to have similar risk of nonfatal serious harms and withdrawals due to harms.

ICS/LABA vs. LABA

- Low strength of evidence from one trial found ICS/LABAs and LABAs to have a similar risk of exacerbations in patients with moderate to severe COPD.
- Indacaterol was associated with less serious adverse events compared to salmeterol/fluticasone propionate (RR 0.29; 95% CI, 0.11 to 0.74).

ICS/LABA vs. LAMA

- Eight studies met inclusion criteria for ICS/LABA vs. LAMA comparisons in COPD patients. Outcome findings were mixed. Findings of individual studies are presented in table 11.

Table 11. Efficacy Comparison of ICS/LABA vs. LAMA in Patients with COPD.[1]

Comparison	**Findings**	**Strength of Evidence**
Tiotropium vs. fluticasone propionate/salmeterol	Fluticasone/salmeterol was found to have a lower risk of mortality, higher hospitalization risk and improved quality of life compared to tiotropium.	Low
Tiotropium vs. vilanterol/fluticasone furoate	No difference in mortality was found.	Low
Tiotropium vs. fluticasone furoate/vilanterol	No difference in mortality was found.	Low
Tiotropium 18 mcg vs. umeclidinium bromide 62.5 mcg/vilanterol 25 mcg	No difference in mortality or quality of life was found.	Low

- Withdrawals due to adverse events were similar between tiotropium and fluticasone propionate/salmeterol but serious harms were significantly lower with tiotropium based on low strength of evidence.
- There is low strength of evidence that tiotropium is similar to fluticasone furoate/vilanterol in the risk of serious adverse events.
- Withdrawals due to adverse events were similar for tiotropium and umeclidinium bromide/vilanterol in patients with COPD.

LAMA/LABA vs. LAMA

- No difference was found between umeclidinium/vilanterol and tiotropium in mortality, quality of life, daily activities, or exacerbations based on low strength of evidence. Moderate strength of evidence found higher utilization in rescue medication use compared to tiotropium.
- Less rescue medication use was associated with umeclidinium/vilanterol compared to umeclidinium monotherapy based on low strength of evidence.
- A comparison between umeclidinium/vilanterol and tiotropium found low strength of evidence of no difference in overall adverse events, pneumonia, death, serious adverse events or withdrawals due to adverse events.

Subgroups

- Data was insufficient to make subgroup comparisons regarding efficacy and safety for asthma or COPD severity, comorbidities, use of other medications, smoking status, genetics or pregnancy.

New Safety Alerts

No new safety alerts identified.

New Formulations or Indications

Glycopyrrolate and formoterol fumarate (Bevespi Aerosphere™)

Glycopyrrolate/formoterol was studied in 2 phase III confirmatory trials involving 3,699 patients with COPD. Both trials were 24-week, randomized, double-blind, placebo-controlled trials.[2] Included patients had moderate to very severe COPD, at least a 10 pack-year history of smoking, a baseline mean FEV1 <80% of predicted normal values (post-albuterol) and a FEV1/FVC ratio <0.7. At baseline patients were a mean age of 63 years old, 54% were smokers, 91% were white, and 44% were female. Patients were randomized to glycopyrrolate 18 mcg/formoterol 9.6 mcg twice daily, glycopyrrolate 18 mcg twice daily, formoterol 9.6 mcg twice daily or placebo in both studies. The first trial also had an open-label active control arm.[2] The primary endpoint in both studies was change in trough FEV1 at week 24 compared to baseline. Minimally important values from research in COPD patients suggest minimally important FEV_1 changes range from 100-140 ml.[3] A key secondary endpoint was change in St. George's respiratory questionnaire (SGRQ), which measures quality-of-life for patients with obstructive airway disease.[4] A 50 item questionnaire determines the score, which can range from 0 to 100, with higher scores indicating more limitations. A change of 4 points is associated with slightly efficacious treatment, 8 points for moderately efficacious treatment, and 12 points for very efficacious treatment.[4]

Glycopyrrolate/formoterol combination improved FEV1 more than all comparators in both studies. The least squares mean change from baseline between glycopyrrolate/formoterol compared to placebo, glycopyrrolate and formoterol monotherapy were 150 mL (95% CI, 114 to 186 mL), 59 mL (95% CI, 31 to 88 mL) and 64 mL (95% CI, 36 to 92 mL), respectively.[2] The second study had similar findings with least squares (LS) mean changes between glycopyrrolate/formoterol and placebo of 103 mL, 54 mL for glycopyrrolate comparison and 56 mL for formoterol comparison. Changes in FEV1 versus placebo comparisons were clinically significant in the both studies, however, at the lower end in the second study. Changes in SGRQ scores were based on a responder rate which was an

improvement in score of 4 points or more. Responder rates were 37% for glycopyrrolate/formoterol, 30% for glycopyrrolate, 35% for formoterol and 28% for placebo in the first trial. In the second trial, responder rates by SGRQ scores favored glycopyrrolate/formoterol compared to glycopyrrolate, formoterol and placebo with odds ratios (OR) of 1.2, 1.3 and 1.3, respectively.[2]

Tiotropium (Spiriva Respimat®)

Tiotropium was previously approved for COPD, but in 2015 it received an indication for use as long-term maintenance therapy for the treatment of asthma in patients 12 years and older. Tiotropium was studied for 12-24 weeks in adult patients who were on ICS therapy with or without other inhalers in 3 trials.[5] Patients were non-smokers 18-75 years of age (mean age of 46 years) with pre-bronchodilator FEV1 ranging from 2.18-2.30 L. Trial 1 primary endpoint was change from pre-treatment baseline in peak FEV1, 0-3hr at week 12. Trials 2 and 3 had co-primary efficacy endpoints: change from pre-treatment baseline in peak FEV1, 0-3hr and change from pre-treatment baseline in trough FEV1 at week 24. Trials 2 and 3 also included salmeterol 100 mcg as a second comparison arm.[5] Key secondary endpoints were asthma exacerbations, Asthma Control Questionnaire (ACQ), and Asthma Quality of Life Questionnaire (AQLQ). The ACQ is an asthma symptom assessment tool with a range of scores from 0 (totally controlled) to 6 (severely uncontrolled), with a score of change of 0.5 representing a minimally clinical important difference.[6] The Asthma Quality of Life Questionnaire (AQLQ) quantifies both the physical and emotional impact of asthma.[6] The AQLQ scores range from 1 to 7, with higher scores indicating better quality of life. [6] A difference of 0.5 overall and for each item is the minimally clinical important difference for this instrument.[6]

Tiotropium 2.5 mcg was found to be superior to placebo in all 3 trials when used in patients on low to medium strength ICS therapy. In Trial 1, change from baseline FEV1, 0-3 hours, between tiotropium and placebo at 12 weeks was 0.16 L (95% CI, 0.09 to 0.23L) (p-value not provided).[5] Results in the second trial found a change in baseline FEV1, 0-3 hours, of 0.24 L (95% CI, 0.18 to 0.29 L) for tiotropium compared to placebo and 0.21 L (95% CI, 0.16 to 0.27 L) for salmeterol compared to placebo. In change in trough FEV1 from baseline, the difference between tiotropium compared to placebo was 0.19 L (95% CI, 0.13 to 0.24 L) and 0.12 L (95% CI, 0.06 to 0.18 L) for salmeterol compared to placebo.[3] Results in the third trial were similar with a change in baseline FEV1, 0-3 hours, of 0.21 L (95% CI, 0.16 to 0.26 L) for tiotropium compared to placebo and 0.18 L (95% CI, 0.12 to 0.23 L) for salmeterol compared to placebo and for trough FEV1 change from baseline, tiotropium compared to placebo was 0.18 L (95% CI, 0.12 to 0.23 L) and 0.11 L (95% CI, 0.05 to 0.16 L) for salmeterol compared to placebo. Studies of tiotropium 5 mcg yielded less benefit than the 2.5 mcg dose and maximal bronchodilator effect took 4 to 8 weeks.[5] The mean rate of asthma exacerbations were 0.08 for tiotropium compared to 0.24 for placebo in Trial 2 and 0.13 for tiotropium and 0.18 for trial 3 (not assessed in trial 1); however, significance level was not provided. In trial 2 the ACQ-7 responder rate (change in score of ≥ 0.5) was 63% for tiotropium 2.5 mcg and 53% for placebo. The responder rate for AQLQ assessments (change in score of ≥ 0.5) were 58% for tiotropium compared to 50% for placebo.[5]

In studies of adolescents 12-17 years, tiotropium 2.5 mcg once daily was found to be more effective than placebo with a mean difference in peak FEV1, 0-3hr of 0.13 L (95% CI 0.03, 0.23) and 0.11 L (0.002, 0.22) for the 48-week and 12-week trials, respectively).[5]

Randomized Controlled Trials

No additional randomized controlled trials provided evidence to prompt changes to current policy.

References:

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2. Bevespi Aerosphere™ (glycopyrrolate/formoterol) [Prescribing Information]. Wilmington, DE: AstraZeneca, April 2016.
3. Cazzola M, Macknee W, Martinez FJ, et al. Outcomes for COPD pharmacological trials: from lung function to biomarkers. *Eur Respir J*. 2008; 31: 416-469.(25)
4. Spiriva Respimat® (tiotropium) [Prescribing Information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc. June 2016.
5. American Thoracic Society. St. George's Respiratory Questionnaire (SGRQ). Available at: https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/sgrq.php. Accessed August 18, 2016.
6. American Thoracic Society - Asthma Control Test (ACT). Available at: http://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/act.php. Accessed August 18, 2016.

Appendix 1: Current Status on Preferred Drug List

Long-acting Anticholinergics (LAMA)

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	CAP W/DEV	SPIRIVA	TIOTROPIUM BROMIDE	**Y**
INHALATION	AER POW BA	TUDORZA PRESSAIR	ACLIDINIUM BROMIDE	N
INHALATION	BLST W/DEV	INCRUSE ELLIPTA	UMECLIDINIUM BROMIDE	N
INHALATION	CAP W/DEV	SEEBRI NEOHALER	GLYCOPYRROLATE	N
INHALATION	MIST INHAL	SPIRIVA RESPIMAT	TIOTROPIUM BROMIDE	N

Inhaled Corticosteroids (ICS)

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	AER POW BA	PULMICORT FLEXHALER	BUDESONIDE	**Y**
INHALATION	AER W/ADAP	FLOVENT HFA	FLUTICASONE PROPIONATE	**Y**
INHALATION	AER W/ADAP	QVAR	BECLOMETHASONE DIPROPIONATE	**Y**
INHALATION	BLST W/DEV	FLOVENT DISKUS	FLUTICASONE PROPIONATE	**Y**
INHALATION	AER POW BA	ASMANEX	MOMETASONE FUROATE	N
INHALATION	AMPUL-NEB	BUDESONIDE	BUDESONIDE	N
INHALATION	AMPUL-NEB	PULMICORT	BUDESONIDE	N
INHALATION	BLST W/DEV	ARNUITY ELLIPTA	FLUTICASONE FUROATE	N
INHALATION	HFA AER AD	ALVESCO	CICLESONIDE	N
INHALATION	HFA AER AD	ASMANEX HFA	MOMETASONE FUROATE	N

Long-acting Bronchodilators (LABA)

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	BLST W/DEV	SEREVENT DISKUS	SALMETEROL XINAFOATE	**Y**
INHALATION	CAP W/DEV	FORADIL	FORMOTEROL FUMARATE	**Y**
INHALATION	VIAL-NEB	PERFOROMIST	FORMOTEROL FUMARATE	N
INHALATION	VIAL-NEB	BROVANA	ARFORMOTEROL TARTRATE	N
INHALATION	CAP W/DEV	ARCAPTA NEOHALER	INDACATEROL MALEATE	N
INHALATION	MIST INHAL	STRIVERDI RESPIMAT	OLODATEROL HCL	N

LAMA/LABA

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	BLST W/DEV	ANORO ELLIPTA	UMECLIDINIUM BRM/VILANTEROL TR	N
INHALATION	MIST INHAL	STIOLTO RESPIMAT	TIOTROPIUM BR/OLODATEROL HCL	N

ICS/LABA

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	BLST W/DEV	ADVAIR DISKUS	FLUTICASONE/SALMETEROL	**Y**
INHALATION	HFA AER AD	ADVAIR HFA	FLUTICASONE/SALMETEROL	**Y**
INHALATION	HFA AER AD	SYMBICORT	BUDESONIDE/FORMOTEROL FUMARATE	**Y**
INHALATION	BLST W/DEV	BREO ELLIPTA	FLUTICASONE/VILANTEROL	N
INHALATION	HFA AER AD	DULERA	MOMETASONE/FORMOTEROL	N

Inhaled Corticosteroids (ICS)

Goals:

- Promote use that is consistent with Oregon Asthma Guidelines and the NIH EPR 3 Guidelines on Asthma. See also: http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Pages/index.aspx and http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report
- Step-therapy required prior to coverage for non-preferred ICS products:
  - Asthma: inhaled short-acting beta-agonist.
  - COPD: short-acting and long-acting bronchodilators (inhaled anticholinergics and beta-agonists). Preferred short-acting and long-acting bronchodilators do NOT require prior authorization. See preferred drug list options at http://www.orpdl.org/drugs/.

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred ICS products

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Will the prescriber consider a change to a preferred product? Message: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class.	**No:** Go to #3

Approval Criteria		
3. Does the patient have a diagnosis of asthma or reactive airway disease (ICD10 J4520-J4522, J45901-45998)?	**Yes:** Go to #7	**No:** Go to #4
4. Does the patient have a diagnosis of COPD (ICD10 J449), chronic bronchitis (ICD10 J410-418, J42, J440-449) and/or emphysema (ICD10 J439)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Does the patient have an active prescription for an on-demand short-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.
6. Does the patient have an active prescription for an inhaled long-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness.
7. Does the patient have an active prescription for an on-demand short-acting beta-agonist (SABA) or an alternative rescue medication for acute asthma exacerbations?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T Review: *9/16 (KS); 9/15*
Implementation: *10/9/15*

Long-acting Beta-agonists (LABA)

Goals:

- Promote use that is consistent with Oregon Asthma Guidelines and the NIH EPR 3 Guidelines on Asthma. See also: http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Pages/index.aspx and http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report
- Step-therapy required prior to coverage of non-preferred LABA products:
  - Asthma: inhaled corticosteroid and short-acting beta-agonist.
  - COPD: inhaled short-acting bronchodilator.

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred LABA products

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Will the prescriber consider a change to a preferred product? Message: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class	**No:** Go to #3
3. Does the patient have a diagnosis of asthma or reactive airway disease (ICD10 J4520-J4522; J45901-45998)?	**Yes:** Go to #6	**No:** Go to #4

Approval Criteria		
4. Does the patient have a diagnosis of COPD (ICD10 J449), chronic bronchitis (ICD10 J410-418; J42; J440-449) and/or emphysema (ICD10 J439)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Does the patient have an active prescription for an on-demand short-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness.
6. Does the patient have an active prescription for an on-demand short-acting beta-agonist (SABA) or an alternative rescue medication for acute asthma exacerbations?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
7. Does the patient have an active prescription for an inhaled corticosteroid (ICS) or an alternative asthma controller medication?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T Review: *9/16 (KS); 9/15; 5/12; 9/09; 5/09*
Implementation: *10/9/15; 8/12; 1/10*

Long-acting Beta-agonist/Corticosteroid Combination (LABA/ICS)

Goals:

- Promote use that is consistent with Oregon Asthma Guidelines and the NIH EPR 3 Guidelines on Asthma. See also: http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Pages/index.aspx and http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report
- Promote use that is consistent with Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines. See also: http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html
- Step-therapy required prior to coverage:
  - Asthma: short-acting beta-agonist and inhaled corticosteroid or moderate to severe persistent asthma.
  - COPD: short-acting bronchodilator and previous trial of a long-acting bronchodilator (inhaled anticholinergic or beta-agonist) or GOLD C/D COPD. Preferred LABA/ICS products do NOT require prior authorization.

Length of Authorization:

- Up to 12 months

Requires PA:

- Non-preferred LABA/ICS products

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Will the provider consider a change to a preferred product? Message: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class	**No:** Go to #3
3. Does the patient have a diagnosis of asthma or reactive airway disease (ICD10 J4520-J4522, J45901-45998)?	**Yes:** Go to #7	**No:** Go to #4

Approval Criteria		
4. Does the patient have a diagnosis of COPD (ICD10 J449), chronic bronchitis (ICD10 J410-418, J42, J440-449) and/or emphysema (ICD10 J439)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Does the patient have an active prescription for an on-demand short-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.
6. Is there a documented trial of an inhaled long-acting bronchodilator (anticholinergic or beta-agonist), or alternatively has the patient been assessed with GOLD C/D COPD?	**Yes:** Approve for up to 12 months. Stop coverage of all other LABA and ICS inhalers.	**No:** Pass to RPh. Deny; medical appropriateness.
7. Does the patient have an active prescription for an on-demand short-acting beta-agonist (SABA) or an alternative rescue medication for acute asthma exacerbations?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness
8. Is there a documented trial of an inhaled corticosteroid (ICS) or does the patient have moderate to severe persistent asthma (Step 3 or higher per NIH EPR 3)?	**Yes:** Approve for up to 12 months. Stop coverage of all other ICS and LABA inhalers.	**No:** Pass to RPh. Deny; medical appropriateness

P&T Review: *9/16 (KS); 11/15; 9/15; 11/14; 11/13; 5/12; 9/09; 2/06*
Implementation: *1/1/16; 1/15; 1/14; 9/12; 1/10*

Long-acting Muscarinic Antagonist/Long-acting Beta-agonist Combination (LAMA/LABA)

Goals:

- Promote use that is consistent with Oregon Asthma Guidelines and the NIH EPR 3 Guidelines on Asthma. See also: http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/Asthma/Pages/index.aspx and http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report
- Promote COPD therapy that is consistent with Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines. See also: http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html
- Step-therapy required prior to coverage:
    - COPD: short-acting bronchodilator and previous trial of a long-acting bronchodilator (inhaled anticholinergic or beta-agonist) or GOLD C/D COPD. Preferred LAMA and LABA products do NOT require prior authorization.

Length of Authorization:

- Up to 12 months

Requires PA:

- All LAMA/LABA products

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Will the prescriber consider a change to a preferred product? Message: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of preferred LAMA and LABA products in each class	**No:** Go to #3

Approval Criteria		
3. Does the patient have a diagnosis of asthma or reactive airway disease (ICD10 J4520-J4522, J45901-45998) without COPD?	**Yes:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.	**No:** Go to #4
4. Does the patient have a diagnosis of COPD (ICD10 J449), chronic bronchitis (ICD10 J410-418, J42, J440-449) and/or emphysema (ICD10 J439)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Does the patient have an active prescription for an on-demand short-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.
6. Has the patient been assessed with GOLD C/D COPD?	**Yes:** Approve for up to 12 months. Stop coverage of all other LAMA and LABA inhalers.	**No:** Go to #7
7. Is there a documented trial of a LAMA or LABA, or alternatively a trial of a fixed dose combination short-acting anticholinergic with beta-agonist (SAMA/SABA) (i.e., ipratropium/albuterol)?	**Yes:** Approve for up to 12 months. Stop coverage of all other LAMA and LABA inhalers or scheduled SAMA/SABA inhalers (PRN SABA or SAMA permitted).	**No:** Pass to RPh. Deny; medical appropriateness.