

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***

Andrew Clerman, M.D., Ph.D.

Senior Physician

Division of Therapeutic Performance I, Office of Generic Drugs

CDER | U.S. FDA

September 14, 2023

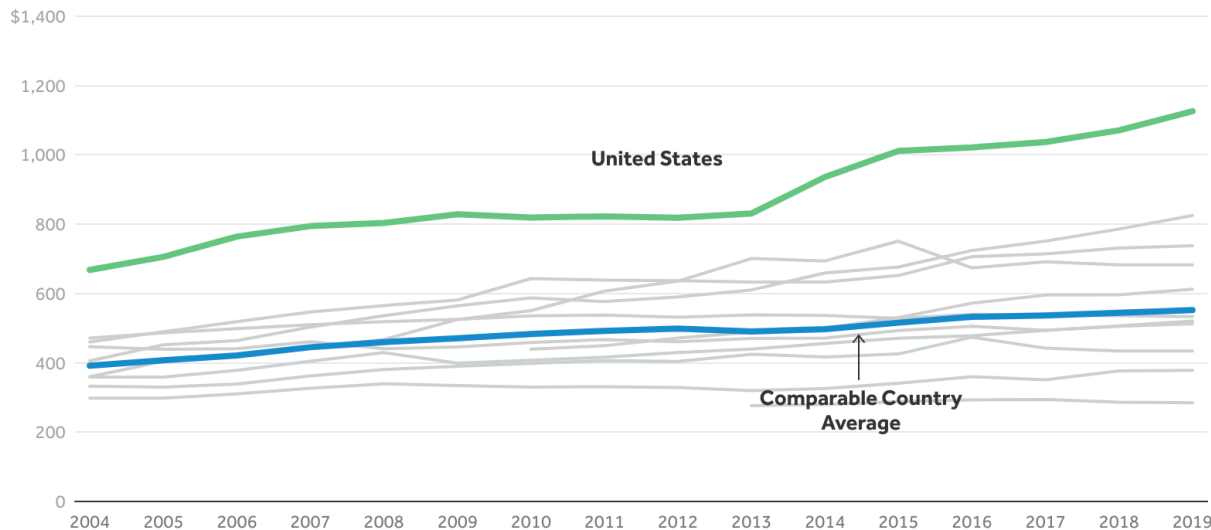
Learning Objectives

- 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

Source: Kurani et al. 2022

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

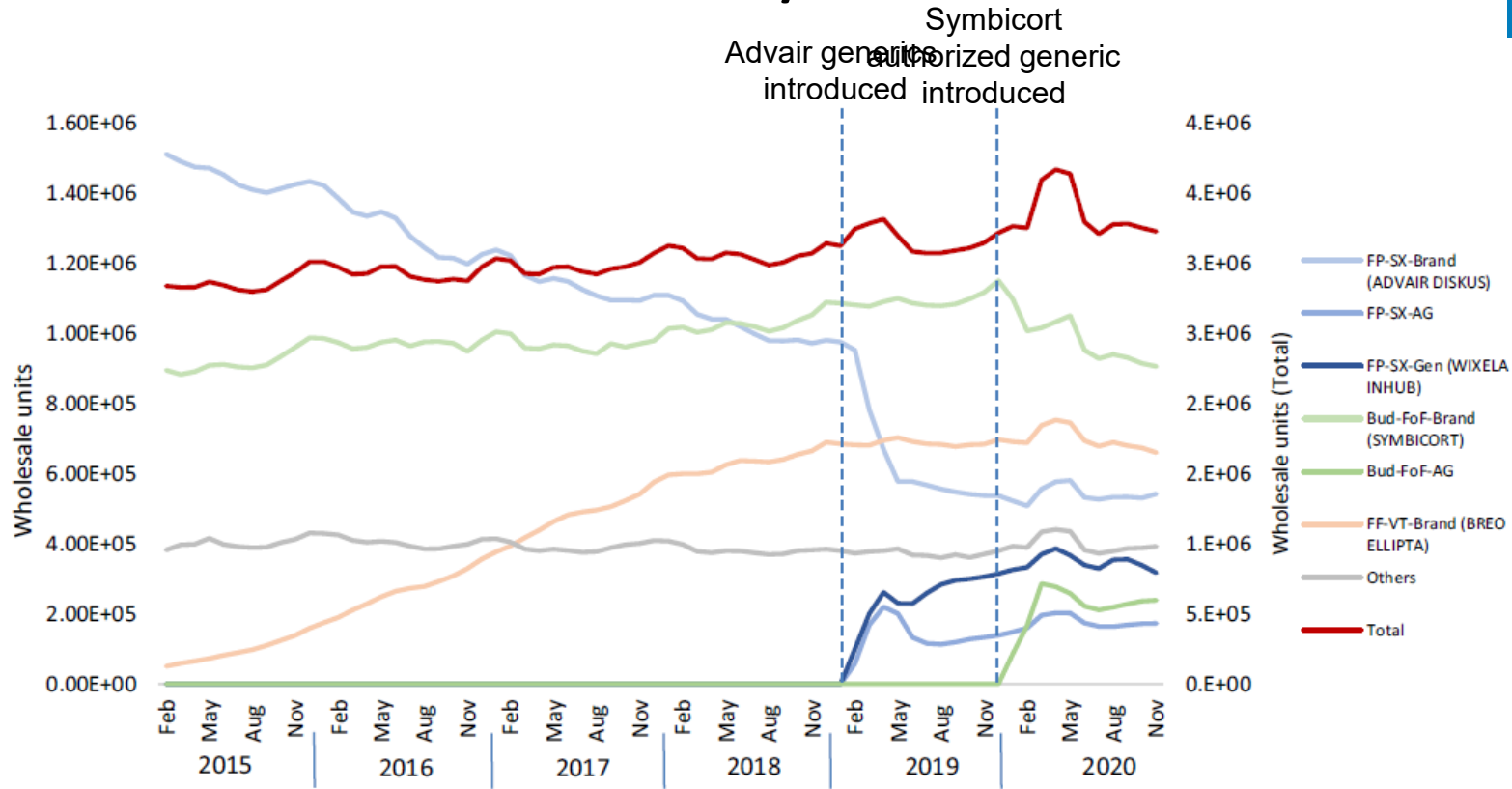


Active ingredient(s)	Dosage form; route	Application number	Category	Company	Approval date or date entered market	Brand name product (application number)
Budesonide; Formoterol Fumarate Dihydrate	Aerosol, Metered: Inhalation	021929	Authorized Generic	Prasco	January 1, 2020	Symbicort (021929)
Fluticasone 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)

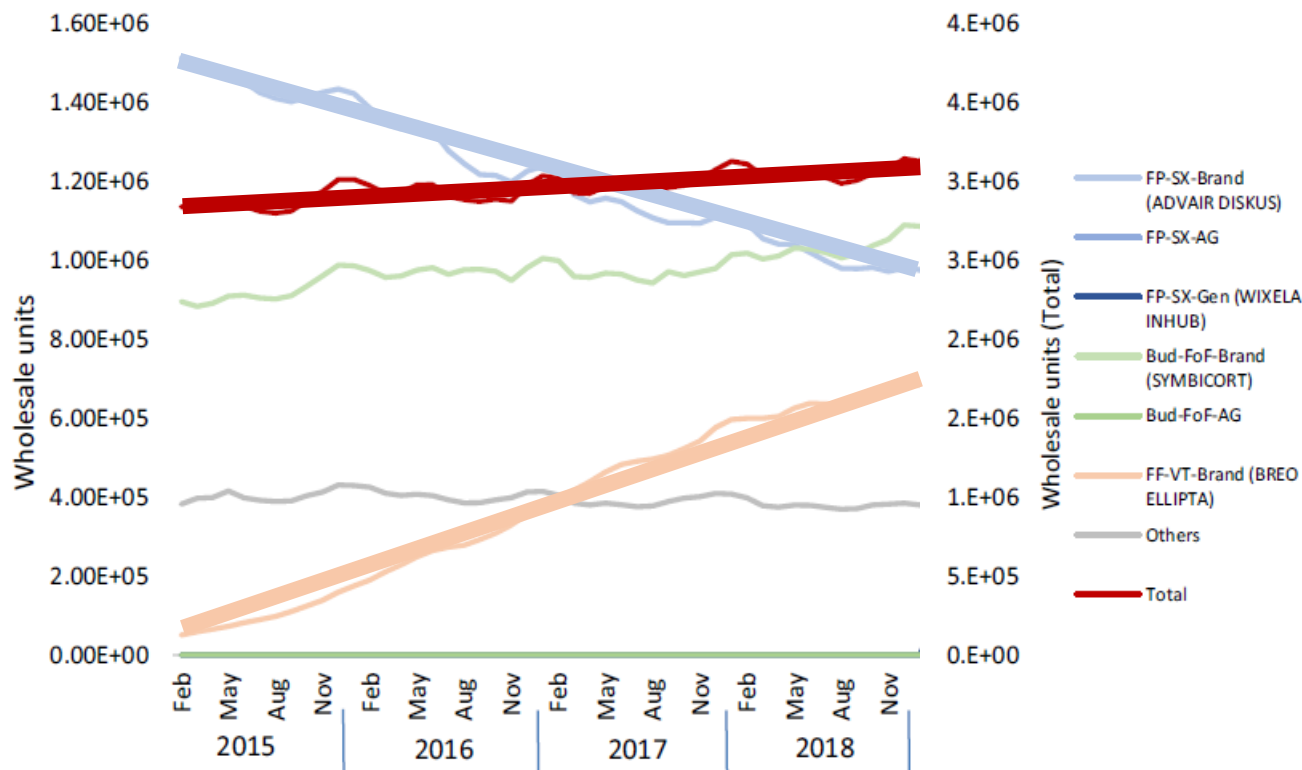
- First approved generic referencing Advair Diskus was introduced in January 2019 following ANDA approval
- Authorized generic of Advair Diskus introduced February 2019
- Authorized generic of Symbicort introduced January 2020

Table modified from: Wang et al. 2022

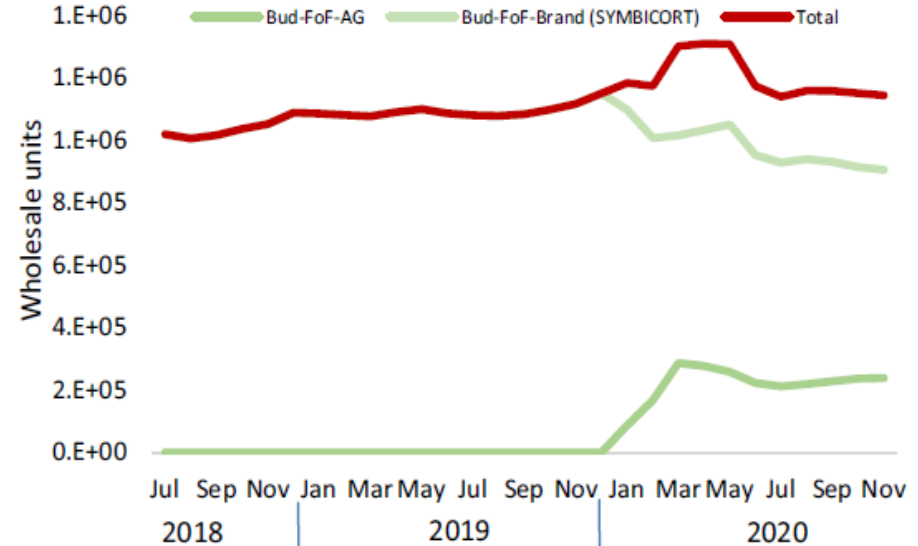
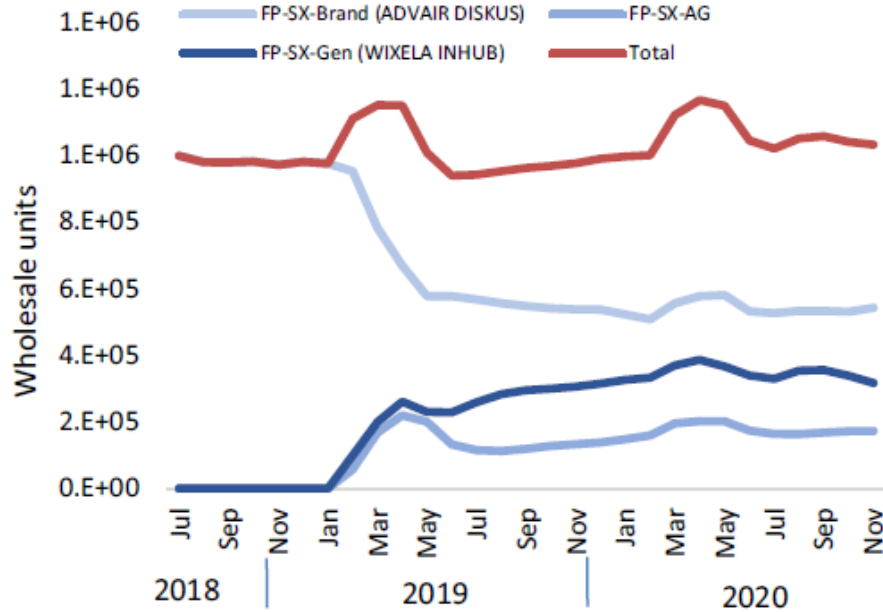
Wholesale units of ICS/LABAs 2015-2020



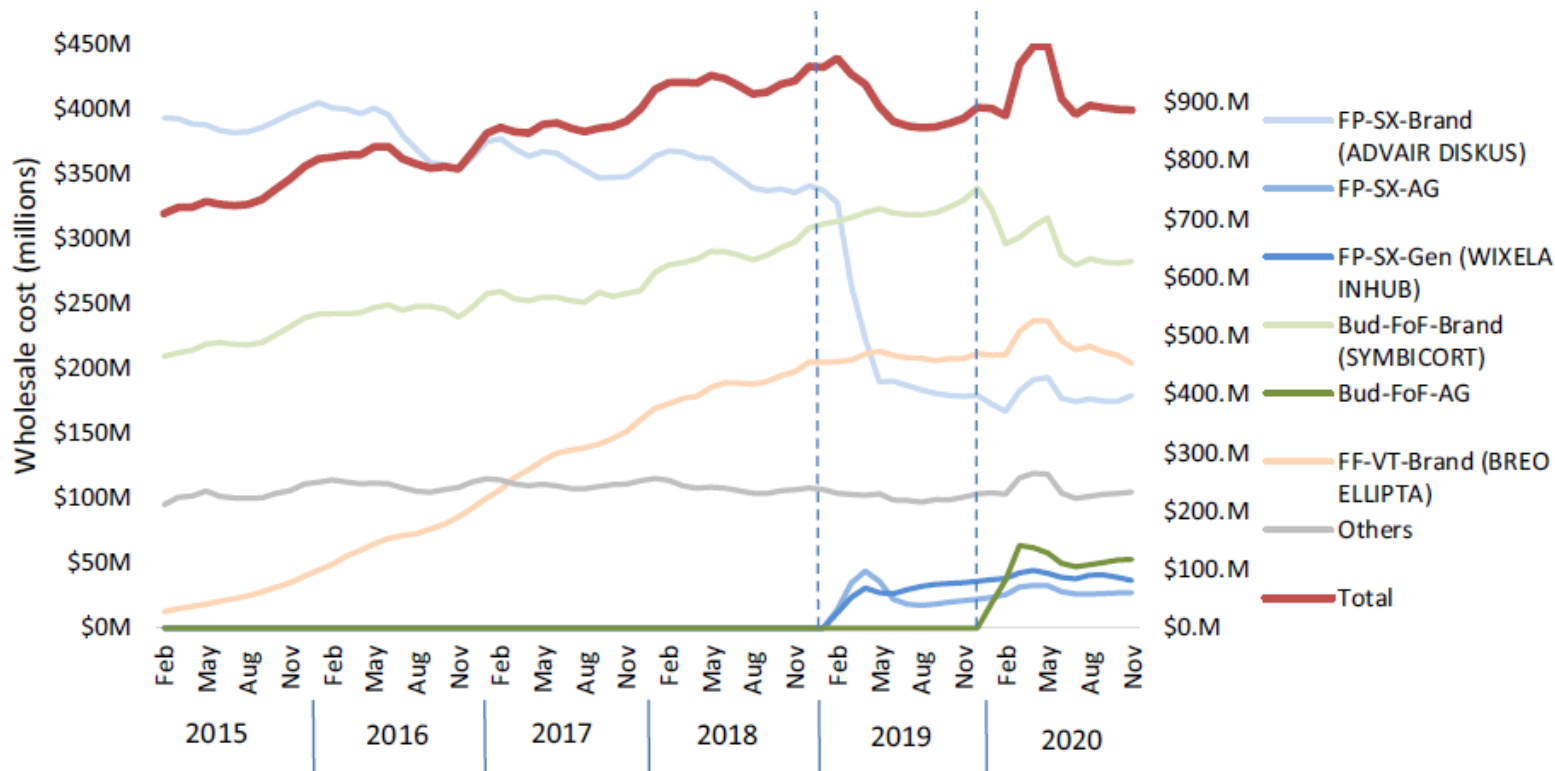
Before generic approval: Wholesale units 2015-2018



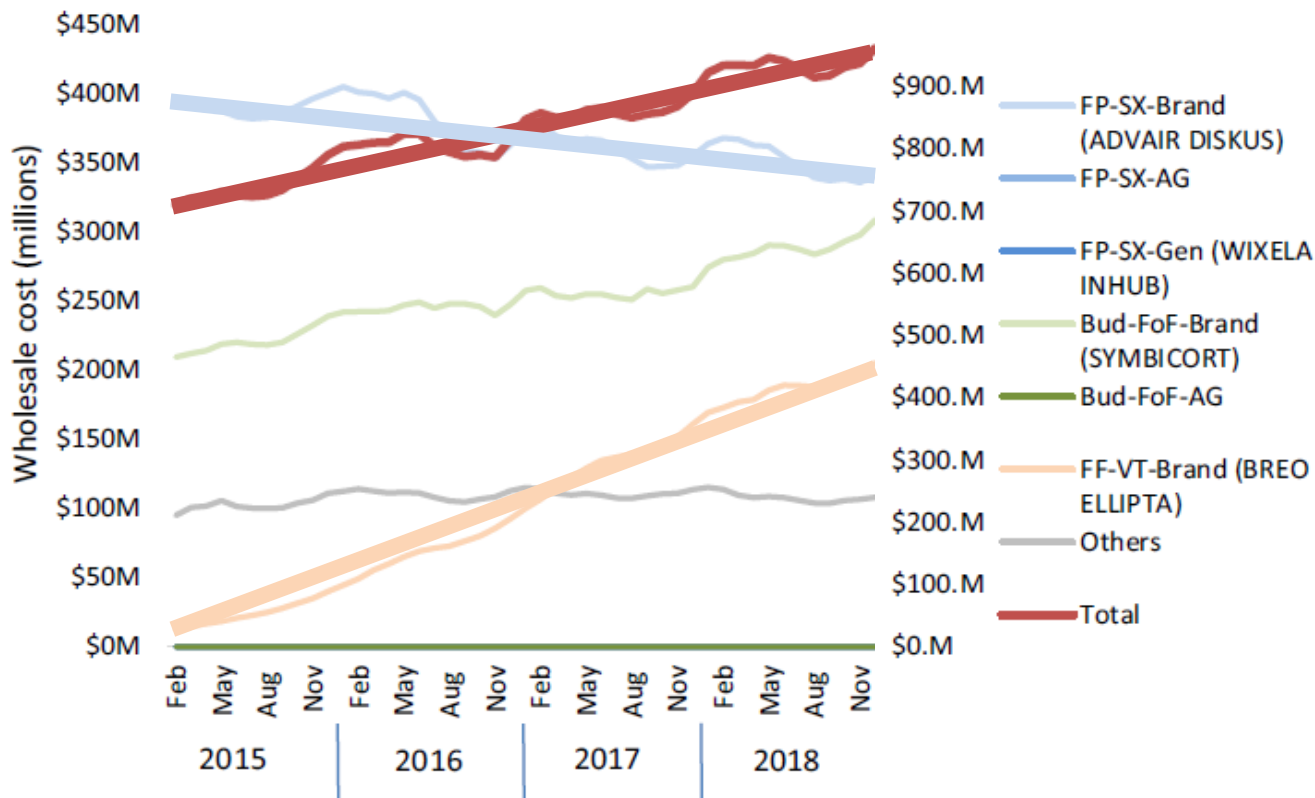
After generic approval: Wholesale units 2019-2020



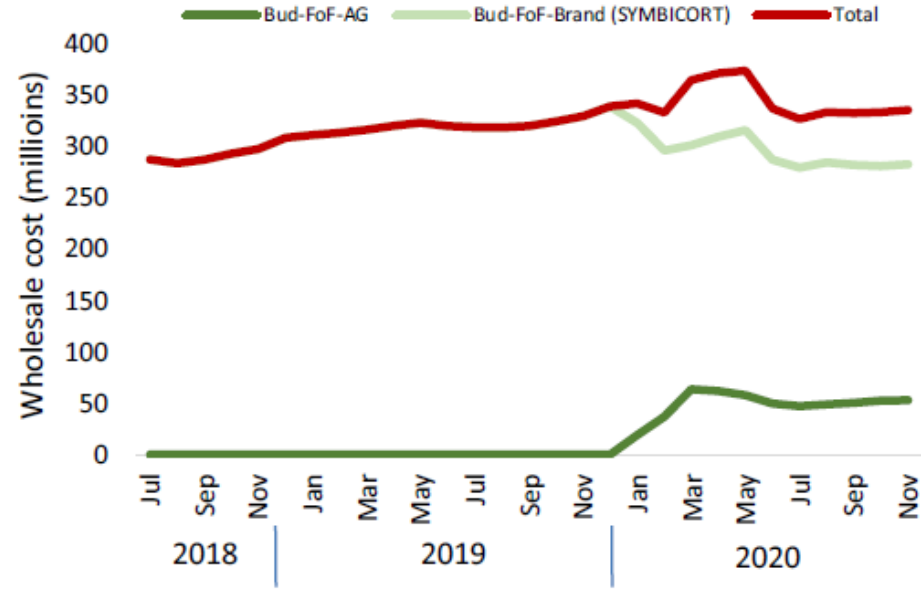
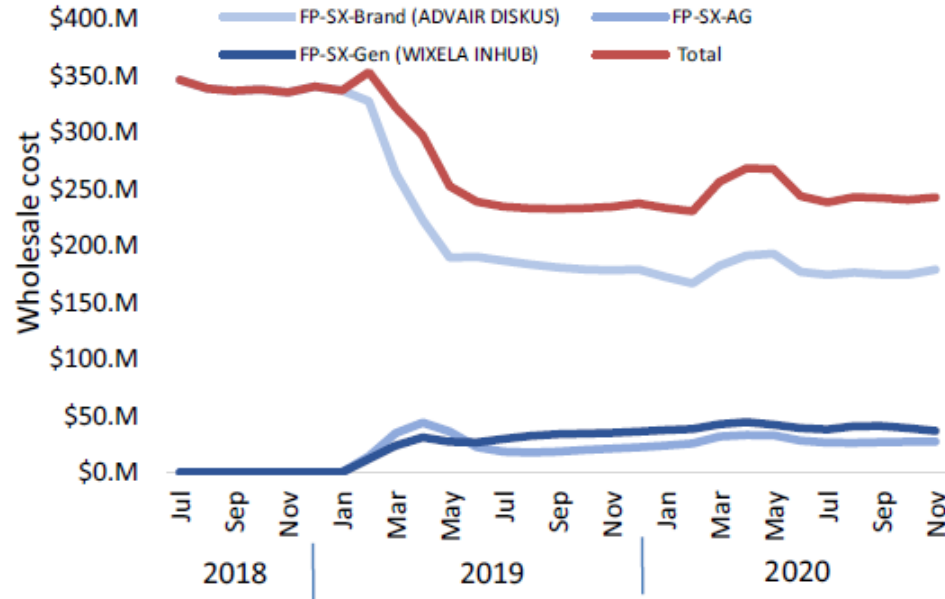
Wholesale cost of ICS/LABAs 2015-2020



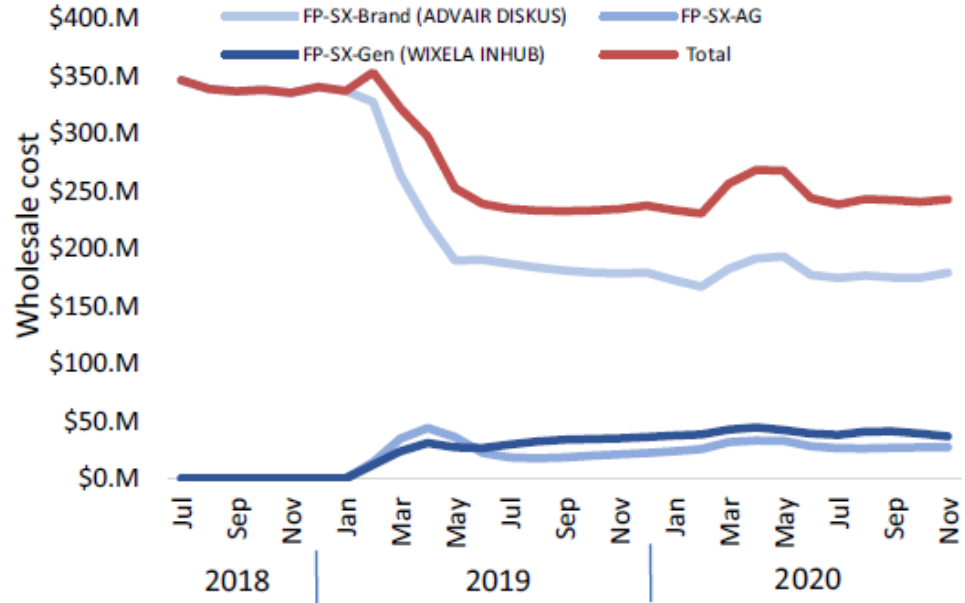
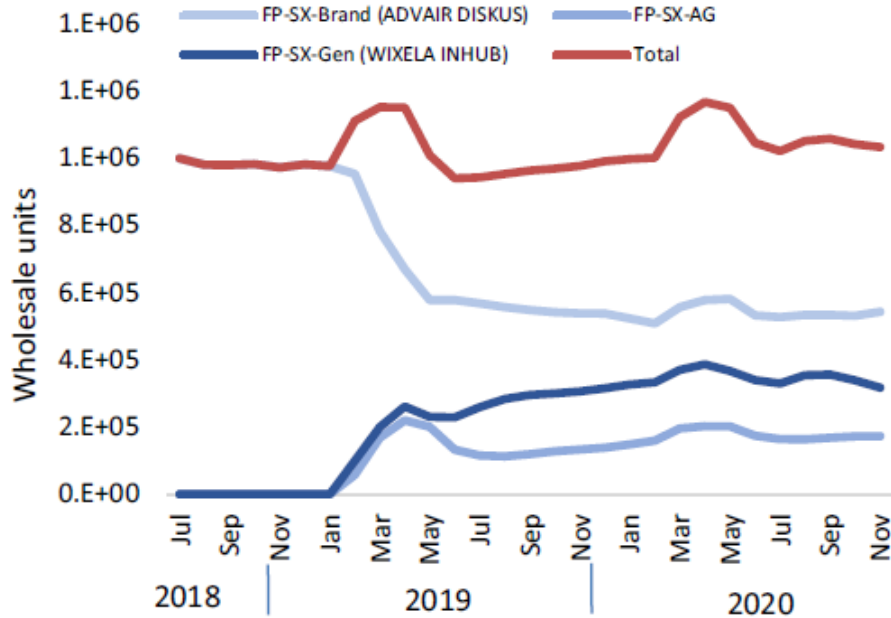
Before generic approval: Wholesale cost 2015-2018



After generic approval: Wholesale cost 2018-2020

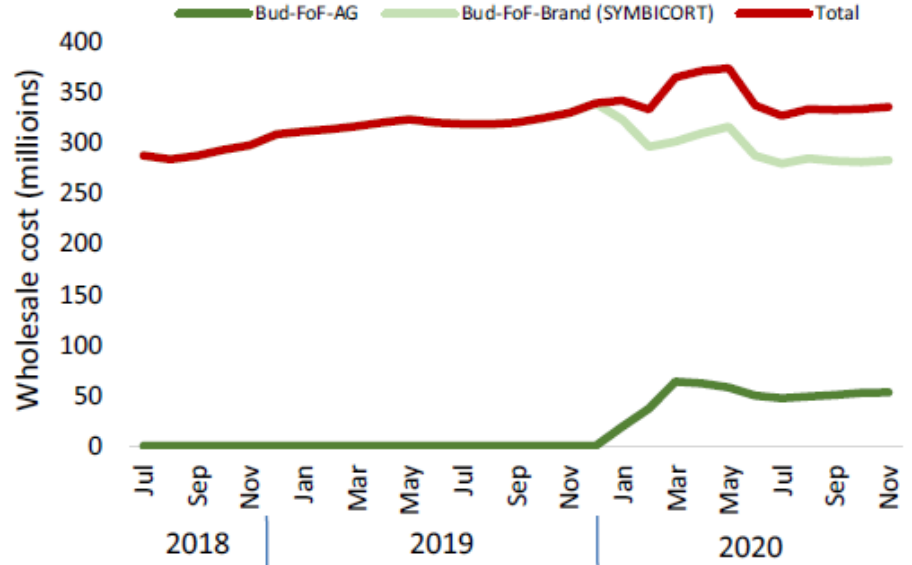
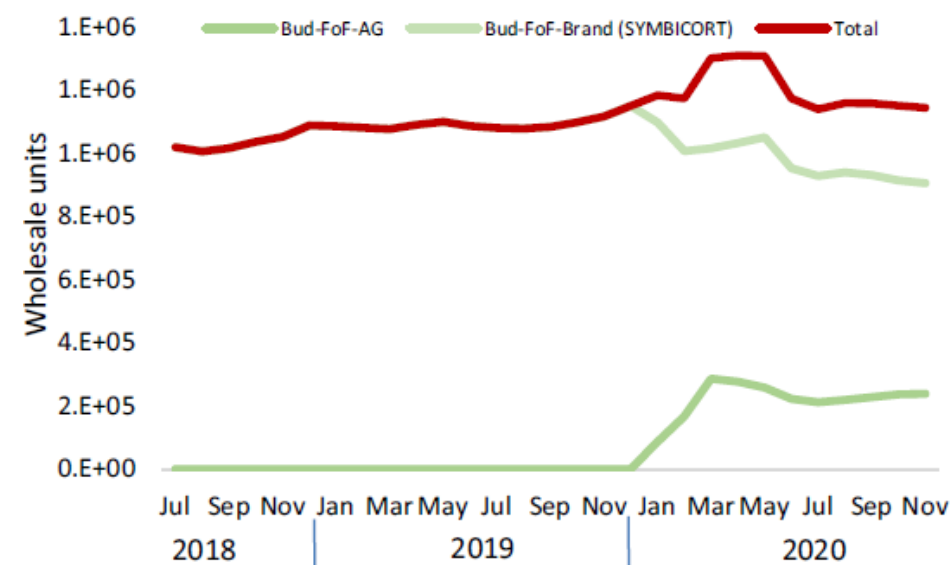


Impact of generic approval on cost



Modified from: Wang et al. 2022

Impact of generic approval on cost



Modified from: Wang et al. 2022

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

Andrew Clerman, M.D., Ph.D.

Senior Physician

Division of Therapeutic Performance I, Office of Generic Drugs

CDER | U.S. FDA

Closing Thought

Post-approval market research is vital to quantify the market effects of generic drug approvals and communicate the impact to stakeholders



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

