



Medication Cost-Savings and Utilization of Generic Inhaled Corticosteroid (ICS) and Long-Acting Beta-Agonist (LABA) Drug Products in the USA

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Abstract

Background In the USA, drug costs associated with the inhaled corticosteroid (ICS) and long acting β agonist (LABA) combination products have been increasing since 2001. In January 2019, the first generic ICS/LABA drug product was approved by the U.S. Food and Drug Administration.

Methods We investigated retrospectively the effects of the first approved generic ICS/LABA drug from 2019 to 2020 on the wholesale cost-savings and prescription dispensing using the IQVIA data system in the USA.

Results The marketing of the first generic for fluticasone propionate and salmeterol xinafoate dry powder inhaler was associated with \$941 million in drug cost-savings during the first year for this class of medications. Although the brand-name drug manufacturer concurrently introduced its authorized generic, these cost-savings were driven by the averaged unit cost of the approved generic at \$115, compared to \$169 for the authorized generic and \$334 for the branded product. Generic initiation and substitution with the first generic were, respectively, higher compared to those with authorized generics; however, overall dispensing of the first generic was lower than that of its branded product. As in the case of budesonide and formoterol fumarate dry powder inhaler, marketing of authorized generics alone was not associated with any noticeable change in sales or prescription cost-saving.

Conclusion We estimated that more than 20% of prescription cost-saving was achieved for the ICS/LABA dry powder inhalers in the first year following the introduction of the first approved generic, even though generic utilization remained lower than that of the branded counterpart.

Keywords Asthma · COPD · Generic substitution · Authorized generics · First approved generic · Prescription cost-savings · Persistence · Adherence

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Introduction

In the USA, generic prescriptions account for 9 out of every 10 prescriptions dispensed, adding up to over 4 billion prescriptions in 2019. Conversely, brand-name drugs account for only 10% of the prescriptions dispensed, but amount to over 75% of total drug spending [1]. In 2020, the average co-pay for brand-name drugs was \$56.32 and for generic drugs it was \$6.97, with 92% prescriptions filled for \$20 or less [1]. Cost-savings of this magnitude can be critically important for patients with chronic conditions, such as those suffering from respiratory diseases like asthma or chronic obstructive pulmonary disease (COPD). In the USA, the prevalence of asthma is approximately 7.7% affecting about 25 million people [2], and the prevalence of COPD is approximately

6.6% among adults (≥ 18 years of age), affecting 16.4 million people [3]. Patients with asthma and COPD frequently require use of one or more inhalers daily to maintain their respiratory health. COPD patients in particular are often elderly and may rely on Medicare for assistance with treatment costs potentially reaching more than \$2800 per year [4]. The average annual per-person medical cost for asthma patients in the USA was found to be \$3366 in 2015, of which \$1830 was attributable to prescription medication [5]. The high cost of maintenance medication is an important factor contributing to non-adherence with orally inhaled drug products (OIDPs) and represents a significant barrier to optimal care for many patients with chronic respiratory diseases such as asthma and COPD [1, 6, 7]. Unsurprisingly, adults and parents of children with asthma and COPD report high rates (30–50% of patients) of cost-related underuse of asthma medicines [8, 9], and the rate of underuse has only increased over time as medication costs increased [7]. Repeated studies have demonstrated that when asthma or COPD medications are not properly adhered to, disease-related morbidity and mortality increase [10–15]. The overall economic burden of asthma and COPD in the USA is driven not just by the high cost of prescription medications, but also by the hospitalizations, emergency room visits, and lost revenue from missed work and school days that occur when disease flares occur [5, 13, 16]. These disease flares are at least partially caused by lack of adherence to daily medication regimens [15, 17]. Improved access to inhalers and asthma medications through increased generic medications in the market should lead to an improvement in medication adherence and to a decrease in the overall economic burden of asthma and COPD in the USA.

To address the increasing cost of brand-name prescriptions that COPD and asthma patients continue to face, the U.S. Food and Drug Administration (FDA) has devoted considerable resources into regulatory science initiatives aimed at improving efficiency in generic development and review through science-based innovation in bioequivalence assessment methods [18]. While product-associated complexities with OIDPs still pose challenges in demonstration of bioequivalence for generic development [19], FDA's research efforts and communication with the generic industry through product-specific guidances [20, 21] has recently resulted in the market introduction of first generics for dry powder inhalers (DPIs) and metered dose inhalers (MDIs) (Table 1). In early 2019, Wixela™ Inhub™ (fluticasone propionate and salmeterol xinafoate) inhalation powder (ANDA 208891) became the first generic DPI approved in the USA referencing the brand-name Advair Diskus® fluticasone propionate and salmeterol xinafoate inhalation powder. This is significant because Advair Diskus® has historically been one of the most prescribed brand-name drugs of any class [22],

and it is used in the daily maintenance treatment of both asthma and COPD. In 2020, the albuterol sulfate metered inhalation aerosol became the first generic MDI referencing ProAir HFA® (albuterol sulfate) metered inhalation aerosol. Introduction of the approved generic drugs for Advair Diskus® and ProAir HFA® to the U.S. respiratory drug market has the potential for a significant public health impact through decreased cost and increased accessibility to medication for the millions of Americans requiring these medications for daily and breakthrough treatment of asthma and COPD.

As more generics enter the market, there is an expectation that the increased competition will result in cost reductions for patients purchasing the medication [23]. Cost reductions may also come from the market introduction of an “authorized generic”. Distinct from the other generics approved under an abbreviated new drug application (ANDA), authorized generics are manufactured by the same company (also referred to as innovator company) as the brand-name drug, under the same processes, and often alongside the brand-name drug. However, authorized generics are not marketed under the brand-name and may not mention their association with the innovator company in their labeling [24, 25]. Despite not using the brand-name, an authorized generic is marketed under the brand-name's new drug application (NDA) number, and as such is not listed separately in the FDA's *Approved Drug Products with Therapeutic Equivalent Evaluations* (more commonly referred to as the Orange Book) [26]. Companies owning and marketing a brand-name drug may choose to also market an authorized generic to its brand-name drug product (often at a discounted price), or license the authorized generic distribution to a separate company. Approved generics, on the other hand, generally may contain permissible differences from their reference listed drug (RLD) and are demonstrated to be bioequivalent (BE) following review and approval of the submitted ANDA. The presence of authorized generics in the generic marketplace has been controversial in terms of their effect on drug price competition, mainly due to their coexistence with approved generics [27].

The recent introduction of generic and authorized generic DPIs and MDIs provides an opportunity to evaluate how the marketing of these products may impact related drug costs for asthma and COPD patients. In particular, ICS/LABA containing DPIs and MDIs were evaluated since these are widely prescribed treatments for asthma and COPD and provided examples of generic and authorized generic products marketed together as well as marketed alone for the latter [28]. We hypothesized that introduction of the first generic would lead to significant drug cost-savings during the first year for its related class of medications, while the savings from an authorized generic marketed alone might be limited.

Table 1 Approved generic and authorized generic orally inhaled drug products (OIDPs)

Active ingredient(s)	Dosage form; route	Application number	Category	Company	Approval date or date entered market	Brand name product (application number)
Albuterol Sulfate	Aerosol, Metered; Inhalation	203760 ^a	Generic	Perrigo Pharmaceuticals Co	February 24, 2020	ProAir HFA (021457)
Albuterol Sulfate	Aerosol, Metered; Inhalation	209954	Generic	Lupin Inc	August 24, 2020	ProAir HFA (021457)
Albuterol Sulfate	Aerosol, Metered; Inhalation	021457	Authorized Generic	Teva Branded Pharmaceutical products R&D, Inc	January 2019	ProAir HFA (021457)
Albuterol Sulfate	Aerosol, Metered; Inhalation	209959	Generic	Cipla Ltd	April 8, 2020	Proventil HFA (020503)
Albuterol Sulfate	Aerosol, Metered; Inhalation	020503	Authorized Generic	Kindeva Drug Delivery L.P	April 2019	Proventil HFA (020503)
Budesonide; Formoterol Fumarate Dihydrate	Aerosol, Metered; Inhalation	021929	Authorized Generic	Prasco	January 1, 2020	Symbicort (021929)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	208891 ^a	Generic	Mylan Pharmaceuticals Inc	January 30, 2019	Advair Diskus (021077)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	203433	Generic	Hikma Pharmaceuticals USA Inc	December 17, 2020	Advair Diskus (021077)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	021077	Authorized Generic	GlaxoSmithKline Intellectual Prop. Ltd. England	February 2019	Advair Diskus (021077)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	208799	Authorized Generic	Teva Branded Pharmaceutical Products R&D Inc	April 2017	AirDuo RespiClick (208799)

^aFirst Generic

Methods

We used IQVIA data to investigate the trends in national monthly estimates of drug wholesale and drug dispensing from January 2015 to November 2020 for Advair Diskus®, Symbicort®, and Airduo Respiclick®, their authorized generic products and newly released generic for Advair Diskus®. Both Symbicort® and Airduo Respiclick® were included in the analysis to evaluate how marketing an authorized generic impacts the brand-name product when a generic is not currently being marketed. Also, Symbicort® and its authorized generic were included because of the increasing role of ICS-formoterol in asthma management guidelines published by the Global Initiative for Asthma (GINA) in 2019 [29] and by the National Asthma Education and Prevention Program (NAEPP) in 2020 [30]. Breo® Ellipta®, approved in May 2013 (lower strength) and April 2015 (higher strength), was included because it is a DPI that contains a similar ICS (fluticasone furoate) as Advair® Diskus® (fluticasone propionate and salmeterol xinafoate) combined with a different LABA (vilanterol) that allows for less

frequent dosing. Furthermore, it is marketed by the maker of Advair® Diskus®, GSK. Airduo Respiclick® and its authorized generic were launched in 2017 and were grouped into “others” along with Advair® HFA, Dulera®, and Airduo® Digihaler® in Figs. 1, 2, and 3. Table 2 lists the brand-name and generic drugs included in this analysis.

IQVIA provides information about invoice transaction pricing of pharmaceutical sales through National Sales Perspective (NSP) and dispensing through the National Prescription Audit (NPA). As units of analysis for our study, NSP provides monthly projected sales volume in dollars (\$) and units of pharmaceutical products purchased by retail and non-retail providers, such as retail drugstores, hospitals, clinics, and other non-retail type outlets such as HMO and long-term care facilities. It captures 89% of raw sales directly from ~100 manufacturers and indirectly from 442 suppliers. The wholesale unit cost for each product were estimated based on sales volumes divided by units purchased.

NPA was used to monitor monthly projected prescriptions dispensed by the pharmacist to the consumer and is based on a sample of approximately 49,900 retail stores, 168 mail-order

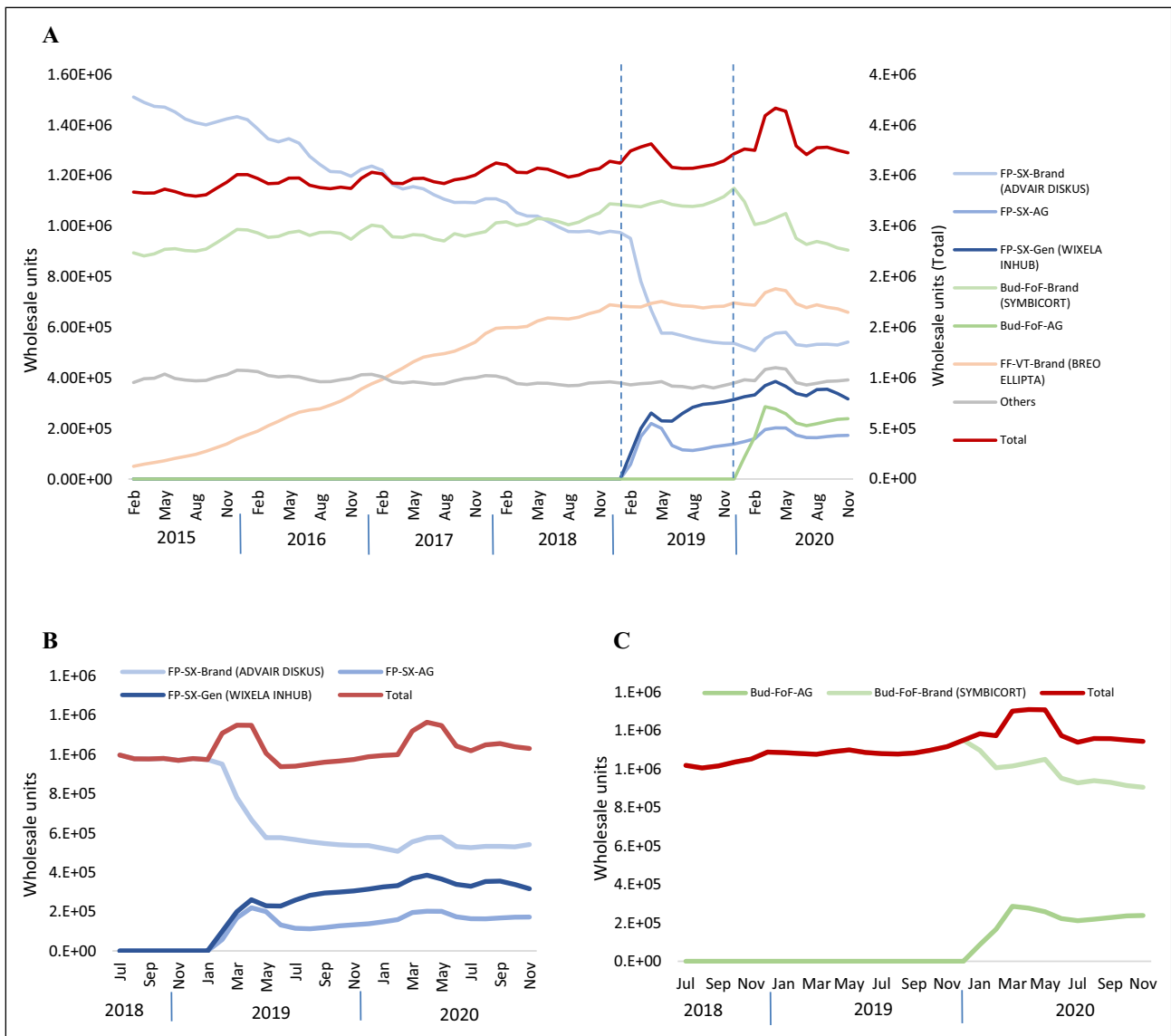


Fig. 1 Wholesale units of selected orally inhaled drug products (OIDPs) with their generics in the USA. **A** Estimates of all ICS/LABA OIDPs. The first gridline indicates the launching of Wixela and the authorized generic (AG) for Advair; the second indicates that

of AG for Symbicort. The total of the sum of all OIDPs. **B** Estimates of Advair Diskus, its AG, and Wixela. The total is the sum of all three products. **C** Estimates of Symbicort and its AG. The total is the sum of both products

distributors, and 2000 long-term care facilities. It includes patient age and gender through NPA Extended Insights, as well as deidentified patient-level data with longitudinal data to capture those who were naïve to the drug products. Three classes of treatments were defined for patients who had a prescription dispensed filling current therapy and, during the assigned look-back period, (1) had not filled any therapy within the defined Uniform System of Classification (USC) 3 or 4 relevant defined market (new therapy start Rx); (2) had never filled the product previously but filled another USC 3 or USC 4 relevant defined market drug (switch to/add-on Rx); and (3) had filled the same product previously (continuing Rx). We used the first two therapy patterns, respectively, to

approximate the generic initiation and substitution for patients treated with generics.

Finally, we used the Total Patient Tracker® to capture the demographics of the patients treated with different types of OIDPs.

Results

Pharmaceutical Whole Sales

Figure 1 shows the units of pharmaceutical whole sales of selected OIDPs from 2015 to 2020: (i) Advair Diskus®

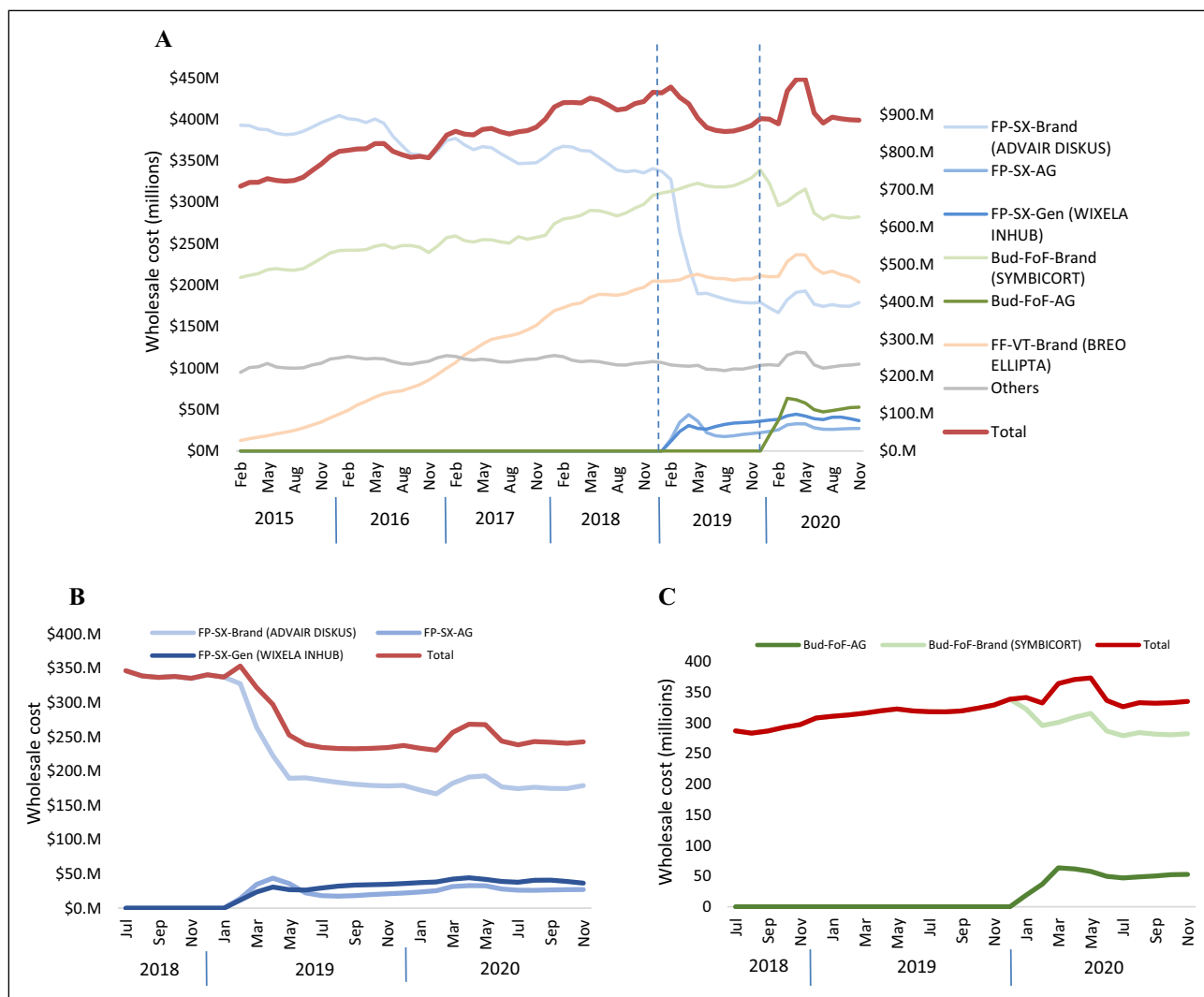


Fig. 2 Cost of selected orally inhaled drug products (OIDPs) with their generics in the USA. **A** Estimates of all ICS/LABA OIDPs. The first gridline indicates the launching of Wixela and the authorized generic (AG) for Advair; the second indicates that of AG for Symbi-

cort. The total of the sum of all OIDPs. **B** Estimates of Advair Diskus, its AG, and Wixela. The total is the sum of all three products. **C** Estimates of Symbicort and its AG. The total is the sum of both products

and its generic Wixela™ Inhub™ and authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder; (ii) Symbicort® and its authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered; (iii) Breo Ellipta®; and (iv) several OIDPs grouped together in an “others” category (i.e., Advair® HFA, Dulera®, Airduo® Respiclick® and its authorized generic, and Airduo® Digihaler®). The number of wholesale units for the ‘others’ category remained relatively constant between 2015 and 2020.

Prior to the marketing of Wixela™ Inhub™ in February 2019, there were increasing trends in sales of Breo Ellipta® and to a lesser extent, Symbicort®, which were associated with a gradual decrease in the wholesale units for Advair

Diskus® (Fig. 1A). Following the concurrent marketing of Wixela™ Inhub™ and authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder, the gradual decrease in Advair Diskus® wholesale units turned into drastic decrease from 951,324 in January 2019 to 577,006 in May 2019 (Fig. 1B). In the last 2 years, the combined (generic, authorized generic, and brand) number of wholesale units for this class of ICS/LABAs only showed transient increases following generic introduction and COVID-19 pandemic. Although there were similar increases in the wholesale units for Wixela™ Inhub™ and authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder in the first three months of marketing, Wixela™ Inhub™ sales have overtaken that of the authorized

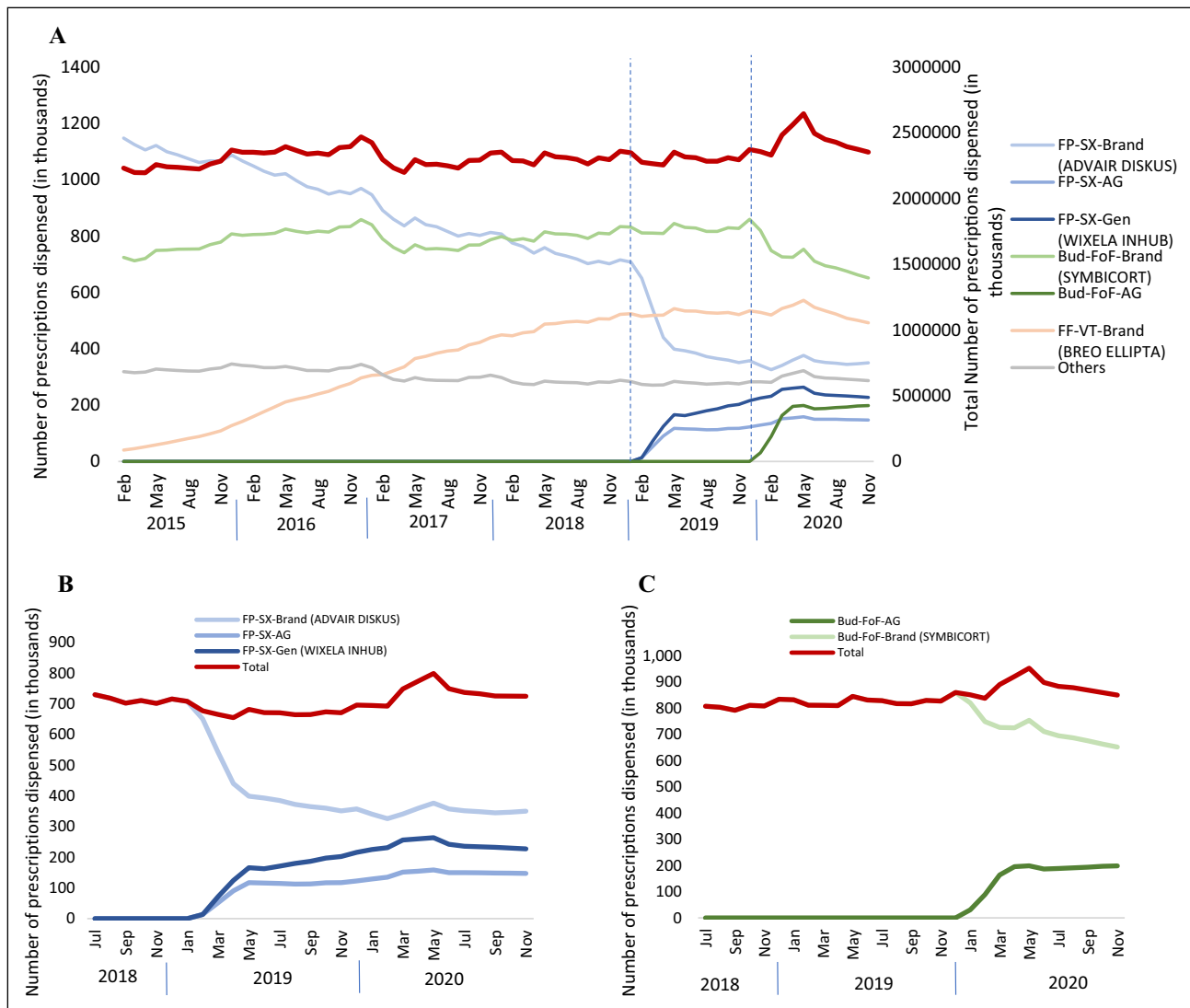


Fig. 3 Prescriptions of selected orally inhaled drug products (OIDPs) with their generics in the USA. **A** Estimates of all ICS/LABA OIDPs. The first gridline indicates the launching of Wixela and the authorized generic (AG) for Advair; the second indicates that of AG for

Symbicort. The total of the sum of all OIDPs. **B** Estimates of Advair Diskus, its AG, and Wixela. The total is the sum of all three products. **C** Estimates of Symbicort and its AG. The total is the sum of both products

generic but still have fallen behind Advair Diskus® sales as of November 2020 in terms of wholesale units in a 3-month moving average. The marketing of authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered in January 2020 resulted in decrease in Symbicort® wholesale units and led to a transient increase in the combined sales units (Fig. 1C).

As for wholesale costs, similar trends were observed as that of the wholesale units (Fig. 2). However, the overall cost for the Advair Diskus® and its associated generics decreased from \$337 million in January 2019 to \$233 million in January 2020 (Fig. 2B). In comparison, the sole marketing of an authorized generic for Symbicort® did not result in a similar level of savings for overall cost (Fig. 2C). The averaged

unit cost for Wixela™ Inhub™ was \$115 compared to \$169 for the authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder and \$334 for the RLD Advair Diskus®. In comparison, the mean unit cost for the authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered was \$229 and that for Symbicort® itself was \$294, a much smaller cost difference between brand-name and authorized generic.

Prescription Estimates

The overall prescription estimates for the selected fluticasone/salmeterol OIDPs remained unchanged upon launching of the first generic Wixela™ Inhub™ (Fig. 3A, B).

Table 2 List of orally inhaled drug products (OIDPs) included in the study

Brand/Generic proprietary name	ICS	LABA	Dosage form; route	Application number	Category	Company	Approval date or date entered market	Figure legend title
ADVAIR DISKUS	Fluticasone Propionate	Salmeterol Xinafoate	Powder; Inhalation	021077	Brand	GlaxoSmithKline Intellectual Prop. Ltd. England	August 24, 2000	FP-SX-Brand
BREO ELLIPTA	Fluticasone Furoate	Vilanterol Trifenatate	Powder; Inhalation	204275	Brand	GlaxoSmithKline Intellectual Prop. Ltd. England	May 10, 2013	FF-VT-Brand
SYMBICORT	Budesonide	Formoterol fumarate dihydrate	Aerosol, Metered; Inhalation	021929	Brand	Astra Zeneca LP	July 21, 2006	Bud-FoF-Brand
WIXELA INHUB	Fluticasone Propionate	Salmeterol Xinafoate	Powder; Inhalation	208891	Generic	Mylan Pharmaceuticals Inc	January 30, 2019	FP-SX-Gen
Fluticasone propionate; salmeterol xinafoate inhalation powder	Fluticasone Propionate	Salmeterol Xinafoate	Powder; Inhalation	203433	Authorized Generic	GlaxoSmithKline Intellectual Prop. Ltd. England	December 17, 2020	FP-SX-AG
Budesonide; Formoterol fumarate dihydrate Inhalation Aerosol	Budesonide	Formoterol fumarate dihydrate	Aerosol, Metered; Inhalation	021929	Authorized Generic	Prasco	January 1, 2020	Bud-FoF-AG

The launching of the authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered was associated with a transient increase (13.7%) in treatment volumes that coincided with the COVID-19 pandemic (Fig. 3A, C).

Generic Substitution

We used number of treatments for switch/add therapy and start of new therapy to monitor the generic substitution and initiation, respectively (Fig. 4). Generic substitution as described by the number of treatments for switch/add therapy, peaked three to four months after the marketing of generics and returned to around 50% of the peak values within a year (Fig. 4A). In comparison, generic initiation as described by the number of treatments for new therapy, peaked only after one year for both Wixela™ Inhub™ and authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder (Fig. 4B).

Overall, the number of treatments for patients substituted or initiated with generic Wixela™ Inhub™ were estimated to be 562,111 and 312,248 per month, respectively. In comparison, fewer patients were treated with authorized generics for either fluticasone propionate and salmeterol xinafoate inhalation powder or budesonide and formoterol fumarate dihydrate inhalation aerosol metered (Fig. 5A). Figure 5B shows the demographic distributions for patients who received the generic or authorized generics studied. With respect to distribution of copayments, 35.1% of patients who received the authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered did not have a copayment. As for Wixela™ Inhub™, over 30% of patients had either no copay or minimal copayment (no more than

\$10), compared to under 25% for those who received Advair Diskus®. Overall, 63.2% of patients paid no more than \$10 in copayment (including zero copay) for the authorized generic budesonide and formoterol fumarate dihydrate inhalation aerosol metered, followed by 61.6% of patients who were dispensed Wixela™ Inhub™, compared to 52.0% of patients who were dispensed the authorized generic fluticasone propionate and salmeterol xinafoate inhalation powder (Fig. 5C).

Discussion

Our study demonstrates that the approval and introduction of the generic for Advair Diskus® (branded by the generic manufacturer as Wixela™ Inhub™) to the U.S. market in January 2019 led to an estimated annual cost-savings of \$941 million, as the overall U.S. prescription cost for the combined Advair Diskus® and generic market decreased from \$337 million/month in January 2019 (in the absence of generic) to \$233 million/month in January 2020.

At the individual patient level, during the period of our study (January 2015 to November 2020), the average cost of an Advair Diskus® inhaler was \$334, while the generic Wixela™ Inhub™ was \$115. This amounts to a significant cost-savings for each unit purchased. The wholesale price comparison portends increased affordability, even though our study did not capture the actual cost for patients at the pharmacy counter, such as savings based on health insurance or coupons. For patients with medication coverage via health insurance, generic availability on the market still leads to cost-savings at the pharmacy since the co-pay for generics

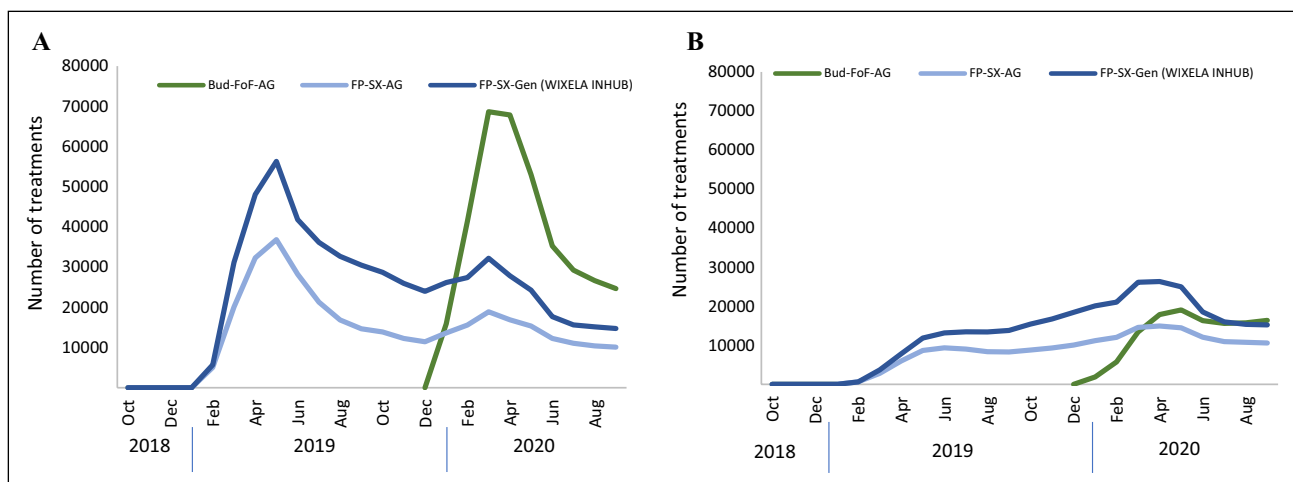


Fig. 4 Generic substitution (A) and initiation (B) of selected ICS/LABA orally inhaled drug products (OIDPs) in the USA from Oct 2018 to Oct 2020. **A** Estimates of treatments switched to Wixela,

authorized generic (AG) for Advair Diskus, or AG for Symbicort. **B** Estimates of treatments initiated with Wixela, AG for Advair Diskus, or AG for Symbicort

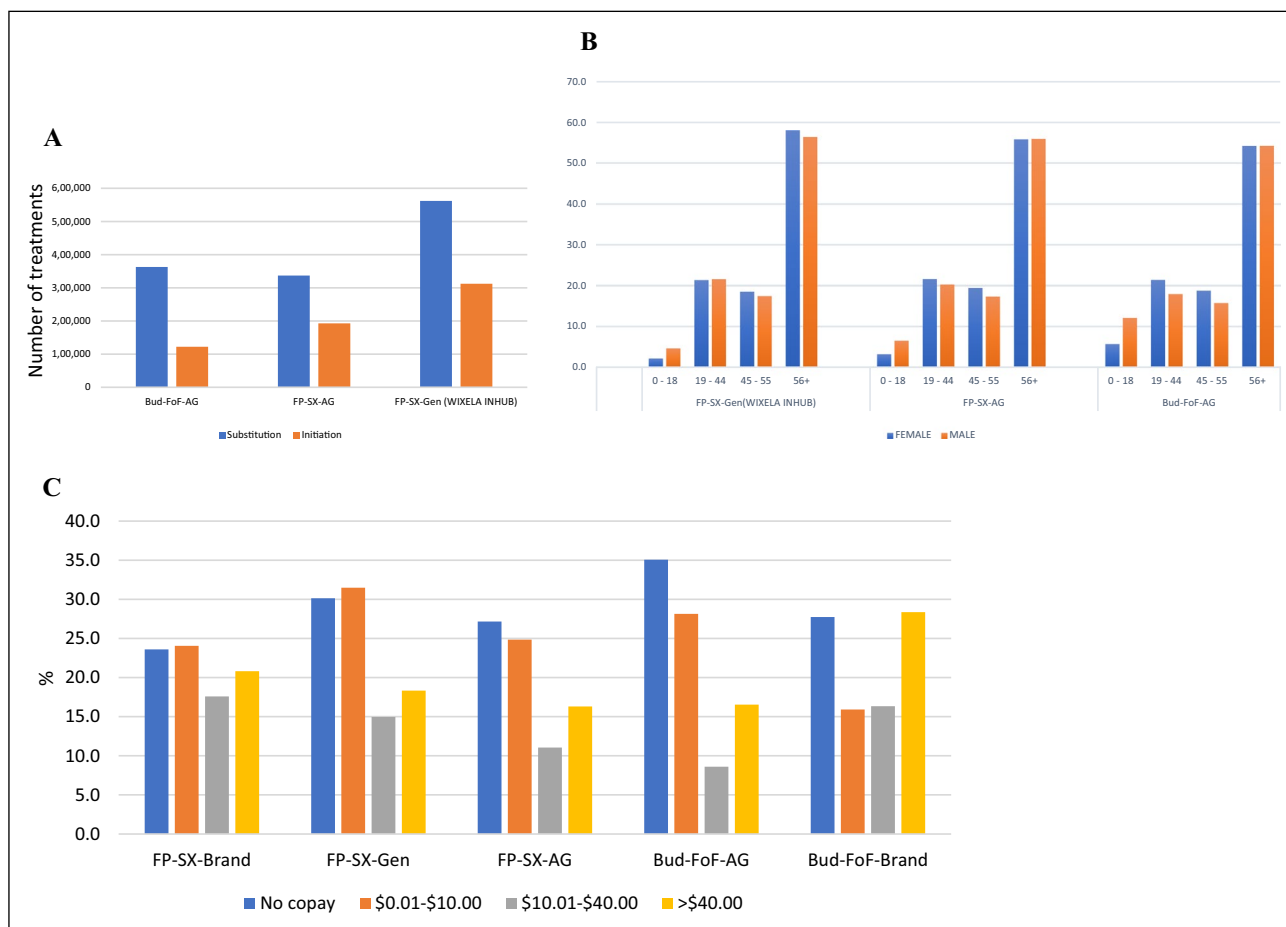


Fig. 5 **A** The total estimates of number of treatments through generic substitution and initiation with Wixela, authorized generic (AG) for Advair Diskus, or AG for Symbicort. **B** Gender and Age distributions

of patients who were treated with Wixela, authorized generic (AG) for Advair Diskus, or AG for Symbicort. **C** Copayment structure for the payments for selected orally inhaled drug products (OIDPs)

tends to be lower than that for the branded and some authorized generic medications (Fig. 5C).

Generally, the authorized generic is priced higher than generics that are reviewed and approved through the ANDA process [27, 31]. As a generic enters the market, the market will typically shift away from the brand-name product, reducing its market share. With each generic approval, this reduction in market share can continue for the brand-name product. Innovator companies may choose to introduce an authorized generic to recapture a portion of this lost market share, or to minimize the impact from the first approved generic following release on a market. While an approved ANDA that is a first applicant entitled to 180-day exclusivity blocks approval of a subsequent applicant's ANDA, the innovator company may introduce an authorized generic of its brand-name product during this exclusivity period. Importantly, as an innovator company controls the marketing of the brand-name and the authorized generic version of their drug product, pricing data suggest that the marketing of an authorized generic likely does not exert significant

pressure on the innovator company to reduce cost of the drug product. Therefore, marketing of an authorized generic may offer a limited benefit to the patient in terms of adherence and overall health outcomes. As an example, only an authorized generic was available for Symbicort® during our study period, and the average cost of the authorized generic budesonide-formoterol was only slightly lower than the cost of the branded product Symbicort® (\$223 vs \$294 per unit).

Based on the market share and averaged unit price/cost of medications, we estimated that percent savings resulting from the Wixela™ Inhub™ inhalation powder and the authorized generic for Advair Diskus® was 22.4% for this class of products, compared to 12.3–16.5% for other medications with only one generic and an authorized generic during the 180-day exclusivity period (percentages derived from Table 4 of reference 32) [32]. For the entire year of 2019, the percentage saving from Wixela™ Inhub™ inhalation powder increased slightly to 23.3%. On average, the marketing of a first generic without a competing authorized generic provided a cost-savings to the patient at 31%

[23, 27, 33–35]. Therefore, the introduction of Wixela™ Inhub™ inhalation powder has performed well compared to other generic products with competing authorized generics, as well as to those without. It is noted that ancillary price concessions such as consumer rebates given by manufacturers for brand-name inhalers have not been accounted in the current analysis, in part because the cost to the consumer is likely to vary depending on the markup at the retail level and types of payments made through the pharmacy supply chain. While rebates for inhaler products may be common, they often require consumer action, which will have a variable effect for different consumers. In addition, rebate utilization data is not publicly available. Finally, we should also keep in mind that rebates are often a by-product of the concern of price reductions caused by the entrance or anticipated entrance of a generic for a given product.

One strength of our study was that we were able to evaluate the trends in the availability and pricing of Advair Diskus® and its generics (including Wixela™ Inhub™) in the context of trends observed for other OIDs on the market concurrently. In fact, drug pricing and utilization can be affected by factors other than the introduction of generics to the marketplace, such as other drugs entering the marketplace and changes in clinical guidelines for the management of asthma. For our study, we evaluated trends in related ICS-LABA products, namely Breo® Ellipta® and Symbicort®. Approved in May 2013, Breo® Ellipta® is a DPI that is also manufactured by GSK with similar indications for the treatment of asthma and COPD as Advair Diskus®, and has less frequent dosing that is expected to help patient adherence. Thus, its market uptake since its introduction is important to consider, as it is correlated with a very slow market decline in Advair Diskus®. Of note, the patents on Advair Diskus® expired in 2016. In the years preceding that expiration, from 2013 to 2015, GSK launched four drug products (including Breo® Ellipta®) related to Advair Diskus® [36]. A decline of more than \$100 million per month in sales of Advair Diskus® during this time period was partially offset by these newly launched related drug products. With the introduction of Wixela™ Inhub™ inhalation powder to the market, market uptake of Breo® Ellipta® appeared to plateau, possibly because Wixela™ Inhub™ is a lower priced option for the same indication. Importantly, the data on changes in wholesale units and dispensing of the studied inhalers was very likely confounded by the increased demand for these products occurring with the emergence of the COVID-19 pandemic in the USA in March 2020. Many doctors prescribed inhalers normally used in the treatment of asthma or COPD to help patients that developed respiratory symptoms due to COVID-19 [37, 38]. It should also be noted that increase in patient adherence to the maintenance treatment may also lead to increased demands for inhalers. In addition, as concerns about use of nebulized medication causing

increased spread of the SARS-CoV-2 virus were prevalent, many patients with asthma and COPD were switched from nebulized maintenance therapies to MDIs and DPIs [39, 40]. As a result, an increase in wholesale units and dispensed drugs was seen in March 2020, as the COVID-19 pandemic progressed in the USA. This was followed by a decline and return to pre-March 2020 levels by June–July 2020 [37]. This transient increase in wholesale units and dispensed drugs was most likely due to the increased demand for these medications during the pandemic, rather than to any market effects from changes in drug availability or pricing. However, the increasing trend in dispensed doses for Wixela™ Inhub™ remained during the period of our study (January 2015 to November 2020), even after the transient changes in demand attributable to COVID-19 had passed, as seen from demand returning to pre-COVID-19 levels (Fig. 3A). Therefore, even accounting for market influences attributable to the COVID-19 pandemic, this study provides support for the positive impact of approved generics like Wixela™ Inhub™ on reducing prescription costs for patients.

Conclusion

For medications that can treat diseases like asthma and COPD, expanding the availability of approved generics continues to be a slow and challenging process, owing to the complexity of dosage forms that treat respiratory diseases, as well as the substantial challenges associated with demonstrating bioequivalence for these drug products. FDA has recognized these challenges and remains committed to facilitating greater access to approved generics for these drug products through regulatory science initiatives funded through the Generic Drug User Fees Amendments (GDUFA). This paper quantified the benefit to the patient with the approval of the first generic fluticasone propionate and salmeterol xinafoate inhalation powder to the brand product Advair Diskus®. While an innovator company may introduce an authorized generic at lower cost than that of the branded product, our study suggests that an authorized generic alone offers limited savings to prescription costs based on the comparison of products with both authorized generic and an approved generic against products with only an authorized generic. We showed that significant cost-savings are associated with the marketing of approved generics even in the presence of authorized generic(s), affirming that continuing efforts to expand the availability of approved generics will likely have a sustained and robust benefit to public health.

Author Contributions

Substantial contributions to the conception or design of the work (ZW, SKA, BN, SD, LZ, MCL); or the acquisition, analysis, or interpretation of data for the work (ZW, SD, MCL); and drafting the work or revising it critically for important intellectual content (ZW, SKA, BN, SD, MCL); and final approval of the version to be published (LZ, MCL); and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated.

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Declarations

Conflict of interest

Authors report no conflict of interest.

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