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

Policy Evaluation: Combination Inhaler Prior Authorization

There has been ongoing controversy about the safety of long-acting beta-agonists over the last decade.[1] A recent meta-analysis found the odds of severe asthma exacerbations were increased with combination inhaler treatment compared to inhaled corticosteroids alone (OR 3.65 95% CI 1.39 – 9.55).[2] A United States Food and Drug Administration (FDA) meta-analysis of over 60,000 patients led to a strengthened public health advisory recommending that long-acting beta-agonists be used only for those who remain symptomatic on other asthma controller medications, for the shortest possible duration and never as a single agent.[3] Combination inhaler recommendations for COPD were not affected by the FDA advisory. The Global Initiative for Chronic Obstructive Lung Disease recommends a stepped approach to COPD treatment with combination inhalers reserved for patients with severe and very severe disease.[4]

Despite the controversy, utilization of combination inhalers has proliferated. In the Oregon fee-for-service Medicaid program, where Advair® was the 9th most costly drug in 2010,[5] only 12% of combination inhaler patients[6] had prior drug claims for any asthma controller in the 90 days prior to therapy initiation contrary to the FDA labeling and practice guidelines.[7] Consequently, the Oregon Medicaid fee-for-service program implemented a prior authorization (PA) policy to align combination inhaler prescribing practices with the FDA guidance and national guidelines.[8] Following implementation, combination inhaler use declined by 45% and inhaled corticosteroid use rose by 6%.[9] The objective of this study was to determine if the PA policy targeting combination inhalers increased short term emergency department or hospital utilization.

METHODS

The Oregon Medicaid fee-for-service program implemented a PA requirement on January 1, 2011. The combination inhaler products affected were all orally inhaled forms of fluticasone/salmeterol, budesonide/formoterol and mometasone/formoterol. PA approval required a trial of inhaled corticosteroid monotherapy or evidence of severe asthma or trial of both an anticholinergic and long-acting beta-agonist inhaler for COPD patients. The policy “grandfathered” (automatically approved payment) all patients with a prior paid claim for a combination inhaler within the previous 90 days, so as not to disrupt current therapy.

This analysis included patients enrolled in the Oregon Medicaid fee-for-service program between January 1, 2010 and August 30, 2011 and that had a minimum of three months continuous Medicaid enrollment before and after an index event. For the

study group, the index event was the earliest date the patient had a combination inhaler claim denied with a message of "PA required" between January 1, 2011 and August 30, 2011. A historical control group was constructed with patients who had a paid combination inhaler claim (the index event) between January 1, 2010 and August 30, 2010, and therefore were not affected by the PA policy. Analogous to the study group grandfathering, control patients were excluded if they had a combination inhaler paid claim in the 90 days prior to their index event.

To ensure the study groups were independent, patients in the study group (2011) were excluded if they had a combination inhaler claim in 2010. To maintain comparability, patients in the control group (2010) were excluded if they had a combination inhaler claim in 2009. Patients were excluded if their demographic data (e.g. age, sex or ethnicity) were not available, they were less than 5 or greater than 64 years old at the time of the index event or if they had dual Medicare eligibility. The asthma treatment guidelines[7] are more clearly defined for patients 5-64 years and Medicare drug claims were not included in the administrative data.

The primary outcome was a composite of an emergency department or hospital claim with an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code for asthma or COPD in the primary diagnosis field within 60 days of the index event. The 60 day interval was selected because in comparative studies of combination inhaler medications, time to first exacerbation survival curves typically separate within 60 days.[10,11] The analyses were repeated using a 30 day and 90 day post index event assessment window. The component outcomes also were evaluated individually. The frequency of oral corticosteroid prescriptions during the same period (excluding the day of index event) were examined because it is recommended treatment for acute asthma and COPD exacerbations.[4,7] Finally, the frequency of all-cause emergency department encounters, hospitalizations, or death in the 60 days following an index event was evaluated.

Administrative data in the year before the index event were used to characterize baseline patient demographics and severity of illness. First, patients were classified with respect to the presence of an ICD-9-CM code for asthma (493xx), COPD (491.2x, 492, 492.0, 492.8, 496, 506.4, 518.1, 518.2), both asthma and COPD, and neither asthma or COPD. Asthma and COPD controller and rescue medication use in the 90 days prior to the index event was also characterized (see Appendix A which identifies and classifies the drugs used). As in indicator of severity of illness, the asthma- or COPD-related emergency department encounters and hospitalizations in the year prior to the index event were quantified.[4,7] Asthma disease severity was also assessed using the Healthcare Effectiveness Data Information Set (HEDIS) persistent asthma indicator, a validated measure using pharmacy, medical and hospital claims, from the year prior to the index date.[12] In addition, a ratio of 0.5 (or lower) asthma controller medication claims to total asthma medication claims (controller and rescue) is

associated with a higher risk of using acute asthma services.[13,14,15] Finally, a combined disease severity variable, that included any of the previously mentioned metrics, was created to provide the greatest sensitivity to severe respiratory disease.

Patients in the study group were followed longitudinally to assess if a PA was requested by their prescriber, and the ultimate disposition of any PA requested. Patient demographics, disease severity, and subsequent drug therapy were then characterized by final PA disposition (i.e. not requested, requested and approved or requested and denied).

For, the primary analysis, multivariate logistic regression models were used to adjust for any imbalance in key baseline prognostic variables. The following baseline covariates were explored during the modeling process: age, sex, race, COPD or asthma diagnosis, HEDIS persistent asthma indicator, baseline respiratory controller medication use, baseline emergency department use, baseline hospital utilization and baseline asthma rescue inhaler use. Covariates were selected for inclusion in the final regression models based on a backwards selection process with a p-value set at 0.05. Both unadjusted and adjusted odds ratio (OR) were generated reflecting the relative increase in odds of the modeled outcome (i.e. emergency department visit or hospitalization). The same covariates were used for individual components of composite primary outcome as well as sensitivity analyses at 30 and 90 days. Statistical analyses were conducted with Stata V13 (Stata Corp. College Station, TX).

RESULTS

There were 794 patients with index events for the study group and 662 patients identified with index events for the control group. After excluding patients less than 5 and greater than 64 years old (study n=8, control n=4), those covered by Medicare (study n= 11, control n=18), those with combination inhaler claims in the prior year (study n=324, control n=139), and those without continuous eligibility (study n=154, control n= 150) the final study group was 297 patients and the control group was 351patients.

Table 1 displays the baseline characteristics of the groups. Demographics and baseline diagnostic groups were very similar. The HEDIS persistent asthma indicator, prior emergency department encounters and prior drug use were also similar between groups. However, the controller ratio and prior hospital encounters indicated lower disease severity in the study group.

TABLE 1 – BASELINE CHARACTERISTICS

	Study Group[a] (n=297)	Control Group[b] (n=351)
Demographics	*No. (%)*[c]	*No. (%)*[c]
Mean Age (min-max)	36 (5-64)	36 (5-64)
Age >= 19	224 (75)	250 (71)
Female	192 (65)	223 (64)
Non-White	54 (18)	61 (17)
Diagnostic Group	*No. (%)*	*No. (%)*
Asthma (no COPD[d])	155 (52)	183 (52)
Asthma + COPD	31 (10)	45 (13)
COPD (no Asthma)	46 (15)	54 (15)
No Asthma & No COPD	65 (22)	69 (20)
Disease Severity 1 year prior[e]	*No. (%)*	*No. (%)*
HEDIS[f] Persistent Asthma	62 (21)	82 (23)
Asthma Controller Ratio <0.5	104 (35)	182 (52)
Asthma or COPD Emergency Department Encounter	38 (13)	51 (15)
Asthma or COPD Hospitalization	5 (2)	18 (5)
Any of the Above	141 (47)	210 (60)
Drug Therapy at Index Event (includes 90 days prior) [e]	*No. (%)*	*No. (%)*
Asthma or COPD Controller	84 (28)	95 (27)
Short-Acting Beta-Agonist	138 (46)	162 (46)

[a]*Study Group = Prior authorization required for combination inhaler*
[b]*Control Group = No prior authorization required for combination inhaler*
[c]*Data presented as No. (%) unless otherwise noted*
[d]*COPD = Chronic Obstructive Pulmonary Disease*
[e] *Categories not mutually exclusive*
[f]*HEDIS = Healthcare Effectiveness Data and Information Set*

Table 2 displays the results of primary and secondary outcomes. There were 31 primary outcome events during the 60 day follow-up period, 17 (5.7%) in the study group and 14 (4.0%) in the control group (OR 1.46, 95% confidence interval [CI] 0.71 to 3.02). After statistical adjustment, the OR increased to 2.26 (95% CI 1.01 to 5.06). This was driven primarily by increased odds of emergency department encounters. The adjusted odds of oral corticosteroid use were also 1.81 times higher (95% CI 1.19 to 2.69) in the study group relative to the control group. The secondary safety composite outcome of all cause hospitalization, emergency department encounter or death was similar in both groups. There were no deaths recorded. Results assessed at 30 and 90 days were similar with overlapping confidence intervals (see Appendix 2 that displays these data).

TABLE 2 - PRIMARY AND SECONDARY OUTCOMES 60 DAYS AFTER STUDY ENTRY

	Study Group[a] (n=297)	Control Group[b] (n=351)		
	No. (%)	No. (%)	OR (95% CI[c])	Adjusted[e] OR (95% CI)
Composite Asthma or COPD[d] Emergency Department or Hospital Encounter	17 (5.7)	14 (4.0)	1.46 (0.71 – 3.02)	2.26 (1.01 – 5.06)
Asthma or COPD Emergency Department Encounter	17 (5.7)	12 (3.4)	1.72 (0.81 – 3.65)	2.76 (1.19 – 6.42)
Asthma or COPD Hospital Encounter	4 (1.3)	3 (0.9)	1.58 (0.81 – 3.65)	2.18 (0.43 – 11.21)
All Cause Hospital or Emergency Department or Death	61 (20.5)	74 (21.1)	0.97 (0.66 – 1.42)	0.98 (0.66 – 1.46)
Oral Corticosteroid	42 (14.1)	33 (9.4)	1.59 (0.977 – 2.58)	2.62 (1.54 – 4.45)

[a]*Control Group = No prior authorization required for combination inhaler*
[b]*Study Group = Prior authorization required for combination inhaler*
[c]*CI = Confidence Intervals*
[d]*COPD = Chronic Obstructive Pulmonary Disease*
[e] *Model adjusted for age less than 18, HEDIS Persistent Asthma, Controller Use and Hospitalization at baseline*

Table 3 explores the correlation of drug therapy at 60 days and disease characteristics for patients in the policy group overall and displayed by whether or not a PA was requested by the prescriber on outcomes. Of the 297 study patients affected by the PA requirement, 83 (28%) requested a PA within 14 days and all 83 were approved. Asthma was more prevalent in patients with a PA request than those without (74% versus 59%) and COPD was less prevalent (17% versus 30%). Those with a PA request also appeared to have higher disease severity. The most notable disease severity differences were in the HEDIS persistent asthma indicator (34% versus 16%), prior asthma or COPD hospitalizations (4% versus 1%) and prior controller drug use (48% versus 21%). Of the 83 patients with an approved PA, 65 (78%) had a paid claim for a combination inhaler at 60 days and 9 (11%) had a claim for another controller. There were 214 (72%) patients that did not have a PA request submitted within 14 days of the index event and of these 100 (47%) had a controller medication prescribed at 60 days. Thirty patients without a PA request received a combination inhaler at 60 days either by subsequently enrolling in a Medicaid managed care plan (n=13) or by requesting a PA after 14 days (n=17). Of the remaining 84 patients without a PA request, 52 received a short-acting beta-agonist only and 32 had no paid respiratory drug claims. The incidence of the primary outcome in these subgroups followed disease severity and combination inhaler drug use: 8% of those requesting a PA, 5% of those not requesting a PA. Notably, the rate of all cause hospitalization, emergency department encounters or death was higher for the patients not requesting PA versus those that did (22% versus 16%).

TABLE 3 – ANALYSIS OF STUDY GROUP BY PRIOR AUTHORIZATION REQUEST SUB-GROUP

Study Group[a] (n=297)	Prior Authorization Requested within 14 days (n=83)	No Prior Authorization Requested within 14 days (n=214)
Outcomes at 60 days	*No. (%)*	*No. (%)*
Composite of Asthma or COPD[b] Emergency Department or Hospital Encounter	7 (8)	10 (5)
Asthma or COPD Emergency Department Encounter	7 (8)	10 (5)
Asthma or COPD Hospital Encounter	2 (2)	2 (1)
All Cause Hospital or Emergency Department or Death	13 (16)	48 (22)
Oral Corticosteroid	11 (13)	31 (14)
Drug Use at 60 days	*No. (%)*	*No. (%)*
Combination inhaler	65 (78)	30 (14)
Asthma / COPD Controller	9 (11)	100 (47)
Short-Acting Beta-Agonist only	5 (6)	52 (24)
None of the Above	4 (5)	32 (15)
Diagnostic Group	*No. (%)*	*No. (%)*
Asthma (no COPD)	53 (64)	102 (48)
Asthma + COPD	8 (10)	23 (11)
COPD (no Asthma)	6 (7)	40 (19)
No Asthma & No COPD	16 (19)	49 (23)
Disease Severity 1 year prior [c]	*No. (%)*	*No. (%)*
HEDIS[d] Persistent Asthma	28 (34)	34 (16)
Asthma Controller Ratio <0.5	32 (39)	72 (34)
Asthma / COPD ED	10 (12)	28 (13)
Asthma / COPD Hospital	3 (4)	2 (1)
Any of the Above	49 (59)	92 (43)
Drug Therapy at Index Event (includes 90 days prior [c]	*No. (%)*	*No. (%)*
Asthma / COPD Controller	40 (48)	44 (21)
Short-Acting Beta-Agonist	47 (57)	91 (43)

[a]Study Group = Prior authorization required for combination inhaler
[b]COPD = Chronic Obstructive Pulmonary Disease
[c] Categories not mutually exclusive
[d]HEDIS = Healthcare Effectiveness Data and Information Set

DISCUSSION

In this analysis, patients encountering the PA requirement had 2.26 higher adjusted odds of the primary outcome compared to a historical control group from the previous year. The increased odds of an oral corticosteroid prescription following exposure to the PA policy also suggest an elevated risk for an exacerbation. However, rates of all cause hospitalization, emergency department encounters or death were similar in both groups.

Study group patients whose prescribers requested a PA were more likely to have indicators of severe asthma, suggesting the PA policy was effective at restricting use consistent with the FDA recommendation. Although this study found encountering a PA requirement increased the odds for the primary outcome, it is unclear if the PA caused the increase.

A striking finding was that less than a third of patients encountering a PA requirement subsequently had a PA requested. That is, for a majority of cases no attempt was made by the prescriber to submit a PA request. It is difficult to infer causality between no PA request and subsequent adverse outcomes because having a PA request submitted was associated with increasing disease severity. Despite this limitation, rates of the primary outcome were, in fact, lower in the group of patients who had no PA request (5% versus 8%), although the absolute numbers were small.

The study is unavoidably limited by a small sample size as a result of the policy applying only to newly started patients. New combination inhaler patients represented 37% all combination inhaler patients in 2011 and 22% in 2010. Additionally, the policy was limited to the fee-for-service program which represented just 16% of Oregon Medicaid patients in 2011 and 18% in 2010.

There were a small absolute number of outcome events (31) and it used a historical control. Therefore, the results are potentially sensitive to background changes in prescribing patterns occurring from 2010 to 2011. Although the study periods for the study group and control group were identical, there were 54 fewer patients in the study group. This may reflect a decline in prescribing following the FDA 2010 safety announcements about long-acting beta-agonist use. The number of combination inhaler index events continued to trend downward throughout the study period. Given the nature of the FDA announcement, it was expected prescribers would reserve combination inhalers for patients with more severe disease in the study group. This is supported by the observation that the control group was less severely ill according to several disease severity indicators. In order to maintain adequate sample sizes continuous eligibility was not required beyond the 90 days before and after the index event. Consequently, there may be missing disease severity information and residual confounding may still exist. A frequency plot of index events found them evenly distributed seasonally with a continuous downward trend. However, there was still potential for differences in the control and study groups due to differences in the

availability of promotional drug samples, differences in prescriber access and differences in environmental factors such as forest fires, allergens and circulating viruses from one season to the next.

The combination inhaler PA policy appeared successful at limiting use to patients with moderate to severe asthma or to those not controlled with inhaled corticosteroid monotherapy. The policy was associated with an increased adjusted odds of 2.26 (95% CI 1.19 to 5.08) of emergency department or hospital encounters. The automated PA process was modified to electronically approve for patients with prior claims evidence of asthma (9/1/2011) or COPD (9/28/2012) within 102 days of the PA. However, further policy adjustments may be necessary.

REFERENCES

1. Sears MR. The FDA-mandated trial of safety of long-acting beta-agonists in asthma: finality or futility? *Thorax* 2013;68(2):195-198. doi:10.1136/thoraxjnl-2012-202414.

2. Salpeter S, Wall A, Buckley N. Long-acting beta-agonists with and without inhaled corticosteroids and catastrophic asthma events. *J. Med.* 2010;123(4):322-8. doi:http://dx.doi.org/10.1016/j.amjmed.2009.07.035.

3. Food and Drug Administration Center for Drug Evaluation and Research. Postmarket Drug Safety Information for Patients and Providers > FDA Drug Safety Communication: New safety requirements for long-acting inhaled asthma medications called Long-Acting Beta-Agonists (LABAs). *U. S. Food Drug Adm.* 2010. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm200776.htm#_Ref252304498. Accessed April 19, 2012.

4. GOLD - the Global initiative for chronic Obstructive Lung Disease. *Glob. Initiat. Chronic Obstr. Lung Dis.* 2014. Available at: http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html. Accessed June 2, 2014.

5. OHP FFS Average Costs PMPM Top 40 Drugs (brand name) - First Quarter 2010. *Or. State Univ. Drug Use Res. Manag.* 2010. Available at: http://oregonstate.edu/pharmacy/drug_policy/sites/default/files/pages/dur_board/reports/topdrugs/2010/topdrugs_2010_q1.pdf. Accessed June 2, 2014.

6. Combination Long-Acting Beta-Agonist Inhaled Corticosteroid: Summary of Clinical Evidence and Drug Utilization Evaluation. *Or. State Univ. Drug Use Res. Manag.* 2010. Available at: http://pharmacy.oregonstate.edu/drug_policy/sites/default/files/pages/dur_board/evaluations/articles/laba_ics_due.pdf. Accessed April 19, 2012.

7. US Department of Health and Human Services, National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma; 2007. *US Dep. Health Hum. Serv. Natl. Heart Lung Blood Inst.* 2007. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed May 23, 2012.

8. Oregon Medicaid PA Criteria, January 2011. *Or. Health Plan* 2011. Available at: http://www.oregon.gov/oha/healthplan/tools/Oregon%20Medicaid%20PA%20Criteria,%20January%202011.pdf. Accessed June 3, 2014.

9. Oregon Health Authority. Policy Evaluation: Step Therapy Prior Authorizati on of Combination Inhaled Corticosteroid / Long-Acting Beta-Agonists. *Or. Pharm. Ther. Comm.* 2012. Available at: http://pharmacy.oregonstate.edu/drug_policy/sites/default/files/pages/dur_board/evaluations/articles/2012_05_31_ICS_LABA%20_Pol_Eval.pdf. Accessed May 2, 2013.

10. Postma D, O'Byrne P, Pedersen S. Comparison of the effect of low-dose ciclesonide and fixed-dose fluticasone propionate and salmeterol combination on long-term asthma control. *Chest* 2011;139(2):311-8. doi:http://dx.doi.org/10.1378/chest.09-1735.

11. Martinez FD, Chinchilli VM, Morgan WJ, et al. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. *The Lancet* 19;377(9766):650-657. doi:10.1016/S0140-6736(10)62145-9.

12. National Committee for Quality Assurance. NCQA HEDIS & Quality Measurement. *Natl. Comm. Qual. Assur.* 2013. Available at: http://www.ncqa.org/HEDISQualityMeasurement.aspx. Accessed April 23, 2013.

13. Samnaliev M, Baxter J, Clark R. Comparative evaluation of two asthma care quality measures among Medicaid beneficiaries. *Chest* 2009;135(5):1193-6. doi:http://dx.doi.org/10.1378/chest.07-2962.

14. Yong PL, Werner RM. Process quality measures and asthma exacerbations in the Medicaid population. *J. Allergy Clin. Immunol.* 2009;124(5):961-966. doi:10.1016/j.jaci.2009.07.027.

15. Vernacchio L, Trudell EK, Muto JM. Correlation of Care Process Measures With Childhood Asthma Exacerbations. *Pediatrics* 2013;131(1):e136-e143. doi:10.1542/peds.2012-1144.

16. Smalley WE, Griffin MR, Fought RL, Sullivan L, Ray WA. Effect of a Prior-Authorization Requirement on the Use of Nonsteroidal Antiinflammatory Drugs by Medicaid Patients. *N. Engl. J. Med.* 1995;332(24):1612-1617. doi:10.1056/NEJM199506153322406.

17. Soumerai S. Benefits and risks of increasing restrictions on access to costly drugs in Medicaid. *Health Aff. (Millwood)* 2004;23(1):135-46.

18. Soumerai SB, Zhang F, Ross-Degnan D, et al. Use Of Atypical Antipsychotic Drugs For Schizophrenia In Maine Medicaid Following A Policy Change. *Health Aff. (Millwood)* 2008;27(3):w185-w195. doi:10.1377/hlthaff.27.3.w185.

19. Brown JD, Barrett A, Caffery E, Hourihan K, Ireys HT. Medication Continuity Among Medicaid Beneficiaries With Schizophrenia and Bipolar Disorder. *Psychiatr. Serv.* 2013;64(9):878-885. doi:10.1176/appi.ps.201200349.

20. Vogt WB, Joyce G, Xia J, Dirani R, Wan G, Goldman DP. Medicaid Cost Control Measures Aimed At Second-Generation Antipsychotics Led To Less Use Of All Antipsychotics. *Health Aff. (Millwood)* 2011;30(12):2346-2354. doi:10.1377/hlthaff.2010.1296.

21. Lu CY, Adams AS, Ross-Degnan D, et al. Association Between Prior Authorization for Medications and Health Service Use by Medicaid Patients With Bipolar Disorder. *Psychiatr. Serv.* 2011;62(2):186-193. doi:10.1176/appi.ps.62.2.186.

22. Lu CY, Soumerai SB, Ross-Degnan D, Zhang F, Adams AS. Unintended impacts of a Medicaid prior authorization policy on access to medications for bipolar illness. *Med. Care* 2010;48(1):4–9.

23. Jackevicius CA, Tu JV, Demers V, et al. Cardiovascular Outcomes after a Change in Prescription Policy for Clopidogrel. *N. Engl. J. Med.* 2008;359(17):1802-1810. doi:10.1056/NEJMsa0803410.

24. Ackman ML, Graham MM, Hui C, Tsuyuki RT. Effect of a prior authorization process on antiplatelet therapy and outcomes in patients prescribed clopidogrel following coronary stenting. *Can. J. Cardiol.* 2006;22(14):1205.

25. Guénette L, Gaudet M. Impact of prior authorization for asthma medications on the use of emergency health services: A retrospective cohort study among newly diagnosed patients with asthma. *Clin. Ther.* 2010;32(5):965-972. doi:10.1016/j.clinthera.2010.05.004.

Appendix 1 – DRUG CLASSIFICATION TABLE

Study Group	Generic Name	Route Code	Asthma Controller	COPD Controller	HEDIS Indicator
ANTICHOL	TIOTROPIUM BROMIDE	IH	0	1	0
ANTICHOL	IPRATROPIUM BROMIDE	IH	0	1	0
ANTICHOL	IPRATROPIUM/ALBUTEROL SULFATE	IH	0	1	0
ComboProducts	GUAIFENESIN/THEOPHYLLINE	PO	0	0	1
ComboProducts	AMINOPHYLLIN/EPHED/POT IOD/PB	PO	0	0	1
ComboProducts	EPHEDRINE SULFATE/GUAIFENESIN	PO	0	0	1
ComboProducts	EPHEDRINE/POTASSIUM IODIDE	PO	0	0	1
ComboProducts	GUAIFEN/AMINOPHYLLIN/EPHED/PB	PO	0	0	1
ComboProducts	GUAIFEN/DYPHYLLINE/P-EPHEDRINE	PO	0	0	1
ComboProducts	GUAIFEN/THEOP ANHYD/P-EPHED	PO	0	0	1
ComboProducts	GUAIFEN/THEOPHYLL/EPHED/PB	PO	0	0	1
ComboProducts	GUAIFENESIN/DYPHYLLINE	PO	0	0	1
ComboProducts	GUAIFENESIN/THEOP SOD GLY	PO	0	0	1
ComboProducts	ISOPROTERENOL/CALCIUM IODIDE	PO	0	0	1
ComboProducts	GUAIFENESIN/OXTRIPHYLLINE	PO	0	0	1
ICS	MOMETASONE FUROATE	IH	1	0	1
ICS	FLUTICASONE PROPIONATE	IH	1	0	1
ICS	FLUNISOLIDE/MENTHOL	IH	1	0	1
ICS	FLUNISOLIDE	IH	1	0	1
ICS	TRIAMCINOLONE ACETONIDE	IH	1	0	1
ICS	CICLESONIDE	IH	1	0	1
ICS	BUDESONIDE	IH	1	0	1
ICS	BECLOMETHASONE DIPROPIONATE	IH	1	0	1
ICS	DEXAMETHASONE SOD PHOSPHATE	IH	1	0	1
ICSLABA	FLUTICASONE/SALMETEROL	IH	0	0	1
ICSLABA	MOMETASONE/FORMOTEROL	IH	0	0	1
ICSLABA	BUDESONIDE/ FORMOTEROL FUMARATE	IH	0	0	1
IgE	OMALIZUMAB	SQ	1	0	1
LABA	SALMETEROL XINAFOATE	IH	1	1	1
LABA	ARFORMOTEROL TARTRATE	IH	1	1	1
LABA	FORMOTEROL FUMARATE	IH	1	1	1
LABA	INDACATEROL MALEATE	IH	0	1	1
leukotriene	ZILEUTON	PO	1	0	1
leukotriene	MONTELUKAST SODIUM	PO	1	0	1
leukotriene	ZAFIRLUKAST	PO	1	0	1

Policy Evaluation: Combination Inhaler Prior Authorization

Study Group	Generic Name	Route Code	Asthma Controller	COPD Controller	HEDIS Indicator
OralSteroids	PREDNISOLONE ACETATE	PO	0	0	0
OralSteroids	CORTISONE ACETATE	PO	0	0	0
OralSteroids	METHYLPREDNISOLONE	PO	0	0	0
OralSteroids	BUDESONIDE	PO	0	0	0
OralSteroids	BETAMETHASONE	PO	0	0	0
OralSteroids	PREDNISOLONE SOD PH/PEAK FLOW	PO	0	0	0
OralSteroids	DEXAMETHASONE	PO	0	0	0
OralSteroids	PREDNISOLONE SOD PHOSPHATE	PO	0	0	0
OralSteroids	TRIAMCINOLONE	PO	0	0	0
OralSteroids	PREDNISONE	PO	0	0	0
OralSteroids	ADRENAL CORTEX (PORCINE)	PO	0	0	0
OralSteroids	HYDROCORTISONE	PO	0	0	0
OralSteroids	HYDROCORTISONE CYPIONATE	PO	0	0	0
OralSteroids	PREDNISOLONE	PO	0	0	0
PDE4I	ROFLUMILAST	PO	0	1	0
SABA	PIRBUTEROL ACETATE	IH	0	0	0
SABA	ALBUTEROL SULFATE	IH	0	0	0
SABA	BITOLTEROL MESYLATE	IH	0	0	0
SABA	ALBUTEROL	IH	0	0	0
SABA	LEVALBUTEROL HCL	IH	0	0	0
SABA	RACEPINEPHRINE HCL	IH	0	0	0
SABA	TERBUTALINE SULFATE	IH	0	0	0
SABA	ISOPROTERENOL HCL	IH	0	0	0
SABA	METAPROTERENOL SULFATE	IH	0	0	0
SABA	EPINEPHRINE BITARTRATE	IH	0	0	0
SABA	EPINEPHRINE	IH	0	0	0
SABA	LEVALBUTEROL TARTRATE	IH	0	0	0
SABA	ISOPROT HCL/PHENYLEPHRINE	IH	0	0	0
THEOPHYLLINE	OXTRIPHYLLINE	PO	1	0	1
THEOPHYLLINE	DYPHYLLINE	PO	1	0	1
THEOPHYLLINE	AMINOPHYLLINE	PO	1	0	1
THEOPHYLLINE	AMINOPHYLLINE	IV	1	0	1
THEOPHYLLINE	THEOPHYLLINE ANHYDROUS	PO	1	0	1
THEOPHYLLINE	THEOPHYLLINE/DEXTROSE 5%-WATER	IV	1	0	1
THEOPHYLLINE	DYPHYLLINE	IM	1	0	1

Appendix 2 – OUTCOMES AT 30-DAYS AND AT 90-DAYS

	Study Group[a] (n=297)	**Control Group[b] (n=351)**		
	No. (%)	No. (%)	OR (95% CI[c])	Adjusted[d] OR (95% CI)
30 Days After Study Entry				
Composite Asthma or COPD[e] Emergency Department or Hospital Encounter	14 (4.7)	7 (2.0)	2.43 (0.97 – 6.11)	4.17 (1.48 – 11.79)
Asthma or COPD Emergency Department Encounter	14 (4.7)	6 (1.7)	2.84 (1.08 – 7.50)	4.69 (1.61 – 13.64)
Asthma or COPD Hospital Encounter	3 (1.0)	1 (0.3)	3.57 (0.37 – 34.52)	4.90 (0.43 – 56.27)
All Cause Hospital or Emergency Department or Death	38 (12.8)	50 (14.2)	0.88 (0.56 – 1.39)	0.88 (0.55 – 1.40)
Oral Corticosteroid	29 (9.8)	16 (4.6)	2.27 (1.21 – 4.26)	3.41 (1.69 – 6.88)
90 Days After Study Entry				
Composite Asthma or COPD Emergency Department or Hospital Encounter	21 (7.1)	15 (4.3)	1.70 (0.86 – 3.37)	2.57 (1.20 – 5.49)
Asthma or COPD Emergency Department Encounter	21 (7.1)	13 (3.7)	1.98 (0.97 – 4.02)	3.08 (1.40 – 6.78)
Asthma or COPD Hospital Encounter	4 (1.3)	3 (0.9)	1.58 (0.34 – 7.13)	2.18 (0.43 – 11.21)
All Cause Hospital or Emergency Department or Death	78 (26.3)	94 (26.8)	0.97 (0.69 – 1.38)	0.97 (0.67 – 1.40)
Oral Corticosteroid	52 (17.5)	49 (14.0)	1.31 (0.86 – 2.00)	1.54 (0.98 – 2.42)

[a] *Control Group = No prior authorization required for combination inhaler*
[b] *Study Group = Prior authorization required for combination inhaler*
[c] *CI = Confidence Intervals*
[d] *Model adjusted for age less than 18, HEDIS Persistent Asthma, Controller Use and Hospitalization at baseline*
[e] *COPD = Chronic Obstructive Pulmonary Disease*