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Original Article

Impact of Regulatory Policy Changes on Generic Drug Prices in the United States

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ABSTRACT

Introduction: Generic Drug User Fee Act (GDUFA) was introduced in 2012 to bring more and more generic drugs into the market in a short time through an effective review process. In the present study, the impact of the GDUFA on prices of the generic drugs has been evaluated. **Materials and Methods:** Various research reports related to drug costs and competition such as (i) reasons for high drug prices, (ii) FDA's research on drug prices pre- and post- GDUFA, and (iii) the current status of generic drugs in the USA produced by different agencies including the Congressional Budget Office (CBO), FDA's Center for Drug Evaluation and Research (CDER), and the Federal Trade Commission (FTC) to understand the challenges of high drug costs have been critically evaluated. **Results and Discussion:** The analysis of research reports generated over some time concludes that the fall in generic drug prices has been accelerated further in recent years, with increased competition. The data analysis also reflects that during the GDUFA period, the Agency has been able to proactively address the challenges posed by brand-product companies. However, some issues remain to be addressed. **Conclusion:** The scope of this evaluation was limited to focus on FDA-related aspects where generic competition can be enhanced by making the generic drug approval process more efficient, continue to facilitate industry on complex products regulation to bring generic equivalents of complex products where patents expired long-time back, help resolve shortages faster and help expedite resolution of site compliance matters more quickly to assist in resuming supplies.

Keywords: Congressional Budget Office (CBO), Federal Trade Commission (FTC), Generic Drug User Fee Act (GDUFA), USFDA, Drug Prices.

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INTRODUCTION

United States is the largest pharmaceuticals market with more than USD 127.8 billion in the world, drug prices do have a significant impact on the economy and healthcare policies of the country.[1] As per the National Health Expenditure Accounts (NHEA) estimates for 2019, US healthcare spending grew to $3.8 trillion or $11,582 per person. Total health spending accounted for 17.7 percent of the USA's Gross Domestic Product.[2] While FDA policy matters did help reduce the prices, off-shoring of manufacturing generic drugs in countries with lower labor costs has also contributed significantly to lowering the drug prices in the US market. Specifically, India has played a pivotal role in the supply of generic drugs globally, and the supply from Indian manufacturers is meeting about 40% of the USA demand and 25% of the UK demand for generic drugs.[3]

Medicare is a major part of the healthcare program in the United States, and after supporting Americans for more than 50 years now it faces huge challenges of effectiveness and sustainability in the coming decades. As the USA population is aging, Medicare beneficiaries are also increasing and will be more than 80 million by 2030.[4,5]

Keeping the above aspects into consideration, in the present evaluation, the authors have analyzed the reasons for high drug prices in the USA and the impact of the Generic Drug User Fee Act (GDUFA) on drug prices in the USA. GDUFA was introduced in 2012 to bring more and more generic drugs into the market in a short time through the effective review process, and to get appropriate funding for resource management to ensure that consumers continue to receive the substantial benefits that are given by the generic drug.[6]

MATERIALS AND METHODS

In this study, the following data was evaluated and critically analyzed,

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- Reasons for high drug prices in the USA, and possible ways to reduce the same.
- Analyze the research conducted by FDA or any other.
- Agencies related to drug prices in the USA before and after GDUFA.
- Efforts done by the FDA in terms of policies or laws during the GDUFA period, helped in increasing competition and reducing drug prices.
- Growing consumption of generic drugs in the USA market because of comparatively lower prices but the same quality as brands.
- Current status of generics in the USA and future perspective.

RESULTS

Reasons for high drug prices in the USA, and possible ways to reduce the same

Although per capita spending on pharmaceuticals is increasing worldwide, the pace is higher in the United States. Until the mid-1990s, Germany and France were having higher per capita spending on drugs which has now changed, and the USA's per capita drug spending as per a 2020 publication is exceeding $ 1,000, which is much higher than Germany and France, and more than twice of many developed European countries (Figure 1). One of the main reasons for higher prescription-drug prices in the USA is because of limited competition among drug companies.[7]

The Drug Price Competition and Patent Term Restoration Act, also known as Hatch-Waxman Act was enacted in the United States in 1984 and brought the formal process of generic drug approval.[8] Implementation of the Hatch-Waxman Act increased both – the probability of generic entry, as well as the market share of low-price generics (Table 1).

There were majorly three factors that led to a dramatic increase in the sales of generic drugs – first, by 1980, pharmacists were allowed to dispense a generic product even when the prescription called for a brand-name drug, as most states of the USA had passed drug-product substitution laws. Second, the Hatch-Waxman Act of 1984 made it easier and less expensive for generic manufacturers to enter the market. And third, many private health insurance plans and even government health programs like Medicaid were promoting generic substitution.[9]

Analysis of research conducted by the FDA or any other Agencies related to drug prices in the USA before and after GDUFA

In July 1998, the Congressional Budget Office (CBO) of the USA published a study on generic drug prices, titled "How Increased Competition from Generic Drugs has affected Prices and Returns in the Pharmaceutical Industry". As per an estimate by CBO in this report, within the first decade after Hatch-Waxman Act, the savings by substituting generic drugs was roughly $8 billion to $10 billion in 1994. Also, generic drug sales grew, and the number of prescriptions filled by generics increased from 19 percent in 1984 to 43 percent in 1996, within twelve years of the Act. This trend has been growing over some time (Figure 2) and as of 2020 data, over 90 percent of the prescriptions are filled by low-price generics.[10,11]

In another study in 2005, FDA analyzed sales data from IMS Health for a period between 1999–2004. This study determined that on average, the first-generic manufacturer keeps the prices of its product slightly reduced than the brand-name product, but when the second generic product gets approved and launched in the market, the average generic price is reduced to almost half of the brand-name drug prices. Although the generic product price keeps falling with the entry of every subsequent generic product, the fall in prices is not as sharp as was for the second generic product. However, the fall in generic product prices goes much lower for products where the number of generic competitors is many (Figure 3).[12]

Most recently FDA released another study report in December 2019 – "Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices". This 2019 study report analyzed the prices and competition for generic products which initially entered the market between 2015 and 2017. The median fall in price was more than 30% after the first generic product entry and 44% after the second product entry. For generic products where the number of manufacturers increased up to 10 or more, the median price fall was about 98% (Figure 4).[13]

When the 2019 study is seen vis-à-vis the 2005 study to understand the changes over this period, it clearly shows that in recent years the price of generic products falls too early and too fast (Figure 5). Comparative information of first 5 generic products in Figure 5 indicates that the fall is 67% in 2005 study (6%, 48%, 56%, 61% and 67%) whereas it was up to 85% in 2019 study (30%, 44%, 55%, 73% and 85%). When the comparison is done up to the tenth generic, the difference is even sharper – 74% fall in the 2005 study and 98% fall in the 2019 study.

Efforts done by the FDA in terms of policies or laws during the GDUFA period helped in increasing competition and reducing drug prices

While GDUFA I (2013-2017) has helped in reducing the backlog of approvals, GDUFA II (2018-2022) has focused on improving approval times, and also expedited approval of first generics, and supported the industry to bring generics for low-competition/no-competition products. The GDUFA III (2023-2027) negotiations are already over and the commitment letter brings promises to help bring more generics to market faster.[14]

Although efforts are being made to bring down the drug prices, however, in many cases the brand manufacturer has been

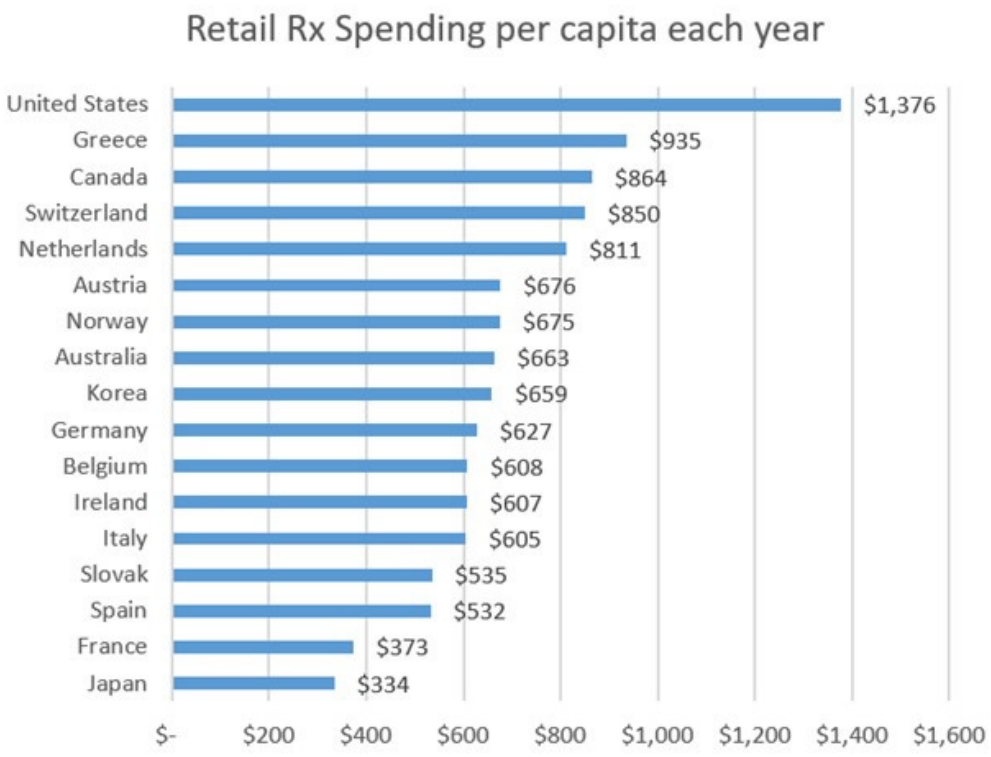

Figure 1: Comparative Retail Drug Spending per capita 2020 data of Countries.

Table 1: Impact of Hatch-Waxman Act on Generic Drug Availability.

Assumption (For an average brand-name drug)	Before Hatch-Waxman Act	After Hatch-Waxman Act
Probability of Generic Entry	40%	91.5%
Generic Market Share		
One year after the generic entry	2.4%	40%
Two years after the generic entry	5.1%	50%
Three or more years after generic entry	5.1%	60%

Source: US Congress Budget Office (CBO) 1998

"gaming" the system to avoid or delay the competition, hence extending the life of their product and hence profits. Competition in the form of generic drugs is the key to bringing down prescription drug prices. However, some brand-drug manufacturers engage in anti-competitive behaviors to block or delay generic approvals by FDA or otherwise delay their market entry. While a lot has been done by FDA and the Congress, much more needs to be done to address some of these issues.

FDA enacted Creating and Restoring Equal Access to Equivalent Samples Act in December 2019, which is commonly known as CREATES Act.[15] The enactment of CREATES established a process for obtaining the RLD samples for the development of generic, 505(b)(2), or biosimilar products. Also, the CREATES Act authorizes generic manufacturers to file a civil action against brand-name drug or biological manufacturers who refuse to sell RLD samples.[16]

Growing consumption of generic drugs in the USA market because of comparatively lower prices but the same quality as brands

The regulatory framework in the USA mandated by FDA ensures that generic drugs undergo a rigorous scrutiny process for approval. This ensures that the generic drugs pass all the quality tests for approval, without the need of repeating toxicological and clinical assessment, which has already been established as innovator product.

Also, the Federal Trade Commission (FTC) has the responsibility to prevent anticompetitive business practices and thereby address any related issues. It is the FTC's responsibility to prevent anti-competitive business practices. But Congress set out certain laws that are meant to strike a careful balance between pharmaceutical innovation and access to lower-cost generic products, and FDA has an important responsibility to enforce those laws in a manner that adheres to the balance struck by Congress.

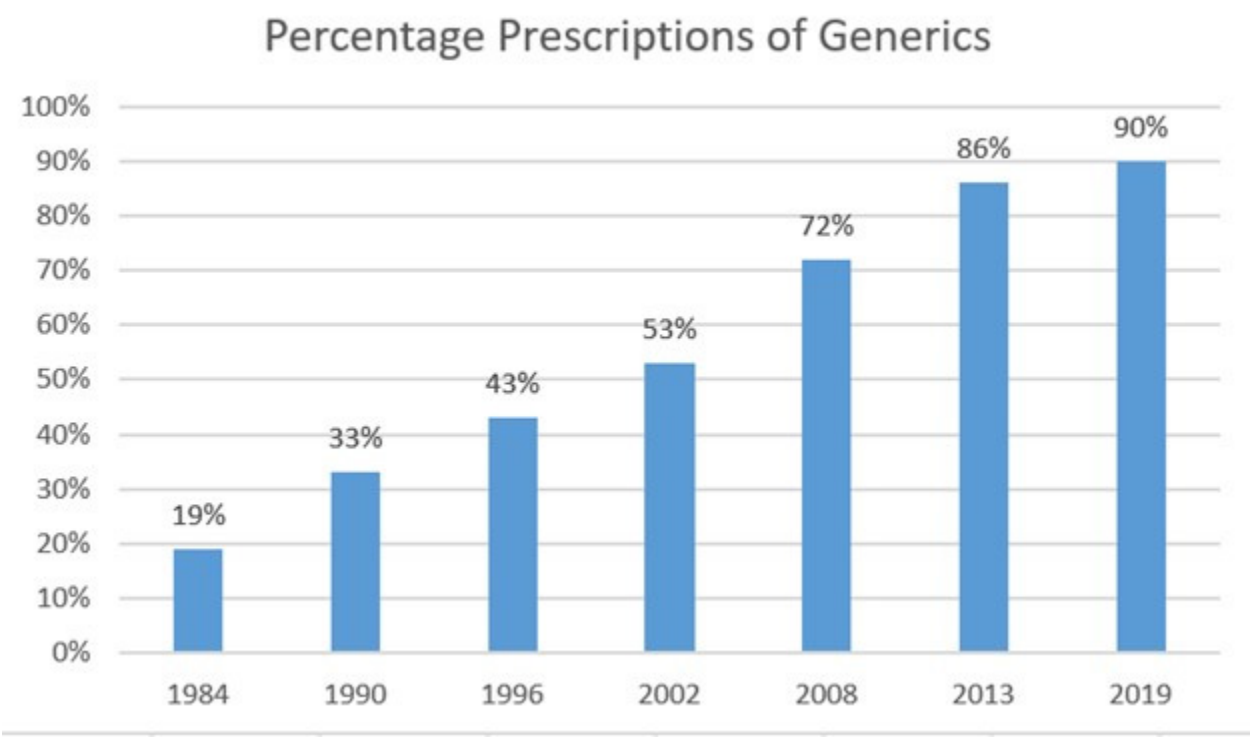

Figure 2: Growth in Percentage Prescription of Generic Drugs.

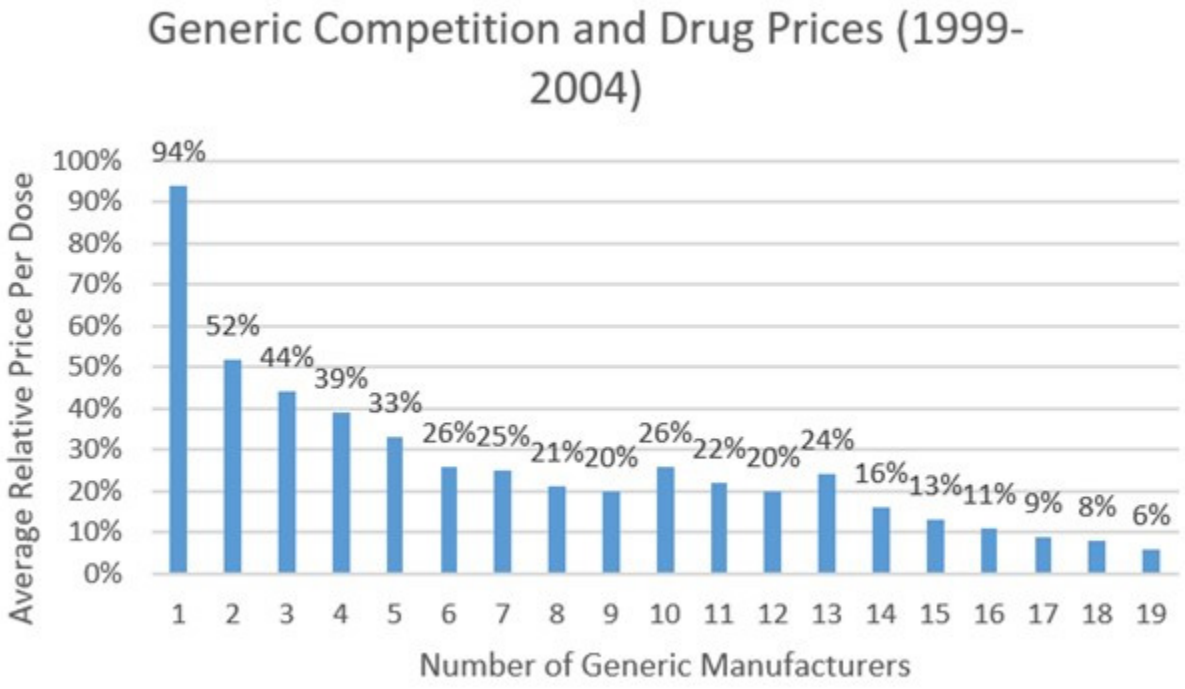

Figure 3: Impact of Competition on Generic Drug Prices – 1999 to 2004 data.

Current status of generics in the USA and future perspective

With the rising cost of drugs, specifically brand products, the USA has constantly updated the regulatory framework for the availability of generic drugs over almost four decades, after the introduction of the Hatch-Waxman Act in 1984. The need to reduce the rising healthcare cost has compelled the need to expedite these efforts further in the last decade for faster approval of generics. As a result of these efforts, currently, more than 90% of prescriptions are filled by generic drugs in the USA for a meager

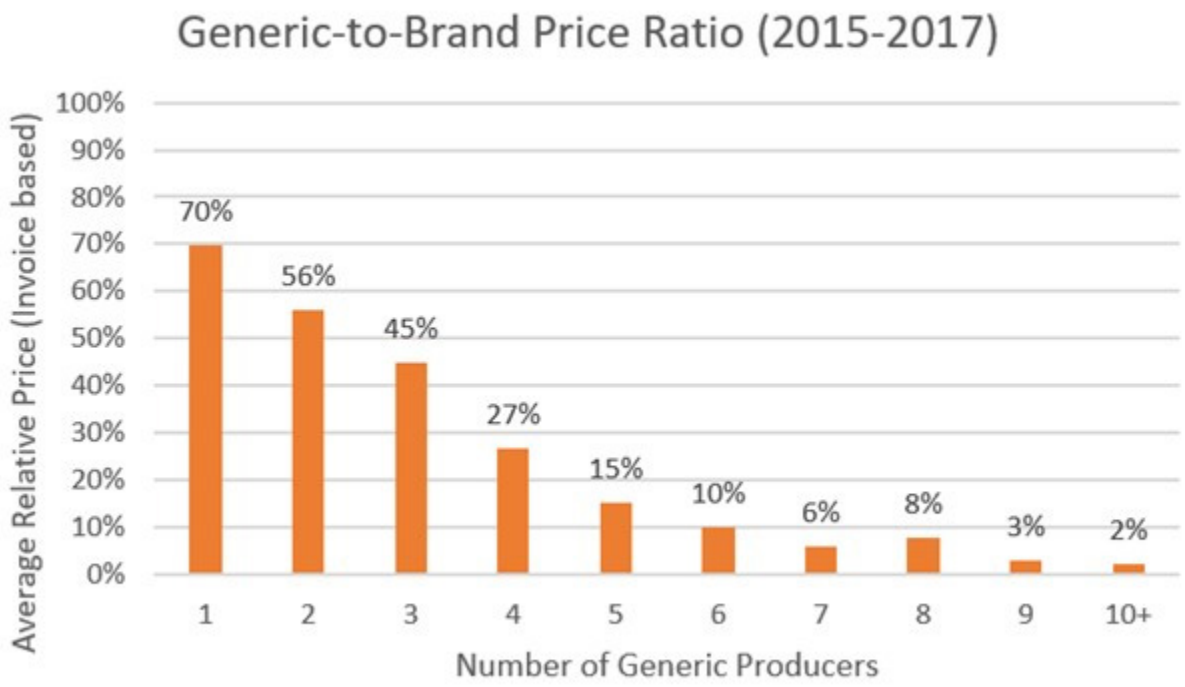

Figure 4: Changes in Generic-to-Brand Price Ratio with Increase in Generic Producers.

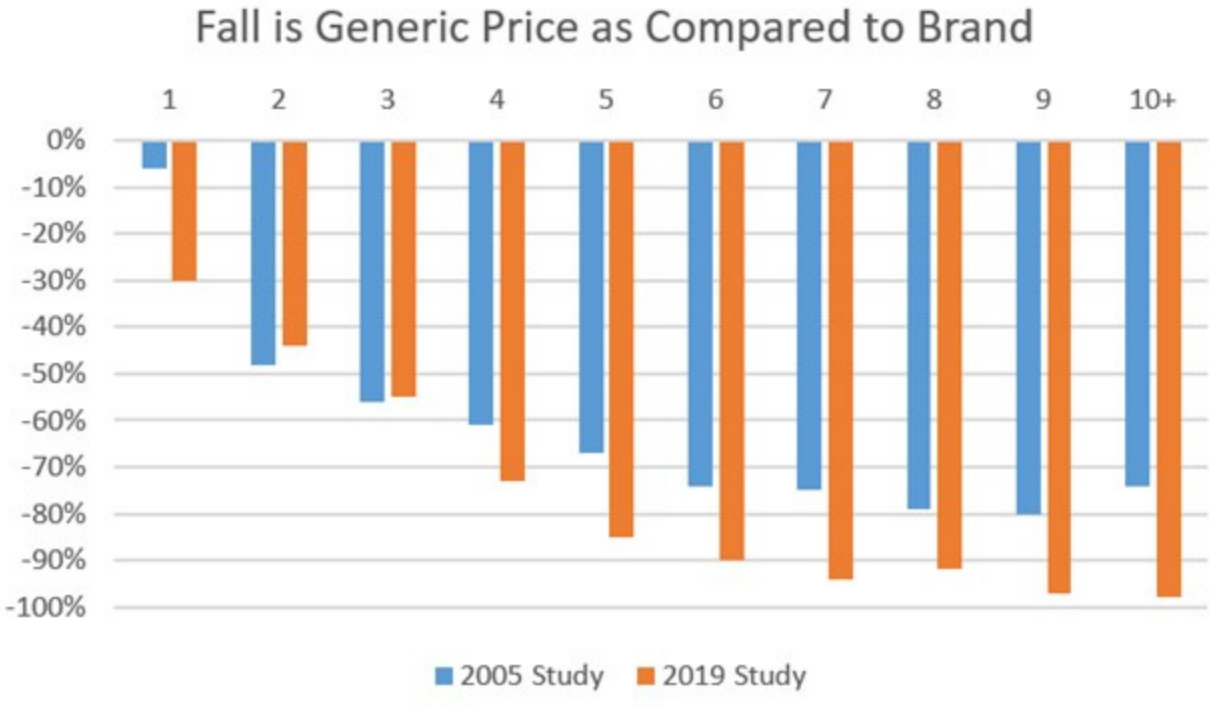

Figure 5: Fall in Generic Drug Prices –as per the 2005 study and 2019 study.

Table 2: 2020 Top 10 Generic Drugs Ranked by Savings.

Brand Product (Generic equivalent)	Brand Pre-expiry Price (per unit)	Price of Generic Equivalent 2019 (per unit)	2020 Savings ($Bn)	Percent Savings	2020 Dispensed Prescriptions (Mn)
Lipitor® (Atorvastatin)	$3.29	$0.08	$19.2	98%	5982
Zofran® (Ondansetron)	$21.67	$0.16	$13.9	99%	745
Prilosec® (Omeprazole)	$3.31	$0.06	$12.0	98%	4116
Crestor® (Rosuvastatin)	$5.78	$0.08	$10.7	99%	1899
Abilify® (Aripiprazole)	$21.68	$0.40	$8.9	99%	423
Neurontin® (Gabapentin)	$1.02	$0.07	$7.5	93%	7864
Norvasc® (Amlodipine)	$1.54	$0.02	$7.4	99%	4799
Singulair® (Montelucast)	$3.74	$0.09	$6.6	98%	1821
Cymbalta® (Duloxetine)	$4.61	$0.21	$6.5	96%	1462
Protonix® (Pantoprazole)	$3.63	$0.03	$6.2	98%	2290

Source: IQVIA, National Sales Perspectives, Dec 2020 (2021 AAM Savings Report)

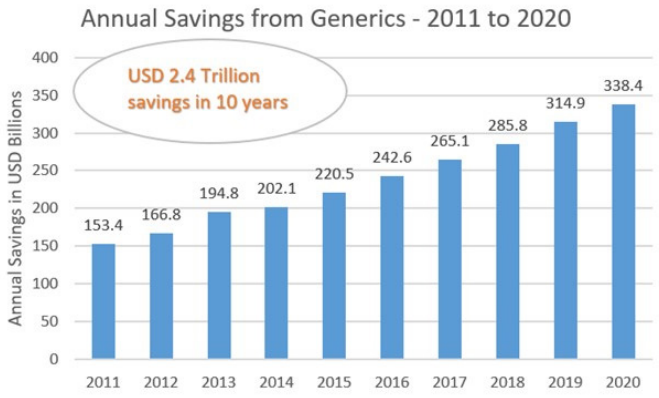

Figure 6: Annual Savings from Generic Drugs over 10 years.

cost of about 18.1% of the total cost. The significant growth in the demand for generics has saved a huge amount of more than USD 2.4 trillion from the American healthcare system over a period of ten years, i.e., 2011 to 2020, Figure 6.[11] Although the cost of a drug decreases with the approval of first-generic products, with the approval of multiple generic products, cost decreases further significantly (Figure 5) because of higher market competition, and in some cases cost decreases by more than 99%, Table 2.[17-19]

DISCUSSION

FDA can approve one or more generics under Hatch-Waxman Act if the patent of a brand-name drug has expired or will expire. However, if the generic manufacturer believes that the patent will not be infringed or is invalid, it may choose to challenge the patent. If the generic manufacturer prevails in the patent challenge either by not being sued by the innovator or winning the litigation, it gets rewarded with 180-day market exclusivity upon approval. Once the patent or exclusivity expires, multiple generics can get FDA approval and enter the market. Although the price of a drug falls to a certain extent after the first-generic entry, however, the fall in price is significant when multiple generics enter the market. Multiple studies and sales-data analysis have been done in the past three decades which proves that an increased number of ANDA approvals and drug product launches leads to competition within the pharmaceutical market, which eventually leads to decreased drug prices.

Further, the study conducted by Dave *et al.* and published in Health Affairs in 2020[20] estimated the cost of delayed generic entry to Medicaid for a period between 2010 and 2016. Since delays in generics entry are not uncommon, this study evaluated the prevalence, reasons, and effects on Medicaid spending of these delays. The delay in the generic entry corresponding to 69 brand-name drugs was studied, and it was concluded that in 45% of cases generic entry was either delayed by more than a quarter (29%) or did not occur (16%). Overall, these delays led to average annual excess Medicaid spending of $109 million annually and totaling $761 million over a period of seven years. The patent challenge was observed as the most common reason for delays in the market entry of generics. It is therefore important to address the inefficiencies resulting from patent challenges to avoid additional cost burden on the USA healthcare system.

Various tricks are played by the brand-drug manufacturers to reduce the competition and thus create hurdles in lowering drug prices. Many of the challenges include blocking the generic approvals by doing some last-minute changes close to generic entry, e.g., filing a Citizen's Petition, updating the RLD labeling with safety-related updates, switching to a different dosage form and stopping existing RLD product, blocking the RLD samples needed for bioequivalence testing for REMS or other products in the name of safety, parking the exclusivities, reverse-payment patent settlements, avoiding shared distribution system or shared REMS program.

Brand-name manufacturers played the trick of paying the generic manufacturer for abandoning the patent challenge. Any such delay in the generic entry is a huge gain for the brand manufacturer. The USA Supreme Court ruled in 2013 that such "pay for delay" cases may violate antitrust laws. Although Federal Trade Commission (FTC) was apprehensive, Court ruled that such cases are not always illegal and left the decisions to the lower courts on a case-by-case basis.

Also, drug shortages have been one of the factors leading to increases in prices. Most recently, FDA has enhanced the drug shortage mitigation efforts through CDER's Coronavirus Aid, Relief, and Economic Security Act, also known as CARES Act.[21] This Act was signed into law on March 27, 2020. Although the main purpose of this Act was to ease the economic impact of COVID-19, it also enhanced FDA's authority to identify, prevent and mitigate possible drug shortages, through FDA's visibility into the drug supply chain and other means.

The CARES Act amended the FD&C Act to provide FDA-specific authorities as below:

-Notifying FDA of Manufacturing Discontinuance and Interruptions.

-Creating Risk Management Plans for Drugs.

-Reporting the Number of Drugs Manufactured.

This is likely to help increase supply chain visibility, reduce drug shortages, and hence prevent an increase in drug prices.

Additionally, there are some other challenges like drug shortages or lack of policy and guidelines for the development of certain complex products for which patent has expired long back. Agency is taking various initiatives, including pre-ANDA meetings and developing guidance documents for complex products to address this challenge.

Good efforts have been done to control the prices, however, considering the importance of having drug prices in control, additional efforts are needed in the future on the following aspects:[22]

Federal Trades Commission's role to contribute on price reduction

-Reduce Hart-Scott-Rodino (HSR) thresholds on merger revenue scrutiny.

-Pursue assertively on pay-for-delay, product hopping, evergreening, etc.

FDA's role to contribute on price reduction

-Lower barriers to entry through GDUFA regulations.

-Expedite resumptions of supplies after temporary supply disruptions.

-Support regulatory processes in an expedited manner for alternate suppliers.

-Ensure quality manufacturing.

CONCLUSION

The scope of this evaluation was limited to focus on FDA-related aspects where generic competition can be enhanced by making the generic drug approval process more efficient, continue to facilitate industry on complex products regulation to bring generic equivalents of complex products where patents expired long-time back, help resolve shortages faster and help expedite resolution of site compliance matters more quickly to assist in resuming supplies. The analysis of research reports generated over some time concludes that the fall in generic drug prices has accelerated further in recent years, with increased competition. The data analysis also reflects that during the GDUFA period, the Agency has been able to proactively address the challenges posed by brand-product companies. However, some issues remain to be addressed.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ANDA: Abbreviated New Drug Application; **CARES:** Coronavirus Aid, Relief, and Economic Security; **CBO:** Congressional Budget Office; **CDER:** Center for Drug Evaluation and Research; **CREATES:** Creating and Restoring Equal Access to Equivalent Samples; **FDA:** Food and Drug Administration; **FD&C:** Food Drug and Cosmetics; **FTC:** Federal Trade Commission; **GDUFA:** Generic Drug User Fee Act; **NHEA:** National Health Expenditure Accounts; **USA:** United States of America; **RLD:** Reference Listed Drug; **REMS:** Risk Evaluation and Mitigation Strategy; **HSR:** Hart-Scott-Rodino.

SUMMARY

Generic Drug User Fee Act (GDUFA) on drug prices in the USA GDUFA was introduced in 2012 to bring more and more generic drugs into the market in a short time through the effective review process, and to get appropriate funding for resource management to ensure that consumers continue to receive the substantial benefits that are given by the generic drug. The present study reports generated over some time conclude that the fall in generic drug prices has accelerated further in recent years, with increased competition. The data analysis also reflects that during the

GDUFA period, the Agency has been able to proactively address the challenges posed by brand-product companies. The scope of this evaluation was limited to focus on FDA-related aspects where generic competition can be enhanced by making the generic drug approval process more efficient.

REFERENCES

1. IMARC US. Generic drug market: Industry trends, share, size, growth, opportunity, and forecast 2021-2026. IMARC-group. 2021;1-4 [cited Mar 18 2022]. Available from: https://www.imarcgroup.com/us-generics-market.
2. NHEA. Centers for Medicare and Medicaid Services; 2021 [cited Mar 18, 2022]. Available from: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical.
3. IBEF. Indian pharmaceutical Industry. India Brand equity foundation. 2018;1-6 [cited Feb 20 2022]. Available from: https://www.ibef.org/industry/pharmaceutical-india.aspx.
4. Blumenthal D, Davis K, Guterman S. Medicare at 50 — origins and evolution. N Engl J Med. 2015;372(5):479-86. doi: 10.1056/NEJMhpr1411701, PMID 25587859.
5. Blumenthal D, Davis K, Guterman S. Medicare at 50 — moving forward. N Engl J Med. 2015;372(7):671-7. doi: 10.1056/NEJMhpr1414856, PMID 25629661.
6. Woodcock J. Implementation of the generic drug user fee amendments of 2012 (GDUFA); testimony before the senate committee on health, education, labor, and pensions. Center for Drug Evaluation and Research. 2016 [cited Mar 9 2022]. Available from: https://www.fda.gov/news-events/congressional-testimony/implementation-generic-drug-user-fee-amendments-2012-gdufa.
7. Mikulic M. Pharmaceutical spending per capita in selected countries as of 2020. Statista – health, pharma and medtech; 2020 [cited Mar 10, 2022]. Available from: https://www.statista.com/statistics/266141/pharmaceutical-spending-per-capita-in-selected-countries/.
8. CDER. Milestones of drug regulation in the United States; 2021 [cited Feb 28, 2022]. Available from: https://www.fda.gov/media/109482/download.
9. CBO. How Increased Competition from Generic Drugs has Affected Prices and Returns in the Pharmaceutical Industry – a CBO Study. United States Congressional Budget Office. 1998.
10. Ann Med Thayer. 30 years of generics. Chem Eng News Arch. 2014;92(39):8-16.
11. AAM. Securing our access and savings. 2020;2020. AAM report on generic and biosimilars access and savings in the U.S. [cited Mar 9, 2022] Available from: https://accessiblemeds.org/sites/default/files/2020-09/AAM-2020-Generics-Biosimilars-Access-Savings-Report-US-Web.pdf.
12. CDER. Generic competition and drug prices – analysis of IMS data. Cent Drug Eval Res [cited Mar 9, 2022]. 1999-2004;2005. Available from: http://fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.
13. CDER. Generic competition and drug prices: New evidence linking greater generic competition and lower generic drug prices; 2019 [cited Mar 9, 2022]. Available from: https://www.fda.gov/media/133509/download.
14. CDER G. Reauthorization performance goals and program enhancements fiscal years 2023-2027 (GDUFA III) [cited Mar 10 2022]. Available from: https://www.fda.gov/media/153631/download. FDA Official [document]; 2022.
15. CDER. Access to product samples: The CREATES act. Food and Drug Administration; 2019 [cited Mar 25, 2022]. Available from: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/access-product-samples-creates-act.
16. CDER. CDER's coronavirus aid, relief, and economic security act (CARES act) drug shortage mitigation efforts. Food and Drug Administration; 2020 [cited Mar 9, 2022]. Available from: https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts.
17. AAM A. Testimony on the generic global supply chain—five takeaways. Association of accessible medicines; 2019 [cited Mar 9, 2022]. Available from: https://accessiblemeds.org/resources/blog/aam-testimony-generic-global-supply-chain-five-takeaways.
18. Dave CV, Sinha MS, Beall RF, Kesselheim AS. Estimating the cost of delayed generic drug entry to Medicaid. Health Aff (Millwood). 2020;39(6):1011-7. doi: 10.1377/hlthaff.2019.00673, PMID 32479219.
19. Khullar D, Ohn JA, Trusheim M, Bach PB. Understanding the rewards of successful drug development — thinking inside the box. N Engl J Med. 2020;382(5):473-80. doi: 10.1056/NEJMhpr1911004, PMID 31995697.
20. CDER. FDA drug competition action plan. Food and Drug Administration; 2020 [cited Mar 9, 2022]. Available from: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan.
21. Aislinn A. Competition lowers drug prices, FDA says. Pharma Times; 2020;88(4):1-9.
22. FTC. Understanding competition in prescription drug markets: Entry and supply chain dynamics. In: Federal Trade Commission; 2017 [cited Mar 9, 2022]. Available from: https://www.ftc.gov/system/files/documents/public_events/1255653/understanding_competition_in_prescription_drug_markets_workshop_slides_11-8-17.pdf.

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