Analysis of Pharmaceutical Products with Large Price Changes in a Regional Hospital System

Christina M.L. Kelton[1], Robert P. Rebelein, Michelle L. Dusing, Yann Ferrand, and Jeff J. Guo

Christina M.L. Kelton, PhD
College of Business, University of Cincinnati
P.O. Box 210223
Cincinnati, OH 45221-0223
Tel.: (513) 556-2983, Fax: (513) 556-2953
Email: chris.kelton@uc.edu

Robert P. Rebelein, PhD
Department of Economics, Vassar College
124 Raymond Ave., Box 290
Poughkeepsie, NY 12604-0290
Tel: (845) 437-7393, Fax: (845) 437-7576
Email: rebelein@vassar.edu

Michelle L. Dusing, PharmD, BCPS
Health Alliance Pharmacy Services
3200 Burnet Ave., 3BAPS
Cincinnati, OH 45229
Tel.: (513) 585-8005, Fax: (513) 585-8003
Email: dusingml@healthall.com

Yann Ferrand, MBA
College of Business, University of Cincinnati
P.O. Box 210130
Cincinnati, OH 45221-0130
Tel: (513) 556-7052, Fax: (513) 556-5499
Email: ferrany@email.uc.edu

Jeff J. Guo, PhD
College of Pharmacy, University of Cincinnati
PO Box 670004
Cincinnati, OH 45267-0004
Tel.: (513) 558-8613, Fax: (513) 558-4372
Email: jeff.guo@uc.edu

[1] Corresponding Author. Christina Kelton is Professor of Economics at the University of Cincinnati; Robert Rebelein is Assistant Professor of Economics at Vassar College; Michelle Dusing is Director, Clinical Pharmacy Programs, at the Health Alliance; Yann Ferrand is a doctoral student in the Quantitative Analysis and Operations Management Department at the University of Cincinnati; and Jeff Guo is Associate Professor of Pharmacoeconomics and Pharmacoepidemiology at the University of Cincinnati. We are very appreciative of the work that Dr. Margaret Pasquale put into assembling the data base for this project and of the support of Marianne Ivey for the continued collaboration between the Division of Pharmacy Services at the Health Alliance and academics at the University of Cincinnati and Vassar College. We thank two anonymous referees for their helpful insights and suggestions. Finally, we thank Oliver Kronawittleithner for his programming assistance. An earlier version of this project was presented as an unpublished poster at the 2nd Asia-Pacific Conference of the International Society for Pharmacoeconomics and Outcomes Research in March 2006; it received a finalist award.

Analysis of Pharmaceutical Products with Large Price Changes in a Regional Hospital System

January 2007

Abstract

PURPOSE: Large price swings for individual drugs complicate the hospital purchasing process, both increasing costs and adversely affecting patient treatment therapy. The objectives for this study are, for a large regional hospital buyer, to describe price changes for individual drugs, therapeutic classes, and drug companies, and to determine factors associated with large price swings.

METHODS: We constructed monthly transaction prices for over 5,000 individual drug products purchased by the Buyer during 2000 and 2001. Of those, we were able to determine annual price changes for 3,085 products, which we describe in detail. 319 products with annual price swings of 20 percent or more between 2000 and 2001 were selected for further analysis. Percentage change in price was regressed on patent expiration (whether a patent expired during the time period), drug shortage (whether one occurred during the time period), whether the drug was branded or generic, and Buyer expenditure on the drug over the study period.

RESULTS: Out of those companies and therapeutic classes, respectively, which accounted for over $1 million in expenditures for the Buyer over 2000–2001, GlaxoSmithKline and sympathomimetics exhibited the highest upswings, while TAP Pharmaceuticals and quinolones were responsible for the largest downswings. Regression results revealed that drug shortages beginning in 2000 ($t=2.25$, $p<0.05$) and 2001 ($t=3.91$, $p<0.01$) were statistically associated with large upward price swings; large downswings were observed for generic drugs whose branded counterpart had a patent expiration in either 1999 ($t=-2.88$, $p<0.01$) or 2000 ($t=-1.66$, $p<0.10$). Price swings were significantly smaller for heavily purchased drugs ($t=-2.74$, $p<0.01$).

CONCLUSION: Underlying the overall drug price inflation rate are many different individual price changes. Upswings are associated with drug shortages, while downswings are caused in part by patent expiration. Generally, with some notable exceptions, high-budget items are not characterized by the largest swings.

KEY WORDS: Price stickiness, Hospital drug purchasing, Hospital drug shortages.

Analysis of Pharmaceutical Products with Large Price Changes in a Regional Hospital System

January 2007

Introduction

In 2003, total pharmaceutical sales in the United States were $216.4 billion, representing an increase of 11.4 percent over $194 billion in sales in 2002. Growth rates of 18 percent and 12 percent, respectively, characterized the 2000–2001 and 2001–2002 periods.[1] These double-digit increases in drug purchases outpaced both the growth in the economy and the growth in overall health-care expenditures. Explaining these rapid increases are new drugs, higher drug utilization, and increasing drug prices. Although mitigated somewhat by generic and over-the-counter entry, large expenditure increases are expected to continue given a growing elderly population, a lengthening life expectancy, and increasing diagnoses of chronic diseases. Furthermore, research and development investment in biotechnology over the last two decades is now paying off in innovative, high-priced therapies. The number of blockbuster products (those with sales exceeding $1 billion annually) totaled 65 in 2003 and 82 in 2004.[2] Both private and public payers are responding with cost-containing strategies (for example, formulary development or drug-rebate negotiations) or protection strategies (for instance, providing high-need and low-income users with prescription drug insurance) in the face of rapidly increasing costs.

The hospital sector accounts for approximately 12 percent of pharmaceutical purchases in the United States. It is a price-sensitive segment that, with the help of strict formularies, strives to keep cost increases to a minimum. Total nonfederal hospital drug expenditures were approximately $23 billion in 2003, representing a 6.3 percent increase compared with 2002. Between 2000 and 2001 (the years featured in our empirical study described below), expenditures grew 11 percent, while, between 2001 and 2002, expenditures grew 9.7 percent.[1] (Note that for 2000 – 2001, 2001 – 2002, and 2002 – 2003, respectively, the U.S. inflation rate, as measured by the annual percentage change in the consumer price index, was 2.9 percent, 1.6 percent, and 2.3 percent.)

Hospital drug purchasing has become more complex over the last decade in the face of rapidly increasing expenditures. Not only must buyers anticipate a higher average pharmaceutical inflation rate, but they must also contend with the very large price swings for individual drugs that tend to occur during high-drug-inflation periods.[3] Moreover, in addition to purchasing complications, large price upswings may lead to clinically adverse outcomes as patients are triaged with respect to their need for the drug. For example, patients may be forced to switch to less expensive alternatives with which clinicians may be less familiar.[4]

Our research has two principal objectives: (1) for a large regional hospital buyer, to describe annual price changes for individual drugs, especially those requiring high expenditures, between the years 2000 and 2001 (after December 2001, the Buyer switched to a different group purchasing organization, causing the data from 2002 and later to be inconsistent with those of prior years); and (2) to identify, describe, and explain any exceptionally large pharmaceutical price swings between the same two years. Since many drugs are sold in noncompetitive markets, price stickiness and large price swings – rather than continuously fluctuating prices – are to be expected.

Price Changes in Noncompetitive Markets

The relationship between market structure and price flexibility has been the topic of an interesting literature in economics for seventy years, dating from Means' study of price behavior during the depression of the 1930s.[5] Since the success of macroeconomic fiscal and monetary policies depends on the degree of price flexibility in the overall economy, empirical documentation of price rigidity is critical. Indeed, a number of economic studies have focused on price stickiness (meaning that prices are slow to change in response to demand and cost changes), and almost all have found a positive relationship between seller concentration (or degree of monopoly power of firms in the market) and price stickiness. Carlton in his influential paper on sticky prices in the *American Economic Review* found that firms in less competitive (more monopolistic) markets tended to have stickier prices than those in more competitive industries.[6] Caucutt, Ghosh, and Kelton confirmed this relationship across approximately 1000 United States manufacturing industries.[7] Powers and Powers studied grocer-to-grocer variation in the size and frequency of price changes for lettuce, and found evidence of infrequent and large price changes in more concentrated grocery markets.[8] Examining wholesale price responses in 188 gasoline markets, Borenstein and Shepard found that firms with market power adjust prices less often than do competitive firms.[9] Arbatskaya and Baye found that online mortgage rates are 30 percent to 40 percent more durable in concentrated markets than in more competitive markets.[10]

The pharmaceutical industry has been described as a collection of differentiated oligopolistic (few-firm) markets,[11] although any branded, patented medication has a monopoly in the sale of a particular chemical formulation for the commercial length of the patent. Regardless, however, of whether pharmaceutical markets are characterized as oligopolistic or monopolistic, all branded pharmaceutical companies are members of the noncompetitive sector of the economy. As such, we would expect a certain degree of price stickiness, accompanied by large price swings at the end of sticky-price spells. Caucutt, Ghosh, and Kelton tested the hypothesis that larger price swings were associated with longer sticky periods and found a statistically significant correlation between length of price constancy and the magnitude of price swing for the majority of industries studied.[7]

Sticky-price spells end when changes in demand or cost are large enough to “unstick” prices; the ensuing price change can be significant. With respect to pharmaceuticals, a substantial downward price swing most likely results from an increase in competition that causes a decrease in demand for the individual drug. Competition increases both with entry of a new branded medication in the therapeutic class or with entry of direct generic competitors. Our expectation, from previous work, is that, although both effects lead to price reduction, the latter effect is generally stronger than the former.[12,13] Another possibility that could result in a price decrease is information discrediting the drug product in either its efficacy or safety attributes. Although a decline in production cost could theoretically explain a price decrease, it is unlikely, in this industry, for cost reductions to be passed on to consumers without a simultaneous increase in competition.

On the other hand, a significant jump in production costs caused, for example, by a shortage in a key input, will lead to a higher profit-maximizing price which most likely will be passed on to drug buyers. The complexity of the pharmaceutical supply chain makes it difficult to identify the reasons for shortages; they can occur not just at the manufacturing stage, but earlier in the supply chain as well. In a comprehensive study of the reasons behind national drug shortages from January 1996 to June 2002, Fox and Tyler report that the most common reason for shortages was "manufacturing difficulties," followed by product discontinuation, a distribution restriction, a raw-material shortage, and a regulatory problem.[4] Other reasons mentioned were "supply and demand" and "business decision." The reason for 26 percent of the shortages studied by Fox and Tyler remains "unknown."[4] The effect of a particular shortage on a buyer's costs depends on the buyer's ability to switch to alternative therapies. The conclusion, however, from the July 2002 symposium of the American Society of Health-System Pharmacists and the American Medical Association on drug shortages, was that drug shortages increased costs for pharmacies and health-care organizations taken as a whole. At one 800-bed hospital, purchases of alternative products and purchases off contract led to an expenditure increase of $25,000 per month. Moreover, increased staff time to deal with shortages is also costly.[14] The Buyer in this study, for example, has devoted considerable human resources to deal with the drug shortages it faces.

Alternatively, an increase in price could be due to an increase in demand as a newer drug in a therapeutic class demonstrates higher efficacy than its competitors or gets approved for additional indications by the Food and Drug Administration. Finally, the pricing strategy for a branded medication may call for an increase in price just prior to patent expiration and generic entry. If the branded manufacturing firm chooses not to compete on price with the generics, it may raise its price to the less price-elastic buyers, settling for a small market share and perhaps eventual discontinuation of production.

The Buyer

The Buyer in this study is a nonprofit system of six hospitals that serve a large community base of approximately 1.5 million people. It is located in the Midwest region of the country. The hospitals are distinct in character. A substantial number of uninsured and underinsured patients are served by one of the hospitals (which is a teaching hospital as well), and an annual tax levy goes part way to covering the cost of indigent care. The Buyer spends approximately $50 million per year on pharmaceuticals, and all drug purchasing decisions are made by the Division of Pharmacy Services. The Buyer, like other health-care providers, has seen its drug expenditures increase dramatically in the last few years. The Buyer has a single formulary, the same for inpatients and outpatients, which it updates on a monthly basis with input from physicians and others in the system.

In purchasing pharmaceuticals, the Buyer may contract directly with a pharmaceutical company (which it seeks to do for its largest purchases); it may work through a group purchasing organization, which contracts on behalf of the Buyer as well as on behalf of other institutional buyers in the group; or it may buy drugs without any contract.

Each of the direct contracts is distinct. There is no simple pricing formula nor is there an industry pricing rule. Some companies offer large discounts for drugs purchased in an inpatient setting expecting spillover into the outpatient setting; other companies do not. Nevertheless, a striking feature of most of the direct contracts is a "market-share" stipulation that the Buyer must maintain a minimum market share (purchases of the company's drug relative to purchases of competitors' products). In other words, discounts are almost always based on market share rather than volume. Each contract specifically defines a market in which the Buyer is to maintain a minimum share. If it fails to do so, the discount falls or disappears altogether. All available forms of a drug are usually covered on the same contract. Often, more complex contracts address purchases in more than one market for an individual company and reflect bundled contracting techniques. Maintaining a certain market share in one market may result in discounted prices not only in that market but also in another market in which buyer and seller "meet."

Our data base covers essentially all of the Buyer's acute-care pharmaceutical purchases during the 2000 – 2001 period. (A few purchases, representing less than one percent of total expenditures, are omitted due to distinct accounting procedures.) Only acute-care drugs are included in the analysis. Pharmaceuticals purchased for outpatient use and/or subject to PHS or Public Health Services pricing, representing less than 20 percent of the Buyer's expenditures, are not included. Pricing for the PHS class of trade is expected to be quite different from acute-care drug pricing and should be studied separately. Total expenditures on drugs in our sample rose 7.4 percent from $39.2 million in 2000 to $42.1 million in 2001. Of the $2.9 million increase in spending, $1.9 million is accounted for by new-drug-form purchases. Increasing utilization of drug products purchased in both 2000 and 2001 accounts for approximately $220,000 of the expenditure increase, while price increases of drugs purchased in both years account for the remaining $780,000 increase. The weighted average (weighted by the Buyer's total two-year expenditures on the drug product) percentage price change for drugs purchased in both 2000 and 2001 was 2.0 percent.

Methods

In this section, we describe our data. We also develop a regression model that provides an explanation for at least some of the variation in price swings across drug products.

Data

We have an extremely rich data set for the regional hospital buyer described above, which provides a rare opportunity to observe the actual prices paid by a large pharmaceutical buyer. Specifically, we have, for calendar years 2000 and 2001, monthly expenditures and unit quantities for 5,250 inpatient national drug codes (NDCs or individual drug products purchased for hospital patients) that were purchased in at least one month during the two-year period. These purchases were summed across the Buyer's six hospitals.

Monthly transaction prices for a given NDC are computed as expenditures divided by quantities. Let P_{it} represent the transaction price for NDC *i* in month *t*. These transaction prices, unlike other price points in the industry such as average wholesale prices (AWPs) or wholesale acquisition costs (WACs), are what the Buyer actually paid. Although there are instances in which the Buyer received rebates from pharmaceutical manufacturers, rebates were far less important than they are to, say, state Medicaid programs, and their omission from consideration here is believed by the Buyer not to have affected the results of this study. Indeed, the Buyer estimates that less than 10 percent of total expenditures is subject to any rebate, and, even for those instances in which there are rebates, the rebate resents less than 5 percent of drug cost. In general, the Buyer prefers contracts without rebates due primarily to the administrative burden, as well as the deferred payment, that they represent.

Evidence of Price Stickiness

There were 348 drug products purchased by the Buyer *every month* between January 2000 and December 2001. For these NDCs, we calculated average spell length (ASL) following the approach to price rigidity suggested by Carlton.[6] Specifically, we computed the average number of months over which the drug price did not change by more than one percent. We found the ASL to be 4.7 months. (The longest spell length in our data was 23 months for an erythromycin NDC purchased by the Buyer.) This average spell length is higher than most ASL values found in Caucutt, Ghosh, and Kelton.[7]

Description of Price Changes

There were 3,085 NDCs purchased at least once during both calendar years 2000 and 2001, that is, had at least two months of purchase data, one in 2000 and one in 2001. For these NDCs, we constructed P_{i00} and P_{i01} as averages of the available monthly transaction prices in 2000 and 2001, respectively. We let ΔP_i be the percentage change in price for NDC *i* between the two years: $\Delta P_i = [(P_{i01} - P_{i00}) / P_{i00}] \times 100$.

For companies that accounted for a significant share (over $1 million) of the Buyer's expenditures over the two-year period, we computed expenditure-weighted averages of individual price changes. That is,

$$\overline{\Delta P}_c = \sum_{i=1}^{C} E_i \Delta P_i / \sum_{i=1}^{C} E_i \ ,$$

where $\overline{\Delta P}_c$ is the weighted average price change for company *c*, E_i is the sum of expenditures by the Buyer on NDC *i* from January 2000 through December 2001, and *C* is the number of drug products purchased by the Buyer from company *c*. We similarly constructed expenditure-weighted average price changes for individual markets *m* ($\overline{\Delta P}_m$) and for individual generic compounds *j* ($\overline{\Delta P}_j$).

Identification of Large Price Swings

We next identified those NDCs that experienced "large" price swings between 2000 and 2001. Figure 1 shows the relative frequencies of percentage price changes across the NDCs. Of the 3,085 NDCs, 2,385 (77 percent) experienced price changes between –10 percent and +10 percent; another 364 experienced positive or negative price changes between 10 percent and 20 percent. The remaining 336 NDCs experienced price swings of at least 20 percent, which we consider "large" given the average price change of approximately two percent. After removing 17 of the drug products, which had incomplete information for the explanatory variables described below, we were left with 319 observations for which $|\Delta P_i| \geq 20$ percent. There were 205 large upswings and 114 large downswings in this group.

Empirical Model

We develop an empirical regression model to help explain variation in price changes across the large-price-change NDCs purchased by the Buyer. Our dependent variable is ΔP as defined above. With one exception, all explanatory variables are dummy (0/1) variables.

Although we have no particular expectation regarding which group of drugs (brand-name or generic) should have a higher price change, we choose to control for differences in pricing strategy between generic and brand-name pharmaceutical companies. Moreover, since we believe there is an important interaction between branded status and patent expiration that affects price change, as explained below, we include branded status (B) as a "main effect" variable. We assign B = 1 if the NDC is branded and B = 0 otherwise.

The possibility that drug shortages cause large price upswings suggests that we should also include shortage variables in the model. Four shortage variables (again, dummies) are included: S99, S00, S01, and S02, respectively, depending on whether a shortage began in 1999, 2000, 2001, or 2002. (We realize that 2002 is after our study period; however, we are interested in expectations as well as current pricing strategies.) Shortages and their starting dates are found in Fox and Tyler.[4] According to an editorial in the *American Journal of Health-System Pharmacy*, the number of national shortages potentially affecting patient care increased from 3 in 1996 to 119 in 2001. The level fell to 87 in 2002 and 73 in 2003.[15]

To capture one of the main reasons for large price downswings, we include four competition variables in the model: P99, P00, P01, and P02 are dummy variables which, respectively, denote whether a patent expired for the relevant generic compound in 1999, 2000, 2001, or 2002.[16,17] We anticipate that a patent expiration for a branded drug leads to a reduction in price for its generic producers as more generic companies enter the market. However, there is no such expectation for the branded drug itself. Depending on the branded pharmaceutical company's pricing strategy, it may reduce price in order to compete with the generic producers, or it may actually choose to increase price since its only sales might be to price-insensitive buyers after the patent expires. The drug company may plan to discontinue production eventually, leaving the market to the generic producers. Hence, we also include in the model (dummy) variables that can capture the interaction between the branded/generic dummy and the patent expiration dummies; these are denoted BXP99, BXP00, BXP01, and BXP02, respectively. Our expectation is that these variables should have a positive impact on drug price change.

Finally, we include a variable denoted EXP which is the natural logarithm of total expenditures by the Buyer on the drug product over the 2000–2001 period. A larger expenditure gives the Buyer a greater incentive to negotiate vigorously with the pharmaceutical manufacturer for a lower price increase (or larger price decrease). We expect EXP's effect on price change to be negative.

Our regression model is as follows:

$$\begin{aligned}\Delta P_i = \ & \beta_O + \beta_1 B_i + \beta_2 S99_i + \beta_3 S00_i + \beta_4 S01_i + \beta_5 S02_i + \\ & \beta_6 P99_i + \beta_7 P00_i + \beta_8 P01_i + \beta_9 P02_i + \beta_{10} BXP99_i + \beta_{11} BXP00_i + \\ & \beta_{12} BXP01_i + \beta_{13} BXP02_i + \beta_{14} EXP_i + \varepsilon_i, \qquad (1)\end{aligned}$$

where ε_i is assumed to have the standard properties.

Results

We begin by describing price changes across all the drug products purchased by the Buyer in both 2000 and 2001. Over 1000 different generic compounds were purchased from over 200 different pharmaceutical companies, which could be categorized into 148 different therapeutic classes.

Full Data Base

Figure 2 shows expenditure-weighted average price changes ($\overline{\Delta P_c}$) for those companies that account for a relatively large share of the Buyer's drug expenditures. For drugs from each of the pharmaceutical companies in Figure 2, almost all of which are branded drug companies, the Buyer spent over $1 million over the two-year period 2000 – 2001. In descending order from left to right, the Buyer spent over $7 million on drugs from Eli Lilly, $6.7 million on drugs from Pfizer, $6 million on drugs from Amgen, and so forth, down to just over $1 million each for drugs from AstraZeneca, TAP, and Nycomed. There are more positive average price changes shown in Figure 2 than there are negative changes. GlaxoSmithKline (with $3.8 million in sales to the Buyer from 2000 – 2001) shows a weighted average price change of 10.9 percent, the highest among the companies depicted. Average price decreases of over 10 percent are observed for Bayer, Fujisawa Healthcare, and TAP Pharmaceuticals.

Similarly, Figure 3 shows average price changes ($\overline{\Delta P_m}$) for those therapeutic classes for which the Buyer spent over $1 million in the 2000 – 2001 period. Again, from left to right, the Buyer spent close to $8 million on hematopoietic agents, $6.8 million on antineoplastic agents, $4.6 million on cardiac drugs, $3.2 million on general anesthetics, and so forth, to just over $1 million for sympathomimetic agents and miscellaneous beta-lactam antibiotics. As in Figure 2, there are more upward price movements than downward price changes. By far, the highest average upward price change is observed for sympathomimetic agents, with close to a 25 percent average price increase. The Buyer faced an average price decrease of over 15 percent for quinolones.

Finally, Figure 4 shows average price changes ($\overline{\Delta P}_j$) for the 25 generic compounds on which the Buyer spent the most over the years 2000 – 2001. Again, drugs are shown from left to right in Figure 4 from the highest to lowest expenditures. The Buyer spent $5.8 million on epoetin alfa, close to $5 million on abciximab, $1.9 million on filgrastim, and so forth down to roughly $644,000 on both carboplatin and reteplase, and $634,000 on lymphocyte immune globulin rabbit. As for Figures 2 and 3, there are more upward than downward price movements. However, none of the price increases exceeds 10 percent. Whereas there are fewer downswings, two of them are substantial. The Buyer faced a price decrease of 26 percent for ciprofloxacin lactate and a price decrease of 24 percent for amphotericin B liposome.

With but a single, albeit large, buyer for our study, one concern may be that the price swings it experiences are not representative of price changes for all purchasers. Hence we compare, for a sample of drugs in different therapeutic classes, the price change experienced by our Buyer to the national average retail price change for the same drug.[18] Table 1 presents our findings. In some cases (notably Aciphex®, Prilosec®, and Zocor®), the price increases experienced by our Buyer were smaller than the average retail price change. Only in one situation, for Zerit®, did the Buyer face a significantly larger price increase than did the retail sector. In general, the price increases experienced by our Buyer were in line with overall retail price increases.

Large-Price-Change Drug Products

This section describes the price changes for the 319 drug products with a price change of at least 20 percent; these 319 products were identified above in the Methods section. Although a few of these products are included in Figures 2 – 4, many others are not; they are not necessarily produced by companies, for example, from which the Buyer purchased over $1 million worth of drugs. The 319 NDCs represent 182 different generic compounds, 80 different pharmaceutical companies (identified by the first five digits of the NDCs[19]), and 79 different therapeutic classes (six-digit American Hospital Formulary Service categories[20]).

The range of price changes was from –96.0 percent for a nalbuphine product to +681.3 percent for a fentanyl citrate NDC. Other drugs with large upswings include dexamethasone sodium phosphate (with price increases of 634.2 percent, 331.9 percent, and 287.6 percent for three different NDCs, respectively), albuterol (price increases of 428.9 percent, 274.5 percent, and 177.3 percent for three drug products, respectively), famotidine, and ampicillin for injection. Large downward swings (over 50 percent decreases) were observed for midazolam hydrochloride products, leuprolide acetate, simvastatin, and pantoprazole sodium sesquihydrate.

In Table 2 are counts of large price swings by selected company and selected market (AHFS 6-digit therapeutic class). The companies and therapeutic classes shown in the table accounted for the largest numbers of price swings. Of the companies selling to the Buyer, Pfizer (PFE) had the highest number (35) of large price swings between 2000 and 2001. Bristol-Myers Squibb (BMS) and Abbott Laboratories (ABT) accounted, respectively, for 18 and 17 swings, while GlaxoSmithKline (GSK) and Merck each accounted for 16 price swings. There were 24 large price swings in the adrenal drug class, and 18 each for benzodiazepines and penicillins. Altogether, the companies in the table accounted for 144 (about half) of the large price swings, while the classes in the table accounted for 149 (again, about half) of the swings in total. Counts in the inside columns and rows show individual company participation in the therapeutic classes. For example, Table 2 shows that Pfizer sold to the Buyer 15 adrenal drug products with large price swings. Merck sold eight large-price-swing antilipemics.

Table 3 gives expenditure-weighted average price changes for the same companies and therapeutic classes as in Table 2. Across the drugs in the large-price-change sample, Abbott's prices dropped on average approximately 25 percent. Those for GlaxoSmithKline rose 54.6 percent on average, while those for UDL Laboratories rose 61.6 percent on average. Prices went up in the adrenal class on average 68.7 percent and went up, on average, 128.7 percent among opiate agonists. Prices for benzodiazepines fell on average by 62.0 percent. On average, across all drugs produced either by one of the companies featured in Table 3 or included in one of the therapeutic classes featured in Table 3, prices rose 1.4 percent (the value in the bottom right corner of Table 3). There are some tremendously large upswings in Table 3; for example, note Baxter's 504.6 percent average price increase for its opiate agonist drug products. For one sympathomimetic drug product, GlaxoSmithKline had a price increase of 428.9 percent.

Regression Results

The average two-year expenditure for drug products in our sample is $18,793. The smallest expenditure was for polyvinyl alcohol ($125), while the largest two-year expenditure ($1,103,692) was for a ciprofloxacin lactate product. Slightly over 60 percent of the products in the regression sample are branded. Approximately one third of our sample (including fentanyl citrate products; dexamethasone sodium phosphate products which required a costly changeover from bovine- to plant-input manufacturing; metoclopramide hydrochloride products; diatrizoate sodium products; and multivitamins) appeared in the shortage list in Fox and Tyler, for one of the years 1999, 2000, 2001, or 2002.[4] Roughly 12 percent of our sample were generic compounds for which a patent expiration occurred during one of the same four years.[16,17]

A correlation analysis revealed perfect correlation (estimated correlation coefficient equal to unity) between P01 and BXP01, two of the independent variables. In addition, there were no branded drugs in our sample whose patent expired in 2002. Hence, we were unable to obtain estimated regression coefficients for P01 and BXP02. The remaining independent variables are sufficiently uncorrelated to imply no other multicollinearity problems.

Table 4 presents ordinary-least-squares regression results for the empirical model in (1) above. The F-statistic for the regression as a whole (testing the null hypothesis that all of the regression coefficients for the independent variables are equal to zero) is 5.58. Compared to the critical F value with 12 and 306 degrees of freedom, the computed F value is significant at the one percent level. The R^2 value for the regression is 0.18.

The regression results reveal the importance of drug shortages in explaining the large price changes experienced by the Buyer. Estimated coefficients for S00 and S01 are positive and statistically significant at at least the five percent level. Relative to a drug product with no shortage, those with a shortage beginning in 2000 are estimated to increase in price by 45.47 additional percentage points, while those with a shortage beginning in 2001 are predicted to increase in price by 59.66 additional percentage points. Neither the estimated coefficient for S99 or for S02 is statistically significant, suggesting shortages beginning in the years surrounding our time period are not important. It appears as though price responses to shortages are fairly immediate, as opposed to a slower price adjustment process, as in the case of generic entry following patent expiration.

Generic competition is shown to have a negative effect on drug price change for generic manufacturers of the previously patented generic compound. The Buyer experienced statistically significant price downswings on generic-manufactured products for which the patent on the branded pharmaceutical expired in 1999 or 2000, with the magnitude of effect strongest for P99. The interpretation is that, for drugs whose patent expired in 1999, we expect prices to fall by 85.83 percentage points on average from 2000 to 2001, while, for drugs whose patent expired in 2000, we expect prices to fall by 77.84 percentage points on average from 2000 to 2001. This result is consistent with the empirical literature on generic entry, in which it takes several years for the impact of generic entry to drive price down to (close to) marginal cost.[12]

Prices of a number of drugs in the sample were affected by patent expirations. Bristol Myers Squibb's patent on Platinol® (cisplatin) expired in 1999. American Pharmaceutical Partners (APP) was the first generic company allowed in the cisplatin market. The Buyer saw a large drop in APP's prices (over 40 percent between 2000 and 2001) as the second generic, produced by Bedford Laboratories, entered the market. Hoffman LaRoche's patent on Versed® expired on December 20, 1999, and generic entry actively drove down the price of midazolam hydrochloride between 2000 and 2001 for the Buyer. All four generic companies (Abbott, Baxter, Bedford Laboratories, and ESI Lederle) from which the Buyer purchased in 2000 and 2001 dropped their prices for this generic compound. Organon's patent on Norcuron® expired on August 20, 1999, and generic entry again drove down the price of the drug, vecuronium bromide. Prices dropped for all generic NDCs produced by Abbott, Baxter, Bedford Laboratories, and ESI Lederle from which the Buyer purchased vecuronium bromide in 2000 and 2001.

The regression results further indicate that the reaction of the branded pharmaceutical company to a patent expiration on one of its drugs is *not* to reduce price. Indeed, the estimated coefficient on BXP00 is 281.64, indicating a higher average price change of 281.64 percentage points for branded pharmaceuticals whose patents expired in 2000. Rather than compete with generic manufacturers by reducing their prices, they are shown to raise price instead, probably with the expectation of losing the Buyer as a purchaser, and perhaps with the expectation of eventually discontinuing production altogether. Note that only one of the three interaction terms has a statistically significant effect. Branded drug products whose patents expired in

1999 or 2001 did not have significantly different price changes from those whose did not. Merck's famotidine (Pepcid®) is responsible for several large drug-product price upswings between 2000 and 2001. The patents for both Pepcid® and Pepcid AC® expired on October 15, 2000. Rather than reduce price to compete with the generic companies, Merck raised its prices significantly between 2000 and 2001 for several famotidine products. Indeed, by July 2001, the Buyer was already purchasing famotidine from four generic manufacturers, that provided stiff competition for Merck.

Finally, the regression results clearly show that the more the Buyer spends on a particular drug product, the smaller the price increase (or larger the price decrease). As expenditures on a product increase, we expect a greater incentive to negotiate with the drug's manufacturer. The estimated regression coefficient of –8.55 implies (with some calculus) that a $1,000 increase in drug-product expenditure on average reduces the percentage increase in price (or increases the percentage decrease in price) by approximately half (0.46) a percentage point, around the average expenditure of $18,793. This particular result, a significant negative coefficient on drug expenditures, is consistent with the data presented in Figures 2 – 4; many of the high-expenditure pharmaceutical companies, pharmaceutical classes, and generic compounds had lower average price swings than those observed in the high-price-change product sample. The relatively small price swings for most of the high-expenditure therapeutic classes suggest the Buyer was able to substitute among therapeutically similar drugs to keep overall class expenditures from rising significantly.

Discussion

Although the regression model points to the importance of drug shortages, patent expirations, and Buyer expenditures in explaining large price swings, there are clearly other variables that influence price change in particular situations. For example, between 2000 and 2001, the Buyer experienced a price drop of 65 percent from Wyeth Laboratories on pantoprazole sodium sesquihydrate (Protonix®) in 40 mg tablet form. The Buyer negotiated a new contract with Wyeth in 2001 following the entry of Nexium® (AstraZeneca) in February 2001. In this case, entry of a new branded drug in the anti-ulcer (miscellaneous gastrointestinal) therapeutic class led to the price drop. Similarly, between 2000 and 2001, both leuprolide acetate (Lupron® produced by TAP Pharmaceuticals) and simvastatin (Zocor® manufactured by Merck) came down in price for the Buyer due to additional competition within the therapeutic class: specifically, Lupron® versus Zoladex® and Zocor® versus Pravachol®, Lescol®, Lipitor®, and Baycol®. The Buyer was able to secure a new contract for both Lupron® and Zocor®. Unfortunately, issues like “change in contract” are extremely difficult to quantify and have been omitted from the empirical model to ensure tractability.

We recognize that our research is limited by a single buyer. As mentioned in Fox and Tyler, each buyer is affected to a greater or lesser degree by national drug shortages or the addition of new branded or generic competitors in a market.[4] In addition, our study spans only a two-year period. Those drugs experiencing a high price upswing in 2001 may well come back down in price in 2002 (and vice versa). According to Fox and Tyler, 2001 was a particularly bad year for shortages, although the trend toward more shortages is clearly described in their paper. The problem of drug shortages is likely to persist or even worsen, given the unpredictability of manufacturing problems and raw-material shortages and continuing consolidation in the pharmaceutical industry.[4] There is no indication that the drug purchasing process will become any easier in the foreseeable future.

Summary and Conclusion

This paper presents an inside look at a unique data set: actual pharmaceutical prices paid by a large regional hospital buyer. We analyze individual drug price changes, which are usually concealed when reporting a single average price statistic. This study stresses the importance of transaction prices (which account for manufacturer discounts), rather than average wholesale prices, in understanding true drug price patterns. Transaction prices for pharmaceuticals are shown to follow the sticky-price-large-price-swing pattern observed in many sectors of the economy.

For drugs, companies, and therapeutic classes which represent large expenditures for the Buyer, we find that most prices went up between 2000 and 2001. However, for “big-ticket” purchases, average price increases were seldom greater than 10 percent. It appears the Buyer is able to substitute among drug products within therapeutic classes to keep overall class expenditure increases to a minimum. Average price declines tended to be small as well, though there are a few large-expenditure drugs whose price fell over 20 percent over the two years. Only one pharmaceutical company (GlaxoSmithKline), from which the Buyer purchased over $1 million worth of drugs, had average price increases over 10 percent, though several others, including Bristol-Myers Squibb, Novartis, and AstraZeneca, had increases over 5 percent.

We examine in detail over three hundred large individual drug price swings. These price swings make the pharmaceutical purchasing process difficult. We find that large downswings can often be explained by patent expirations on branded drugs, while large upswings may result from drug shortages. These swings are important consequences of the way that pharmaceutical markets are structured. Recognizing these phenomena, and planning for them to the greatest extent possible, should keep clinical effects to a minimum.

REFERENCES

1. Hoffman JM, Shah ND, Vermeulen LC, Hunkler RJ, and Hontz KM. Projecting future drug expenditures – 2005. *Am J Health-Syst Pharm.* 2005; 62: 149–167.
2. Standard & Poor's. *Industry Surveys Healthcare: Pharmaceuticals*. 2005.
3. Caucutt, EM, Ghosh M, and Kelton, CML. Pricing behavior in United States manufacturing industries: a statistical study using disaggregated data. *Rev Indust Org*. 1994; 9: 745–771.
4. Fox ER and Tyler LS. Managing drug shortages: seven years' experience at one health system. *Am J Health-Syst Pharm*. 2003; 60: 245–253.
5. Means GC. *Industrial Prices and Their Relative Inflexibility*. 1935. Washington, D.C.: U.S. Senate Document 13, 74th Congress, 1st Session.
6. Carlton, DW. The rigidity of prices. *Am Econ Rev.* 1986; 76: 637–658.
7. Caucutt, EM, Ghosh M, and Kelton, CML. Durability versus concentration as an explanation for price inflexibility. *Rev Indust Org*. 1999; 14: 27–50.
8. Powers, ET and Powers NJ. The size and frequency of price changes: evidence from grocery stores. *Rev Indust Org*. 2001; 18: 397–416.
9. Borenstein S and Shepard A. Sticky prices, inventories, and market power in wholesale gasoline markets. *RAND J Econ*. 2002; 33: 116–139.
10. Arbatskaya M and Baye MR. Are prices "sticky" online? Market structure effects and asymmetric responses to cost shocks in online mortgage markets. *Intl J Indust Org.* 2004; 22: 1443–1462.
11. Elzinga KG and Mills DE. The distribution and pricing of prescription drugs. *Intl J Econ Bus.* 1997; 4: 287–299.

12. Guo JJ, Kelton CML, Pasquale MK, Zimmerman J, Patel A, Heaton PC, and Cluxton RJ. Price and market-share competition of anti-ulcer gastric medications in the Ohio medicaid market. *Intl J Pharm Med.* 2004; 18: 271–282.

13. Dusing ML, Guo JJ, Kelton CML, and Pasquale MK. Competition and price discounts for a hospital buyer in the anti-infective pharmaceutical market. *J Pharm Fin, Econ and Pol*. 2005; 14: 59–85.

14. American Society of Health-System Pharmacists. Special Feature: Provisional observations on drug product shortages: effects, causes, and potential solutions. *Am J Health-Syst Pharm*. 2002; 59: 2173–2182.

15. American Society of Health-System Pharmacists. Editorial: Measuring the impact of drug shortages. *Am J Health-Syst Pharm*. 2004; 61: 2009.

16. Locum Publishing House. *Drugs Off-Patent Report 1999: Drugs Under $100 Million U.S. Dollars.* 1999. http://www.locumusa.com/pdf/members/under100-1299.pdf. (accessed 2006 Jan 3).

17. Locum Publishing House. *Drugs Off-Patent Report 2000: Over USD $100 Million*. 2000. http://www.locumusa.com/pdf/members/100m+00.pdf. (accessed 2006 Jan 3).

18. National Institute for Health Care Management. *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs*. 2002.

19. Medical Economics Company, Inc. *2004 Drug Topics® Red Book*. 2004. Montvale, New Jersey.

20. American Society of Health-System Pharmacists. *Am Hosp Form Serv Drug Info.* 2002. Bethesda, MD.

Table 1. Buyer Price Changes versus Retail Price Changes for Selected Drug Brands: 2000 – 2001

Drug Brand	Percentage Price Change for Buyer[a]	Percentage Retail Price Change[b]
Aciphex®	–10.2	4.1
Allegra®	6.2	10.9
Cipro®	5.5	7.0
Depakote®	6.3	5.7
Glucophage®	14.2	14.4
Lipitor®	4.7	2.9
Prilosec®	–4.3	3.7
Prozac®	10.2	10.6
Seroquel®	5.8	7.1
Vioxx®	4.7	7.9
Zerit®	28.2	5.8
Zocor®	–36.0	7.5

[a] Weighted average of NDCs purchased by Buyer

[b] Source: National Institute for Health Care Management (May 2002).

Table 2. Counts of Large Price Swings for Selected Companies[a] in Selected Therapeutic Classes[b]

	ABT[c]	APP[d]	AZN	BAX	BMS	GSK	MRK	PFE	UDL	All Companies
Adrenals[e]	1	3	---	---	---	---	---	15	---	24
Antilipemics	---	---	---	---	---	---	8	---	---	10
Antineoplastics	---	2	---	---	---	1	---	3	---	16
Antiretrovirals	1	---	---	---	4	6	---	---	---	12
Benzodiazepines	3	---	---	4	---	---	---	---	1	18
Cardiac Drugs	---	---	2	---	---	---	---	---	1	9
Misc. Antibiotics	1	1	---	---	---	---	---	5	---	10
Misc. GI Drugs	---	---	---	1	---	2	5	---	1	12
Opiate Agonists	---	---	1	2	---	---	---	---	3	11
Penicillins	---	---	---	---	13	---	---	---	---	18
Sympathomimetics	1	---	---	---	---	1	---	---	---	9
All Drugs	17	9	9	9	18	16	16	35	15	144/149

[a] The companies are Abbott Laboratories (ABT), American Pharmaceutical Partners (APP), AstraZeneca (AZN), Baxter HealthCare Corporation (BAX), Bristol-Myers Squibb (BMS), GlaxoSmithKline (GSK), Merck & Co. (MRK), Pfizer (PFE), and UDL Laboratories (UDL).

[b] The therapeutic classes with AHFS classification in parentheses are adrenals (680400), antilipemics (240600), antineoplastics (100000), antiretrovirals (081808), benzodiazepines (281208, 282408), cardiac drugs (240400), miscellaneous antibiotics (081228), miscellaneous gastrointestinal drugs (564000), opiate agonists (280808), penicillins (081216), and sympathomimetics (121200).

[c] Abbott's NDCs in adrenals, antiretrovirals, and sympathomimetics are branded. Its benzodiazepine and antibiotic drugs are generic.

[d] American Pharmaceutical Partners, Baxter, and UDL Laboratories produce generic drugs. AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Merck, and Pfizer produce branded medications. Although Abbott produces a few branded medications in our data sample, it primarily manufactures generic drug products.

[e] The adrenals, antilipemics, antiretrovirals, miscellaneous gastrointestinal drugs, and penicillins are primarily branded. The benzodiazepines, opiate agonists, and sympathomimetics are primarily generic. The remaining therapeutic classes are mixed.

Table 3. Weighted Average Percent Price Change for Drugs Manufactured by Selected Companies[a] in Selected Therapeutic Classes[b]

	ABT[c]	APP[d]	AZN	BAX	BMS	GSK	MRK	PFE	UDL	All Companies
Adrenals[e]	-47.7	299.9	---	---	---	---	---	45.2	---	68.7
Antilipemics	---	---	---	---	---	---	-36.0	---	---	-34.8
Antineoplastics	---	-43.0	---	---	---	104.1	---	1.4	---	-44.5
Antiretrovirals	21.6	---	---	---	30.5	25.2	---	---	---	26.3
Benzodiazepines	-52.5	---	---	51.7	---	---	---	---	69.5	-62.0
Cardiac Drugs	---	---	36.6	---	---	---	---	---	-53.6	14.5
Misc. Antibiotics	-36.4	-30.5	---	---	---	---	---	45.7	---	6.1
Misc. GI Drugs	---	---	---	49.2	---	42.0	20.2	---	193.9	16.9
Opiate Agonists	---	---	60.3	504.6	---	---	---	---	60.4	128.7
Penicillins	---	---	---	---	91.3	---	---	---	---	72.2
Sympathomimetics	-76.7	---	---	---	---	428.9	---	---	---	200.7
All Drugs	-25.0	-0.00	30.9	124.7	50.0	54.6	3.3	37.5	61.6	1.4

[a] The companies are Abbott Laboratories (ABT), American Pharmaceutical Partners (APP), AstraZeneca (AZN), Baxter HealthCare Corporation (BAX), Bristol-Myers Squibb (BMS), GlaxoSmithKline (GSK), Merck & Co. (MRK), Pfizer (PFE), and UDL Laboratories (UDL).

[b] The therapeutic classes with AHFS classification in parentheses are adrenals (680400), antilipemics (240600), antineoplastics (100000), antiretrovirals (081808), benzodiazepines (281208, 282408), cardiac drugs (240400), miscellaneous antibiotics (081228), miscellaneous gastrointestinal drugs (564000), opiate agonists (280808), penicillins (081216), and sympathomimetics (121200).

[c] Abbott's NDCs in adrenals, antiretrovirals, and sympathomimetics are branded. Its benzodiazepine and antibiotic drugs are generic.

[d] American Pharmaceutical Partners, Baxter, and UDL Laboratories produce generic drugs. AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Merck, and Pfizer produce branded medications. Although Abbott produces a few branded medications in our data sample, it primarily manufactures generic drug products.

[e] The adrenals, antilipemics, antiretrovirals, miscellaneous gastrointestinal drugs, and penicillins are primarily branded. The benzodiazepines, opiate agonists, and sympathomimetics are primarily generic. The remaining therapeutic classes are mixed.

Table 4. Regression Results

Independent Variable	Estimated Coefficient	Standard Error	t-Statistic
Constant	88.54***	24.42	3.63
Branded (B)	3.52	11.89	0.30
1999 Shortage (S99)	11.02	29.44	0.37
2000 Shortage (S00)	45.47**	20.20	2.25
2001 Shortage (S01)	59.66***	15.26	3.91
2002 Shortage (S02)	-1.17	22.41	-0.05
1999 Patent Expiration (P99)	-85.83***	29.82	-2.88
2000 Patent Expiration (P00)	-77.84*	46.81	-1.66
2002 Patent Expiration (P02)	-76.45	93.95	-0.81
1999 Interaction (BXP99)	49.00	40.07	1.22
2000 Interaction (BXP00)	281.64***	58.54	4.81
2001 Interaction (BXP01)	53.19	41.65	1.28
Log of Expenditures (EXP)	-8.55***	3.12	-2.74
F-Statistic	5.58***		
R^2	0.18		
Number of Observations	319		

* Significant at the 10 percent level (two-tailed test).

** Significant at the 5 percent level (two-tailed test).

*** Significant at the 1 percent level (two-tailed test).

Figure 1. Frequency of Price Changes for 3085 Drug Products

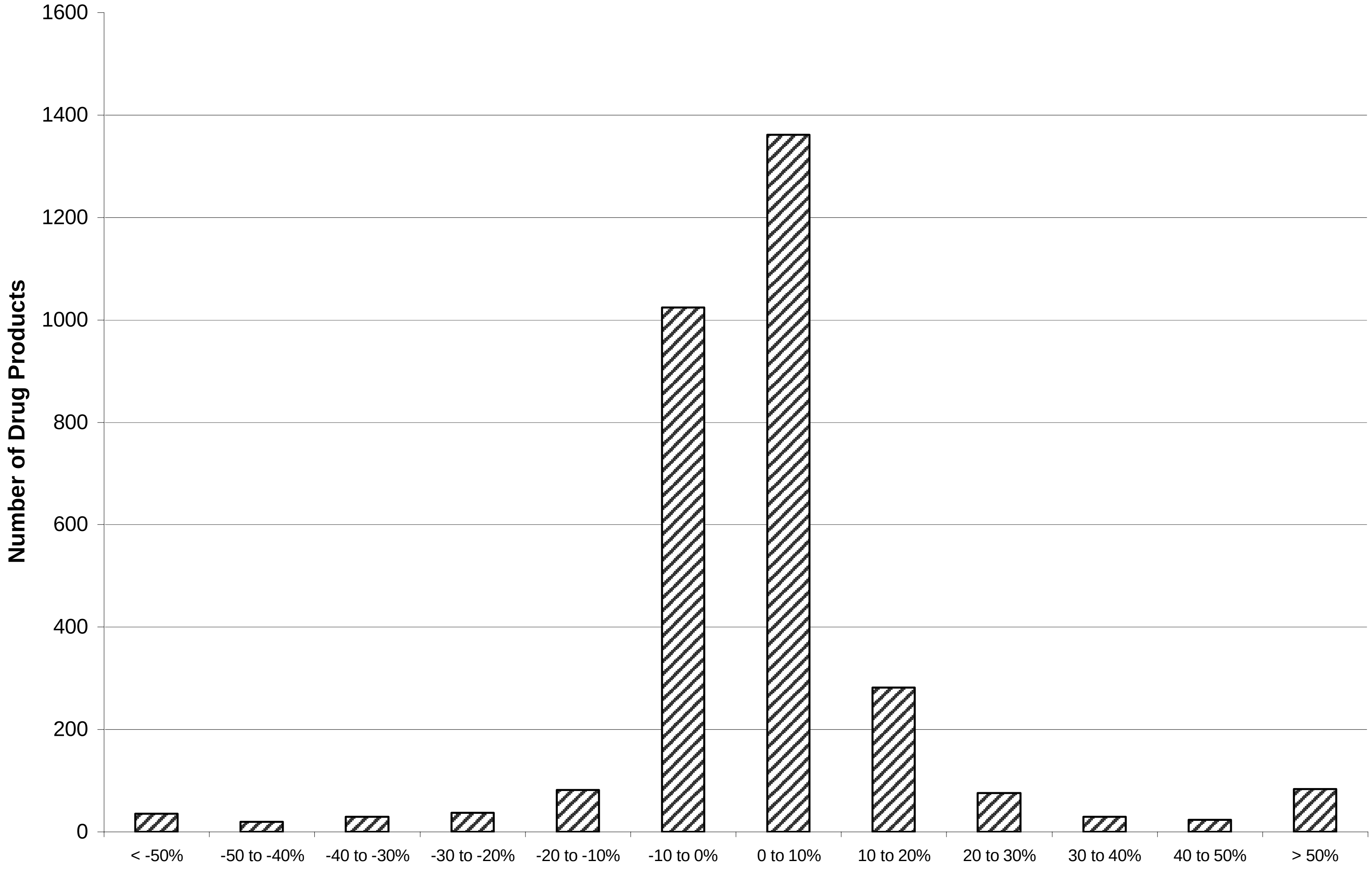


Figure 2. Weighted Average Price Change for Companies Selling Over $1 Million in Drugs to the Buyer Over 2000 - 2001

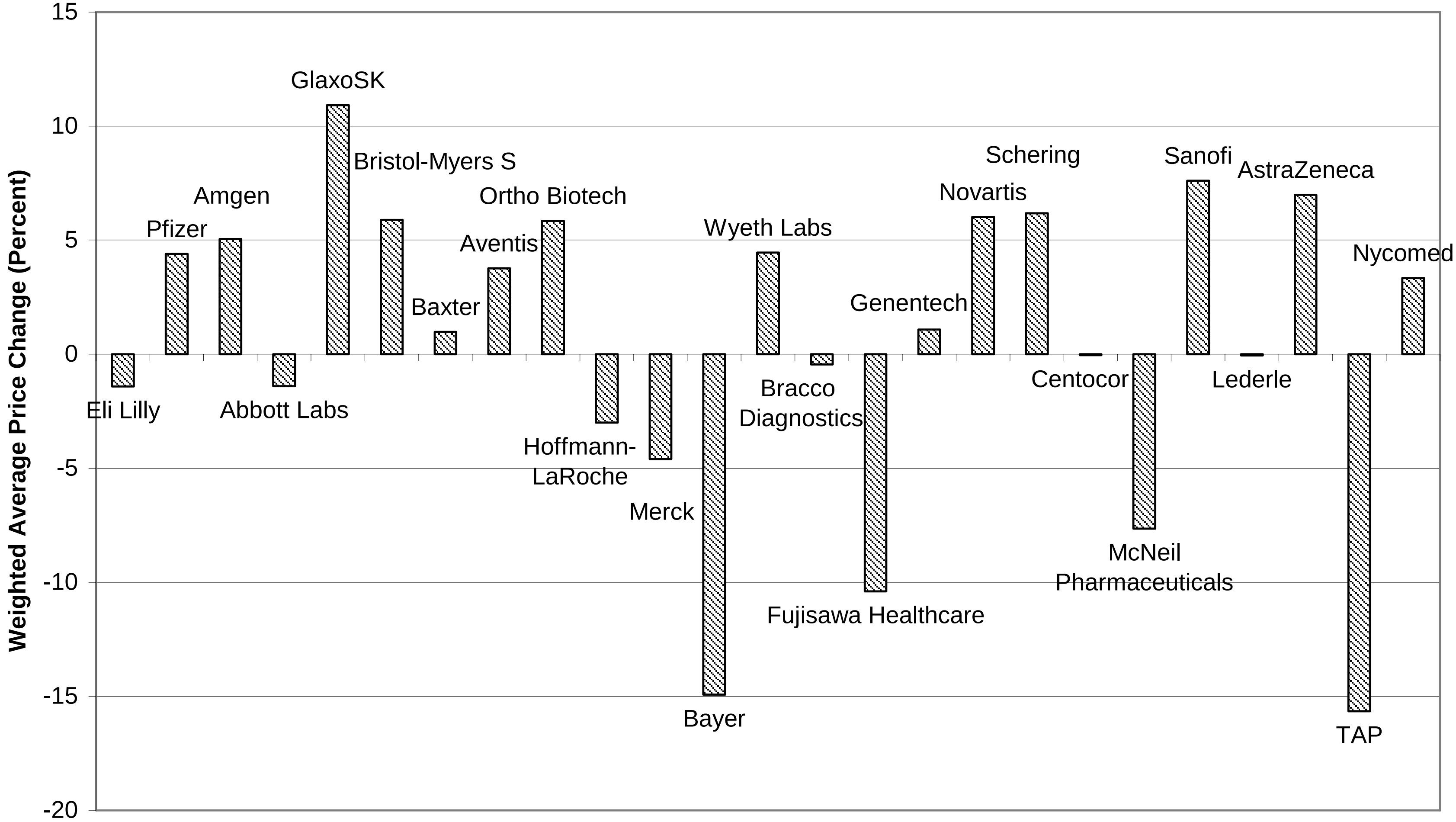


Figure 3. Weighted Average Price Change for Pharmaceutical Classes with Buyer Expenditures of Over $1 Million Over 2000 - 2001

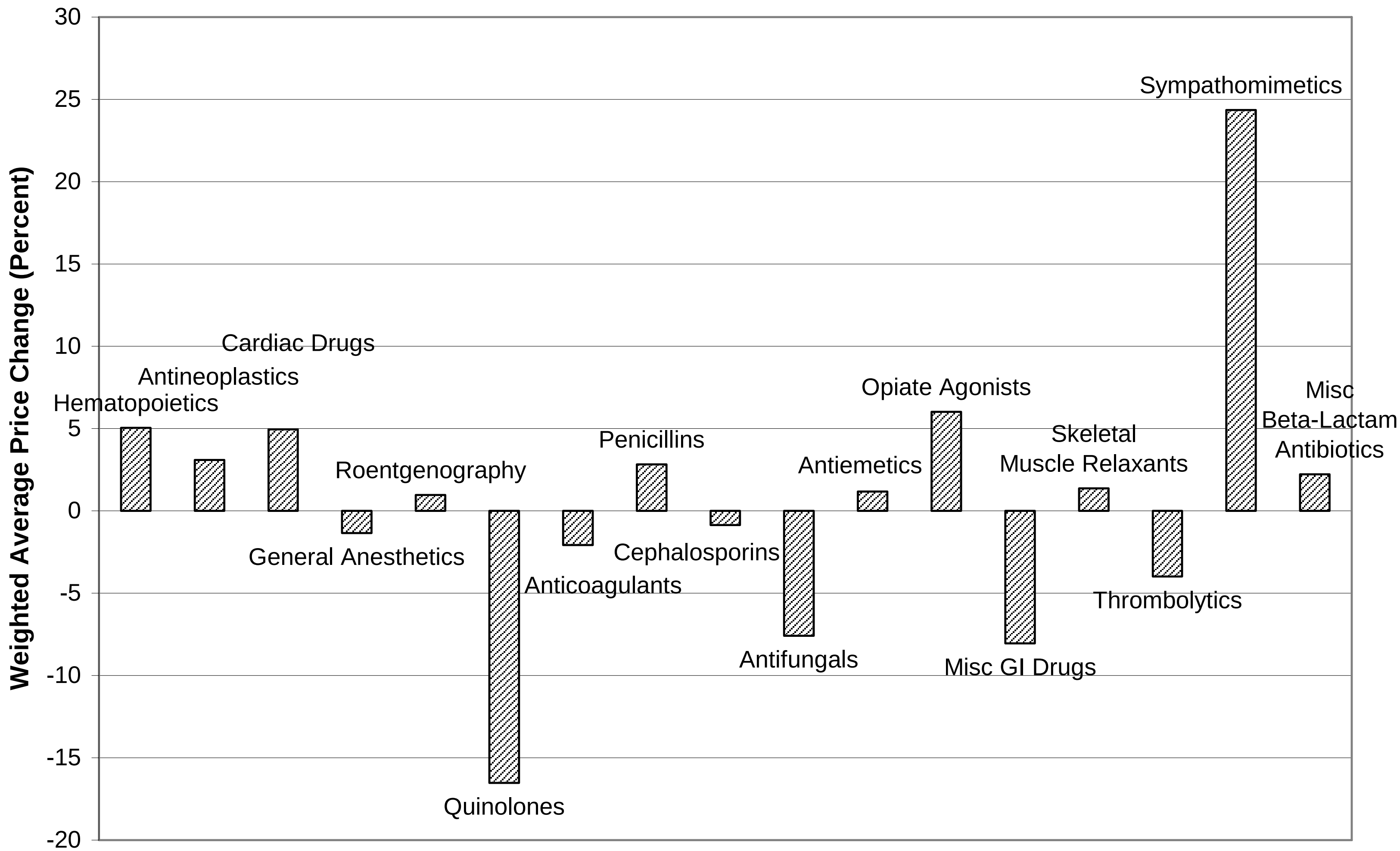
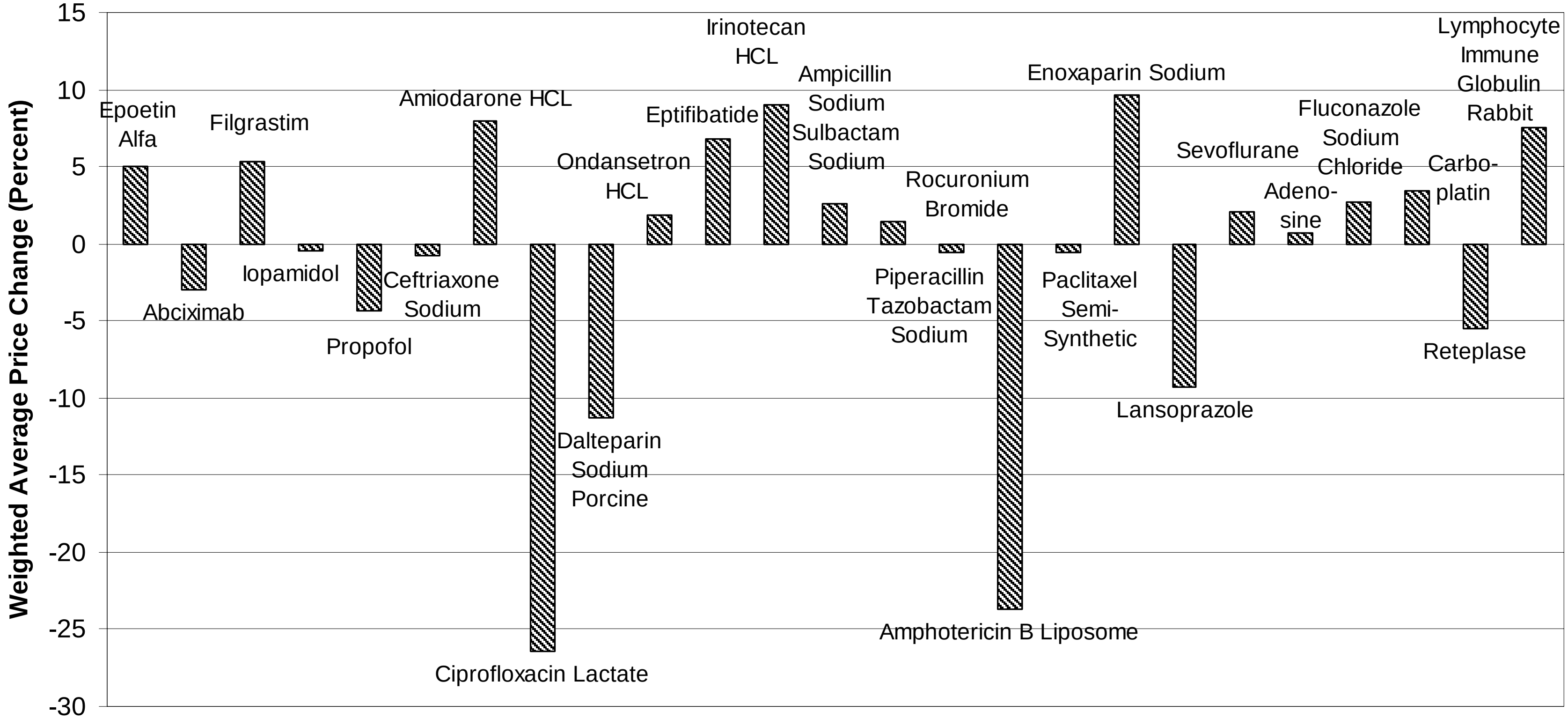


Figure 4. Weighted Average Price Change for the 25 Generic Compounds with Greatest Buyer Expenditures Over 2000 - 2001



We argue that pharmaceutical pricing is a growing challenge for all countries, calling into question the sustainability of the systems that are supposed to drive pharmaceutical innovation. Innovation and market power.Â The prices of new treatments for rare diseases represent even less affordability. In the US in 2016, the median annual price for each patient a year treated with top selling orphan drugs was $83 883.Â Gileadâ€™s global sales of sofosbuvir and related combination products totalled $59bn from 2014 through 2018.18 It has been estimated that the total cost of treating all patients with hepatitis C at posted prices for sofosbuvir products would be equal to at least a tenth of the current annual cost for all medicines in 30 countries.19 Such extraordinary revenues for. According to the research study by PricewaterhouseCoopers, healthcare is projected to be the largest R&D spending sector in a few years, and the emergence of the COVID-19 pandemic has diverged the R&D spending towards coronavirus disease. There has been a surge in healthcare spending for the past ten years due to the burden of treating untreatable disorders and chronic diseases. According to the IQVIA report, healthcare investments are growing rapidly and are reflecting confidence in medical innovations. For instance, Venture Capital firms invested over USD 23 billion in 2018, coupled with the This report outlines and critically analyses the current pharmaceutical pricing and reimbursement policies and regulation in the MENA region and pays special att ention to External Reference Pricing (ERP), the most commonly used pricing policy in the region. The focus of the report is on 11 countries: Algeria, Egypt, Morocco, Lebanon, Jordan, Saudi Arabia and the rest of the Gulf Cooperation Council (GCC) countries : Kuwait, United Arab Emirates (UAE), Qatar, Bahrain and Oman. Beyond mapping, analysing and critically The application of Pharmaceutical Quality Systems in pharmaceutical products can extend to pharmaceutical development, which should facilitate innovation and continual improvement of prescribed medication.2,6 It is the tool with which to achieve product realisation by designing, planning, implementing, maintaining and continuously improving a system, to allow the consistent delivery of pharmaceuticals with appropriate quality attributes.4,6.Â Anastasia Petropoulu is a Radiopharmacy Technician / Clinical Scientist in the Radiopharmacy Department of University Hospital Bristol NHS Foundation Trust, Anastasia obtained a certificate in Health and Science followed by a BSc Hons degree in Pharmaceutical Science at the University of the West of England. Â In addition, new medicines are often developed through actions taking place in a variety of countries, making it increasingly difcult to attribute the innovative output to a single country.