DRUG PRICING PRINCIPLES

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Pharmaceutical pricing and utilization are influenced and, in some cases, controlled by a patchwork of government laws and regulations overlaying a diverse web of private insurance plans, self-paying individuals, and charity healthcare services. Biotech companies need to understand how to integrate these factors into their product development plans. Although this chapter focuses on pharmaceutical pricing in the U.S., foreign pricing systems are also discussed.

GENERAL PRINCIPLES

A new therapeutic's price reflects a combination of factors: the price of competing treatment options, the value provided to patients and society, and an assessment of what the market will accept. As a "real" benchmark, the first is easiest to grasp. However, with a breakthrough medicine -- one for a disease with no pre-existing treatment options — appreciating the latter two factors becomes essential. In these cases, a starting benchmark can be the price of an existing medicine for a disease of comparable severity affecting a similarly sized population. For example, the first biologic treatment for advanced rheumatoid arthritis (TNF-alpha inhibiter), entered the market at roughly the same annual treatment cost (about $12,000) as the previously approved first biologic for multiple sclerosis (beta-interferon).

When comparing a new biotech medicine with existing treatments for the purpose of setting a price, first consider its relative clinical effectiveness. This includes not only the efficacy seen in clinical trials, but also the drug's side effects, its interactions with other medicines or foods, dosing intervals, and other characteristics that influence the patient's compliance.

Then consider the drug's economic value for payers. The new drug must either demonstrate cost savings over competing pharmaceuticals or show that it can reduce overall healthcare costs. Pharmaceutical-specific cost savings are direct and can be calculated simply: compared to an older once-a-day medicine, a new medicine dosed once a week yields cost savings even if each individual dose costs three times as much. Overall healthcare savings are difficult to calculate comprehensively as one must quantitate the value of shorter hospitalizations, fewer emergency room visits, eliminating the need for tests to monitor side-effects such as liver or bone marrow toxicity, and other benefits a drug may offer.

Ideally, real-world studies will demonstrate both clinical and economic value. For example, a once-a-week medicine produces better compliance, better control of the patient's disease, reduced ER visits and hospitalizations, and, thus, lower overall healthcare costs. During the clinical development stages of any new pharmaceutical or biotech medicine, a company should include plans for collecting this type of information to demonstrate the value of the new medicine to potential partners and payers. Sometimes, such pharmacoeconomic studies are included after FDA approval either in Phase IV trials or as part of Phase III trials for additional indications.

Pharmacoeconomic data and information about competing treatments enable the biotech company to "ballpark" the launch price of its new medicine. To fine-tune the process, a company may hire a consulting firm that anonymously market-tests pricing scenarios for new treatments. These consultants assemble patient and payer groups to ask test groups questions aimed at gauging market response to a new drug; i.e. "What would you think of a new medicine that did X, Y & Z and that was priced at A per dose, or B per month of treatment?" However, there are no exact formulas for introductory pricing. For example, Pfizer launched Zithromax® at a premium compared to similar antibiotics believing that the drug presented major advantages over its competitors. This was not born out by its initial market performance because payers and prescribers (i.e. insurers and physicians, respectively) did not agree. In response, the manufacturer lowered the price of Zithromax®, leading to increased sales volume.

The ultimate "value" of a medicine in both clinical and economic terms is often not well understood until late development or even post-approval. For example, the cholesterol-lowering power of Lipitor® was not appreciated until its Phase III trials, prior to which its development had almost been terminated because it was going to be the fourth or fifth medicine of its type on the market. Lipitor® eventually became the most frequently prescribed branded prescription drug in the US. Also, the market value of Diflucan®, a potent antifungal, increased significantly post-approval when the number of patients with compromised immune systems grew dramatically due to HIV/AIDS and advanced cancer treatment.

US PRICING AND DISTRIBUTION

Although one often hears references to the "price of a medicine" in the United States, this is really an oversimplification, since for any given medicine there are a wide range of prices. At the high end, retail prices vary

not only by city, but among local pharmacies. At the low end, free medicines are delivered as samples and through patient assistance programs.

GOVERNMENT PROGRAMS

In between full retail and free, prices range widely, influenced by the patient's insurance status and other factors. The lowest prices are generally paid by government programs such as Medicaid and the Veterans' Health Administration (VHA). Under Federal law, state Medicaid programs receive a 15.1% discount off the average manufacturer price (AMP) or the "best price" at which the company sells a medicine to any private sector customer in the United States, whichever is lower. AMP is the proprietary price at which the manufacturer sells the medicine to wholesalers, while Average Wholesale Price, or AWP, is a published "list price" compiled by industry analysts. A frequently cited source for AWPs is the Red Book, published by the Medical Economics Company, the same company that publishes the Physicians' Desk Reference.

Many Medicaid programs use a "Preferred Drug List" to exert pricing pressure on manufacturers. Drugs that aren't discounted below the minimum price may be excluded from the list and thus can only be prescribed with prior authorization from the state Medicaid agency. This imposes a level of administrative burden that can act as a powerful deterrent against physicians prescribing an expensive medication, ultimately hurting sales of the drug.

The VHA receives discounts that are similar to Medicaid's, although the formula is different. In addition, the VHA uses a bidding process for the "closed classes" of its National Formulary system to secure prices below those that are legally required. Securing coverage by the VHA for medicines excluded from its closed classes is even more difficult for physicians than obtaining prior authorization for a drug from Medicaid.

Medicare currently pays only for a limited number of outpatient prescription drugs -- mostly cancer chemotherapy agents, administered as intravenous infusions in a clinic or doctor's office. However, new Federal legislation has created a limited and voluntary Medicare prescription drug benefit for all Medicare enrollees, starting in 2006. In addition, for 2004 and 2005, this law included transitional prescription drug discount cards and, for low-income Medicare beneficiaries, a $600 annual subsidy. The law also changes Medicare's methods of paying for the medicines it already covers. Specifically, before 2004, Medicare reimbursed the doctor or clinic 95% of the Average Wholesale Price (AWP), a system that has been repeatedly criticized in government reports for over-reimbursing doctors and clinics. Starting in 2004, Medicare's reimbursement amounts for some of these medicines decreased to 80-85% of AWP and in the future may be subject to "competitive acquisition program" pricing.

Although the new law precludes the Federal government from dictating prices or formularies, there will likely be pressure in the long run for the government to reduce the prices it pays for prescription medicines, just as it currently does for all healthcare products and services. Expensive biotech medicines may find themselves particularly vulnerable to this pressure, since the government may represent a large part of the U.S. market for these drugs, particularly if they are used primarily by the elderly and if private plans manage to avoid providing Medicare prescription drug coverage to the high risk/high cost patients using these therapies.

Overall, there will likely be considerable uncertainty over the next 5-10 years about how Medicare will price or pay for medicines, particularly new medicines, within the new benefit. Clearly, the government's continued leveraging of its legal and buying powers to minimize spending will have significant pricing implications for pharmaceuticals. The effect on drug sales depends, in part, upon whether lower prices can be offset by increased usage due to expanded insurance coverage for millions of Medicare beneficiaries.

How the changes in Medicare will ultimately affect seniors' prescription drug coverage and use will depend upon Congressional modifications to the new law, the Federal government's implementing regulations, the rate at which seniors enroll in the new benefit (inasmuch as it may initially prove of only limited value to them) and employers dropping or modifying their retiree coverage in response to the new law.

PRIVATE MARKET

In the private insurance market, discounts and rebates vary by company and medicine, with the Medicaid "best price" often creating a floor for markdowns. Contracts frequently provide for variable discounts depending on a drug's market share, rather than strictly on the volume of units purchased. Private insurers can affect a drug's market share by using prior authorization, formularies, and financial incentives. Private payers create financial incentives for patients by placing medicines in "tiers" requiring different co-payments. For example, a plan might require that patients make co-payments of $10 for generics, $20 for "preferred" medicines, and $40 or 50% of the cost for "non-preferred" medicines. Within some plans, if a medication is not "on formulary" it is classified as non-covered or "excluded," requiring patients to pay 100% of its cost. Health plans and insurance companies may also create financial incentives for physicians to use certain medicines. Particularly in staff-model health systems, these incentives can take the form of risk sharing, bonus pools, or other systems where the

physician is partially responsible for the total cost of prescription drugs used by their patients.

One effect of the new Medicare pharmaceutical benefit law is to make Medicare beneficiaries more attractive to private managed care plans. Early trends indicate that managed care plans are boosting their pharmaceutical benefit and lowering premiums for Medicare beneficiaries, with the likely effect of increasing enrollment. This will place a greater percentage of the pharmaceutical market under the restrictions of managed care plans.

By establishing incentives for physicians, prior authorization policies and formularies create de facto pharmaceutical expenditure-control programs. Therefore, when formulating a compelling pricing argument, a biotech company needs to appreciate each customer's internal budgetary operations and incentives for cost control. Those with direct pharmacy spending budgets will probably be more stringent in imposing limits on drug prices and usage. Health systems that take a more integrated approach may view pharmaceutical expenditures within the context of overall healthcare spending and recognize, for example, that spending more on drugs may reduce hospitalization costs. Generally, vertically integrated health systems, such as staff-model HMOs, tend to have more integrated budgetary approaches and are thus more open to cost-saving arguments for expensive biotech products. Yet, a system that includes both physician groups and hospitals must still pay for the fixed cost of maintaining hospitals and may not derive savings from a new drug's ability to prevent hospitalizations.

A private health insurance system may also rely on a third-party company, called a pharmacy benefit manager (PBM), to develop and manage formularies, negotiate discounts, and manage prior authorization processes. (Integrated health systems like HMOs and the VHA may have their own internal PBMs.) In some cases, PBMs have their own internal financial incentives that can affect pharmaceutical usage.

None of these market pressures are likely to remain static. Most programs, whether private or governmental, change their pharmacy systems and contracts every year in response to new approvals of branded and generic medicines and other events. The resulting changes in prices and sales volume for individual medicines can be dramatic.

FOLLOW THE MONEY

Complex behind-the-scenes financial transactions paralleling the distribution chain also affect potential drug revenues. As a general rule, the manufacturer receives 70-75% of the retail price of a medicine, 5% goes to the wholesaler, and 20-25% percent to the pharmacist. These revenue distributions can be influenced by rebates and discounts, as well as by the individual payment policies of different payers. For example, companies pay state Medicaid programs a quarterly rebate: 15.1% of either the AMP or the best price to private purchasers in the US. Additionally, the Federal rebate formula increases this percentage if the company has raised its price by greater than the Consumer Price Index. Because of the retail markup on drugs, pharmacies have traditionally been able to offer discounts (usually 10%) to seniors who lack prescription drug coverage. Some payers try to drive down their retail payments for medicines to near the pharmacist's actual acquisition costs, while compensating pharmacists with a higher dispensing fee. A biotech company should "follow the money" to understand how economic incentives influence the various links of the distribution chain.

MARKET SEGMENTS

Pharmaceutical customers can be broadly divided into two categories: institutional decision-makers and individual prescribers. A biotech company will typically have one or more sales teams assigned to each segment, either directly or through a marketing partner. The decisions made by an institution will vary according to its type – for instance, long-term care facilities will differ from tertiary care hospitals. Sales forces for institutions may be divided between those focusing on managed care plans and those directed towards hospitals and nursing homes. Virtually all institutions have a Pharmaceutical & Therapeutics (P&T) Committee that decides which medicines to stock and may also establish guidelines or rules for the use of certain high-cost treatments. Consequently, a pharmaceutical sales force often includes specialists focused on institutional P&T Committees.

Individual prescribers, technically free to use any FDA approved medicine, typically develop their own personal formulary based upon their training and the formularies of their patients' managed care plans. Sales forces targeting physicians may be divided into groups focusing on specific medical specialties, particularly if the biotech product is used predominantly by only a few types of physicians, e.g. nephrologists, oncologists or rheumatologists. However, even in the case of specialized drugs, it is important to market to internists and general practitioners as they provide needed specialty referrals and educate patients about new treatment options.

OTHER DEVELOPED COUNTRIES

Most other developed nations, including Canada, Germany and England, have more uniform health systems than the U.S. In these countries, the government is essentially the sole purchaser and uses its monopsony power to establish reimbursement amounts for all

medicines. Therefore, companies trying to introduce a new drug in these countries face a "fourth hurdle" after the three initial market entry barriers of discovery, development and approval.

These government-managed markets also involve discounts and rebates, usually tied to either total volume of sales or profits. In some countries, reference pricing systems enable the government to set a price based on either the price of the drug in other countries or the price already established for other treatments, branded and generic, that address the same condition. Furthermore, countries such as France have instituted policies to support local industries, providing government reimbursement for products which in the US would be sold as nutritional supplements.

Pricing differences between countries results in transshipment of medicines across national boundaries. This "parallel trade" practice is legal in the EU, and drug companies try to limit it by restricting supplies to wholesalers in countries where their products are low-priced. Increasingly, drugs are now coming into the U.S. from Canada, Mexico and elsewhere, even though it raises significant safety concerns. Since US laws and regulations only allow individuals to carry a 90-day supply of medication for their own personal use across the border, shipping medicines from outside the country is illegal in almost all cases.

DEVELOPING COUNTRIES

International pricing comparisons and purchasing are likely to put more downward pressure on U.S. prices. However, there is a flip side to globalization; developing countries are creating a growing middle class with the discretionary resources to spend on healthcare. The lifestyle and longevity of these populations also lead to chronic diseases typical of developed nations, including cardiovascular diseases, diabetes, cancer, and Alzheimer's. While this trend presents opportunities for increasing sales volume in international markets, actually generating revenues and profits will require that developing countries enforce intellectual property rights and establish market-oriented healthcare systems.

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Dr. Miller helps early, middle and late stage biomedical companies and other healthcare innovators maximize the value of their research portfolios and businesses. Dr. Miller specializes in creating coherent marketing messages and strategies that enable key audiences such as payers, investors, patient groups and potential Pharma development or marketing partners to fully realize the clinical and economic value of experimental treatments and new medicines. Prior to founding his own consulting firm, Dr. Miller spent over a decade in Washington DC helping organizations such as Pfizer, the U.S. Congress, and the National Institutes of Health speed the development and adoption of medical innovations. For example, Dr. Miller's knowledge and skills have led to accelerated development, insurance coverage and utilization of new treatments for cancer, cardiovascular diseases, erectile dysfunction, infectious diseases and mental illnesses.