

ADHERENCE, CONTROL AND QUALITY OF LIFE

An evaluation of asthma medication utilization for risk evaluation and mitigation strategies (REMS) in the United States: 2005–2011

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Abstract

Purpose: The purpose of this study was to assess drug utilization patterns of fluticasone propionate (FP)/salmeterol (SAL) combination (FSC) and SAL over the 7-year period of 2005–2011 in patients with asthma as part of the Risk Evaluation and Mitigation Strategies (REMS). **Methods:** A descriptive, retrospective observational study utilizing national pharmacy data and employer-based claims data to characterize drug utilization patterns. **Results:** For patients with asthma, the total number of FSC and SAL dispensings and users of FSC and SAL has declined between 2005 and 2011. During this period, FSC and SAL dispensing for asthma decreased 24% and 76%, respectively, with a more pronounced decline between 2010 and 2011 relative to other years. The total number of patients with asthma who were dispensed FSC has decreased by 10% among adults and by 40% in children and adolescents. While SAL-containing medications decreased, dispensing of FP monotherapy increased 39% during the same 7-year period. The number of patients dispensed FP for asthma has increased 47% in children 4–11 years of age, 72% in adolescents 12–17 years of age, and 6% in adults. SAL use without a controller was infrequent and decreasing, reported by 1.7% and 0.5% of patients with asthma in 2005 and 2011, respectively. **Conclusions:** In patients with asthma, use of FSC and SAL decreased between 2005 and 2011, while the use of FP increased. Use of SAL monotherapy was infrequent and declined during the study period. The data suggest that the substantial communication activities have encouraged appropriate prescribing of long-acting β_2 -adrenergic agonist (LABA).

Keywords

Drug utilization, fluticasone propionate/salmeterol combination, salmeterol, fluticasone propionate

History

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Introduction

Two large clinical trials reported data on a potential association between salmeterol (SAL; trade name SEREVENT), a long-acting β_2 -adrenergic agonist (LABA), and an increased risk of asthma-related death [1,2]. Subjects randomized in these trials were requested to continue their other asthma medications but were dispensed SAL or placebo. In the Salmeterol Multicenter Asthma Research Trial, fewer than 50% of subjects reported using a concomitant inhaled corticosteroid (ICS). Despite the increased risk of asthma fatality in patients with concomitant ICS + LABA, the trial was not prospectively designed to directly answer this question. As a result of these studies and an extensive literature review, the United States treatment guidelines recommend that LABAs should only be used in combination with ICS for the treatment of asthma in patients with moderate or severe persistent asthma requiring more than low- to medium-dose ICS [3]. Since 2003, GlaxoSmithKline and the United States Food and Drug Administration (FDA) have initiated a series of activities to better understand the

safe use of LABAs, and a series of measures were implemented to communicate this information to prescribers. These activities have included four FDA advisory committee meetings; a boxed warning with several revisions and updated labeling for LABA-containing medications; an FDA-conducted meta-analysis of safety data; two FDA-issued communications on the safe use of LABAs [4,5] and a class-level Risk Evaluation and Mitigation Strategy (REMS) for LABA-containing medications [6]. In preparation for the 2008 advisory committee, the FDA-conducted meta-analysis noted an increased risk of asthma-related hospitalizations associated with LABA use, particularly in children [7]. These activities are discussed in more detail elsewhere [8].

The REMS for LABA-containing medications included a communication plan with letters to current and potential prescribers of LABAs, printed/web-based information for healthcare providers, and letters to the leadership of relevant professional societies [6]. Under the REMS, the FDA issued revised prescribing information which no longer characterized LABAs as long-term maintenance medications for asthma treatment and encouraged discontinuing LABA use if the patient's asthma could be controlled with ICS monotherapy. Additionally, the LABA prescribing information was updated to indicate that the available data were inadequate to determine whether concurrent use of ICS or other long-term

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asthma medication mitigates the observed increased risk of asthma-related death associated with LABAs.

As part of an assessment of whether the REMS [9,10] was meeting its goals, GlaxoSmithKline examined drug utilization trends to evaluate prescribing patterns over time. The primary objective was to characterize drug utilization trends for fluticasone propionate (FP; trade name FLOVENT)/SAL combination (FSC; trade name ADVAIR) and SAL, between 2005 and 2011 in the United States among patients with asthma. Secondary objectives were to characterize drug utilization class-level trends for ICS/LABA medications and to characterize drug utilization for FP. This analysis was submitted to the FDA in March 2012, and the FDA released these medications from their REMS in August 2012 [6].

Methods

Study design

This was a retrospective data analysis using healthcare claims data to summarize asthma drug utilization trends from 2005 to 2011 by age categories for LABA-containing and ICS medications. Analyses were conducted at the aggregated level for prescription dispensing and at the patient-level for concurrent medication use and length of therapy. This analysis was to support the GlaxoSmithKline REMS, and therefore GlaxoSmithKline medications including FSC, SAL and FP were the medications of interest; however, class-level analyses are also provided in the online appendix (Supplemental Table S1).

Data sources

Drug utilization trends were determined using several data sources. Source Healthcare Analytics (SHA; Phoenix, Arizona, USA) prescription-level data include estimates of prescription-level data representing 82% coverage of retail pharmacy dispensing, and 50–80% of mail order (depending on product) in the United States [11]. Patient-level originates from 75 million covered lives per year, representing 75% coverage of retail pharmacy dispensing, 55–80% of mail order (depending on product) and 60% of the long-term care dispensing [12]. Source Healthcare Analytics data were used to estimate patient counts and concurrent use of LABA and other controllers.

IMS health data (IMS health, Danbury, Connecticut, USA), including the IMS National Prescription Audit™ [13] and the National Disease and Therapeutic Index™ [14], were used to determine the market shares of medications within the asthma market. The National Prescription Audit™ measures volume and shares of medications dispensed in the United States based on a representative sample of the prescribing universe, including 74% of retail pharmacies, 40–70% of non-governmental mail service pharmacy outlets, and 45–50% of long-term care facilities. The National Disease and Therapeutic Index™ includes disease encounters in 4140 office-based practices in the continental United States, which provide treatment dispensings by diagnosis. IMS data were combined with Source Healthcare Analytics data to estimate the total number of prescription dispensings by class within the asthma market.

Optum™ Impact™ National Managed Care Benchmark Database [15] (OptumInsight, Eden Prairie, Minnesota, USA) was used to obtain measures of adherence based on medication dispensing. This national database comprises claims from more than 50 sources and covers more than 20 million lives, yielding patient-level healthcare claims data.

Definitions

Concurrent dispensing

Concurrent use of SAL with a controller was tabulated using Source Healthcare Analytics data. Concurrent use was defined as controller dispensing identified within 90 days of a LABA dispensing (± 90 days) to account for variable adherence with respiratory medications. Categories included FSC, SAL with ICS, SAL with other controller, and SAL monotherapy.

Length of therapy

To examine the length of therapy, the proportion of days covered and the medication possession ratio in a 1-year period were calculated using Optum™ Insight™ employer-based claims data. The proportion of days covered provides the length of time a patient is covered with the medication for a 1-year period, and was calculated as the sum of the days supplied within the 1-year period from index prescription to the end of the period divided by 365 days [15]. To be included in the proportion of days covered tabulations, patients were required to have at least one medication fill for the medication of interest during the 1-year study period. The medication possession ratio was calculated as the number of days supply dispensed from the first index fill to the last fill (not including the days supply of the last medication fill) divided by the days between the first and last fill in a 1-year time period [16]. Patients were required to have at least two medication fills, with the first and last dispensing at least 6 months apart in order to measure persistence over time. By requiring at least two prescriptions, medication possession ratio measures tend to be skewed to more adherent patients relative to the proportion of days covered.

The identification period for these measures was 1 January 2010 to 30 June 2011. The first prescription fill in the first 6 months of this period was selected as the index prescription. Patients were required to have continuous health plan coverage for 12 months from the index date and a diagnosis of asthma in the 6 months prior to or during the 12 months after the index date.

Assumptions required for the length of therapy measures included: (1) Days supplied for dispensed medications that overlap with the previous fill were added to the end of the days supplied rather than truncating the prior dispensing. (2) If there was a dispensing at the end of the period that went past the 365 day interval, the coverage was truncated to coincide with the 365th day. (3) Medication fills with missing days supplied were deleted from the analysis due to potential data errors.

Statistical analysis

The number and proportion (%) of dispensing and patients was assessed annually by age (4–11 years, 12–17 years, ≥ 18

years) at the class-level and GlaxoSmithKline medication level. The number of patients with concurrent prescription of SAL with and without a controller was tabulated by age for patients with asthma. No statistical testing was performed.

Results

Total dispensing

The total number of dispensings of FSC, FP and SAL for asthma from 2005 to 2011 is presented in Figure 1 and Supplemental Table S2. Dispensing of FSC and SAL decreased during this time period with a 24% reduction of FSC dispensing (12 486 637 to 9 512 223 dispensing), and a 76% reduction in SAL dispensing (counts decreasing from 847 200 to 203 149 dispensing). In contrast, dispensing of FP increased 39% (3 449 461 to 4 791 544 dispensing) during the same period. FSC and SAL dispensing decreased annually by

an average of 3.4% and 11%, respectively, and the decrease was most pronounced between the years 2010–2011.

GlaxoSmithKline-level patient information

The calculated number of patients using FSC, FP and SAL for asthma between 2005 and 2011, by age group are presented in Figure 2 for children aged 4–11, Figure 3 for adolescents aged 12–17, and Figure 4 for adults aged ≥ 18 ; and in Supplemental Table S3. The patient data follow the same trends as the prescription dispensing data. The number of patients with asthma dispensed FSC and SAL has decreased for all age groups since 2005, and the greatest decrease was observed in children and adolescents.

In this analysis, the number of patients with asthma treated with FSC decreased 48% in children, 44% in adolescents, and 10% in adults between 2005 and 2011. In contrast, the number of patients dispensed FP between 2005 and 2011 increased

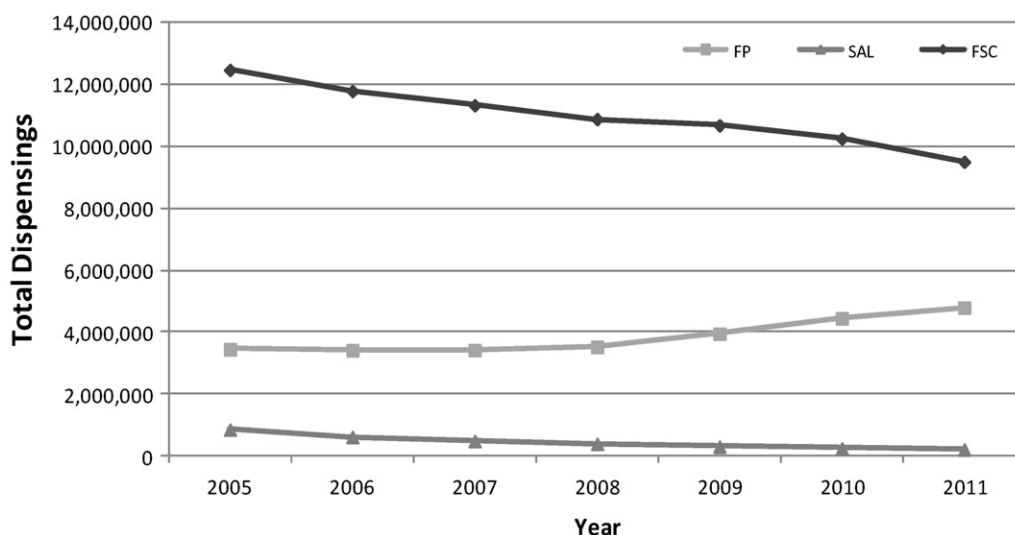


Figure 1. –Drug utilization: total number of dispensings of GlaxoSmithKline medicines for patients with asthma during 2005–2011, by year. FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol. Sources: IMS Health, IMS National Prescription Audit™, IMS National Disease and Therapeutic Index™, and GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool.

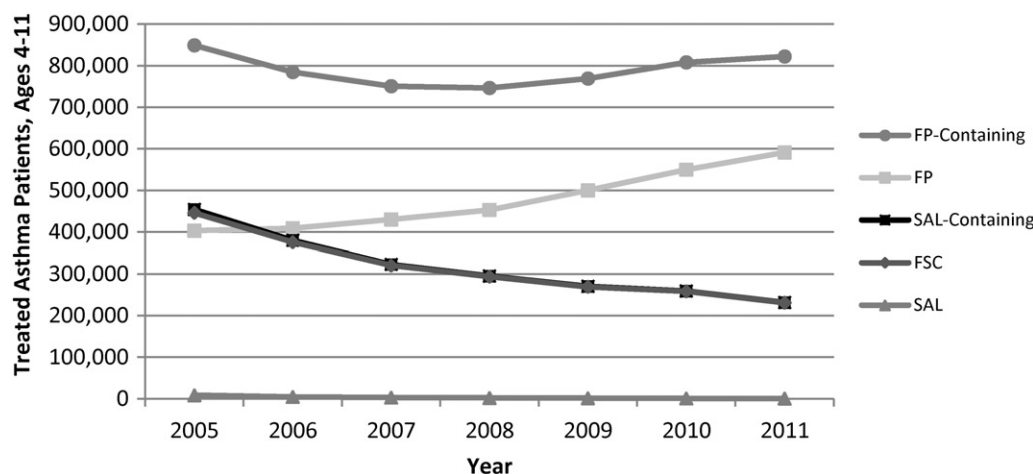


Figure 2. –Drug utilization in total number of patients with asthma aged 4–11 years, for GlaxoSmithKline medications during 2005–2011. Note: FSC line is overlapped by SAL-containing line in the graph above. FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol. Sources: Source Healthcare Analytics, GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool and Annual Unique Patient Counts.

47% in children, 72% in adolescents, and 6% in adults. SAL monotherapy was infrequent among patients with asthma (<2%).

Concurrent salmeterol with controllers in asthma

The use of concurrent SAL with a controller as FSC or SAL plus a controller has increased for all age groups since 2005 (98.2% in 2005 vs. 99.8% in 2011 in children; 97.5% in 2005 vs. 99.5% in 2011 in adolescents; 91.9% in 2005 vs. 97.3% in 2011 in adults). The use of SAL alone has decreased since 2005 across all age groups as presented in Table 1. When dispensed SAL, the majority of patients with asthma were dispensed a concurrent controller medication (e.g., ICS or other therapy such as a leukotriene receptor antagonist).

Length of therapy

Medication persistence: proportion of days covered

Medication persistence measured as a proportion of days covered during a 1-year period for FSC, FP and SAL is presented in Table 2. Among the 74 070 patients treated with FSC, the average proportion of days covered was 43% for asthma in 1 year. Results were lower in children

and adolescents. Proportion of days covered for FP was 28% for all patients with asthma ($n = 40\,198$), and similar in all age groups. Five percent of all patients with asthma using FP had $\geq 80\%$ coverage during the 1-year study period. Proportion of days covered for SAL was 54% for all patients with asthma ($n = 1\,522$; mostly adults).

Medication adherence: medication possession ratio

Medication adherence measured as medication possession ratio during a 1-year period for FSC, FP and SAL is presented in Table 3. Patients were required to have more than one prescription within the 1-year interval for this analysis, resulting in smaller sample sizes but higher measures of adherence than proportion of days covered.

The average medication possession ratio for patients treated with FSC was 56%. MPR in children and adolescents was lower: 50% and 48% respectively. Twenty-four percent of all patients with asthma had a medication possession ratio $\geq 80\%$, with 16% of children and 15% of adolescents having a medication possession ratio of $\geq 80\%$.

Medication possession ratio for FP was 43% for all patients with asthma ($n = 26\,813$), and was similar among age groups.

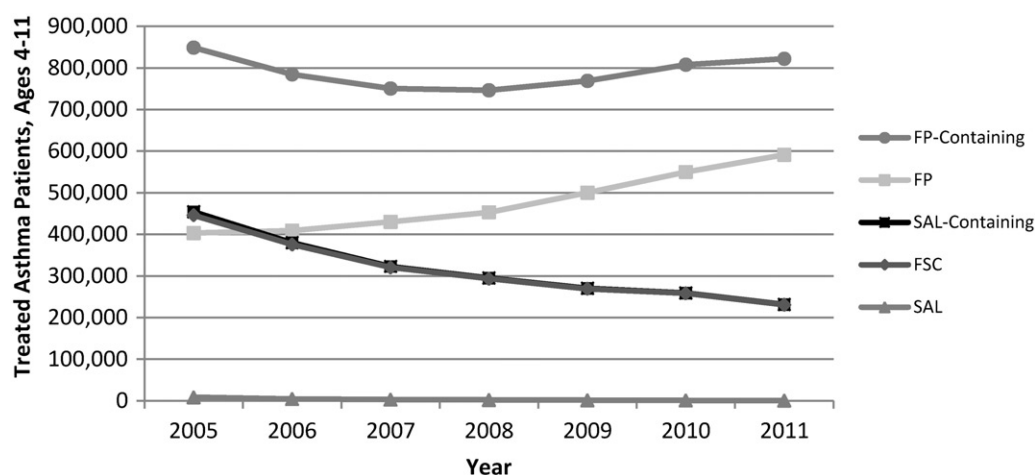


Figure 3. –Drug utilization in total number of patients with asthma aged 12–17 years, for GlaxoSmithKline medications during 2005–2011. Note: FSC line is overlapped by SAL-containing line in the graph above. FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol. Sources: Source Healthcare Analytics, GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool and Annual Unique Patient Counts.

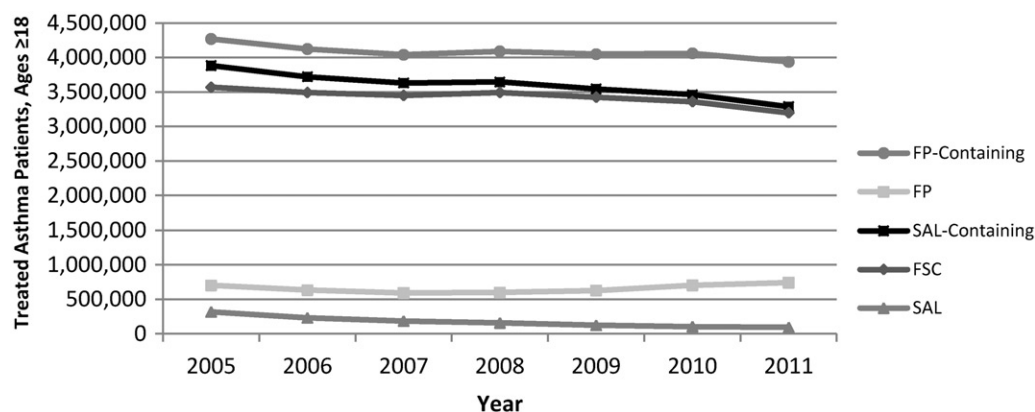


Figure 4. –Drug utilization in total number of patients with asthma ≥ 18 years old, for GlaxoSmithKline medications during 2005–2011. FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol. Sources: Source Healthcare Analytics, GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool and Annual Unique Patient Counts.

Table 1. Drug utilization in patient counts for concurrent GlaxoSmithKline medicines at age group level in patients with asthma, by year.

Patient counts								Total patient count (%)	
Asthma 4–11	2005	2006	2007	2008	2009	2010	2011	2005*	2011*
FSC	4 457 88	375 352	320 000	293 092	268 970	257 862	230 514	98.2%	99.8%
SAL alone	864	331	233	167	81	59	65	0.2%	0.0%
ICS + SAL	5351	3 046	1 778	1160	832	580	321	1.2%	0.1%
SAL + other	1960	859	686	391	229	168	97	0.4%	0.0%
Total	453 963	379 588	322 697	294 810	270 112	258 669	230 997	100%	100%
Asthma 12–17	2005	2006	2007	2008	2009	2010	2011	2005 (%)	2011 (%)
FSC	434 181	387 077	346 532	313 842	302 636	284 174	243 686	97.5%	99.5%
SAL alone	2218	954	646	460	344	216	175	0.5%	0.1%
ICS + SAL	5397	3223	2 371	1 717	1 177	939	807	1.2%	0.3%
SAL + other	3363	1739	1 214	796	519	335	307	0.8%	0.1%
Total	445 159	392 993	350 763	316 815	304 676	285 664	244 975	100%	100%
Asthma 18+	2005	2006	2007	2008	2009	2010	2011	2005 (%)	2011 (%)
FSC	3 565 747	3 489 736	3 448 009	3 489 532	3 421 194	3 356 553	3 195 260	91.9%	97.3%
SAL alone	64 218	44 485	34 272	30 786	23 613	20 040	17 962	1.7%	0.5%
ICS + SAL	160 939	121 295	96 310	80 550	63 639	53 840	47 387	4.1%	1.4%
SAL + other	90 102	62 548	50 245	42 760	33 339	27 562	24 387	2.3%	0.7%
Total	3 881 006	3 718 064	3 628 836	3 643 628	3 541 785	3 457 995	3 284 996	100%	100%

Sources: Source Healthcare Analytics, GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool and Annual Unique Patient Counts. FSC, fluticasone propionate/salmeterol combination; ICS, inhaled corticosteroids; Other, other controller; SAL, salmeterol.

*Expressed as a % of total patients.

Table 2. Proportion of days covered in 1 year among patients with asthma.

	Asthma			
	Ages 4–11	Ages 12–17	Ages 18+	All patients
FSC (n)	5 023	6 502	62 434	74 070
Avg. proportion of days covered	0.36	0.34	0.45	0.43
% at $\geq 80\%$	8	7	17	15
% at $\geq 70\%$	13	11	23	21
FP (n)	15 121	5 231	17 422	40 198
Avg. proportion of days covered	0.27	0.21	0.30	0.28
% at $\geq 80\%$	3	2	7	5
% at $\geq 70\%$	6	3	10	8
SAL (n)	10	21	1 491	1 522
Avg. proportion of days covered	0.19	0.24	0.55	0.54
% at $\geq 80\%$	n/a	5	30	29
% at $\geq 70\%$	n/a	10	37	36

Source: Optum™ Impact™ National Managed Care Benchmark Database. Avg., average; FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol.

Less than 20% of asthma patients using FP had $\geq 80\%$ coverage during the 1-year study period. Medication possession ratio for SAL was 69% for all patients with asthma ($n = 1253$), which was an adult population with only 17 combined children and adolescents with more than one SAL dispensing in the database.

Discussion

This study provides information on United States drug utilization patterns for FSC, SAL and FP, as well as the overall class of these respiratory medications between 2005 and 2011. The results suggest that the series of communications regarding LABA safety in the United States, prior to and including the REMS, may have contributed to decreased SAL-containing medication use and increased use of FP monotherapy. The use of FSC and SAL in asthma has declined and the use of FP has increased between 2005 and 2011. SAL was used in a fixed dose combination or with

another controller for the vast majority of patients with asthma. The measures of persistence and adherence for the medications studied suggest that these medications were commonly used intermittently as opposed to continuously, suggesting patients or healthcare professionals may have down titrated these medications when patients' asthma was controlled.

Frequent and concurrent use of SAL with another anti-inflammatory controller has been reported previously in the United Kingdom [17]. In patients receiving SAL prescriptions (excluding FSC), 90% of patients initiating SAL used a concurrent controller within 90 days of the index date. When accounting for all SAL-containing prescriptions (SAL and FSC), 95% of all patients, and 97% of children 4–11 years of age, were prescribed concurrent controllers.

Others have demonstrated that LABA monotherapy is infrequent in patients with asthma. In a Medicaid population between 2006 and 2008, the use of LABA monotherapy was uncommon ($<1\%$ in patients with asthma), decreased with

Table 3. Medication possession ratio in 1 year among patients with asthma.

	Asthma			
	Ages 4–11	Ages 12–17	Ages 18+	All patients
FSC (n)	3 862	4 856	50 757	59 555
Avg. medication possession ratio	0.50	0.48	0.57	0.56
% at ≥80%	16	15	26	24
% at ≥70%	24	22	34	32
FP (n)	10 759	3 073	11 252	26 813
Avg. medication possession ratio	0.40	0.38	0.47	0.43
% at ≥80%	9	9	18	13
% at ≥70%	14	13	23	18
SAL (n)	5	12	1 236	1 253
Avg. medication possession ratio	0.51	0.47	0.69	0.69
% at ≥80%	20	25	45	45
% at ≥70%	20	33	52	52

Source: Optum™ Impact™ National Managed Care Benchmark Database. Avg., average; FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol.

time, and was less frequent in children [18]. In a United States healthcare claims dataset, LABA monotherapy comprised 9% and 3% of LABA-containing medications in the first half of 2003 and 2009, respectively [19]. Infrequent use of LABA has also been observed in Scotland, where <1.5% of patients with asthma (991 of 73 486) used LABA as monotherapy between 2005 and 2007 [20]. In the Scottish study, use of sustained LABA monotherapy was more frequent in patients >60 years of age, and sustained LABA monotherapy was significantly reduced with primary care asthma reviews. Similar to our findings with proportion of days covered, Stempel et al. demonstrated that FSC was filled more frequently than FP [21]. The mean number of medication dispensings obtained using FSC during a 1-year study (3.98; 95% confidence interval [CI] 3.78–4.18), was nearly double that observed in the FP cohort (2.29; 95% CI 2.11–2.47). The difference in the number of dispensings and proportion of days covered between FSC and FP likely reflect the differences in severity or seasonality of disease for treated patients. Consistent with the treatment guidelines, patients dispensed FSC were more likely to have indicators of more severe or uncontrolled asthma and require more medication than those patients who were dispensed ICS monotherapy.

Drug utilization analyses are useful to characterize trends of medication use over time. However, there are limitations in interpreting the results of these studies based on available data. Drug utilization studies are limited by the information recorded and available for analyses in retrospective healthcare databases. Prescription-level trend data (as presented here) have a relatively short lag (2–4 months) which allows us to examine data through 2011; however, it is limited by the lack of patient-level information that would allow for tabulation beyond indication and age. Alternatively, healthcare encounters that require payment are well captured in most healthcare claims and electronic medical record databases; yet, these data may lag up to 18 months. Therefore, trends in LABA-containing medication use following the 2010 LABA safety communication and labeling changes have not yet been evaluated using these sources [19]. Unfortunately, nearly all databases are deficient in either systematically collected measures of asthma symptoms or patient-reported level of

asthma control and cannot provide insight into the physician's judgment that might explain the reasons for the observed trends in prescribing these medications (e.g., reasons for patients maintaining, stepping up, or switching various asthma medications).

Others have evaluated appropriate use of LABAs based on disease severity, and considered the use of LABAs appropriate if patients had prior single controller use (ICS, leukotriene receptor agonist), prior healthcare utilization, courses of oral corticosteroids, or excessive short acting β_2 -adrenergic agonist use in the year prior to initiation of ICS/LABA combinations. Using healthcare claims data, the authors could explain less than half of the LABA-containing medications as being appropriate in the context of their criteria, and cited similar limitations of databases regarding the absence of symptoms and physician judgment [19,22].

Conclusions

The use of FSC and SAL for asthma has declined progressively since the dissemination of targeted information describing the safety risks associated with the use of LABA from 2005 to 2011, with the largest annual decline observed between 2010 and 2011. Conversely, during the same period, the use of FP and other ICS monotherapy have increased. In addition, the majority of LABA use was concurrent with a controller, typically in the same device such as FSC, or less commonly LABA used with a separate controller. Finally, only 15% of patients dispensed FSC had high levels of adherence (proportion of days covered ≥80%) during the 1-year study period, and the average proportion of days covered was 43%, suggesting that FSC may be down titrated when patients achieve asthma control. These data suggest that the substantial communication about LABA safety, prior to and including the REMS, have resulted in a reduction of FSC use and encouraged appropriate use of LABA for the treatment of asthma.

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Declaration of interest

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An evaluation of asthma medication utilization for risk evaluation and mitigation strategies (REMS) in the United States: 2005–2011

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Online supplementary material

Table S1. —Medications classification at class-level.

Class	Class description	GSK medication(s)
LABA-containing	LABA monotherapy and ICS/LABA fixed dose combinations	Salmeterol-containing: SEREVENT, ADVAIR
ICS-containing	ICS monotherapy and ICS/LABA fixed dose combinations	FP-containing: ADVAIR, FLOVENT
ICS/LABA	ICS/LABA fixed dose combinations	ADVAIR (FSC)
ICS	ICS monotherapy	FLOVENT (FP)
LABA	LABA monotherapy	SEREVENT (SAL)

FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; GSK, GlaxoSmithKline; ICS, inhaled corticosteroids; LABA, long acting beta-agonist; SAL, salmeterol.

Table S2. Drug utilization in total number of dispensings at class-level for GlaxoSmithKline medications in patients with asthma during 2005–2011, by year.

Asthma	2005	2006	2007	2008	2009	2010	2011	% Change	
								2011 vs. 2010	% Change since 2005
LABA-									
Containing	13 661 565	12 713 935	12 214 014	12 321 313	12 633 776	12 596 421	12 060 520	–4.4%	–11.7%
ICS-									
Containing	17 984 827	17 746 773	17 790 734	18 180 052	19 399 278	19 933 839	20 005 510	0.4%	11.2%
ICS/LABA	12 486 637	11 803 554	11 473 483	11 735 060	12 198 652	12 255 370	11 799 293	–3.9%	–5.5%
FSC	12 486 637	11 803 554	11 340 721	10 895 208	10 692 584	10 263 785	9 512 223	–7.9%	–23.8%
ICS	5 498 190	5 943 219	6 317 250	6 444 991	7 200 627	7 678 469	8 206 216	6.4%	49.3%
FP	3 449 461	3 415 629	3 419 834	3 520 451	3 945 399	4 444 609	4 791 544	7.2%	38.9%
LABA	1 174 928	910 381	740 531	586 253	435 124	341 051	261 227	–30.6%	–77.8%
SAL	847 200	605 785	472 644	385 360	291 781	236 553	203 149	–16.4%	–76.0%

FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; ICS, inhaled corticosteroids; LABA, long acting beta-agonist; SAL, salmeterol.

Sources: IMS National Prescription Audit™, IMS National Disease and Therapeutic Index™, and Source Healthcare Analytics

GlaxoSmithKline Custom Asthma/Chronic Obstructive Pulmonary Disorder (COPD) Hierarchical Regimen Analysis Tool.

Table S3. —Drug utilization of GlaxoSmithKline medicines in patient counts at age group level in asthma patients, by year.

								% Change
Asthma 4–11	2005	2006	2007	2008	2009	2010	2011	since 2005
SAL- containing	453 962	379 587	322 698	294 810	270 113	258 670	230 997	–49.1%
FP- containing	848 653	784 292	750 107	745 954	768 834	807 589	821 640	–3.2%
FSC	445 788	375 352	320 000	293 092	268 970	257 862	230 514	–48.3%
FP	402 865	408 941	430 107	452 863	499 863	549 727	591 126	46.7%
SAL	8174	4236	2698	1719	1142	807	483	–94.1%
Asthma 12– 17	2005	2006	2007	2008	2009	2010	2011	% change since 2005
SAL- containing	445 159	392 993	350 763	316 814	304 676	285 664	244 975	–45.0%
FP- containing	544 202	494 686	456 662	434 602	449 905	456 920	433 124	–20.4%
FSC	434 181	387 077	346 532	313 842	302 636	284 174	243 686	–43.9%
FP	110 021	107 609	110 130	120 760	147 269	172 746	189 438	72.2%
SAL	10 978	5916	4230	2972	2040	1489	1289	–88.3%
Asthma 18+	2005	2006	2007	2008	2009	2010	2011	% change since 2005
SAL- containing	3881 006	3718 065	3628 835	3643 627	3541 785	3457 995	3284 996	–15.4%
FP- containing	4265 893	4120 137	4037 947	4086 131	4046 873	4057 774	3935 210	–7.8%
FSC	3565	3489	3448	3489	3421	3356	3195	–10.4%

	747	736	009	532	194	553	260	
FP	700 146	630 401	589 939	596 600	625 679	701 221	739 949	5.7%
SAL	315 259	228 329	180 827	154 095	120 591	101 441	89 736	−71.5%

FP, fluticasone propionate; FSC, fluticasone propionate/salmeterol combination; SAL, salmeterol.

Sources: Source Healthcare Analytics, GlaxoSmithKline Custom Asthma/COPD Hierarchical Regimen Analysis Tool and Annual Unique Patient Counts.