
23 Pharmaceutical pricing

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Abstract

In this chapter, we discuss the multiple institutional characteristics that affect prescription drug pricing. We organize our discussion around the 5Cs that define the prescription drug industry: companies (the innovative process), competitors (the limits of patent protections), customers (how insurance markets affect pricing), collaborators (roles played by physicians and various channel players), and context (government regulation of pricing). We conclude the chapter with implications for drug pricing research. We categorize areas for future research in three distinct areas. First, future research should continue to clarify the nature of the current market. Second, we believe that more research is needed on how to optimize the current system. Finally, given the dynamic nature of the regulatory and institutional environment that defines the pharmaceutical industry, continued research on how these changes influence pricing will be needed as the industry continues to evolve.

1. Introduction

The reader might ask at this point why devote a special chapter to pharmaceuticals and make it the only chapter in the whole book devoted to a specific category. The answer to this question is twofold. First, the pharmaceutical industry is of particular interest not only because of its sheer size (five times the entire cosmetics industry and ten times the personal computers industry) and its leading place in marketing expenditures (it spends more on sales force than any other industry and it ranks among the most advertised to consumers), but also due to availability of detailed data that allow researchers to study many general marketing phenomena such as sales force effectiveness, product adoption, social networks, or optimal marketing mix allocation. The caveat is that it is an industry with many institutional characteristics that affect pricing. This leads us to the second and perhaps the primary reason for this chapter – a diligent researcher must understand how industry dynamics affect the critical aspect of pricing, whether or not it is the primary focus of his or her research.

In our exploration, we focus on four critical facets that contribute to how pharmaceutical prices are determined. First, in contrast to the case for most other products, consumers of prescription drugs rarely make consumption decisions on their own. Rather, many different actors influence which drugs patients consume. Patients use physicians as learned intermediaries whose education, experience and access to specialized tools allow them to diagnose the patient's health problem and determine the appropriate treatment. The physician acts as an agent for the patient, but this agency may be imperfect because the objectives of the physician and patient may not coincide.¹ Insurers and pharmacy

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¹ For example, suppose two drugs, A and B, treat a given condition. All else equal, an insured patient may prefer the cheaper drug A (as determined by the benefit manager), but his physician may prefer to prescribe drug B because she believes it to be of higher quality, she is more familiar

benefit managers (PBMs), who often administer drug benefits for insurers, also influence consumption patterns by determining what patients need to pay out-of-pocket for various drug alternatives.

Second, widespread insurance coverage shields patients from the true cost of prescription drugs. In the USA, over 80 percent of people have some form of prescription drug coverage, and high levels of private or public insurance coverage are common in many other nations. The discrepancy between patient prices and retail prices distorts consumer demand for prescription drugs. Aside from the increase in consumption levels, insurance also distorts choices between different drugs when patients do not face the true price differences among different drugs. Perhaps because out-of-pocket payments for insured patients have so little to do with actual retail prices, it is standard terminology to refer to 'patient costs' rather than 'patient prices'.

Third, pharmaceutical prices are influenced by the presence of the patent system, which ensures products a degree of market power while the patent is active but also imposes a well-defined life cycle to the product. A product will face dramatically different pricing environments over its life cycle, with greater ability to maintain higher markups while the patent is active, and then by operating in a highly competitive environment, which is created when generic competitors enter the market.

Fourth, many countries regulate prices of prescription drugs because of their payer role and the political importance of healthcare to voters. However, the standard notion of efficient pricing at marginal cost of production – the goal of regulators in other contexts – is not sustainable in a research-intensive industry like pharmaceuticals where the marginal cost is negligible while R&D is incredibly costly. This extreme divergence between marginal cost of production and fixed costs creates a tension between static and dynamic efficiency. Pricing at marginal cost would maximize static efficiency but would halt future development in the industry. Higher price, on the other hand, promotes dynamic efficiency, giving pharmaceutical firms an incentive to invest in R&D and introduce new products (Berndt, 2002) while lowering current consumer welfare.

In our presentation, we follow the 5Cs framework so commonly used in marketing analyses, organizing our discussion around the companies, competitors, customers, channels and context that define the prescription drug industry. We begin in Section 2 by discussing some high-level industry statistics before turning to the innovative process and the typical product life cycle imposed by patents. In Section 3, we expand on this discussion with a description of the competitive framework that the drug patent system presents. We then explore how the insurance market affects pricing in Section 4. The subsequent discussion of collaborators is divided into two parts: in Section 5 we discuss the role of physicians and then follow that with a detailed discussion of channel players and their role in drug pricing in Section 6. To complete our 5Cs analysis, in Section 7 we analyze the regulatory constraints placed on pharmaceutical prices. We conclude the chapter with implications for pricing research.

As a final note, we would like to point out that, for several reasons, we primarily focus on the US market. First, the USA is the largest national market for prescription drugs,

with that product, she is influenced by detailing for drug B, etc. See McGuire (2000) for an exhaustive review of the physician–patient relationship.

with more than 40 percent of global sales (IMS Health, 2006). Second, facing less regulation, the US market presents greater opportunities for marketing research than is more generally applicable to other product categories. For example, there is significantly less government regulation of pricing in the USA and it is also one of only two countries that allow direct-to-consumer advertising. Finally, we expect that most marketing researchers will have access to US data reinforcing our focus on this market. Therefore, unless we make specific references to international markets, the reader can assume that our discussion pertains to the US market. For similar reasons we focus on drugs available through the retail channel rather than physician-administered drugs such as oncology drugs.

2. Companies

The pharmaceutical industry comprises companies that develop, manufacture, distribute and market branded and generic drugs. In general, companies focus on developing either branded drugs or generics because the respective business models are sufficiently different. For example, the branded drug business model requires very heavy investments in R&D and marketing, while the generic drug model requires particularly strong competence in manufacturing, channel management and patent litigation.

Global pharmaceutical sales have grown on the order of 10 percent per year, rising to \$602 billion in 2005 with the top ten firms accounting for 45 percent of this total (Forbes.com, 2006; IMS Health, 2006). Because of the discrepancy in general price levels between branded and generic drugs, dollar sales are weighted more towards branded drugs and thus are a better representation of drug spending, while unit sales better represent actual utilization. Although prescription drugs, both branded and generic, account for only about 10 percent of total health spending in the USA, it is the fastest-growing segment of health care spending, and in 2005, 20 percent of all out-of-pocket spending was for prescription drugs compared to 17 percent for physicians and clinical services, and 8 percent for hospital care.²

A new prescription drug is the outcome of a process that can take many years from discovery to regulatory approval, cost hundreds of millions of dollars, and tie up valuable capital that could be used in other ventures. Firms that bring these products to market spend heavily on R&D, and, although patents impose a finite lifespan on brand name pharmaceuticals, the profit opportunities that they furnish encourage such investments.

2.1 R&D

Product innovation in the pharmaceutical industry is characterized by high research and development costs. DiMasi and colleagues (2003) surveyed ten large manufacturers and estimate that the average economic cost of bringing a new drug to market is \$802 million.³ This probably overestimates the average development cost for all patented drugs because it focuses only on new chemical entities (NCEs) and does not consider the cost of reformulations of existing products, such as extended release versions of a pill (Frank, 2003). Nonetheless it does capture the fact that bringing a new product to

² Authors' calculations from the National Health Accounts (<http://www.cms.hhs.gov/NationalHealthExpendData>)

³ Economic costs include the opportunity cost of capital that is tied up in the R&D process.

market can be exceedingly expensive even though pharmaceutical research is now potentially more efficient than ever, thanks to more effective methods and technologies such as high-throughput screening and rational drug design. What counteracts improvements in research methods is the reality that many of the foremost targets of pharmaceutical research are more complex than the pharmacological challenges of years past. The most common explanation for this is that all of the low-hanging fruit has been picked, and the recent drop in Food and Drug Administration (FDA) approvals for NCEs would seem to support this contention.⁴ These high research costs are coupled with the regulatory pressures to have even more extensive and expensive clinical trials, thereby further driving up development costs.

The high cost of bringing a new product to market influences the pricing dynamics we observe in the pharmaceutical industry. First, R&D costs represent an imposing barrier to entry that limits the competition that firms face, which in turn allows incumbents to sustain higher prices. Second, because R&D costs are so high, firms must be able to expect significant profits if they are to continue investing in innovation. The relationship between profitability and innovation is well documented (Abbott and Vernon, 2005; Giaccotto et al., 2005; Scherer, 2001). Patents are an important tool through which governments attempt to mitigate the innovation problems that arise when lower expected returns make continued investments in R&D less attractive.

2.2 *The product life cycle*

Governments use patents to compensate for the potential dynamic inefficiency that stems from high development costs. Patents encourage innovation by granting a limited period of market exclusivity to firms that develop new pharmaceutical products. This shapes the characteristic life cycle for pharmaceutical products that can end within months of patent expiration depending on how quickly generic competitors enter the market. Patents remain active for 20 years from the date of filing, but because firms file patents before beginning clinical trials, the average effective patent life is 11.5 years (PhRMA, 2006). While a patent can forestall direct competition, it does not secure monopoly power because a patented molecule has to compete with other distinct molecules approved to treat the same general condition.

Patent holders may attempt to extend the patent life of their drugs in a variety of ways. For example, generic entry could be delayed if patents were staggered so that, for example, the molecule patent expires at a different time than the patent on the production process or delivery method.⁵ Occasionally firms obtain patent extensions for reasons unrelated to changes in the underlying product – consider the relatively common six-month extension for filing a pediatric indication or the two-year extension Claritin received in an addendum to the 1994 GATT treaty.⁶ Brand name manufacturers can also introduce new presentations (e.g. change dosage strength, delivery mechanism, or form)

⁴ See Cockburn (2006) for a discussion of productivity in the pharmaceutical industry.

⁵ Many drugs hold multiple patents, which are filed and approved on different dates. Information on patents is available from the FDA Orange Book, which lists information about all approved patents for prescription drugs. <http://www.fda.gov/cder/ob/>.

⁶ Stephen Hall, 'The Claritin effect', *New York Times Magazine*, 11 March 2001.

of an existing product in the year prior to patent expiration.⁷ This subsequently requires that competing firms either incur higher entry costs as they develop generic versions of each formulation or risk reducing the potential market share that they can capture. In addition, patent holders sometimes launch their own authorized generic products, license authorized generics to another generic manufacturer, or reduce the price of their branded product prior to patent expiration.

3. Competitors

Patents protect pharmaceutical products from direct competition of same-molecule copycats for a period of time – 20 years in the USA. However, patents cannot completely foreclose competition, because they do not prevent competing manufacturers from bringing to market distinct molecules to treat the same condition. Once patents expire, generic manufacturers are free to introduce products that are virtually undifferentiated from the branded product, which heightens competition, reduces the average price for a molecule, and ultimately often results in a shrinking market because of diminished marketing support by manufacturers.

3.1 Brand name drugs

While a prescription drug is under patent protection, the market conditions it faces can best be described as an oligopoly with a number of differentiated, patent-protected products competing within a therapeutic class. As distinct molecules, they may work through a different chemical pathway and thus vary in efficacy, they may target patients with different risk factors or slightly different symptoms, and they may have different side-effect profiles. Because of high entry costs associated with developing a distinct drug molecule, entry into a given therapeutic class is limited, although larger markets tend to attract more entrants (Scott Morton, 1999).

Brand name products are often categorized as either innovative or ‘me-too’ drugs based on how much therapeutic advantage they represent over existing drugs in a therapeutic class. This distinction is a significant factor explaining launch prices of drugs (Lu and Comanor, 1998). Drugs that represent significant therapeutic advantages over existing drugs in a therapeutic class launch, on average, at prices three times higher than other brand name drugs in that class. ‘Me-too’ drugs, on the other hand, generally introduce modest improvements over existing products, and therefore add a measure of price competition into the market. Lu and Comanor (1998) find that launch prices of me-too drugs are comparable to the average price of existing drugs in the market. They also find that the number of drugs in a therapeutic class reduces entry prices and that long-run pricing strategies differ by drug type. Innovative drugs in their sample drugs followed a skimming strategy with high initial prices that fall over time, while ‘me-too’ drugs employed a penetration strategy with entry prices low, in order to gain market share, but rising over time.

⁷ Ellison and Ellison (2000) find that firms are most likely to deter entry in medium-sized markets. They explain that entry deterrence is less common in small and large markets because it is not worthwhile to deter entry in small markets that attract fewer generic entrants, and deterrence strategies will not be effective in large markets where the payoff to entry is sufficiently high.

Non-price competition is equally, if not more, important. Researchers looking at strategies related to the order of entry have found that ‘me-too’ entrants into a therapeutic class would launch at prices similar to the breakthrough incumbent but they would pursue non-price competition in the form of heavy physician marketing (Berndt et al., 1997). In fact new drug introduction is always accompanied by large investments in product promotion regardless of the type of therapeutic advantage that a new product brings to market. Bhattacharya and Vogt (2003) empirically support a model showing that pharmaceutical manufacturers do this to build product recognition and consumer goodwill, which helps facilitate rising prices later in the product life cycle.

3.2 *Generic competition*

The competitive environment facing a prescription drug changes considerably with patent expiration. The rules governing the launch of generic pharmaceutical products in the USA were set forth in the Drug Price Competition and Patent Term Restoration Act of 1984 (the so-called Hatch–Waxman Act). Hatch–Waxman altered the FDA’s approval process so that generic entrants need only to demonstrate that their product is bioequivalent to the brand name product without having to conduct costly safety and efficacy trials. Moreover, under the Hatch–Waxman rules, generic manufacturers are allowed to produce the patented molecule, and submit their marketing applications to the FDA while the original patent is still in effect. This significantly lowers barriers to entry, thereby opening the market up to potentially intense competition. In markets with at least one generic molecule, own- and cross-price elasticities for branded products appear to be higher than in markets with no generic competition (Ellison et al., 1997). In other words, demand is much more sensitive to the prices of a drug and its competitors in the presence of generic products.

Even when a patent expires, generic entry may not have an immediate effect on the prices that consumers pay for a given molecule. Under the Hatch–Waxman rules, the first generic entrant to obtain FDA approval can earn a market exclusivity period of 180 days and thereby delay the further entry of competing generic products.⁸ During this period, the generic manufacturer shares the market only with the original innovator company, which may or may not choose to compete directly with the generic. The generally higher level of pricing sustained during the exclusivity period creates an incentive to be the first to gain FDA approval. During this exclusivity period, the first generic entrant tends to set a price equal to about 80 percent of the brand name price (Berndt et al., 2007; Reiffen and Ward, 2005).

Generic drug prices fall as additional entrants come into the market (Caves et al., 1991; Grabowski and Vernon, 1992; Frank and Salkever, 1997) and approach marginal cost only after several generic firms enter the market (Reiffen and Ward, 2005). But this need not happen in all markets because intense competition depends on the attractiveness of market entry, which varies across therapeutic categories. Not surprisingly, large markets are the most attractive (Ellison and Ellison, 2000). Drugs that treat chronic conditions and drugs that are administered in inpatient settings are also attractive targets for generic entry because consumers have more elastic demand, so they are more likely to switch to

⁸ http://www.fda.gov/cder/about/smallbiz/generic_exclusivity.htm.

the generic product (Scott-Morton, 1999). Mandatory substitution laws and the emergence of pharmacy benefit managers (PBMs) that encourage switching to generic products encourage a fairly rapid rate of generic penetration, which further boosts generic entry.⁹

Most of the evidence pertaining to how incumbent prices respond to generic entry is based on data that pre-date the rise of managed care. In addition, the findings conflict on how manufacturers respond to entry, perhaps because the data used in these studies do not properly capture off-invoice price concessions. Caves et al. (1991) model markups for prescription drugs as a function of a drug's age, patent status, and drug-specific effects such as the type of condition that it treats and where the drug is primarily dispensed. They test their model using the prices of a sample of drugs that lost patent protection between 1978 and 1987 and find that, while the prices of some brand name drugs continued to rise after patent expiration, they increased more slowly than they would have in the absence of generic entry. They find that brand name list prices are declining in the number of generic entrants, and list prices faced by hospitals are much more sensitive to generic entry than are retail list prices. In contrast, Grabowski and Vernon (1992) and Frank and Salkever (1992, 1997) use pricing data from a similar period of time (1983–87 and 1984–87 respectively) and find that over time brand name list prices rise relative to those of generic drugs. Frank and Salkever propose that market segmentation explains this pricing behavior. Once generic firms enter, brand name manufacturers focus on less elastic segments of the market rather than trying to compete with generic products. Thus volume falls, but pharmaceutical firms are able to raise prices for the less elastic customers that remain.

These segmentation-based pricing patterns are probably less attractive now that most states have generic substitution laws that allow pharmacists to fill prescriptions with generic drugs when available. (Note that these generic substitution laws apply only to same-molecule switches and not cross-molecule substitutions.) Even without such laws, the majority of insured patients carry plans that utilize formularies to encourage switching to generic products by increasing the co-payment for the branded version and lowering the co-payment for the generic versions of a drug. As managed care has become more prevalent, the inelastic share of the market has shrunk considerably, and it may no longer be profitable to target this share of the market upon patent expiry.

An alternative strategy to increasing brand name price upon patent expiration is for brand name manufacturers to introduce their own generic products and directly compete with generic copycats. Because there would be no entry costs, this is a winning proposition if the firm can earn more profits during the generic exclusivity period than if they were to focus on the inelastic side of the market. In 2006 Merck followed a similar strategy when it negotiated a deal with United Healthcare and Blue Shield of California to dramatically lower the price in exchange for more favorable consumer-level pricing, which is opposite to what is typically done. When the branded version of a drug loses patent, insurers usually require that patients pay more out of pocket for the brand version of that drug (Won Tesoriero and Martinez, 2006). How such a strategy plays out remains

⁹ Berndt and colleagues give the example of Paxil, which lost 70 percent of its market share to generic entrants within two months (Berndt et al., 2007).

to be seen, but this kind of competitive threat from a branded manufacturer could lower incentives for generic manufacturers to challenge patents.

4. Customers

In the market for pharmaceutical products, the end-user, payer and decision-maker roles are shared by distinct parties: patients, insurance companies and physicians. In this section we focus on distinctions between the end-user and payer roles and on their implications for pricing.

4.1 Insurance

In most industrialized countries, national governments are the predominant source of health insurance coverage. This contrasts with the USA, where employers provide health insurance coverage and, in almost all cases, prescription drug benefits for approximately 60 percent of the population. Twenty-seven percent of the US population receives some form of government health insurance such as Medicare for those 65 years and older (13.7 percent), Medicaid for the disabled and qualified low-income citizens (13.0 percent) or military health insurance (3.8 percent).¹⁰ There is some overlap between the employer and government-sponsored groups, as some Medicare beneficiaries also obtain supplementary retirement coverage through their former employers or are eligible for Medicaid. Both Medicaid and Medicare cover prescription drugs, but prior to the 2006 implementation of the prescription drug benefit for the elderly (the so-called Medicare Part D), more than a quarter of the population eligible for Medicare lacked any sort of prescription drug coverage.¹¹

Insurance distorts consumption patterns by creating a divergence between what a patient pays and what a retail pharmacy charges for the drug. As a result, insurance may effectively lower the elasticity of demand for pharmaceuticals. Because insurance reduces the out-of-pocket cost, it may also increase the quantity of pharmaceutical products consumed as insured patients may choose to take drugs that they might not have been willing to pay for were they facing their full cost.

Many private insurers and government-sponsored plans use a variety of cost management strategies to influence patient behavior to mitigate the adverse effect of health insurance coverage. One such measure is the drug formulary – a preferred list of drugs that a PBM selects based on efficacy, side-effect profile, and cost-effectiveness. Being a list, it will affect utilization patterns only if it is aligned with proper incentives. Common tiered formularies require varying levels of cost-sharing from patients. A common structure for a tiered formulary is to require no or minimal cost-sharing for generic drugs (e.g. a flat fee of \$5 for a 30-day supply of pills), higher for brand name drugs that have ‘preferred’ designation (e.g. \$15 for a 30-day supply), and often significantly higher for drugs that are not on the preferred list (e.g. \$45 for a monthly supply). When cost-sharing relies on a fixed dollar fee for each prescription, it is referred to as co-payment. This is in contrast

¹⁰ US Census Bureau, ‘Income, poverty, and health insurance coverage in the United States: 2005’, <http://www.census.gov/prod/2006pubs/p60-231.pdf>. Percentages do not add up because some people are eligible for more than one type of coverage.

¹¹ Kaiser Family Foundation, Prescription Drug Trends Fact Sheet, November 2005, <http://www.kff.org/insurance/upload/3057-04.pdf>.

to co-insurance, which requires patients to pay a defined percentage of the total cost, usually also increasing with tier preference.

4.2 Effects of insurance on price sensitivity

Much of the early empirical evidence on the effect of health insurance on prescription drug consumption comes from the RAND Health Insurance Experiment (Newhouse and the Insurance Experiment Group, 1993), which assigned people to plans with different levels of prescription drug coverage and found that those who were enrolled in plans with higher cost-sharing requirement consumed fewer prescription drugs.

Gibson et al. (2005) provide a review of recent research on the effects of cost-sharing on drug consumption. As a whole, the evidence that they review supports the notion that insurers can use tiered formularies to alter patient consumption patterns. It has been found, for example, that increasing the number of tiers in a formulary and thus the out-of-pocket prices for some drugs, changes the mix of drugs consumed but not the total volume of drugs consumed (Huskamp et al., 2005). Other research reports that elasticity of demand varies across different therapeutic classes and types of treatment. In particular, demand elasticity ranges from -0.1 to -0.16 for chronic conditions and from -0.6 to -0.24 for acute conditions (Landsman et al., 2005; Goldman et al., 2004).

The studies above show that insurers can influence both the total amount of drugs consumed and choices among drugs by changing the out-of-pocket costs that patients pay. While these studies do not consider prices charged by manufacturers, their results imply that, by influencing consumer behavior, changes in out-of-pocket costs could lead to downward pressure on drugs prices. Pavcnik (2002) explicitly addresses this question, taking advantage of a change in reimbursement practices in Germany in 1989 to analyze how drug prices respond to changes in out-of-pocket spending. These new reimbursement rules made patients responsible for the full cost difference of a specific drug in a therapeutic class and other, more expensive drugs that they might wish to consume. Using a sample of anti-diabetics and anti-ulcer drugs, Pavcnik demonstrates that the policy change led to lower prices for all drugs in those classes by 10 percent to 26 percent, with particularly dramatic decreases occurring among branded drugs.

4.3 Search and switching behavior

The existence of search costs and switching costs in a market leads to higher prices and greater price dispersion. Search costs are a feature of prescription drug markets that is particularly relevant for cash-paying customers who potentially face price dispersion among like drugs across different pharmacies. Sorensen (2000) models search behavior for patients consuming prescription drugs, where a patient will continue going from one pharmacy to the next if the expected benefits from searching exceed the cost of searching. The patient will stop searching once they believe that they cannot make themselves any better off through shopping around. Sorensen documents considerable price dispersion and high search costs for cash-paying customers. The findings are telling – even when patients are responsible for the full cost of the drugs that they consume, they are either not willing to or not able to gather enough information about prescription drugs on their own to limit price dispersion.

Patients who have insurance coverage do not face this kind of price dispersion because their co-payments are pegged to the formulary status of the drug rather than its retail

price. However, insured patients also face costs in their search for the best drug match for them. Gaining the requisite knowledge to effectively evaluate products can be costly for patients, and, indeed, this is one of the reasons why patients rely on physicians to make the choice for them. As we discuss in more detail below, physicians also face search costs that may influence their prescribing choices. Crawford and Shum (2005) observe a sample of patients taking anti-ulcer drugs in Italy and find that very few patients diverge from the initial prescription. This suggests that either the initial prescription is a good match, that there is considerable risk aversion towards switching among patients or doctors, or that search costs of finding a better match are too high. It is important to note that patients are weighing the search cost against the expected benefit, which may not be accurate if patients are not well informed about the quality or existence of different products. Because search costs dampen price shopping, high search costs could contribute to higher prices even when several products exist within a therapeutic class.

5. Collaborators

For the most part, physicians neither consume nor pay for the drugs they prescribe for their patients, but they nonetheless have an institutionalized role as the primary decision-maker. After diagnosing a problem, physicians determine not only whether drug therapy is appropriate, but also what drug and dose should be prescribed. Presumably, physicians' primary objective is to offer their patients a level of care consistent with broadly accepted best practices, but it is not so clear that they have the incentive to account for economic considerations when prescribing a drug. The most medically effective care may not necessarily be the most cost-effective care, and when applied to prescribing behavior, this could be manifested in prescriptions whose marginal value is less than the marginal cost over another drug that treats the same condition. Furthermore, physicians face severe time constraints, making it costly for them to take the time to learn about new pharmaceutical products. While brand name drugs are heavily marketed, generic manufacturers do not promote their products, so it takes relatively more effort for physicians to learn about new generic products.

Despite their lack of direct financial involvement in the decision, research shows that physicians do sometimes alter their behavior in response to cost considerations. There are several reasons for this. First, insurers and PBMs can directly entice physicians to prescribe certain drugs over others. This approach is particularly effective in settings where physician salary is tied to performance on the cost-effectiveness front, as in the case of staff health maintenance organizations. Patients' economic considerations also play a role, despite the general belief to the contrary. According to the Kaiser Family Foundation (2006), 53 percent of physicians frequently discuss out-of-pocket costs with patients when they prescribe drugs. This finding is supported by research showing that tiered patient co-payments matter (Huskamp et al., 2005). This is especially apparent when patients have no insurance coverage or have limited resources (Reichert et al., 2000; Hux and Naylor, 1994).

Nonetheless, physicians neither fully internalize the patient's price incentives nor the insurer's cost burden. This further exacerbates the incentive distortion posed by insurance. This effect is also magnified by the fact that physicians tend to prescribe habitually, with many doctors persistently prescribing brand name drugs after generics have become available (Hellerstein, 1998). The stickiness of prescribing patterns allows brand name

firms to maintain higher prices upon generic entry; although, in the case of generics, the impact of this behavior is mitigated somewhat by the fact that pharmacists are generally allowed to substitute generics when available.¹² Habitual prescribing also helps differentiate products within a therapeutic class, which, according to economic theory, should lead to higher prices.

6. Channels

Because the resale of prescription drugs is closely regulated, pharmaceutical manufacturers can charge very different prices to different buyers without facing the threat of arbitrage (Frank, 2001). These negotiated prices are commonly not available to parties outside the agreement. Therefore, when describing channel structures in the pharmaceutical industry, it is worthwhile to distinguish between the channel structure for the physical product distribution and the financial flow. The former has the typical channel structure that involves wholesalers and retailers. The latter is complicated by the existence of the insurance system, which introduces new players and payments that sidestep the channel partners involved in the physical distribution of the product. We follow this logic after a brief introduction of the various players involved in the distribution and reimbursement of prescription drugs. The discussion in this chapter draws heavily on conversations with industry insiders, on recent reports by the CBO and the Kaiser Family Foundation (CBO, 2007; Kaiser Family Foundation, 2005), and on Kolassa (1997). We summarize some of the key pricing terms in Box 23.1.

6.1 Channel players

Wholesalers Approximately two-thirds of all US prescription drug sales flow through wholesalers (CBO, 2007). The wholesale function is highly concentrated in the top three firms, McKesson, Cardinal Health and AmerisourceBergen, holding an 80 percent market share in 2005 (Kaiser Family Foundation, 2005). Wholesalers distribute products to different types of pharmacies and to some non-retail buyers such as hospitals and nursing homes.

Pharmacies There is a wide spectrum of pharmacy ownership forms: chain pharmacies (e.g. CVS, Duane Reade, Walgreens), mass merchandisers (e.g. Costco, Wal-Mart, Target), food supermarkets (e.g. Safeway, Albertsons), independent pharmacies and mail order pharmacies. Chain pharmacies account for the largest share of the market with over 40 percent of the dollar and unit share (see Table 23.1). The fastest-growing pharmacy segment includes mail pharmacies, of which the largest ones are owned by PBMs. Because mail pharmacy prescriptions are generally for 90 days rather than the standard 30 days in retail, they represent a disproportionate share of dollars (relative to units measured by prescriptions). In addition, these pharmacies dispense a disproportionate share of typically newer and more expensive drugs that treat chronic conditions (Wosinska and Huckman, 2004).

¹² Line extensions, such as ‘extended release’ or ‘extra strength’ may limit the effect of such mandatory substitution laws because such formulations are not affected by them.

BOX 23.1 KEY PRICING TERMS

Average manufacturer price (AMP) AMP is the average price that wholesalers pay to manufacturers for a drug that is distributed through the retail pharmacy channel. AMP incorporates all discounts that the wholesaler negotiates with the manufacturer, but does not include any rebates that insurers or PBMs negotiate. Congress established the AMP in 1990 as a way to calculate rebates for Medicaid prescription drug expenditures.

Wholesale acquisition cost (WAC) WAC is generally the price that manufacturers charge wholesalers. This price does not include any of the discounts that the wholesaler receives.

Average wholesale price (AWP) AWP does not actually represent any average price and it does not reflect what wholesalers pay. Instead, it is best thought of as a benchmark price that may be used as a reference for negotiating discounts and rebates. For example, prior to the 2003 Medicare Modernization Act, CMS set the prices for Medicare Part B drugs as a percentage of AWP. Now CMS uses ASP as its reference point since that price better reflects actual prices that manufacturers receive. (ASP is analogous to AMP for physician-administered drugs.)

Chargeback Sometimes wholesalers provide drugs to organizations that have negotiated discounts directly with the manufacturer. In these cases, the wholesaler offers the drug to these organizations at the lower, negotiated price. The chargeback, which wholesalers receive from manufacturers, is the difference between the WAC and the discounted price that the wholesaler receives.

Rebate Manufacturers pay rebates to customers after the customers have purchased the drug. PBMs, insurers and pharmacies may all negotiate rebates with the manufacturer, and the rebate allows the manufacturer to retroactively lower the net prices that different customers pay. The AWP is commonly used as a starting point in these negotiations. These rebates are confidential.

Non-retail buyers The class of non-retail buyers includes parties such as hospitals, select HMOs (such as Kaiser Permanente) and nursing homes. These health care providers both purchase and administer prescription drugs, and CBO (2005) estimates that they dispense around 28 percent of the prescription market measured in dollars. Non-retail buyers distinguish themselves from other members of the distribution chain in that they can influence consumption patterns. Concordantly, non-retail buyers are able to negotiate significant discounts from manufacturers.

Pharmacy benefit managers Most health insurance plans use separate entities called pharmacy benefit managers (PBMs) to administer prescription drug coverage. While

Table 23.1 *Sales, market share and pharmacy type in the USA (2005–06)*

Pharmacy type	Sales					
	(\$ billions)		Dollar share (%)		Unit share (%)	
	2006	2005	2006	2005	2006	2005
Chain	102.83	94.49	41.2	40.7	47.2	46.6
Mass merchandiser	24.34	22.48	9.7	9.7	11.0	10.9
Supermarket	28.82	27.64	11.5	11.9	13.9	14.2
Independent	43.48	41.90	17.4	18.1	21.1	21.5
Mail order	50.37	45.50	20.2	19.6	6.8	6.8

Source: National Association of Chain Drug Stores, 'Industry facts at a glance'.

many PBMs began as claims processors, they have evolved into full service entities that develop formularies, negotiate prices with manufacturers, establish pharmacy networks (lists of pharmacies where covered patients can fill prescriptions), and offer mail order pharmacy services. Although the PBM industry is not as concentrated as the drug wholesale industry, most of its activity is consolidated in a small number of large multi-billion-dollar firms. In 2005, four PBMs accounted for half of all covered lives: Caremark Rx (19 percent), Medco Health Solutions (13 percent), Express Scripts (11 percent) and WellPoint Pharmacy Management (7 percent) (AIS, 2006). Outside of their mail order operations, PBMs rarely take possession of drugs, but they play a critical role in determining the net price of pharmaceuticals.

Insurers and employers Some private insurers and employers do not outsource the management of pharmacy benefits to PBMs, but rather run them internally. In some cases, self-insured employers form coalitions, such as Rx Collaborative, to improve their bargaining power against manufacturers. In this chapter, our references to PBMs also encompass these entities that perform the PBM functions internally.

6.2 *Channel partners involved in physical product distribution*

The physical distribution of drugs presented in Figure 23.1 is straightforward – wholesalers purchase drugs from manufacturers and then sell these drugs to pharmacies, which in turn dispense to patients. Any potential discounts and the ability to extract higher markups earned by these channel partners depend on their value added, in particular their ability to affect downstream demand.

The first party downstream from manufacturers – wholesalers – are not able to negotiate substantial discounts for branded pharmaceuticals because of their inability to move market share. They are, however, able to negotiate discounts for volume, prompt payment, and for taking on products close to expiration, but these discounts are minimal. A system of 'chargebacks' allows a manufacturer to offer negotiated discounts to end customers without the risk of arbitrage by the wholesaler. Under this system, the amount that wholesalers generally pay to manufacturers for inventory is an undiscounted invoice or list price, often referred to as wholesale acquisition cost (WAC)

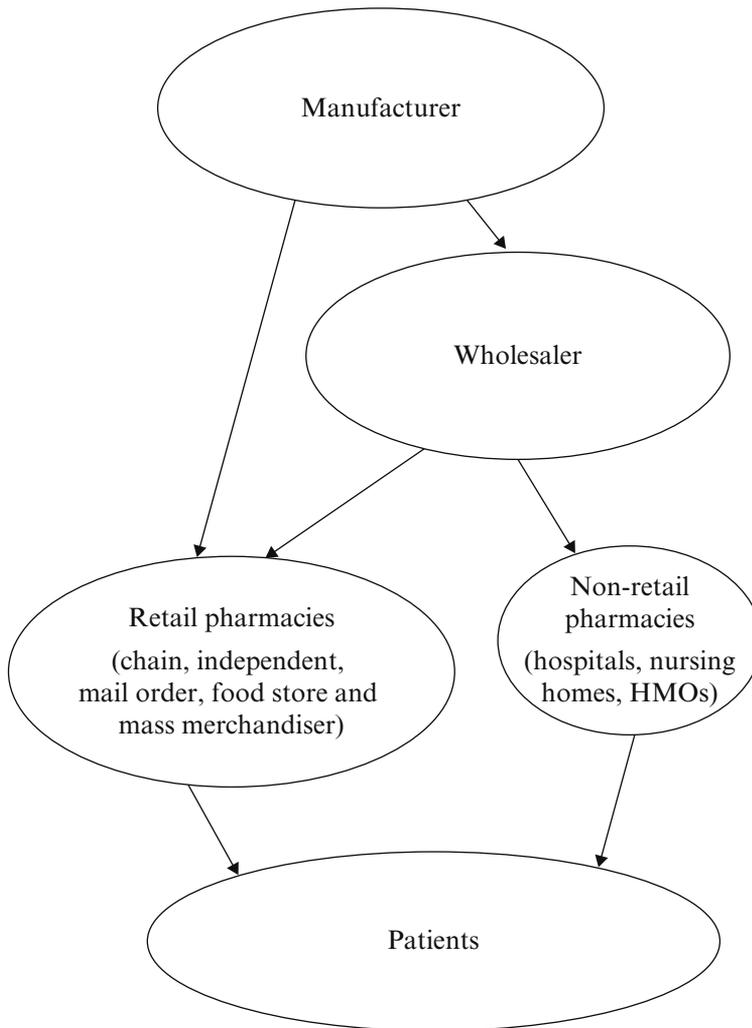


Figure 23.1 Product flows

(Schweitzer, 1997, p. 11). The end purchaser obtains its contractual discount immediately from the wholesaler at the time of purchase, while the wholesaler subsequently is reimbursed for the amount of the discount after submitting a claim to the manufacturer. This payment, known as the chargeback, is mainly used in sales of branded drugs to non-retail entities and sales of generic drugs to retail pharmacies. The net price that the wholesaler pays to the manufacturer is typically the WAC price net of discounts and chargebacks. Customers that do not have discount agreements with the manufacturer typically pay prices near WAC because that is the cost of inventory on hand for the wholesaler.

At the retail level, pharmacy acquisition costs and margins differ drastically between branded and generic drugs and across pharmacy ownership types. In all cases, they are

driven by the ability to influence consumer demand. In the case of branded drugs, pharmacies simply fulfill demand by stocking a wide variety of drugs. In the case of generic drugs, pharmacies make decisions about which manufacturer's generic version to stock. In addition, third-party payers have exhausted their bargaining power with pharmacies for generic markups because any threat to steer patients away from generics would not be credible. Differences in bargaining power across pharmacy types also drive variation in pharmacy acquisition price levels. While independent pharmacies buy almost all of their drugs from wholesalers, chain pharmacies purchase a large share of drugs from their own warehouses, which results in a price differential to the benefit of large retailers. Mail order pharmacies are able to achieve consistently lower prices than other dispensers not only because they are able to take advantages of efficiencies in distribution, but they can ensure a higher degree of formulary compliance.

The amounts that pharmacies receive for drugs vary from payer to payer and also depend on whether the drug is branded or generic. Payments to pharmacies for branded drugs are generally fixed in a formulaic fashion based on the acquisition cost plus a pharmacy margin, which consists of a fixed percentage markup on the drug and a flat dispensing fee. For generic drugs, payers frequently impose a fixed maximum allowable cost (MAC) for reimbursement plus a flat dispensing fee that may vary by payer or drug type. Nevertheless, pharmacies are often able to earn higher margins on generic drugs because they can perform switches from brand to generic. A recent study by the Congressional Budget Office (CBO, 2004) makes that point explicit. The study measured the difference between the average manufacturer price (AMP) and the average price paid by independent pharmacies, which represents both wholesale and pharmacy markups, and found that markups per prescription were \$3.80 for brand name drugs, \$5 for new generics and \$1.40 for old generics. The report also stated that wholesalers retain most of the markup for branded, on-patent drugs while pharmacies keep most of the markup for post-patent branded drugs and generics. The pharmacy markup also depends on a patient's insurance status.

6.3 Payments by entities not involved in physical product distribution

Because of insurance and formularies, the flow of money from the patient back to the manufacturer is more complex than the physical product distribution would suggest (see Figure 23.2). For one, the revenues that pharmacies receive are based on patient co-payments and payments from insurance companies, which are most commonly handled by PBMs. In addition, formularies give PBMs an ability to negotiate manufacturer discounts to bring down the net price they pay to the retail channel.

There are two reasons why PBMs and the insurers they represent are able to bargain with manufacturers. First, an individual PBM represents a large number of health plans and thus pools a large share of the prescription market. Second, PBMs not only influence the formulary line-up, but are also actively involved in enforcing it by mapping it to patient out-of-pocket costs, educational programs, prior authorization requirements, and drug utilization reviews. Ellison and Snyder (2003) argue that it is the ability to manipulate patient behavior, and not size, that confers bargaining power to PBMs. Formularies improve buyers' positions when they negotiate drug prices because they provide a credible means to punish a drug manufacturer for not offering an attractive price. The ability to affect purchase patterns through the formulary is also the reason why

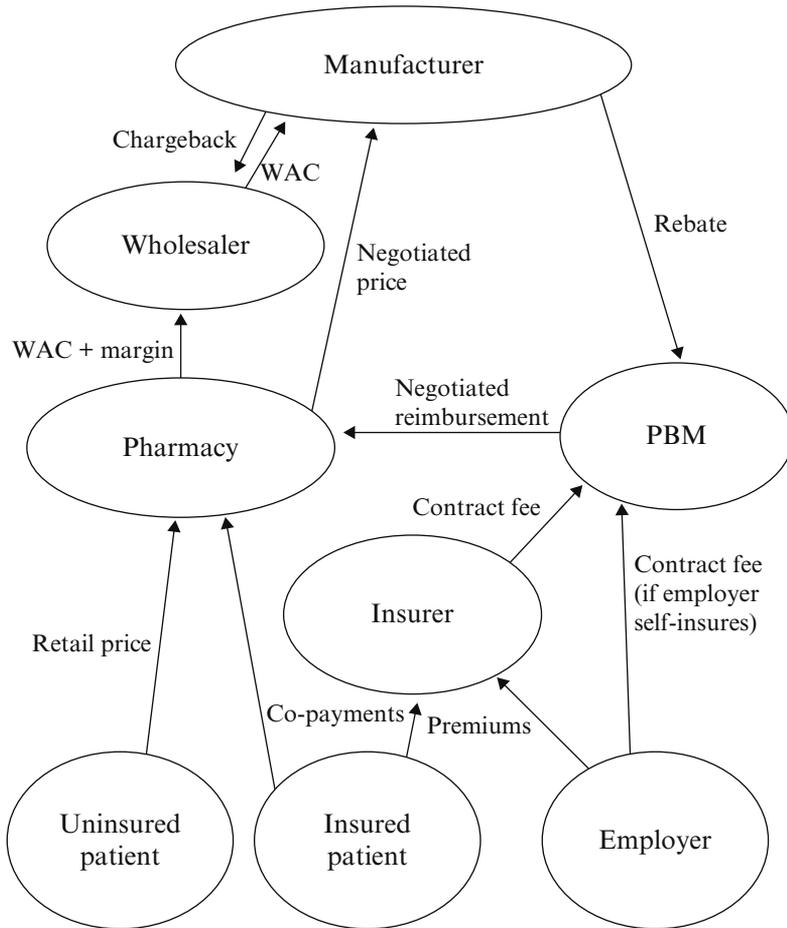


Figure 23.2 Payment flows

hospitals and other non-retail buyers can obtain discounts from the retail price found in pharmacies.

Rebates are a form of *ex post* discounting that PBMs may be able to obtain. Unlike chargebacks, rebates often bypass market intermediaries and change hands after retail transactions are completed. For example, one type of rebate that can flow from manufacturers to payers or PBMs is called a formulary rebate. Such rebates may be tied directly to performance metrics such as achievement of market share goals. Since these metrics cannot be computed until well after transactions are completed (often on a quarterly basis), they are not generally reflected in transactional data. Moreover, in this example, the rebate goes to the payer or PBM and bypasses the pharmacy and wholesaler, which means that transactional data from those entities would not reflect the full discounted prices that PBMs and insurers obtain for their formulary performance – a fact that could bias elasticity estimates based on such data. In addition, mapping rebates to specific transactions is very difficult if not impossible because a

rebate may pertain to purchases aggregated over a long period of time or to a bundle of products.

In addition to bargaining with manufacturers, PBMs use their ability to define which retail pharmacies participate in a network as a way to negotiate lower payments to pharmacies.

7. Context

Pharmaceuticals, together with other health care segments, tend to generate much political interest and therefore regulation. An important reason is the influence that drug quality has on someone's physical well-being in a way that other products do not, and the fact that adverse effects of going without treatment are very different from the adverse effects of going without, say, a new operating system on your computer. Furthermore, because health care accounts for a large share of public spending in the USA and other countries, policy-makers face pressure to limit prices, especially on pharmaceuticals, which represent a fast-growing segment of health care spending.

7.1 Forms of price regulation

In the USA, the main regulatory agency for the industry, the Food and Drug Administration (FDA), regulates the development, approval and marketing of prescription and over-the-counter medicines. It does not, however, regulate pricing. This is in contrast to most other industrialized countries where a single government purchaser is responsible for administering drug benefits. Differences stem from the fact that while many industrialized nations have universal or single-payer health care systems, the USA relies on a system that is predominantly financed by employers.

Methods of price regulation fall into the following general categories: price ceilings, reference pricing and profit regulation (GAO, 2007). Price ceilings, where the government sets a maximum price, are used in France and Australia. If non-governmental purchasers are free to negotiate lower prices than those set by the regulator, then the established price becomes a price ceiling. A related practice, reference pricing, occurs when the regulator links reimbursement to price levels of other drugs in the therapeutic class (as in Germany) or of the same drug in other countries (as in Canada or Australia). Profit or rate of return regulation, which is practiced in the UK, allows pharmaceutical manufacturers to earn a specified rate of return across a portfolio of products sold in the country, and manufacturers are free to set prices for each drug so long as they stay within the acceptable profit corridor. If profits exceed a specified level, the drug company would have to lower prices to bring profits within an acceptable range, and the drug companies can request price increases if profits are too low.

In general, the US government does not regulate the market prices of prescription drugs, although it plays an important role as the largest payer for prescription drugs, primarily through the Medicaid program for the disabled and low-income and the relatively new Medicare program for the elderly (Medicare Part D). State and federal agencies are responsible for financing a considerable amount of prescription drug spending in the USA. A large share of federally financed drug spending flows through private insurance plans and PBMs that are responsible for administering Medicare Part D.

In addition to Medicare Part D and Medicaid, the government finances prescription drugs under the auspices of Medicare Part B (which primarily covers drugs administered

in physician clinics), the relatively small programs in the Veterans' Administration (VA), and the Department of Defense (DOD). These programs directly negotiate with manufacturers or follow legislated reimbursement rules and are able to obtain highly discounted prices. The Congressional Budget Office (2005) estimated that the average prices that the DOD and VA pay for prescription drugs are 41 and 42 percent of the average wholesale price (AWP) respectively. The average price that Medicaid pays is 51 percent of AWP relative to a best price in the private sector of about 63 percent of AWP.

7.2 Firm response to price regulation

The intent of any price regulation is to secure lower prices for prescription drugs. However, consequences unintended by regulators can result from poorly conceived regulation. Exactly how a pharmaceutical manufacturer responds to pricing regulation depends on the regulatory approach taken, but a growing body of evidence suggests that price regulation does not necessarily lead to lower drug costs and it can have adverse effects on both the short- and long-term supply of prescription drugs.

Medicaid's adoption of a 'most-favored-customer' pricing rule in 1991 is a good example of how price regulation can influence industry dynamics. Because Medicaid was a passive payer, it was not securing the same discounts that private purchasers were able to negotiate. In response, the US Congress established that Medicaid price net of rebates would be the lesser of the AMP minus 15.1 percent or the lowest price made available to any private purchaser. In turn, manufacturers responded by offering smaller discounts to private purchasers (Congressional Budget Office, 2004; Scott-Morton, 1997). Furthermore, the pricing regulation created an incentive to introduce new versions of drugs as a way to skirt price regulation because launch prices are not regulated (Duggan and Scott-Morton, 2004). This led to an inefficiently high rate of incremental innovation for certain drugs and effectively raised spending as Medicaid programs began to pay for new and more expensive presentations of the same drugs (Duggan and Scott-Morton, 2004).

Ekelund and Persson (2003) provide an example from Sweden of how regulation changes pricing in the pharmaceutical industry. Using the model of Lu and Comanor (1998), they investigate launch price strategies for innovative and me-too drugs. The model predicts that the profit-maximizing strategy for me-too drugs is setting a low entry price that would rise over time, while the best strategy for unique drugs entails setting a high entry price that would fall over time. However, the Swedish government negotiates prices with manufacturers, who are then prohibited from raising them without government approval. In such a regulated regime, a penetration strategy is not possible because firms cannot raise prices freely. Ekelund and Persson find that launch prices are higher for drugs that represent more significant therapeutic advances, and they find that the relative launch prices are higher in the regulated market. Because regulation does not affect launch prices, they do find evidence for skimming strategies for all drug types.

In similar vein, Danzon and Chao (2000b) argue that regulating prescription drug prices reduces competition. They find that price competition among generic drugs is more robust in less regulated markets, while highly regulated markets have less generic entry and, in turn, higher prices for off-patent drugs. Kyle (2007) finds that firms tend to delay entry into markets where prices are highly regulated, which is consistent with the studies above, which show that price regulation reduces price competition. That price regulation

reduces price competition is a somewhat obvious conclusion. Price regulation, after all, fixes prices or at least binds prices within some range.

So, does price regulation lower prices or does it raise prices? The answer to this depends on how the regulator sets prices. Price regulation will surely lead to lower prices for existing drugs, but it is not clear that regulation leads to lower prices for newer products. Ekelund and Persson's (2003) findings suggest that in a regulated market, the me-too drug sets its price higher than it would do in an unregulated market, so now the average price for treating the condition when two products exist is higher in the regulated market than it would be in the unregulated market. However, price regulation will only have a chilling effect on competition if prices are set upon market entry and renegotiated infrequently or not at all. If regulators can renegotiate prices when substitutes become available, they can induce price competition among firms.

One further concern with price regulation is that, if it depresses prices and current revenues, it will lead to less innovation. Pharmaceutical innovation is funded through both internal revenues and external venture capital, and profit-reducing price regulation can reduce access to both sources of R&D funding. Furthermore, firms may find it more profitable to divert funds towards product promotion if the returns to R&D fall as a result of price regulation. Again, this is not necessarily a bad thing from a regulator's perspective. Both innovation and low prices are valuable to public welfare, but there is a tradeoff between innovation and profits (Abbott and Vernon, 2005; Scherer, 2001). The goal of the regulator is to strike a balance between these two objectives.

7.3 International price variation and arbitrage

Just as there is price variation among different purchasers within the USA, there is substantial international price variation. Price variation among consumers in the USA is sustained by purchasers' inability to resell the drugs that they purchase. Similar restrictions exist in international markets, which partly explains why average prices can differ so much across countries.

Measuring exactly how much prices vary is a difficult task. Danzon and Chao (2000a) and Danzon and Furukawa (2003) discuss some of the difficulties involved with comparing prices for prescription drugs across countries and explain that many comparisons of prices overstate differences. But a consistent finding from the literature on cross-country pricing differences is that the USA and Japan have higher prices than other countries. This is generally attributed to the fact that these countries do not regulate prices and do not take advantage of parallel imports that arbitrage such price differences.

In general, international price variation is sustained by global patent laws that restrict the movement of prescription drugs across borders. The European Union (EU) represents an exception to this rule because of free movement of goods among EU states. Interestingly, this is in spite of patent laws that would restrict such movement. The resulting parallel imports of drugs allow EU governments to arbitrage the existing price variation. When Ganslandt and Maskus (2004) measured the effect that parallel imports had on prices in Sweden after its 1995 EU entry, they found that prices fell between 12 and 19 percent for drugs that faced competition from parallel imports.

Whether the experience from Sweden generalizes to other countries is an open question. In fact, economic theory suggests that while parallel importation could reduce prices in high-priced, importing countries, this effect would be mitigated if pharmaceutical

manufacturers raised prices in exporting countries, or credibly threatened to foreclose a market altogether if their reservation price was not met.¹³ At the same time, the exporting country can sometimes credibly threaten to either nullify a drug's patent or require that it be licensed in country. With few exceptions, such compulsory licensing is prohibited by the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs), but Thailand recently responded to high prescription drug prices by licensing the production of generic versions of Plavix, a drug that treats heart disease, and HIV/AIDS drugs Efavirens, Kaletra and Stocrin (Fuller, 2007).¹⁴

Even when parallel trade is restricted, prices across different countries seem correlated. Chintagunta and Desiraju (2005) look at pricing and detailing levels for three antidepressants and find significant across-market interactions in the pricing of these drugs in the USA, the UK and Italy. They present anecdotal evidence that local and global units of pharmaceutical firms work together when setting prices, and explain that when firms compete in multiple markets, a global, rather than a regional, approach to pricing would generate the observed across-market effects.

Political pressure in key markets, such as the USA, could also explain correlation of prices across countries. When markets are perfectly segmented, profit-maximizing firms with market power will set prices according to the willingness to pay in each market. Large disparities in prices among countries could invite legislative action in high-priced countries that would be unfavorable to pharmaceutical firms. For example, firms may feel that if prices are too low in one country, legislators in the USA could respond by imposing price controls or permitting importation. When setting prices across countries, pharmaceutical firms consider the possibility of inviting such political backlash. Kremer (2002) explains that this is one factor that helps explain the shortage of prescription drugs in the developing world.

8. Areas for future research

From our discussion in this chapter, it should be clear that the pharmaceutical industry is unique, and pricing in this environment merits special attention. A substantial literature addresses pricing in the pharmaceutical industry, but several avenues for future research exist. We would categorize areas for future research in three distinct areas. First, future research should continue to clarify the nature of the current market. Second, we believe that more research is needed on how to optimize the current system. Finally, given the dynamic nature of the regulatory and institutional environment that defines the pharmaceutical industry, continued research on how these changes influence pricing will be needed as the industry continues to evolve.

Research that focuses on the actual measures of price would facilitate a better

¹³ Grossman and Lai (2006) and Pecorino (2002) outline game-theoretic models of pharmaceutical pricing when drug importation is allowed. The key insight of these models is that drug importation changes the possible payoffs for both the drug manufacturers and price-regulating governments. The different payoffs change behavior relative to a regime where drug importation is not allowed.

¹⁴ Under TRIPs, countries are permitted to manufacture a patented drug under a compulsory license if the drug is necessary to address a national emergency and the government cannot otherwise obtain the drug. TRIPs does not clearly define what constitutes a national emergency.

understanding of the industry today. As Figure 23.2 illustrates, payment flows are anything but straightforward. The payment system is made up of several different agents, each of which pays a unique price. Some of these prices are negotiated, but most of the observable prices are list prices. The multiplicity of different price measures can be confusing to the uninitiated. Should one consider the out-of-pocket cost that the patient pays, the pharmacy acquisition price, pharmacy retail price, wholesaler's net price, AWP or WAC? The answer depends on the issue at heart and the segment of the market in question. But it is worth noting that one important price, the price that the manufacturer receives net of rebates, is unobserved because of the private nature of negotiations among drug manufacturers and various purchasers. While this situation is not necessarily unique to the pharmaceutical industry, in the absence of a direct measure, researchers must make do with the price measures available and hope that these prices are at least correlated with the price of interest.

In addition, much of the extant literature on pharmaceutical pricing utilizes data from the 1980s and early 1990s, but, as the market has changed considerably since that time, there is a need for research that demonstrates how and whether these changes have influenced competitive pricing dynamics in the industry. As managed care companies began to actively participate in the pharmaceutical market during the 1990s, pricing in the pharmaceutical industry evolved to the three-tiered co-payment systems we see today. More recently it has been affected by the widespread adoption of PBMs. Through their use of formularies and other negotiating tactics, PBMs injected market power into the buyer side of the market. While it is well known that PBMs secure significant rebates, research that quantifies this effect would be a welcome addition to the literature. This could however be a difficult task, given the confidential nature of the rebates that PBMs negotiate.

Besides improving our understanding of current industry dynamics, research is needed on the optimal way to structure or restructure the systems and contracts that determine prescription drug prices. On the one hand, the growing role that PBMs perform, coupled with their expanded capabilities, could create conflicting incentives for the clients they represent. On the patient-insurer front, misalignment of incentives also is present because the structure of pharmacy benefits has clear implications for patients' drug utilization. These structures are often overly simplistic; for example patients usually face the same co-payment structure regardless of therapeutic category or can fill 90-day scripts through mail pharmacy for both chronic and episodic conditions (e.g. hay fever). We expect that much of this line of research may necessarily be theoretical, although we believe that researchers should also seek out the rare natural or controlled experiments because of their power to aid decision-making.

Finally, the political and therefore regulatory context in which the industry functions is constantly evolving. The introduction of Medicare prescription drug benefits for the elderly will have a substantive impact on industry dynamics and this will undoubtedly be a ripe area for research. The anticipated public release of average manufacturer prices (AMP) is likely to increase transparency in the marketplace, which will probably impact competitive dynamics although the direction of that impact appears ambiguous (CBO, 2008). Even the change in political party controlling the US government's policy is likely to impact the type and likelihood of price regulation. All these changes will provide plentiful opportunities for relevant policy research.

Outside of the USA, several interesting questions are left unanswered. Compulsory licensing and the free trade of prescription drugs across borders significantly changes how pharmaceutical firms think about patents and will change the way they set prices across countries. Pharmaceutical firms charge different prices for the same drug in different countries, but it is not clear that these prices are completely uncorrelated. A small amount of research investigates the correlation of prices across markets, but this is an area that is open for continued research and will become more important if changes in international agreements influence how patents operate internationally.

Aside from the ever-shifting regulatory pressures, advances in the science that drives the industry will affect pricing dynamics in the industry and indirectly fuel regulatory interest. Many newer pharmaceutical and biological products target very specific populations, and the introduction of these highly specialized drugs could place upward pressure on prices. The increased use of biologics may also alter the generic industry dynamics because these complex compounds are difficult to replicate cheaply and consistently.

As noted in the introduction, spending on prescription drugs constitutes an increasingly important share of spending on both the personal and national level. Together with the fact that prescription drugs influence a consumer's well-being like few other products, it is self-evident that a clear understanding of pricing in this industry is important, but research in this area may have a broader appeal. Perhaps because the pharmaceutical industry is regulated on many fronts, many of the transactions are closely recorded, providing a wealth of data that researchers can use to investigate consumer behaviors such as responses to marketing or decision-making when product attributes are not well known. We leave it to the authors of other chapters in this book to identify some of the important areas for such research.

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