

Post-Approval Impact of Generic Fluticasone Propionate & Salmeterol Inhalation Powder (RLD: Advair Diskus)

***SBIA 2023—Advancing Generic Drug Development:
Translating Science to Approval***

***Day 2, Session 5: Noteworthy Complex Generic Drug Approval & Research: Orally Inhaled
Products***

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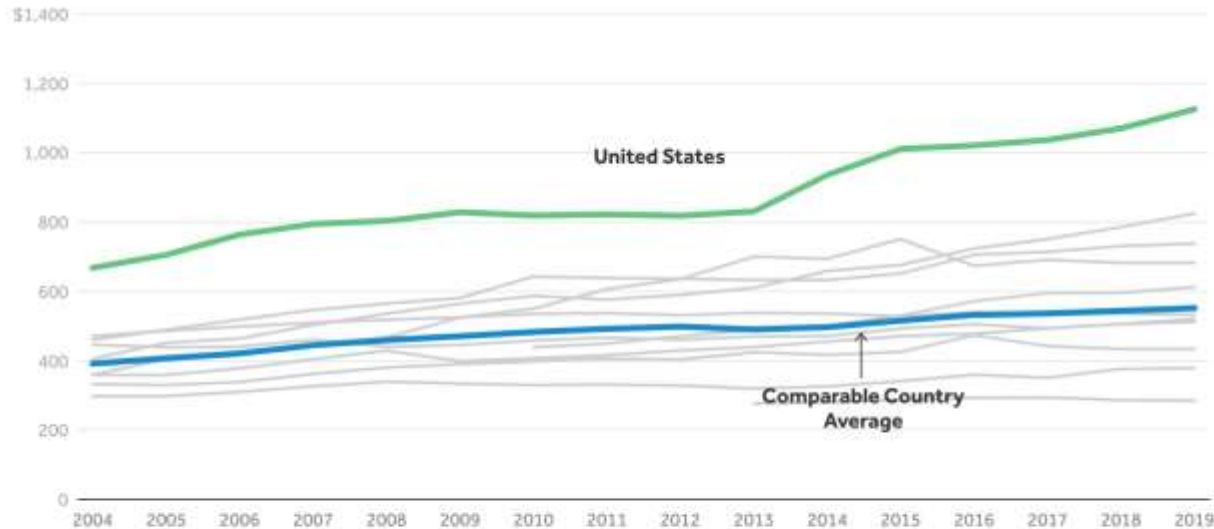
Learning Objectives

- Describe the high costs of inhalers in the United States and the effect on patient outcomes
- Identify the difference between an approved generic (ANDA) and an authorized generic
- Describe the post-market impact of ANDA approved generic and authorized generic inhalers

U.S. per capita prescription spending is higher than comparable countries



Per capita prescribed medicine spending, U.S. dollars, 2004-2019



Notes: Data not available for Switzerland from 2004-2009; for the United Kingdom from 2004-2012; Australia and Japan for 2019 (data from 2018 for these two countries are extrapolated for the 2019 comparable country average). Canada's 2019 value is provisional.

Source: OECD

Peterson-KFF
Health System Tracker

Inhalers are a substantial cost to the U.S. healthcare system



- Medicaid spent \$26.2B on inhalers from 2012-2018 with annual spending increasing from \$2.1B to \$4.6B (120%)
- Inhaled corticosteroid/long-acting beta-agonist (ICS/LABA) combination inhalers represented 53% of that spending and increased 607%
- Almost 7% of the \$168B spent by Medicare Part D in 2018 went toward inhalers for asthma or COPD

Sources: Sistani et al. 2021, Feldman et al. 2021

In the United States, cost barriers to obtaining medicine is associated with:



- Uncontrolled asthma in adults and children
- Experiencing at least one asthma-related hospitalization in patients 65 and older
- Higher likelihood of abandoning inhaler therapy in COPD patients



Sources: Zahran et al. 2015, Hsu et al. 2018, Patel et al. 2022

Investigating the impact of generic inhaler approval



- Wixela Inhub, a generic dry powder inhaler (DPI) referencing Advair Diskus, was approved in January 2019 through submission of an ANDA
- An authorized generic of Advair Diskus entered the market in February 2019
- FDA investigators published research investigating the medication cost savings and utilization of generic ICS/LABA products in the United States using IQVIA data
- The investigators hypothesized that introduction of the first approved generic would lead to cost savings compared to an authorized generic

Source: Wang et al. 2022

Authorized generics are distinct from approved generics



- Authorized generics are identical to a brand-name drug and are marketed under the same new drug application (NDA) but do not display a brand name
- Approved generics may have differences from the brand-name drug but are required to demonstrate bioequivalence through an ANDA

Authorized generic market impact



- A 2011 U.S. Federal Trade Commission (FTC) report found that authorized generics impact the marketplace in several ways:
 - Authorized generic competition during the 180-day exclusivity period of an approved generic led to modestly lower prices (4-8%)
 - Authorized generics have a substantial negative effect on the revenues of competing generic firms
 - Brand companies may be using the threat of authorized generics to prompt generic companies to delay their products, leading to limited market competition and higher prices for consumers

Source: U.S. FTC 2011

Key generic products included in FDA's investigation

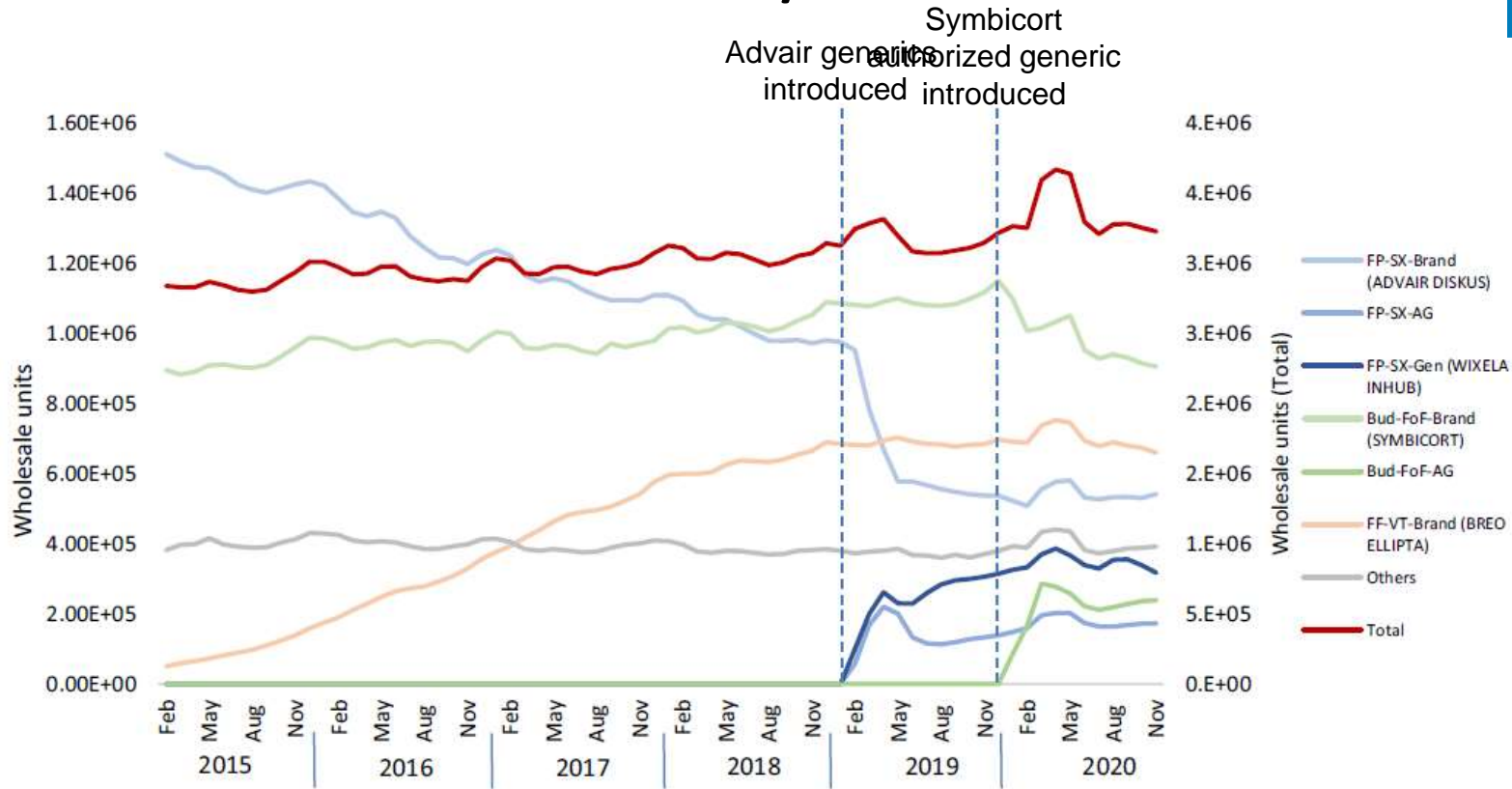


Active ingredient(s)	Dosage form; route	Application number	Category	Company	Approval date or date entered market	Brand name product (application number)
Budesonide; Formoterol Fumarate Dihydrate	Aerosol, Metered: Inhalation	021929	Authorized Generic	Prasco	January 1, 2020	Symbicort (021929)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	208891 ^a	Generic	Mylan Pharmaceuticals Inc	January 30, 2019	Advair Diskus (021077)
Fluticasone Propionate; Salmeterol Xinafoate	Powder; Inhalation	021077	Authorized Generic	GlaxoSmithKline Intellectual Prop. Ltd. England	February 2019	Advair Diskus (021077)

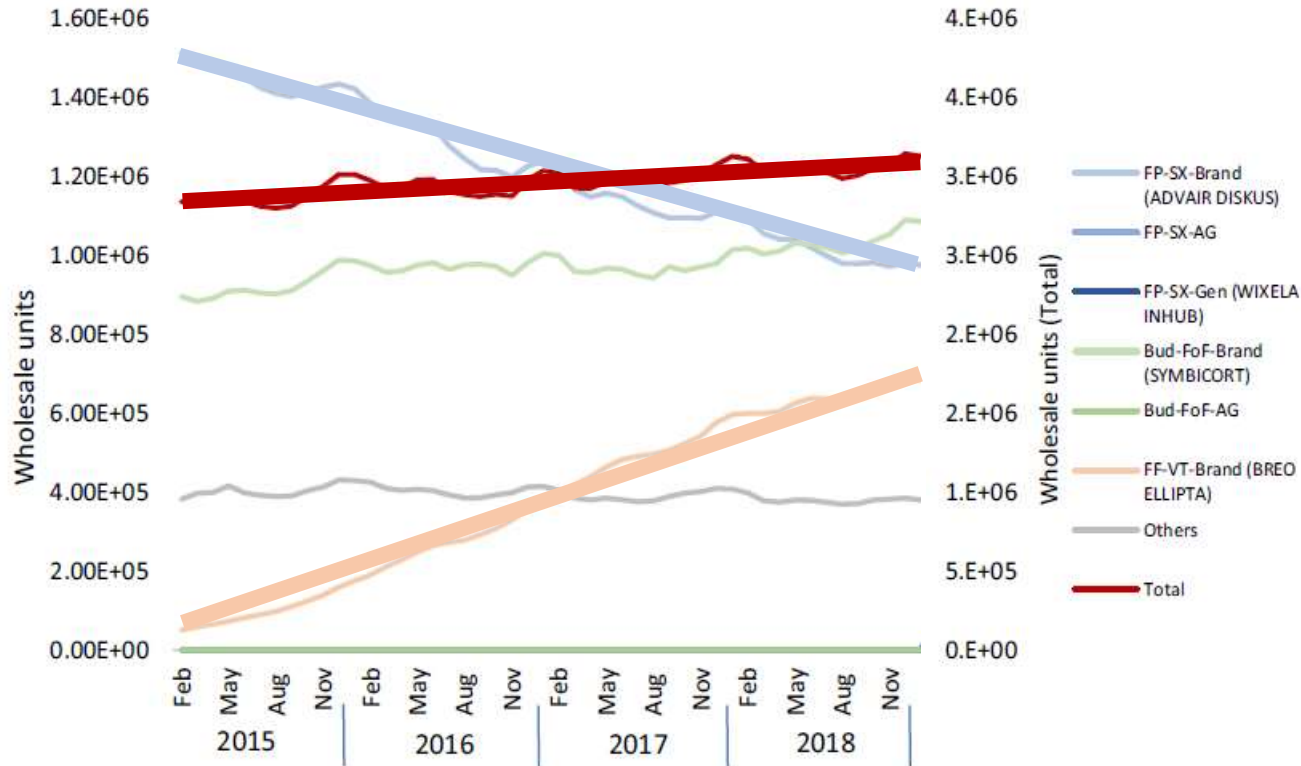
- First approved generic referencing Advair Diskus was introduced in January 2019 following ANDA approval
- Authorized generic of Advair Diskus introduced February 2019
- Authorized generic of Symbicort introduced January 2020

Table modified from: Wang et al. 2022

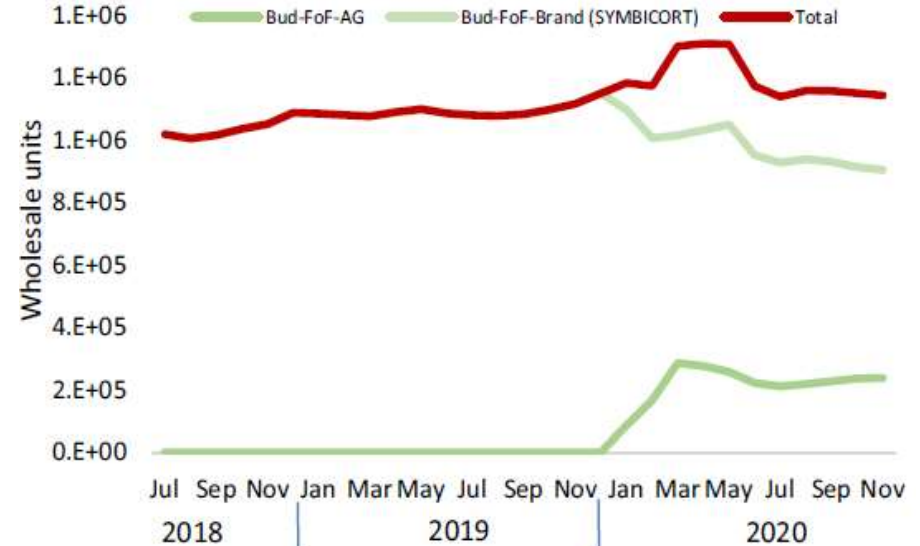
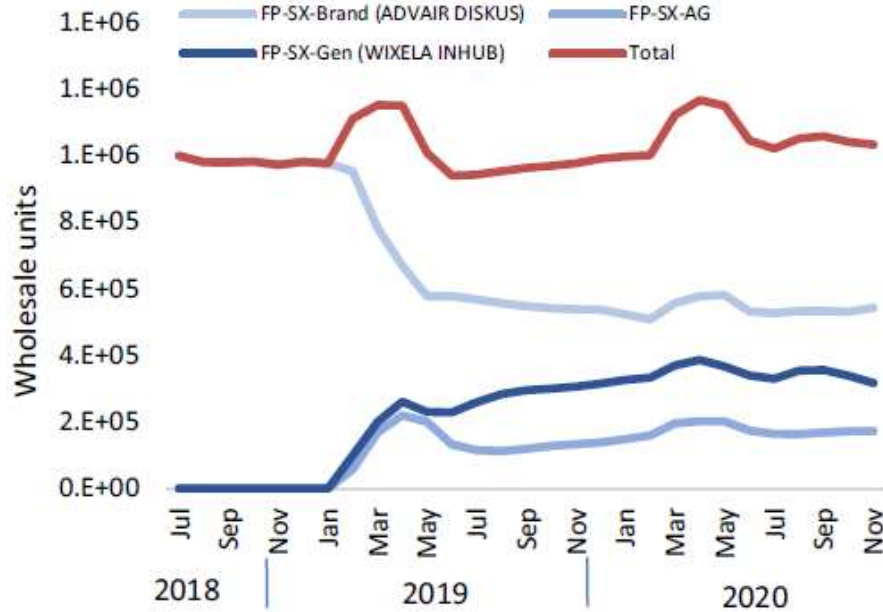
Wholesale units of ICS/LABAs 2015-2020



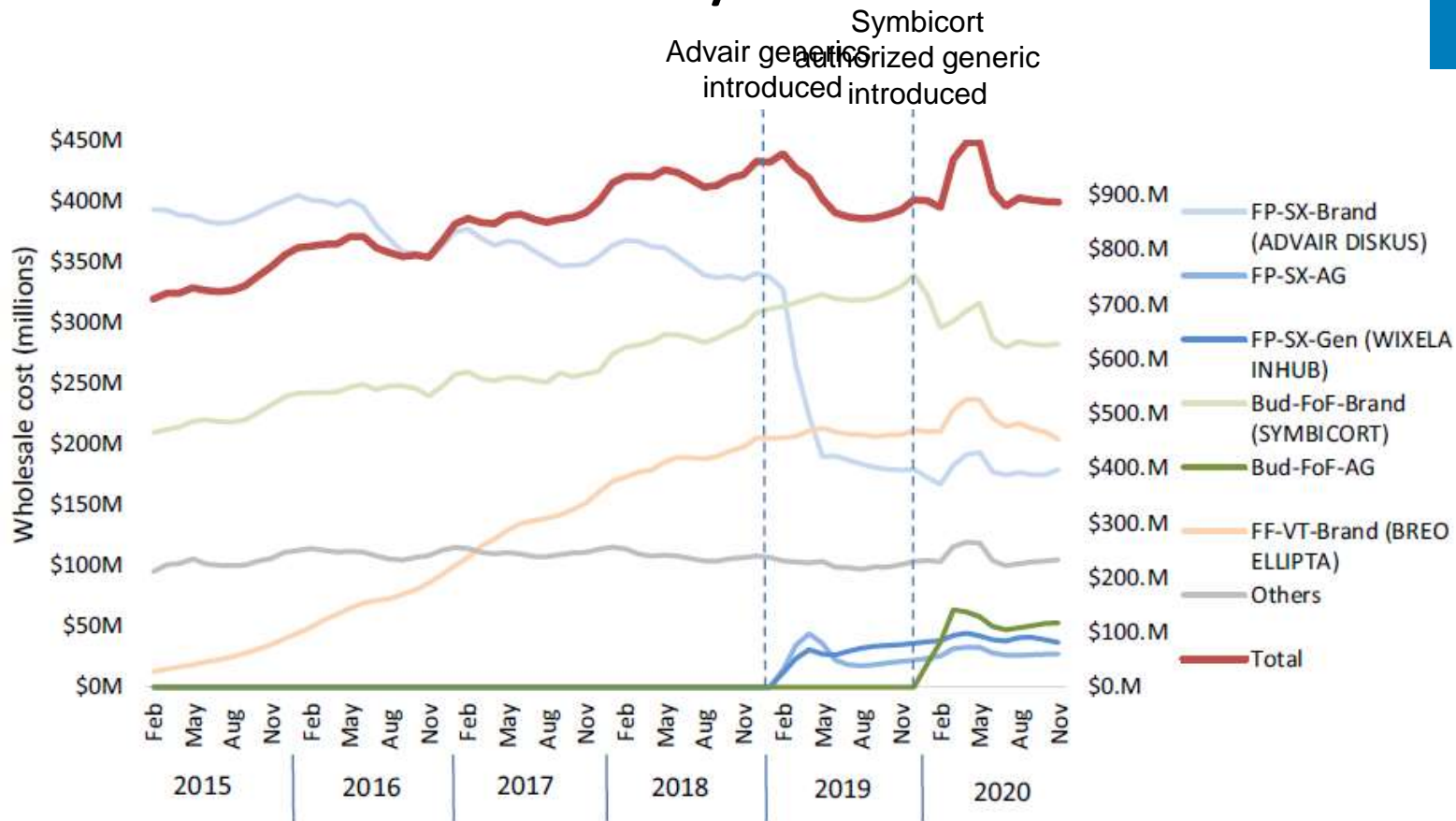
Before generic approval: Wholesale units 2015-2018



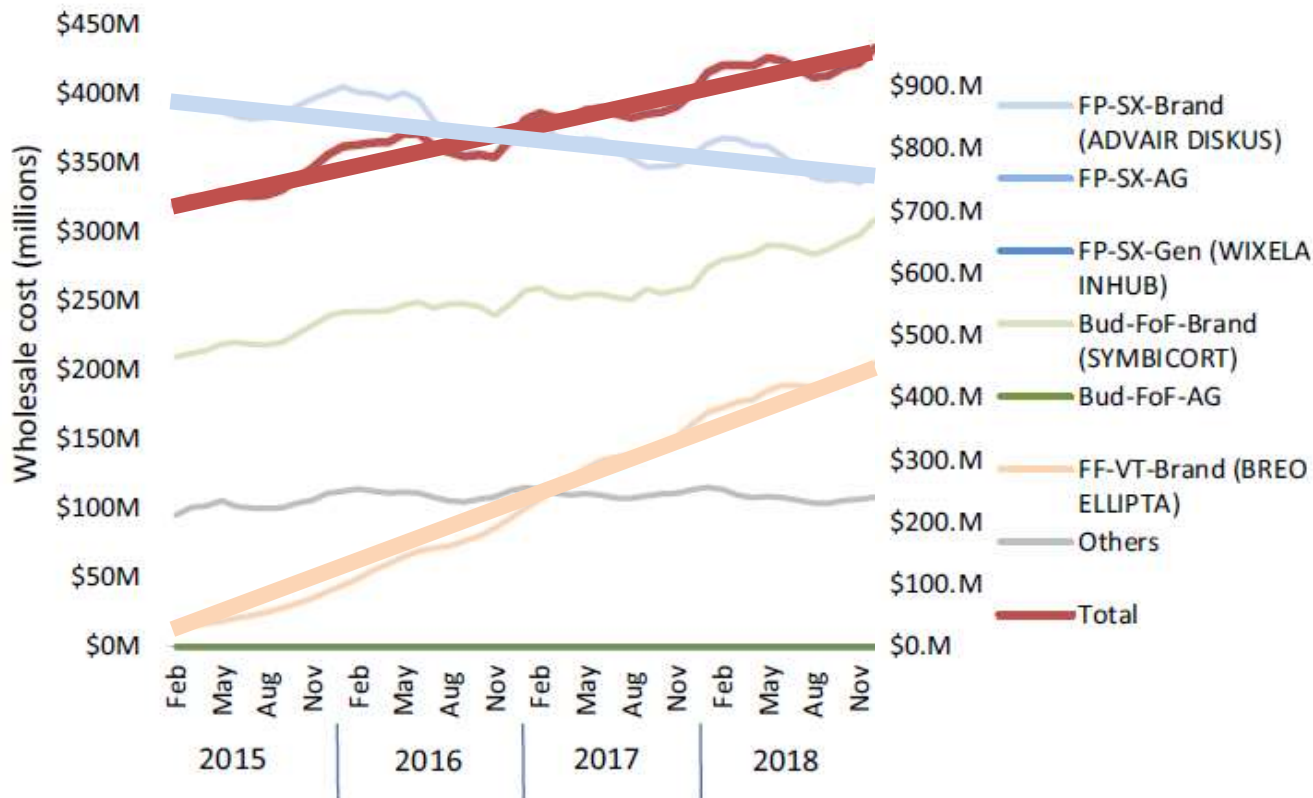
After generic approval: Wholesale units 2019-2020



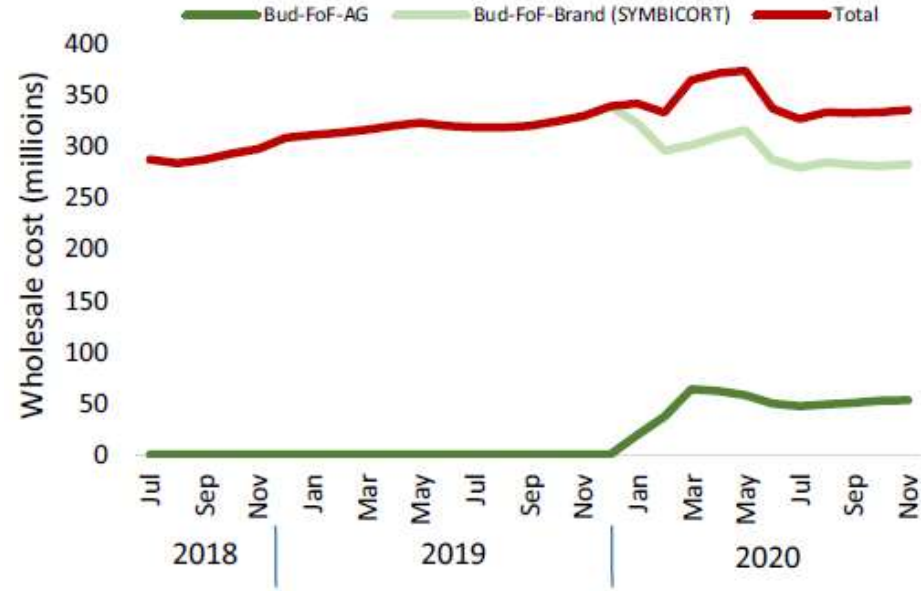
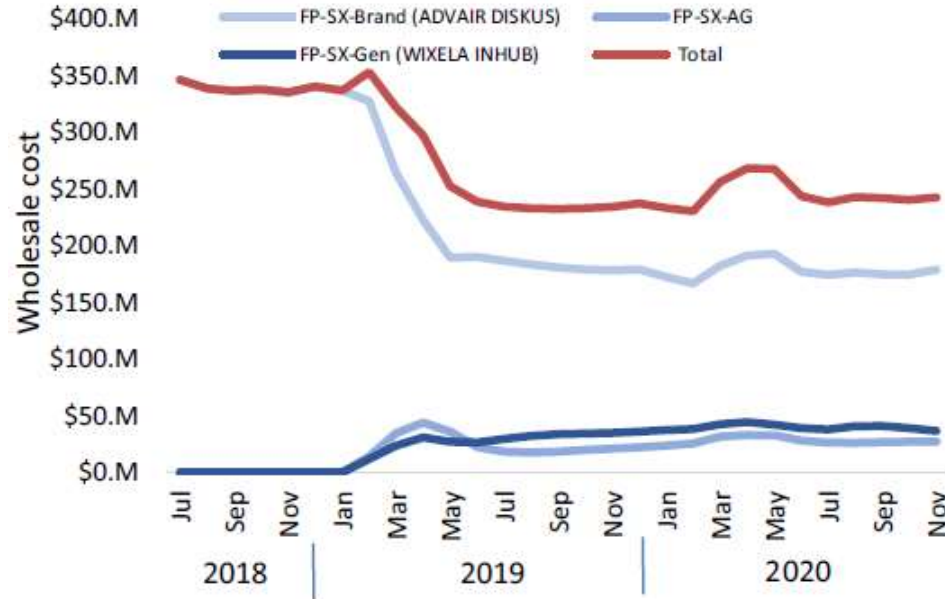
Wholesale cost of ICS/LABAs 2015-2020



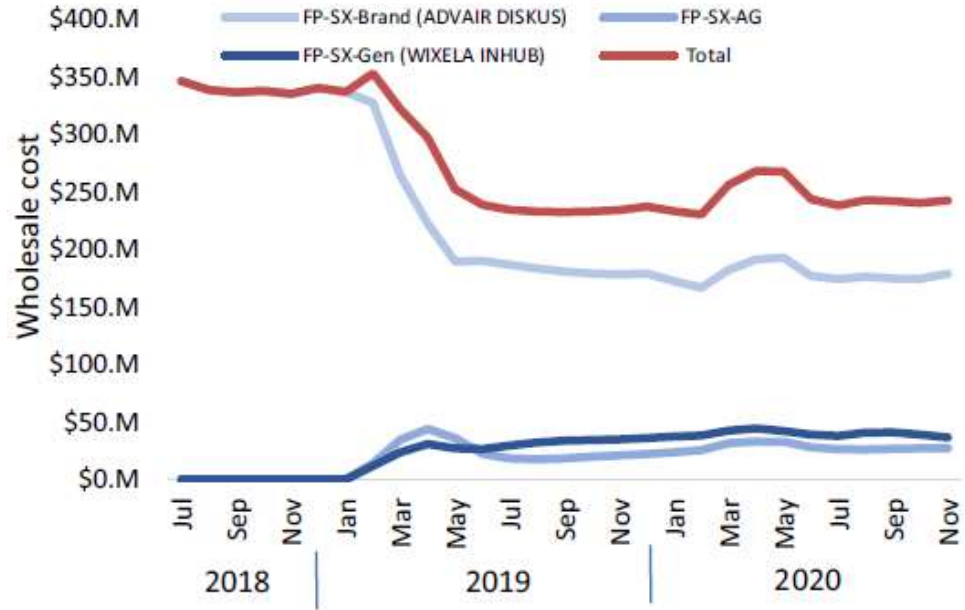
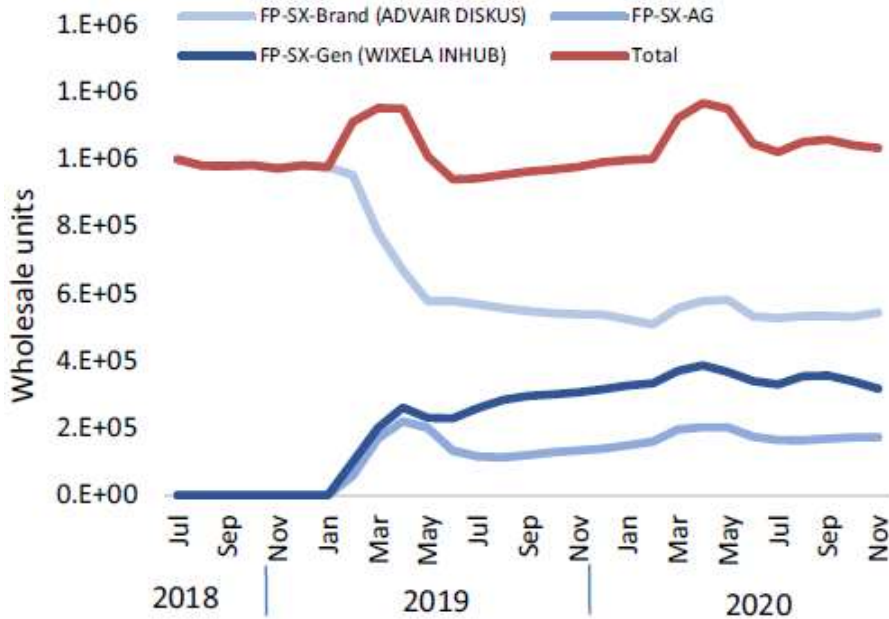
Before generic approval: Wholesale cost 2015-2018



After generic approval: Wholesale cost 2018-2020

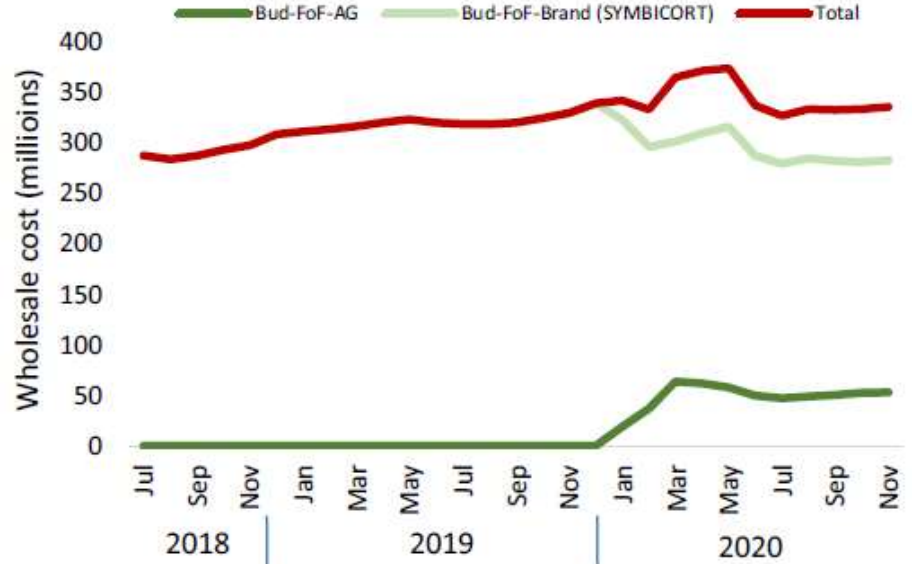
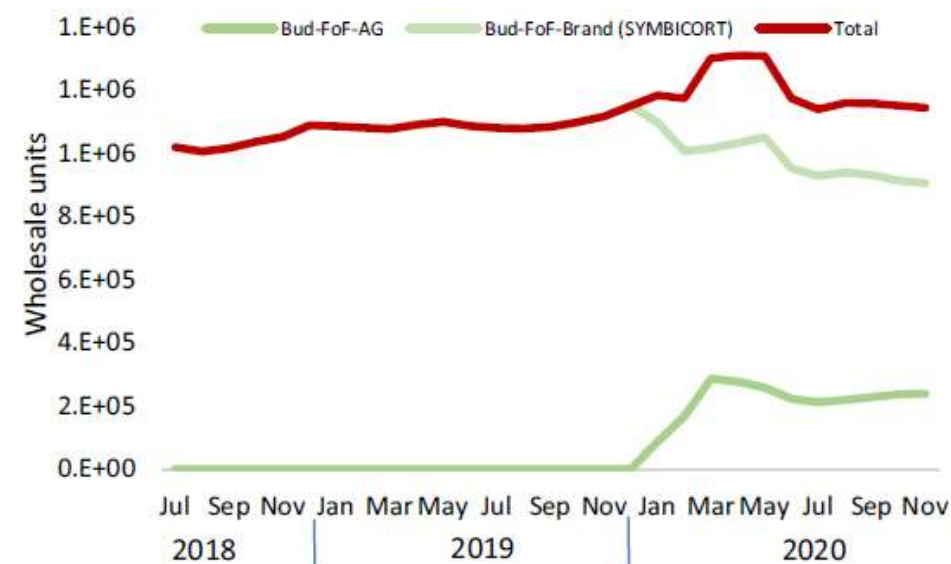


Impact of generic approval on cost



Modified from: Wang et al. 2022

Impact of generic approval on cost



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Impact of generic approval on cost



- Total cost for Advair and its generics decreased from \$337M in January 2019 to \$233M in January 2020 despite stable wholesale units
- Averaged unit cost for the approved generic of Advair was \$115 compared to \$169 for the authorized generic and \$334 for the brand name










Source: Wang et al. 2022










Recent real-world prices



FP/SX approved generic
250mcg/50mcg

Advair Diskus
250mcg/50mcg

 CVS \$98.03	 Giant \$105.12	 Walgreens \$128.42
 Target \$98.03	 Walmart \$100.18	 Harris Teeter \$74.87 <small>Low price</small>
 Safeway \$91.04	 Wegmans \$91.04	 4 more...

 CVS \$411.43	 Safeway \$397.38	 Giant \$385.38
 Walgreens \$414.29	 Walmart \$415.41	 Costco \$441.90
 Wegmans \$385.38	 Harris Teeter \$412.54	 4 more...

Summary



- Inhalers are a substantial cost to the U.S. healthcare system, and high inhaler costs are associated with worse patient outcomes
- An FDA investigation found reduced costs with the ANDA approval of a generic referencing Advair
- Comparatively, introduction of an authorized generic for Symbicort had limited impact on costs

Challenge Question #1

According to a CDC study, U.S. asthma patients 65 years of age and older who had at least one asthma-related hospitalization in the past year were more likely to report:

- A. Pets in the bedroom
- B. Cost barriers to obtaining medication
- C. Secondhand smoke exposure
- D. Obesity



Challenge Question #2

According to an FDA investigation, introduction of an approved generic ICS/LABA through the ANDA pathway resulted in significant cost savings, whereas introduction of a/an _____ did not:

- A. Nebulized formulation
- B. Companion app to monitor inhaler adherence
- C. Authorized generic
- D. Leukotriene receptor antagonist



References

1. "FDA List of Authorized Generic Drugs." (2023) Retrieved June 23, 2023, from <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/fda-list-authorized-generic-drugs>.
2. Federal Trade Commission. (2011). FTC Report Examines How Authorized Generics Affect the Pharmaceutical Market.
3. Feldman, W. B., J. J. Gagne and A. S. Kesselheim (2021). "Trends in Medicare Part D Inhaler Spending: 2012–2018." Annals of the American Thoracic Society 18(3): 548-550.
4. Hsu, J., J. Chen and M. C. Mirabelli (2018). "Asthma Morbidity, Comorbidities, and Modifiable Factors Among Older Adults." J Allergy Clin Immunol Pract 6(1): 236-243 e237.
5. Kurani, N., D. Cotliar and C. Cox. (2022). "How do prescription drug costs in the United States compare to other countries?" Peterson-KFF. Retrieved June 21, 2023 from <https://www.healthsystemtracker.org/chart-collection/how-do-prescription-drug-costs-in-the-united-states-compare-to-other-countries/>.
6. Patel, B., P. Mayne, T. Patri, J. Vandigo, P. T. Yin, K. Bratti and S. Howell (2022). "Out-of-Pocket Costs and Prescription Filling Behavior of Commercially Insured Individuals With Chronic Obstructive Pulmonary Disease." JAMA Health Forum 3(5): e221167.
7. Sistani, F., R. M. Reed, C. H. Shah and Z. Zafari (2021). "Trends in Medicaid spending on inhalers in the United States, 2012-2018." J Manag Care Spec Pharm 27(12): 1744-1749.
8. Wang, Z., S. K. Ahluwalia, B. Newman, S. Dhapare, L. Zhao and M. C. Luke (2022). "Medication Cost-Savings and Utilization of Generic Inhaled Corticosteroid (ICS) and Long-Acting Beta-Agonist (LABA) Drug Products in the USA." Ther Innov Regul Sci 56(2): 346-357.
9. Zahran, H. S., C. M. Bailey, X. Qin and J. E. Moorman (2015). "Assessing asthma control and associated risk factors among persons with current asthma - findings from the child and adult Asthma Call-back Survey." J Asthma 52(3): 318-326.

Questions?

Submit for the Q&A Session

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We Are OGD

Ask me why...

"I make sure that the **generic** drug and the **brand** drug work **the same**."

"The first time I was able to buy my son's inhaler as a generic and realized that my out of pocket dropped, I cried and was able to breathe a sigh of relief."

www.fda.gov

