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ISSUE BRIEF

Understanding Recent Trends in Generic Drug Prices

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Executive Summary

Generic drugs have for several decades offered relief from rising prescription drug costs. This occurs because there is robust competition among multiple interchangeable products that drive prices for generic drugs to be a fraction of that of the corresponding brand name drug. The result is that decreases in generic drug prices have partially offset large increases in prices for brand drugs. Reports of spikes in the prices of some generic drugs have raised concerns that generic drugs are contributing to increases in overall prescription drug spending. This has led policy makers to ask whether markets for generic drugs are operating efficiently. In this paper, we review existing evidence on generic drug prices and spending. Our review of evidence strongly supports the conclusion that generic drug prices are not an important part of the drug cost problem facing the nation. In fact, about two-thirds of generic products appear to have experienced price declines in 2014. Although the generic drug market as a whole is quite competitive, some segments of the market have experienced large price increases. These spikes are on one hand troubling in that they disadvantage particular patient groups but also sufficiently limited so they exert no sizable influence on overall drug spending. Some explanations for these occurrences include: small markets with limited entry; the impact of mergers, acquisitions, and market exits; the ability to obtain new market exclusivities; and distribution activities. These problems apply to relatively small segments of the market and, while they lead to increased costs in certain therapeutic areas, they have little influence on overall spending increases.

Background

The rising costs of prescription drugs are an important concern for ensuring patient access to prescription drugs, as well as for public and private budgets. For the past several decades, a source of relief from rising prescription drug costs has been the increased availability and utilization of lower cost generic versions of branded drugs (sometimes referred to as innovator drugs)¹. While branded drugs can frequently command high prices because patents or regulatory

¹ Branded drugs are approved or licensed by FDA through a New Drug Application (NDA) or Biologic Licensing Application (BLA). Generic drugs are approved through an abbreviated new drug application (ANDA).

exclusivities give them market power over prices, once these patents and regulatory exclusivities expire or are resolved by agreement, multiple generic versions of the branded drug can enter the market. The competition among multiple interchangeable products drives down prices, resulting in generic drugs typically being sold at much lower prices than their branded counterparts². Use of generic drug leads to substantial cost savings for patients and the health care system, reflected in the fact that 88 percent of dispensed prescriptions are for generic drugs, yet they account for only 28 percent of total drug spending³. However, reports of recent spikes in prices for some generic drugs have raised concerns about whether markets for generic drugs are operating efficiently such that generics will continue to offer a counterbalance to expensive branded drugs.

In this paper, we explore recent prescription drug pricing trends, the fundamentals of the generic drug market, and potential reasons for generic price increases in some segments on the market.

Trends in Prescription Drug Prices

Drug Price Indexes

Price indexes offer a convenient way to summarize the overall behavior of drug prices over time. Using different price indexes can provide some insight into drug price trends. The Bureau of Labor Statistics publishes a consumer price index (CPI) for prescription drugs. This index is constructed from transaction prices received by pharmacies and includes both branded and generic prescription drugs, but does not include drugs administered in a hospital setting, nor does it distinguish between branded and generic drugs. The sample includes about 350 to 400 distinct molecules⁴. From December 2009 to December 2013, the CPI for prescription drugs increased by about 11 percent compared to about 8 percent for the overall CPI during the same time period. In 2014, the CPI for prescription drugs increased by about 6 percent whereas the overall CPI increased less than 1 percent⁵. This shows that overall prices for prescription drugs appear to be increasing at a rate higher than general inflation.

Express Scripts, one of the largest pharmacy benefit managers in the U.S., creates its own prescription price indexes for branded and generic drugs⁶. Express Scripts' prescription price indexes measure inflation in prescription drug prices by monitoring changes in consumer prices for a fixed market basket of commonly used prescription drugs. They define separate market baskets for branded and generic drugs that are based on the top 80 percent of highest selling drugs. For 2014, they found that generic prescription drug prices decreased by 20 percent and branded prescription drug prices increased by 15.4 percent⁷. Relative to a base price of \$100 in

Additionally, there can be so-called branded generics that are approved through an ANDA, but are marketed under a brand name. For the purposes of this paper, branded generics are not considered branded drugs.

² Interestingly, prices for the branded drugs typically increase after generic entry. See Frank, Richard G. and David S. Salkever. 1997. "Generic Entry and the Pricing of Pharmaceuticals," *Journal of Economics and Management Strategy* 6(1):75-90.

³ GPHA. Generic Drug Savings in the U.S. Seventh Annual Edition: 2015

⁴ Bureau of Labor Statistics. 2011. The pharmaceutical industry: an overview of CPI, PPI, and IPP methodology.

⁵ <http://data.bls.gov/cgi-bin/survey/most>

⁶ The Express Scripts Lab. The Express Scripts 2014 Drug Trend Report. March 2015.

January 2008, prices for the studied branded drugs increased to \$227.39 (2008 dollars), while studied generic drugs fell to \$37.13 (2008 dollars). This suggests that overall prices for generic drugs are decreasing, while prices for branded drugs are increasing significantly. Nevertheless, branded price growth is often moderated by changes in off-invoice rebates and discounts. IMS estimates that for 2014 invoice prices for brand drugs increased by 13.5 percent, while net prices increased by 7-8 percent accounting for off-invoice discounts and rebates⁸.

Looking at overall price changes, the Kaiser Family Foundation reports that after declines in prescription drug growth rates from 2000 to 2013, spending increased by 11.4 percent in 2014 and is projected to have increased 9.6 percent in 2015⁹. Similarly, the IMS reports spending on prescription drugs increased 13.1 percent on a nominal basis in 2014. IMS suggests that the increased spending is due to the launch of new brand drugs, price increases for protected brands, and fewer branded drugs losing exclusivity protections than in past years¹⁰.

Breakdown of Generic Drug Price Changes by Different Cost Measures

Changes in Pharmacy Acquisition Costs

Express Scripts' data shows that overall generic drug prices are decreasing even if trends for specific generic drugs may differ. Indeed, analyses of trends in individual drugs indicate that prices are increasing for a notable proportion of generic drugs. The Centers for Medicare and Medicaid Services (CMS) analyzed generic drug prices for prescriptions reimbursed under Medicaid fee for service (FFS) between July 1, 2013 and June 30, 2014¹¹. They used data from the National Average Drug Acquisition Cost (NADAC) pricing files that measure drug acquisition costs for retail pharmacies and the CMS National Summary of State Utilization Data file.

CMS found that generic drugs represented approximately 81 percent of Medicaid prescriptions, but only 26 percent of expenditures during the study period. They also found that nearly 65 percent of Medicaid generic prescriptions were for generic drugs that experienced cost decreases. Generic drugs with very significant acquisition cost increases (more than 100 percent) accounted for approximately 2 percent of \$23.3 billion in total Medicaid expenditures on all prescription drugs (generic and branded) and approximately 9 percent of \$6.0 billion in total Medicaid expenditures on generic drugs over the study period. Expanding the definition of a significant increase in acquisition costs to include increases of more than 20 percent means that less than 4 percent of total Medicaid expenditures on all prescription drugs and less than 15 percent of Medicaid expenditures on generic drugs experienced a significant increase.

⁸ IMS Institute for Healthcare Informatics. Medicines Use and Spending Shifts. A Review of the Use of Medicines in the U.S. in 2014. April 2015.

⁹ <http://www.healthsystemtracker.org/chart-collection/what-are-the-recent-and-forecasted-trends-in-prescription-drug-spending/>

¹⁰ IMS Institute for Healthcare Informatics. Medicines Use and Spending Shifts. A Review of the Use of Medicines in the U.S. in 2014. April 2015.

¹¹ Internal CMS analysis.

Figure 1 provides a description of the shares of generic expenditures affected by different percentage changes in the generic drug acquisition cost. Table 1 provides this breakdown as a percent of generic and total pharmaceutical expenditures and as a percent of generic and total prescriptions.

Figure 1: Percent of Total Medicaid FFS Generic Prescription Expenditures, by Percent of Acquisition Cost Change between July 1, 2013 and June 30, 2014

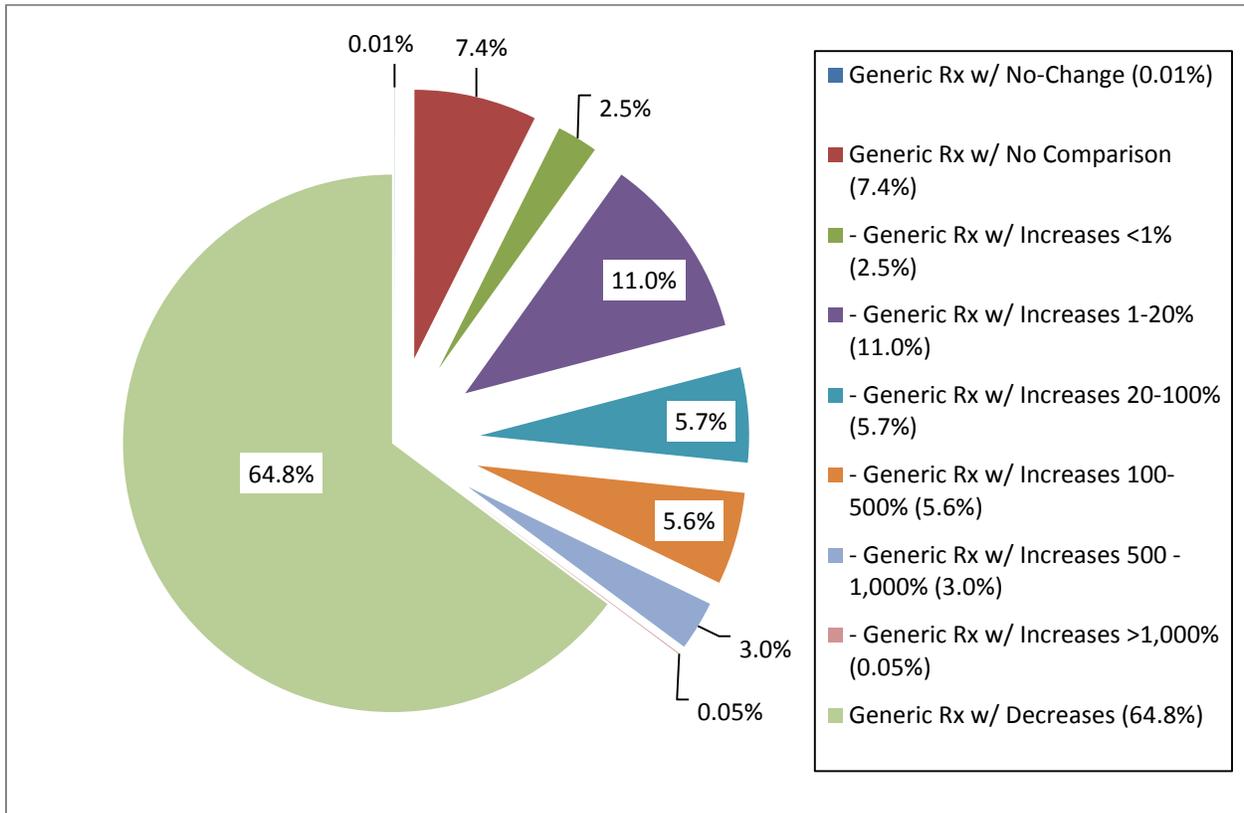


Table 1: Summary of Total Medicaid FFS Prescription Drug Groups

Generic Prescription Drug Acquisition Cost Changes in Millions (7/1/2013 - 6/30/2014)						
Acquisition Cost Change	Medicaid FFS Generic Rx Expenditures (millions)	Percent of Overall Generic Rx Expenditures	Percent of Overall Rx Expenditures	Number of Generic Rx Prescriptions (millions)	Percent of Overall Generic Prescriptions	Percent of Overall Prescriptions
Generic Rx w/ Increases	\$1,674.2	27.8%	7.2%	78.5	41.9%	33.9%
Generic Rx w/ <1% Increase	\$148.6	2.5%	0.6%	5.3	2.8%	2.3%
Generic Rx w/ 1%-20% Increase	\$665.2	11.0%	2.9%	39.3	21.0%	17.0%
Generic Rx w/ 20%-100% Increase	\$343.5	5.7%	1.5%	14.7	7.9%	6.3%
Generic Rx w/ 100%-500% Increase	\$334.8	5.6%	1.4%	15.3	8.2%	6.6%
Generic Rx w/ 500%-1,000% Increase	\$179.1	3.0%	0.8%	3.8	2.1%	1.6%
Generic Rx w/ >1,000% Increase	\$3.0	0.1%	0.01%	0.05	0.03%	0.02%
Generic Rx w/ Decreases	\$3,900.8	64.8%	16.7%	104.4	55.7%	45.1%
Generic Rx w/ No Change	\$0.7	0.01%	0.00%	0.04	0.02%	0.02%
Generic Rx without enough NADAC data	\$444.4	7.4%	1.9%	4.5	2.4%	1.9%
Overall Generic Rx	\$6,020.1	100.0%	25.8%	187.4	100.0%	80.9%

Table 2 presents the change in acquisition costs for some of the generic drugs that have been the focus of media scrutiny. Although these drugs have had very large percentage increases in acquisition costs, the impact on overall Medicaid prescription drug expenditures is relatively small. For example, tetracycline had an increase in acquisition cost of more than 17,000 percent, but it represents only 0.001 percent of Medicaid prescription drug expenditures and 0.001 percent of overall Medicaid prescriptions dispensed.

Table 2: Examples of Generic Drug Groups with Significant Percentage Changes in Acquisition Costs between July 1, 2013 and June 30, 2014

Drug Name	NADAC as of 7/1/2013	NADAC as of 6/30/2014	Percent Change in NADAC	Medicaid FFS Generic Rx Expenditures	Percent of Overall Medicaid Rx Expenditures ^a	Medicaid FFS Generic Rxs	Percent of Overall Medicaid Rxs
Tetracycline 500mg Capsules	0.04823	8.59172	17,714%	\$0.2M	0.001%	1,757	0.001%
Captopril 50mg Tablets	0.03346	1.30700	3,806%	\$0.2M	0.0008%	10,109	0.004%
Clomipramine 75mg Capsules	0.42492	8.15163	1,818%	\$1.9M	0.008%	5,896	0.003%
Doxazosin Mesylate 1mg Tablets	0.04863	0.61716	1,169%	\$0.3M	0.001%	15,505	0.007%
Fluconazole 100mg Tablets	0.13704	1.50144	996%	\$1.5M	0.006%	93,136	0.040%
Digoxin 125mcg Tablets	0.10981	1.01854	828%	\$1.9M	0.008%	100,167	0.043%
Divalproex Sodium ER 500mg Tablets	0.26540	2.38072	797%	\$98.6M	0.423%	542,863	0.234%

Overall, it appears that generic drugs continue to account for the majority of Medicaid prescriptions, but a much smaller amount of Medicaid drug expenditures than branded drugs. Consistent with this, drug acquisition costs fell for the majority of generic Medicaid prescriptions measured by both volume and total generic expenditures. Among Medicaid generic prescription drugs that experienced an increase in acquisition cost, most were drugs with an increase of less than 20 percent. For the generic drugs that experienced an increase in acquisition costs, nearly a quarter more than doubled their acquisition cost. The generic therapeutic drug classes that did experience substantial increases in acquisition costs had relatively low Medicaid drug expenditures and number of prescriptions filled.

Changes in Average Manufacturer Price (AMP)

The HHS Office of the Inspector General (OIG) undertook a separate analysis of AMP¹². The AMP is the price paid to manufacturers and reported to CMS for sales to retail organizations. The OIG analyzed changes in the actual AMP relative to an inflation-adjusted AMP from 2005 to 2014 for the top 200 Medicaid generic prescription drugs as ranked by Medicaid reimbursement each year during the time period. They found that on average 22 percent of generic prescription drugs had an actual quarterly AMP that exceeded the inflation-adjusted AMP over the study period, ranging from 18 percent in 2006 to 35 percent in 2014. For comparison, the OIG previously completed an analysis of actual quarterly AMP relative to inflation-adjusted AMP from 1991 to 2004 and found that on average 35 percent of generic drugs had an actual AMP that exceeded the inflation-adjusted AMP. This indicates that since 1991, a significant percentage of generic drugs have had AMP increases greater than the inflation-adjusted AMP.

Changes in Retail Prices

The AARP examined generic drug prices¹³ using the Truven Health MarketScan Commercial Database and Truven Health MarketScan Medicare Supplemental Commercial Database to analyze changes in retail prices¹⁴ for the 280 generic drugs most commonly used by older Americans from 2006 to 2013. The AARP found that from 2006 to 2013, prices for the generic drugs most commonly used by older Americans fell each year, with the largest annual generic drug price decrease of 14.5 percent occurring in 2012. They also found the smallest annual generic drug price decrease in 2013, 4 percent, with 73 percent of generic drugs experiencing a price decrease. Of the drugs with retail price increases in 2013, eleven of them (4 percent) had increases greater than 30 percent, and two of these exceeded 1,000 percent. Additionally, AARP found that large price increases appear to be associated with certain manufacturers. For the majority of generic manufacturers with at least two drugs in the study (22 out of 26 or 85 percent), the retail prices of their generic drugs decreased. Of the four with price increases, one drug manufacturer had a weighted average annual price increase of 827 percent for its four drugs, more than 60 times higher than any other drug manufacturer with an increase during the study period. The generic drug manufacturer with the next largest weighted average increased retail prices by 12.8 percent.

The AARP analysis also found that while generic drug prices have declined, branded drug prices have increased, resulting in a growing gap between generic and branded drug prices. In 2010, the average annual retail price of therapy for a generic drug was \$551; this fell to \$283 in 2013. Meanwhile, the average annual retail price of therapy for a branded drug rose from \$2,068 in 2010 to \$2,960 in 2013. This means the ratio between branded and generic prices has risen from 3.8:1 to 10.5:1 between 2010 and 2013.

Summary

¹² HHS OIG. 2015. Average Manufacturer Prices Increased Faster Than Inflation For Many Generic Drugs. A-06-15-00039.

¹³ AARP 2015 *Trends in Retail Prices of Generic Prescription Drugs Widely Used by Older Americans, 2006-2013*

¹⁴ The retail price is the total price billed to the insurer.

Analysis of various drug price data indicate that overall branded drug prices are increasing substantially, while overall generic drug prices are decreasing. The large percentage of prescription drugs dispensed as generics continues to hold down overall price inflation for prescription drugs. However, the data indicate that prices are increasing dramatically for some generic drugs, raising questions as to why this is occurring..

The Generic Drug Market

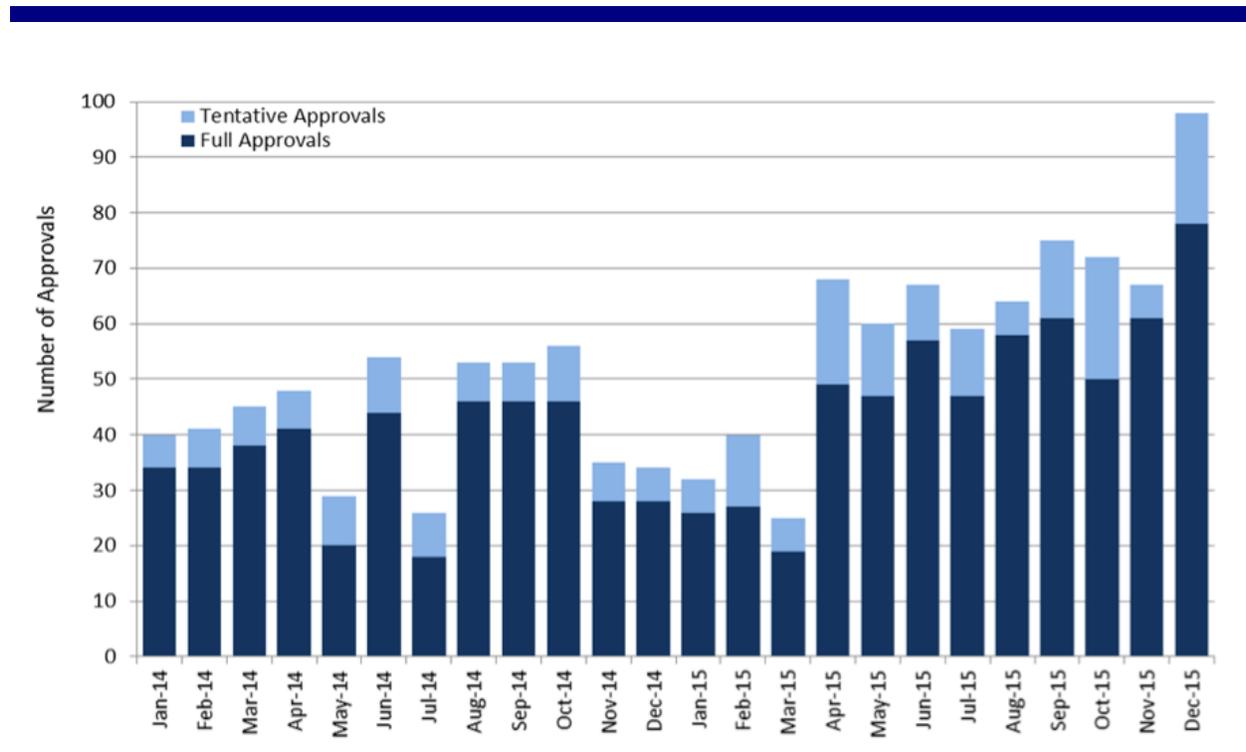
In order for new branded products to gain approval, drug manufacturers must submit a new drug application (NDA) to the Food and Drug Administration (FDA) that contains data demonstrating the new drug is safe and effective for its intended use. Generic drugs manufacturers are able to submit abbreviated new drug applications (ANDAs) to the FDA that rely on the safety and efficacy evidence previously submitted by the branded drug manufacturer. In order to gain approval, a generic drug has to have the same active ingredient, strength, dosage form, and route of administration as the branded drug, and generally must have the same labeling and indications for use as the branded drug. The generic drug manufacturer also must demonstrate that the generic drug is bioequivalent to the branded product, and must meet the same quality and manufacturing standards as branded products.

FDA Review Time for ANDAs

As part of the Food and Drug Safety and Innovation Act, Congress enacted the Generic Drug User Fee Amendments (GDUFA) of 2012, which provides additional funding for FDA's generic drug program, so that the Agency can expedite review of generic drug applications.

The cumulative result of FDA efforts since enactment of GDUFA is a significant increase in the productivity of the FDA generics program. As the chart below indicates, FDA ended last year at a new monthly high of 99 approvals and tentative approvals in December.

Figure 2. Approvals and Tentative Approvals



Under GDUFA, generic drug companies have paid user fees to FDA when they submit ANDAs. As part of the user fee agreement, FDA is phasing in performance goals for reviewing ANDAs. For FY2016, the goal is to review 75 percent of ANDAs within 15 months, and in FY2017, the FDA’s goal is to review 90 percent of ANDAs within 10 months.

Historically, it has taken several review cycles before an ANDA is approved often related to the completeness and quality of the application. As noted in the public minutes published as part of the GDUFA II negotiations now underway, FDA and industry are discussing a pre-ANDA process by which FDA and industry would address approval challenges for particular drugs prior to ANDA submissions, which could make a meaningful difference in the completeness and quality of applications. Drug companies may need to provide more information to the FDA than was included in their initial ANDA, or adjust the formulation of the drug to meet the FDA’s standards. In 2014, the median time from receipt of an ANDA to approval was 42 months. This median review time reflects in part factors outside the control of the FDA reviewers, including application quality issues, time spent with the sponsor responding to deficiencies, and patents that block approval of an ANDA. In addition, the 42 month timeframe reflects time that the backlog of pre-2012 ANDAs spent in the review queue before FDA received additional resources under GDUFA. At the end of FY2015, FDA had issued an approval, tentative approval, or a complete response letter for about 82 percent of the 4,739 backlogged applications and 88 percent of prior approval supplements.

FDA prioritizes the review of ANDAs for “first generics,” which are those products for which there is no generic competition and patent and exclusivity barriers to approval have been lifted or will be lifted soon. FDA also prioritizes ANDAs for which the product is in shortage, is subject to special review programs like the President’s Emergency Plan for AIDS Relief (PEPFAR), is

related to public health emergencies and certain government purchasing programs, or is subject to statutory or other legal requirements.

It should also be noted that FDA is fulfilling, and in many cases substantially exceeding, its negotiated GDUFA commitments. FDA's productivity is consistent and it is currently sustaining record or near record levels of generic drug approvals.

Paragraph IV Drug Patent Challenges

Branded drug manufacturers are required to list patents claiming their drug or a use of their drug product. Generic drug companies may submit ANDAs with the intention of challenging the validity of the patents listed for the branded drug that their application references. The generic applicant must certify that the patent is invalid or that the generic drug will not infringe on the patent through the manufacture, use or sale of the generic product. It must also notify the NDA holder and if different, the patent holder of the reference drug listed in the submission of the ANDA. The first company (or companies) to submit an ANDA and successfully challenge the patent of the branded drug may be approved for marketing prior to patent expiration and may receive 180 days of marketing exclusivity. During this time the first generic drug (or drugs, if there was more than one "first" applicant) would compete only with the branded drug (and each other if there is more than one "first" applicant), and generally no other generic drugs may enter the market. Once this period of exclusivity has expired, other companies may market competing generic drugs, and prices typically decline further.

Competition in the Generic Drug Market

Traditionally, the generic drug market has been characterized by aggressive competition. After relevant patents and claims to exclusivities for a branded drug expire (and after any 180 day exclusivity for "first" generic applicant(s) has expired) many generic drugs may enter the market quickly and prices decline rapidly. One analysis examining data from 2005 to 2009, found that generic prices fell by half, on average, in the 12 months following generic entry and fell by 77 percent in the 24 months after entry. Frequently, there are more than 10 generic manufacturers competing for market share by 24 months after generic market entry¹⁵. The number of competitors is important, as larger numbers of competitors result in more competition and lower prices. One study estimated the price of generics to be 90 percent of the branded drug's price if there is one generic drug, 63 percent of the branded drug's price if there are five generic drugs, and 40 percent of the branded drug's price if there are ten generic drugs¹⁶.

Economic Explanations

¹⁵ Berndt and Aitken. October 2010. Brand loyalty, generic entry and price competition in pharmaceutical in the quarter century after the 1984 Waxman-Hatch legislation. NBER working paper 16431.

¹⁶ Grabowski, Ridley, and Schulman. 2007. Entry and competition in generic biologics. *Managerial and Decision Economics*. 28:439-451.

Although the overall the generic drug market remains very competitive with the typical branded drug having numerous generic competitors putting downward pressure on prices once exclusivities and patents have expired, some drugs are experiencing very large price increases. We consider some economic forces that may produce these results.¹⁷

As with new drug pricing, what a company can charge for an existing drug, whether an old generic or not, depends on the medical value of the drug as well as the competitive landscape for the drug. Demand for some drugs can be quite insensitive to price if users do not have very good alternatives from both clinical and economic perspectives. In such a situation, users will continue to purchase the drug even if firms dramatically increase the price. The relevant alternatives include not only generic versions of the drug, should they exist, but also other drug molecules that treat the same condition (so-called therapeutic substitutes).

In this section, we explore several dynamics that affect the competitive landscape for a given drug and therefore enable prices to rise.

Markets With Limited Entry

Smaller markets tend to attract fewer competitors. In the extreme, there may be no market entry at all. Of the 1,328 approved branded drugs, there is a sizable group, about 10 percent, whose exclusivities and patents have expired, but no drug companies have come forward to submit ANDAs.¹⁸

Grabowski, Ridley, and Schulman are the latest to show that the number of generic drug competitors increases with market size¹⁹. Drug markets with smaller revenues (well below the median for patent-protected drugs) may not attract as many entrants, and prices may persist at higher levels than would be the case in a larger market²⁰. A strong version of this point was made by Anderson who argued that regulatory burden cannot explain the rapid increases in generic drug prices while also noting that large generic manufacturers may be unwilling to enter markets with less than \$100 million in sales because of the administrative barriers to entry²¹.

When generic drugs have very small markets and are unable to support multiple competitors, there is an increased risk for extreme price increases. Analysis of Medicaid data showed that the generic drugs with the largest price increases had low levels of Medicaid spending. Small

¹⁷ It should be noted that following generic entry the market tends to segment with the vast majority of consumers shifting to the generic version of the drug. Those consumers that remain “loyal” to the branded product experience price increases since they are not very responsive to price changes leaving the branded manufacturer with a set of customers that are not sensitive to price. This enables the branded company to raise its prices with little fear of further loss of customers. See Frank RG and Salkever DS. “Generic Entry and the Pricing of Pharmaceuticals,” *Journal of Economics and Management Strategy*, 6(1):75-90, 1997 for a complete explanation and evidence.

¹⁸ Source: Food and Drug Administration (2016)

¹⁹ Grabowski, Ridley, and Schulman. 2007. Entry and competition in generic biologics. *Managerial and Decision Economics*. 28:439-451.

²⁰ *Generic Drug Industry Dynamics*. Reiffen, David and Ward, Michael R. 1, February 2005, The Review of Economics and Statistics, Vol. 87, pp. 37-49.

²¹ Anderson G. Sudden Price Spikes in Off-Patent Drugs: Perspectives from the Front Lines. Testimony for the U.S. Special Senate Subcommittee on Aging. December 9, 2015.

markets mean that the return on investment is low compared to the cost of establishing manufacturing and marketing arrangements for the drug.

Market Concentration

Mergers and acquisitions involving generic drug manufacturers means that there may be fewer competitors producing a given generic. Given the importance of the number of competitors in driving down generic drug prices, the Federal Trade Commission routinely scrutinizes pharmaceutical company mergers. Acquisitions, while not necessarily changing the number of firms in the market, may lead to a reassessment of the product portfolio. Firms may decide that the market can bear higher prices and reset prices accordingly.

For these reasons, the recent trend toward the consolidation among generic drug manufacturers is of concern. For example, in 2015, Teva purchased Allergan Plc's generic business in a \$40.5 billion deal,²² and Endo International agreed to buy Par Pharmaceutical Holdings, increasing the size of Endo's generics business.²³ Valeant, which has received scrutiny about its acquisition strategy, acquired about 100 companies since 2010²⁴ and reset prices for many drugs that came with these acquisitions.²⁵ Analysts expect to see a continuing increase in the number of mergers²⁶.

In addition, firms may decide to reassess pricing even in the absence of merger and acquisition activity. A sizable share of older generic drugs have only two or three competitors, particularly in the case of sterile injectable products, some because of exit and some because the market was not particularly attractive and therefore did not experience much entry. Other older generic drug markets may have many manufacturers, but for reasons of capacity constraints, there are one or two dominant players. Such concentrated markets can sustain prices that are above-competitive level even if products are essentially identical. This is an area well studied in other sectors of the economy such as airlines and wholesale energy markets. In generic drugs, digoxin tablets are a good example of such forces limiting competition to only two competitors in spite of price increases.²⁷

Temporary and Permanent Market Exit

As discussed earlier, concentrated markets create market power over prices. Just as entry and mergers can change market concentration, so can market exit, whether temporary or permanent.

²² <http://knowledge.wharton.upenn.edu/article/why-teva-paid-40-5-billion-for-allergans-generic-business/>

²³ Yu. May 18, 2015 Endo buys Par Pharma for \$8 billion to expand generics. USA Today.

²⁴ <http://www.theglobeandmail.com/report-on-business/valeant-faces-increasing-scrutiny-as-shares-plunge-by-20-percent/article27129779/>

²⁵ <http://www.nytimes.com/2015/10/05/business/valeants-drug-price-strategy-enriches-it-but-infuriates-patients-and-lawmakers.html>

²⁶ Koons, C. Teva's just the start as more generic drug makers poised to merge. www.bloomberg.com. August 5, 2015.

²⁷ <http://www.bloomberg.com/bw/articles/2013-12-12/generic-drug-prices-spike-in-pharmaceutical-market-surprise>

Because shortages are a result of one or more firms suspending their manufacturing operations,²⁸ some of the drugs affected by shortages experienced price increases.

In some cases, shortages result from industry decisions to abandon production of a drug in favor of higher value product lines, which in turn leads to higher market concentration and more pricing power on the part of the remaining competitors. Market exit can also be temporary as with temporary production shut downs to address serious manufacturing quality problems. Shortages in the sterile injectable products market have been caused by disruptions in manufacturing due to quality problems. Coupled with limited potential to increase production capacity²⁹, this dynamic can lead to increased prices.

Two drugs identified in our analysis with large price increases were also in shortage, doxycycline and tetracycline. Acquisition costs for tetracycline increased more than 17,700 percent in the CMS NADAC data and AARP reported that retail prices for doxycycline hyclate 100 mg capsules increased more than 1,900 percent. Tetracycline was available from multiple manufacturers before going into shortage in 2011. A sole manufacturer reintroduced the drug to the market in 2013 and the price was subsequently increased. Doxycycline continues to be available from multiple manufacturers. However, in early 2013 when there was supply disruption resulting from one manufacturer experiencing manufacturing problems, the pricing was increased. Further exploration is needed to determine how often manufacturers change pricing in response to supply disruption or shortages.

Patents, Approvals, and Exclusivity

Significant price increases have occurred after branded drug companies received new patents or market exclusivity associated with new approvals that aim to create incentives for innovation. For example, some asthma drugs, including inhalers containing albuterol, have largely been returned to patent protected status because of a ban on chlorofluorocarbons (CFCs) that took effect for inhalers in 2008³⁰. This meant that generic CFC propelled albuterol inhalers were removed from the market and were replaced by patented hydrofluoroalkane (HFA) propelled inhalers. This resulted in prices increasing from \$13 per inhaler to more than \$50³¹.

Colchicine for the treatment of gout is an example of the effect of new approvals and associated exclusivity. Prior to 2009, the FDA had never formally approved colchicine, as it had been marketed prior to the requirements for new drug approval. In 2009, the FDA approved NDAs for Colcrys (oral colchicine), and the product received marketing exclusivity under the law.

²⁸ GAO. 2014, Drug shortages: public health threat continues, despite efforts to health ensure product availability. GAO-14-194.

²⁹ HHS ASPE. October 2011. Economic analysis of the causes of drug shortages. ASPE Issue Brief.

³⁰ FDA. Transition from CFC Propelled Albuterol Inhalers to HFA Propelled Inhalers: Questions and Answers. Available at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm077808.htm>.

³¹ Ross and Fedberg. On Chlorofluorocarbon bans and inhaled albuterol prices. JAMA Internal Medicine.2015. 175(7):1179.

While the unapproved versions of the product had previously been available for 9 cents per pill, the sponsor of Colcris priced the drug at \$4.85 per pill³².

Another example of the effects of approvals and exclusivity is hydroxyprogesterone caproate for injection. After an approved hydroxyprogesterone caproate for injection product was removed from the market by its sponsor for business reasons, compounders began to offer the product for about \$10 a dose. In 2011, FDA approved KV Pharmaceutical's NDA for Makena (hydroxyprogesterone caproate for injection) for a new use for a very limited patient population, which qualified for 7 years of orphan drug exclusivity. KV Pharmaceuticals priced Makena at \$1,500 per dose. The FDA has since approved an ANDA for a hydroxyprogesterone caproate for injection product for the original indications that do not have orphan exclusivity protections.

Distribution Activities

Along with taking advantage of opportunities to gain marketing exclusivities, manufacturers (including generic manufacturers) may raise prices due to the complex distribution systems and opaque pricing schemes. For example, Valeant Pharmaceuticals, which has aggressively raised prices for a number of its generic drugs, has been cited for using a strategy in which doctors submit prescriptions to a pharmacy affiliated with the drug manufacturer. The pharmacy insulates the doctor from reimbursement difficulties and mails the drug directly to the patient. The manufacturer absorbs the risk that the insurer will refuse to pay, but because prices are so high, even if some insurers do not pay, the manufacturer still comes out ahead. The pharmacy will also engage in aggressive tactics to obtain payment, such as resubmitting a prescription at different prices until the insurer agrees to pay³³.

Conclusions

Based on the analyses conducted to date, a vibrant generic market can exert downward pressure on overall drug prices. Generic drugs account for the majority of prescriptions filled in the US and represent much lower costs to the healthcare system. The review presented in this paper shows that, in fact, the market for generics continues to be competitive and to provide downward pressure on drug prices overall. There are, however, segments of the market that appear to be operating less efficiently. This means that it is important to ensure that we continue to promote a competitive generic drug industry.

Factors such as drug shortages, the ability to obtain new market exclusivities, the distribution system, small market size, and consolidation in the generic drug industry present potential barriers to ongoing competition in the generic drug market, and will be subject of continued study.

³² Kesselheim and Solomon. Incentives for Drug Development: The Curious Case of Colichicine. *NEJM* 2010 326(22):2045-2047.

³³ Whalen, J. Valeant Flap Puts Focus on Drug Maker's Ties to Pharmacies. www.wsj.com. October 30, 2015.

