The Drug Pricing Challenge

The pharmaceutical industry has been under a lot of public pressure, facing criticism over promotional practices, direct-to-consumer (DTC) advertising, and drug pricing. Particularly in the United States the drug industry reputation has been deteriorating over the last decade, resulting in a public image that seems worse than that of the gun and tobacco industries. It is a stunning observation, particularly for an industry that has, and continues to bring, important health benefits as it offers alleviation and cure for the many devastating diseases, compared with two industries whose products kill people.

Drug pricing in particular, is a topic that has captured the attention of many people, including pharmaceutical industry professionals, payers, healthcare providers, politicians and patients. The topic causes emotion and difference in views as people’s lives and general well-being are dependent on access to the drugs that they need. In this chapter we will discuss some fundamental aspects of drug market access and pricing and the reasons why drug pricing is so different from other industries. Many of the observations in this chapter provide a basis for understanding the host of issues covered in the rest of this book.

Drug Pricing

Global drug pricing is highly complicated in comparison with pricing for most other products. It is subject to a lot of political debate, government intervention and public dissatisfaction.

Many governments have a very strict approval process in place for pricing and/or reimbursement decision making for drugs. For reasons explained later, governments in many countries feel the need to control drug pricing. It is obviously a nearly impossible task to design effective, but reasonable, pricing and reimbursement controls that take individual patient situations into
consideration. As a result, many of these systems have become very complex and cause many unintended “side effects.”

In many cases in the past, governments have also mandated price reductions across all drugs, usually to address drug budget shortfalls. This is an interesting aspect of the drug monopsony privilege of government system buyers. Imagine that you go to your oil or gas supplier at the end of the year and demand a refund for going over your household heating budget. Your supplier would be in doubt whether you were pulling a prank on him or you were an escaped patient from a mental institution. Only governments can get away with this and have done so and will continue to do so frequently in many countries!

Over the last few decades, we have seen waves of political and public dissent over drug pricing. Price differences between countries have frequently been the basis for complaints and initiatives to control. In many countries, governments have instituted international price referencing laws on that basis. This will be further discussed later in this chapter. In the United States, price differences with Canada have particularly been subject to media coverage in the days leading up to Medicare reform and the institution of Medicare Part D. Bus trips to Canada for the elderly to purchase cheaper drugs were effectively advertised to gather support for drug coverage for senior citizens and to complain about high prices of drugs in comparison to Canada.

International price differences have probably been one of the most contentious of the issues that the industry has faced. It is not surprising that global price differences of drugs are a contentious issue. It can be hard to evaluate what should be a reasonable price for a product. For a gallon of milk it may be relatively easy as it is considered a commodity with a sufficient number of similar options in the store. For some branded products it is very hard. What is a reasonable price for a Porsche, a high-end brand perfume, or a ticket to a World Cup soccer game? Sitting on an airplane, we would be shocked to find out what the prices are that each passenger on the plane has paid for his or her ticket. It is hard to put a reasonable value on each product feature or benefit. How much is the brand image of a Porsche worth, the “hope” that is bought with the exclusive perfume or the exclusivity of attending a unique sports event. This is hard to say and it will be different from individual to individual. We have a hard time to identify a correct price for a product, but we are all upset when we find out that someone else paid substantially less. Why would we pay more than someone else? This is the question that is posed for international pharmaceutical pricing and the industry has been struggling in
providing an acceptable answer. In this chapter, I will make my own attempt to explain the complexities of global drug pricing.

**Market Access**

Market access is the new buzzword in the pharmaceutical industry. Companies re-focus, restructure and add staff to their organizations to better address today’s market access needs. More disciplines and people get involved in an already complex multidisciplinary process to further optimize development and commercial strategies aimed at preparing fewer new chemical entities for an increasingly demanding payer environment. However, there is a lot of confusion over the term “market access.”

As with every new term, individuals from different disciplines translate a meaning, sometimes twisting it in the context of their own functional specialty, particularly when it seems to be the new hot trend. This reminds me of an analogy from the aircraft industry, which uses the functional perspectives and priorities discussed above, but applied in an aircraft design setting. The wing design group sees the aircraft as a wing with a small fuselage attached, the service group emphasizes all the access panels to reach their service items, whereas the armament group merely sees the plane as an opportunity to hang weapons.

In an attempt to eliminate some of the confusion, this chapter starts with a definition of market access as it is used in this book. Each reader can be the judge which one of the caricatures fits the description and perhaps distorted view of the author.

Pricing, reimbursement and access or market access are terms that are used in any set of combinations to describe the activities related to setting a drug price across markets that addresses third-party reimbursement or cash pay affordability in the context of each payer system and segment. The term pricing is usually well understood to be the activity of evaluating willingness-to-pay among key customers, resulting in an assessment of the optimal price.

For most consumer goods, pricing involves the assessment of customer price elasticity of demand. Not considering middlemen for now, the two key players are the seller and the buyer and the micro-economics laws of supply and demand drive optimal price. In the drug market, the purchasing process
is much more complicated due to the involvement of third-party payers such as insurance companies. Depending on country and healthcare system, the payer acts as a gatekeeper in order to control drug and overall medical cost of treatment in some way or form. In some cases, for example in the United States, payers decide on a co-payment (fixed dollar amount of say $25) or co-insurance (fixed percentage of cost of say 20 percent). In markets such as China and Mexico, there is very limited insurance coverage for prescription drugs. Patients frequently pay for drugs cash out-of-pocket as they can afford it. Issues related to full or partial reimbursement by a payer, or patient affordability, are usually all captured under the term “market access.”

A broader set of activities can be considered part of market access. For instance, it is important for a drug to be included in clinical treatment guidelines as they are frequently agreed upon and published, for example, in the US for hypertension, by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Some argue that gaining marketing authorization by the FDA is part of market access. I would argue that this is a bit of a stretch.

The term “access” is also used to address the ability to reach patients in developing countries or even the ability for the sales force to speak to physicians. In this book this is not considered part of the market access definition. Obtaining regulatory market authorization by the FDA or a similar foreign body is not considered market access either. Healthcare technology assessments and health economics evaluations, frequently used in reimbursement decision making, is part of market access.

In this book, the following definition will be used for market access:

Market access is the discipline that addresses any financially based consideration or hurdle to drug prescribing and use, whether imposed by public or private third-party payers, or experienced as a consequence of patient affordability.

Regulatory and Other Drug Approval Systems

In every healthcare system, drug companies must obtain regulatory approval or market authorization before they can promote prescription drugs.
Regulatory approval is contingent on demonstrating drug efficacy and safety for the proposed indications and at the proposed dosing regimen to the Food and Drug Administration (FDA) in the US, the European Medicines Agency (EMA) in Europe and to the appropriate national authorities in other countries. Balancing speed of approval with safety concerns has been a contentious issue over the years, and has once more become a hot issue over the market withdrawal of Vioxx and emerging side effect concerns for Avandia a number of years ago. Drugs go through a robust efficacy and safety evaluation over years of research preceding the approval, however unfortunately it cannot completely guarantee that no additional side effects and rare toxicities present itself after treatment of millions of patients. For most drugs, these side effects are unfortunate, but they do not change the risk-benefit trade-off of using the treatment for the underlying patient condition. However, in a number of cases, serious health concerns have emerged a number of years after launch, resulting in market withdrawal of the drug or the inclusion of “black box” warnings on the product label.

A key factor in our legal society is whether anybody can be blamed for a potentially debilitating effect of an unknown and previously unreported side-effect. Clearly, drug companies are and should be held to the highest ethical standards with respect to transparency in reporting clinical outcomes for all company sponsored trials, as well as any other third-party results that they become aware of. Drug companies only very rarely violate this principle, but when they do, they certainly deserve to be legally pursued to the fullest extent of the law. Beside these legitimate cases, there are a lot of “ambulance chasing” frivolous class actions initiated, which will eventually only end up benefiting lawyers, thus further increasing the cost of healthcare and limiting opportunities for much needed new treatments to reach patients. It is actually puzzling that the responsible approval agencies, such as the FDA and the EMA, who write the approval requirements and implement them, don’t seem to have any accountability for their decisions.

REGULATORY APPROVAL – WHAT’S NEXT?

Obtaining regulatory approval or market authorization for a new chemical entity is an important milestone in gaining the entry ticket for launch and promotional activities in most markets. In the United States, a company can start marketing and selling a new drug within its approved labeling immediately after regulatory approval by the FDA.
In most healthcare systems, effective market entry is not possible without pricing and/or reimbursement approval. Pricing and reimbursement approval is handled after regulatory approval. Process and requirements are very different between the various payer systems. In Europe, contrary to the regulatory process, pricing and reimbursement is not approved by the EMA on a European level, as the individual EU member countries have insisted on maintaining national control over healthcare expenditures. Healthcare funding and the pricing and reimbursement approval process for drugs are very different between countries such as France, Germany, Italy and the UK. Figure 1.1 is giving an illustrative listing of agencies and terms that are encountered in the payer space in contrast to the regulatory environment.

Differentiation between regulatory and pricing and reimbursement approvals is important in the context of the information and evidence needs in each of the two processes. Demonstrated efficacy and safety are crucial conditions for registration. For market access and pricing they are also important, but there are important commercial and budgetary objectives that play a role in decision making. Questions that may rise during these discussions may be:

Figure 1.1   Key global pricing and market access players
• What is the anticipated use of a new drug, what is the impact on the healthcare budget and, in the context of budget limitations, is this deemed an appropriate use of funds?

• What is a reasonable price of the drug, in the context of alternatives already available and the innovation demonstrated?

• What share of the cost or up to what amount should drug cost be reimbursed?

• Should any limitations be imposed on drug prescribing?

• What are the potential consequences if a drug at agreed-upon prices, exceeds its anticipated (or agreed upon) sales volume or average daily dose?

Depending on the payer system, a mix of the above questions will have to be addressed during the pricing and reimbursement approval process in each country.

Information needs for pricing and reimbursement negotiations have important implications for the drug development process. Clinical end points required to demonstrate drug efficacy and safety to the FDA or equivalent non-US agency, generally do not meet evidence requirements for pricing and reimbursement discussions. Placebo-controlled trials and non-inferiority claims, frequently sufficient for registration approval, will generally not impress public and private payers. This will be further discussed in Chapter 7: Pricing and Drug Development.

**Market Access and Pricing Controls – Why?**

What is different in the pharmaceutical industry that entices many governments to build controls related to price, reimbursement and drug company profitability? Market access and pricing controls are not very common in any product category other than drugs and are usually only introduced where national authorities are concerned over the lack of a natural market mechanism, insufficient competition and potential for price gouging by the industry. Examples of price controls can be found in the utilities industry, where governments have either put specific price controls in place or have
brought the service completely under direct government management. Fear of bureaucracy and inefficiencies due to these controls have led to a search for revision of market mechanisms, for example in the US in the electrical power industry, where private enterprises have been encouraged to build supply sources to the public network and bid for supply prices, thus offering consumers choice. It is an interesting experiment, although it is questionable how much it will enable a sustainable competitive market structure, as the infrastructure is shared and consequently the consumer cannot be offered any meaningful service differentiation beside price. One can argue that if market mechanisms can be restored in the utilities with all its infrastructure limitations, it certainly provides a basis for trying harder in the drug industry, where controls have been both complicated and ineffective with respect to cost control.

In a competitive market, buyers and sellers are balancing supply and demand at a “market price.” Consumer reactions to price can be characterized through price elasticity relationships. In a market with relatively high returns on investment, additional sellers are attracted, provided that there are no insurmountable regulatory hurdles or other barriers to entry. Thus, it is reasonable to expect that industries that make excessive profits will, over time, face more competition, resulting in squeezing of margins and bringing the industry in line with a “normal” return on capital.

Most international governments have in some form exerted control over market access and pricing of drugs. As a result, when trying to gain favorable market access and pricing decisions, we have to be prepared to deal with a myriad of healthcare agencies and national and regional regulations.

Why do governments feel the need to interfere in drug pricing? Why is drug pricing so contentious and subject to public scrutiny? What is the cause of the poor reputation of the industry despite the life-saving character of many of its products?

To better understand the perceived need by government to interfere in drug pricing, we should consider the main factors that cause this complexity:

- Drugs are subject to an unusual purchase decision model as payer, prescriber and patient engage in an increasingly complex tripartite product selection process.
• *Industry cost structure* is different, as high and risky upfront investments in research and development are offset by relatively high margins during commercialization.

• Heavy reliance on *patent protection* to allow for a pay-back period of development cost.

• Governments partly or entirely act as *monopsony* payers in many countries with socialized healthcare systems, such as in Europe, Japan, Canada and Australia.

• Social complexity related to what many consider to be the *right to affordable healthcare*.

These pharmaceutical industry characteristics, particularly in conjunction, create a very complicated environment with a lot of temptation for government involvement as natural market mechanisms are deemed to be impaired. Unfortunately, government involvement on a national basis only creates further problems, as most of the issues are global in nature. Frequently, new rules are introduced to tackle unwanted side effects and market reactions from existing rules, thus causing an increasingly complex web of rules and regulations. For example, therapeutic referencing systems in The Netherlands were recognized to cause substantial increases in prices of generics. By creating fixed reimbursement limits, generics manufacturers were incentivized to increase price up to the reimbursement limit rather than lower them under competitive pressures. Any price competition that did take place did not benefit the healthcare system, but flowed to the pockets of entrepreneurial pharmacists. Unintentionally, the cost containment system went completely contrary to the universally adopted European intent and policy of using savings through use of inexpensive generics to fund for innovative new therapies, also referred to as the “Headroom for Innovation” principle.

Changes in the environment naturally impact the drug industry’s strategies, as they try to optimally adjust to the new customer requirements. Unfortunately, it may take 10 years before a change in strategy sees its impact in market performance. Rapid and frequent changes in healthcare systems are hampering the ability of drug companies to plan for success.
PURCHASE DECISION MODEL

For most consumer goods, the decision maker, payer, and user are the same, thus providing the basis for a natural balance between product benefits and willingness to pay. Micro-economic theory explains how in a free market economy, a natural balance will occur between supply and demand at a market price.

A prescription drug purchase is very unusual, as it involves the writing of a prescription by a physician and, frequently, funding by a third party. Most characteristically different for the drug selection process is that payer, decision maker, and consumer are three different entities. Since each of the players has different perspectives, responsibilities, and preferences, the purchasing process is complicated in nature. Payers are likely to argue that patients, in absence of a substantial co-pay or co-insurance, are not sensitive to drug cost. Consequently, they will favor expensive therapies more than would be the case in a natural market system where payer and consumer are the same.

Payers, whether a US Managed Care organization or the Italian government, tend to be less sensitive to patient benefits than the patients themselves, particularly where convenience and non-life-threatening side effects are concerned. Naturally, payers judge drug performance on a statistical basis where individual patients have a more emotional relationship to their health, which leads to a higher aversion for risk. Governments and insurance companies are frequently faced with budget trade-offs to apply limited resources to competing causes. Health economic cost-effectiveness calculations can be used to make trade-offs in terms of cost per life saved and other similar measures. Although rational, these considerations run into difficult ethical discussions, as it is hard to value a life. This is further discussed in Chapter 5. Patients will obviously insist on any life-saving treatment, regardless of cost.

Co-pays and co-insurance rates are a means of raising patient involvement with drug funding and creating at least some price elasticity towards a natural market mechanism. In the United States, insurance companies have drastically increased co-pays and deductibles for drugs. Due to the fragmented nature of the market and lack of transparency on behalf of physicians and patients, these mechanisms have probably been relatively ineffective. Fixed co-pays, rather than a percentage co-insurance, also do little towards achieving a higher awareness of drug cost with the patient. Co-insurance rates for high-cost biologics have a great impact on patient cost, but may in many cases only
frustrate a patient when he or she has no other choice. In these cases it creates an ethical dilemma for the physician, who has taken an oath and has some legal liabilities to provide the best possible care for a patient, but may be tempted to choose a less favorable choice for the patient on the basis of patient co-pay or co-insurance.

The drug purchasing decision is an interesting situation once described to me as an unusual “dinner for three.” Imagine three people, Bob, Ben and Betty going to a restaurant, where Bob makes a meal choice from the menu, Betty is consuming the meal and Ben is paying the bill. Sounds ridiculous? In drug terms, Doctor Bob prescribes the drug, patient Betty takes the drug and insurance agent Ben pays the bill. Common practice! Is it surprising that Ben has issues? He pays for what he perhaps perceives to be extravagant dishes that he can only hope that Betty will appreciate and benefit from. For Ben, the cheapest meal would certainly have done the job. Bob may be sensitive to Ben’s pleas to order something less expensive, but he has his own responsibility to help Betty and wants to make sure that she is happy with the treatment. The absurdity of the situation illustrates the issue with respect to the role of the payer/insurance in drug prescribing (see Figure 1.2). Preferences between each of the three with respect to quality and cost of the ordered meal can be seen to be very different from each of their perspectives. It illustrates the importance of examining each healthcare system with respect to its ability to provide reasonable healthcare coverage to its citizens, while providing effective incentives to be cost conscious and avoid waste. Decisions of healthcare funding are both economically and ethically complex as they force a value to be placed on improvements of human life.

This “dinner for three” phenomenon is the cause of what many government healthcare agencies refer to as a lack of market mechanism. To address this apparent lack of market mechanism in the drug purchase model, they have felt it necessary to take action through the institution of price and/or reimbursement controls. These systems have grown into very complex sets of measures, each aimed at correcting “imperfections” in another control. Payer Ben has taken charge of the menu decisions, which is creating a new set of issues, particularly when the payer is a monospony, a single payer with control over all government drug expenses. It is not surprising that national healthcare systems with monospony purchasing power have chosen to push for control of drug prices as a mechanism to correct market imperfections. A better model would probably have been the institution of patient co-insurance (percentage co-pay) rates, as they restore a natural market mechanism, provided that open
The cost of development of a new drug was estimated to be in excess of $1.3 billion in 2006 (DiMasi, 2007). Given the past steep growth curve in the cost of drug development, today's average cost of drug development is probably much higher than $1.3 billion dollars. See Chapter 7 for more discussion on drug development cost. Payback of drug investments is very uncertain and only starts after successful completion of a 10- to 15-year development program.
The cost of drug development is likely to continue to rise, as the FDA and drug companies are increasingly under scrutiny for having approved and marketed drugs which only show unacceptable side effects after years of patient use. The market withdrawal of Vioxx has significantly added to this concern and pressures on the FDA to intensify safety drug reviews.

Due to the high cost of development and small probability of success for each compound, drug companies have worked extensively on work processes for early identification of promising compounds and an early failure of problematic ones. Drug revenue forecasts need to be substantial to justify a billion-dollar investment and companies that do hit the “pharmaceutical jackpot” need to employ significant marketing muscle to ensure their share of voice in a very competitive fragmented market.

Whether even a successfully approved drug delivers payback and potentially profit to the innovating company depends on the ability to claim a reasonable price and sufficient sales volume over its limited patent life.

Due to the high cost of drug development, the industry has a cost structure that is much different from most other industries. Let’s look closely at the cost structure shown in Figure 1.3. The illustration shows a comparison in cost structure between a drug and a “widget,” an average consumer product. The numbers are fictitious and not representative of any specific drug company and are just intended to illustrate differences with typical consumer goods.

The drug company cost structure has some remarkable characteristics:

- Very high upfront R&D and other fixed cost. Global R&D and commercialization cost is essentially sunk, independent of the actual number of countries that launch the drug;

- Relatively low marginal cost of goods (manufacturing materials and labor) and local marginal marketing cost;

- A high contribution margin to help offset the high upfront cost of R&D and other fixed cost of development and commercialization.

In this illustrative example, the contribution margin towards profitability is much higher for the drug than for the widget, as the marginal cost is 25 percent for the drug versus 70 percent for the widget. This implies that any price above
25 percent of total allocated cost will contribute to company payback of its upfront investments.

When a drug company is making price concessions in one or more countries, it will help to offset its investments. However it does need higher price levels for the majority of its sales to ensure overall profitability of the business and sustainability of the firm.

What happens if a customer (or a monopsony government) insists that it is only willing to pay a relatively low price for a drug? When the price is at a sufficient level above the marginal cost of manufacturing and marketing the drug, one of the market players is likely to take the deal, knowing that if it doesn’t, it may put itself at a competitive disadvantage versus companies that do accept the deal. This is the reason why the United States is indeed subsidizing monopsony governments. Under competitive pressure, companies accept the risk of downward price cascading to other countries and potential public criticism in the United States.

From the government’s perspective it is tempting to demand a company to make its innovation available at a very modest price level that everybody can afford. But what does that mean for the future? Will we be able to continue to
convince Biotech and traditional Pharma companies to develop new drugs? Or do we think that we do not need next generation drugs to treat HIV/AIDS, cancer and other diseases?

For our widget example, the situation is fundamentally different. At the much higher cost of goods, only an irrational company would sell a widget at a substantial discount, as it would give a negative contribution to corporate profits.

PATENT PROTECTION

The pharmaceutical industry is heavily dependent on patents to pay for its innovation and provide a return on investment for its shareholders. This is how pharmaceutical products can command relatively high prices. Without patent protection, companies would not be willing or able to invest more than $1.3 billion to bring a product to market. Generic manufacturers would be able to make copy products available at much lower prices, since they don’t have to engage in a 10-year risky development program where perhaps only one in a 1,000 products see commercial daylight. The theoretical patent life of a molecule is 20 years in most countries. However, the real effective patent life from the moment of first sale to patent expiration is usually not much more than 10 years, as evidence needs of efficacy and safety take a large portion of its protected life cycle away. At least 10 years market exclusivity after launch is usually guaranteed in the US and Europe through patent and related exclusivity laws, such as the Hatch-Waxman Act in the US. Setting a reasonable, but adequate, price for a new product is therefore crucial for the survival of a pharmaceutical company. If the price is set too low, the return on investment is not sufficient to fund continuing business; if the price is set too high, customers may decide not to use the new product, leading to equal financial problems for the company.

GOVERNMENT MONOPSONY

In most countries, the government is responsible for the funding of healthcare. Organizations such as the National Health Service in the UK are directly funded by the government. In Germany, sick funds play an intermediary role, but are also funded by federal taxes. Employer-sponsored insurance programs, such as the Mutuelles in France, fund part of the drug bill, but the government is the main payer.
Facing budget pressures, governments have historically been tempted to interfere in the drug markets with pricing and reimbursement control measures by using their monopsony buying power. Government interference on drug market access and pricing has already been discussed in detail earlier in this chapter. However there are many other ways of interference beyond these systems. In many instances, governments have dictated drug price reductions to resolve budget problems. Price reductions were enforced in Germany as part of their healthcare reform and in the UK as part of a PPRS renewal. It is a bit ironic that the industry has to accept a 7 percent price cut in order to continue the profit control scheme. Similar price cuts have occurred, sometimes multiple times, in a list of countries that is too long for this book. The latest round of steep price cuts in Greece and other EU markets, following recession-related economic problems in 2010, illustrate the magnitude of this problem.

Monopsony power can result in significant market distortions in the international arena. It is much debated that the US is subsidizing healthcare in other markets with lower prices. The cause of this is at least partly found in monopsony power.

RIGHT TO AFFORDABLE HEALTHCARE

The right to affordable healthcare is a difficult and sensitive topic. Should everybody have equal access to the best healthcare, independent of personal affordability? Idealistically that sounds right to many of us. Within many healthcare systems in individual countries this also may be the case to a large extent. Many countries have universal healthcare coverage that is available and affordable for everyone. Prior to President Obama’s Affordable Care Act (ACA), more than 15 percent of the United States population was uninsured. Under US law, hospitals are obliged to provide emergency care to any patient, independent of insurance coverage or personal financial conditions. Lack of insurance and unwillingness or inability to pay for preventative or early treatments left many inner city emergency care units overcrowded. Unfortunately, lack of insurance coverage thus resulted in much more expensive care in the emergency room, as important treatments were postponed.

What if we look at this internationally? This is obviously much harder, as solidarity tends to not reach as far across borders as it does within the borders of a country. Who would pay for a heart transplant for a patient in Nigeria? The Nigerian healthcare system is likely to have different priorities, as it can save more lives with other, less expensive interventions. Lack of hospitals, training and critical supplies cause the quality of care to be at a lower standard than
it would be, for example, in the United States or Italy and this is generally accepted as part of reality.

The World Health Organization (WHO) has for many years now, maintained a list of “essential drugs.” These drugs, which are mostly generically available compounds, should in WHO’s vision be available to anyone in need as part of its philosophy that healthcare should be accessible to all, independent of income. Challenges arose, when as a consequence of the world crisis on HIV/AIDS, several patented drugs became crucial for developing countries healthcare needs. Given the price of these drugs and the inability to fund for large amounts of drugs that were required to address the emerging needs, huge issues emerged related to pricing for these drugs. Drug companies ultimately responded to pressures to engage in “differential pricing” practices and made the drugs available to the least developed countries at essentially cost of manufacturing, and dramatically reduced cost to lower- and middle-income countries.

It is notable that drug companies are subject to so much criticism and pressure over international pricing. Emerging and middle-income markets use threats of compulsory licensing, that is TRIPS (Trade-Related Aspects of Intellectual Property Rights) agreement based emergency-driven overruling of a patent right, to obtain drugs at a fraction of its cost. It creates complicated issues with respect to international trade and price referencing that are further discussed in Chapter 2.

**A COMPARISON WITH OTHER INDUSTRIES**

When considering the differentiating elements, described in the preceding sections, it may have become apparent that the drug industry is different from other consumer product industries. This is probably the main reason why drug pricing is a unique discipline that is hard to compare with price optimization for other products.

Which other industry has the same mix of complexities as the drug industry. None come to mind. The utilities industries have some similarities in terms of investments and cost structures, but are very different in every other aspect. The software and DVD movie businesses have similar intellectual property and cost structure aspects. DVD markets are regionally divided through regional zones in DVD players and DVDs, an interesting way of segmenting markets and allowing for price differentiation. This industry does not have the social aspects of life-or-death needs or the government monopsony aspects.
One wonders if the regionalization of DVDs would have been challenged if it was a high government expense item in European countries.

**Global Pricing Issues**

Price differences between markets can be substantial for any product, not just pharmaceuticals. For consumer goods, such as cars, DVDs and books, we sometimes find substantial price differences. For some goods, such as for example milk, price differences can be justified by local cost differences. Also most services are priced at local labor rates and as such, are likely to be much lower in a village in Argentina, than they are in, for example, Manhattan. For consumer goods that can be easily transported, such as batteries, computer software and memory chips, international price differences can result in legal or gray market importation. For products with natural or legal trade hurdles, such as water with transportation cost, price differences are less of a commercial threat.

*The Economist* publishes an annual Mac Index overview, which compares prices of a McDonald’s Big Mac in a large number of countries (*Economist*, 2013). Interestingly, *The Economist* draws parallels between the price differences of the Big Mac and the over- or undervaluation of currencies. In most non-American minds, the use of a hamburger as an economic standard may be a bit of a stretch, however the index does demonstrate the wide variety in retail prices for a product which is identical in every market. With the increasing number of open borders, resulting from trade agreements, price differences for many goods may disappear as a consequence of arbitrage.

Figure 1.4 shows the distribution of Big Mac prices across countries. The highest price in Norway ($7.51) is five times higher than the price in India ($1.50). The US and European markets are at the high price range; lower-income countries have prices that are at the low end of the range. Differences in mainly local cost of production seem to allow McDonald’s to address differences in willingness-to-pay and affordability between countries. If it was possible to practically ship a Big Mac from India to Norway without losing its appeal, price differences for the Big Mac would probably be smaller than they are today.

Figure 1.5 shows a similar price comparison for the iPad Retina (16Gb Wi-Fi model), as reported by CommSec (2013) in their CommSec iPad index. Interestingly, the US price is almost the lowest in the selection of countries.
With the exception of Argentina and Brazil, most prices are actually within a relatively narrow band between $500 and $700. The most important observation to make is that Apple did not feel a need to provide its iPad at a lower price to the less affluent populations in developing countries. The chosen, higher than US prices seem to be local profit optimizing prices. Obviously, Apple need not be too concerned about political consequences of high-priced iPads in developing countries; an iPad may not be high on the list of needs of a relatively poor population. Figure 1.6 shows a comparison of the Big Mac and iPad prices, indexed to the US price.
Beside freshness-related considerations, such as with a Big Mac, there are other barriers to trade which enable the sustainability of international price differences. The movie industry has successfully introduced global zones for DVDs making Chinese or Spanish retail DVDs practically unusable in the United States and vice versa. It is hard to think of any reason besides market segmentation that justifies this industry-wide agreement. The zones clearly allow the DVD manufacturers to charge vastly different prices between countries.

Global price differences for drugs have increasingly become an issue for the pharmaceutical industry. Ethical issues prevent drug companies from adopting global pricing strategies similar to the one adopted by Apple for iPad. It would not be right to sell an anti-cancer drug or HIV/AIDS drug at double the US price in Malaysia. Financially, Apple may be able to sell its iPads at US prices in developing countries. However, the cost structure of an iPad will prevent Apple from adopting the relatively very low prices in developing countries that have been given for HIV/AIDS drugs.

The HIV/AIDS pandemic has globally raised concern about drug pricing issues. Affordability of new and innovative drugs for diseases such as AIDS has motivated many developing countries and new economies such as Brazil and South Africa to introduce generics under compulsory licensing provisions.
Compulsory licensing threats have further complicated an already complex global pricing and trade environment. This topic is discussed more extensively in Chapter 13.

Government payers have used international price differences to negotiate better terms with companies by introducing price referencing laws. Starting in Europe, but now expanding to other countries, companies have also been encouraged to engage in international trade or “parallel trade” for pharmaceuticals. Also on the political arena, international price differences have caused many issues around the world. Since 1994, every few years and again recently, the United States has seen a flurry of political attention concerning global price differences for drugs, resulting, increasingly, in support for initiatives with respect to importation legislation for drugs.

INTERNATIONAL PRICE REFERENCING

Starting in Europe about 20 or so years ago, countries have increasingly introduced international price referencing laws to take advantage of lower prices in other countries. These mechanisms put a cap on in-market prices (ex-factory or retail) on the basis of the price in the country of origin, the average price of a list of countries or in some cases even the lowest price of a list of countries. This trend is still expanding rapidly with, for example, now Brazil and Mexico adopting such measures.

Figure 1.7 shows that considering just two major countries, an already complex picture develops. As an example, in Canada a price for a new drug cannot exceed the median level of prices for the same compound in the United States, France, Germany, Italy, Sweden, Switzerland and the United Kingdom. Japan’s “Foreign Price Adjustment” rule can adjust the approved price either upward or downward through a relatively complex formula based on the price difference compared with the average of the US, the UK, France and Germany.

Many countries have international reference pricing laws in place. Figure 1.8 gives a more complete picture of all global price referencing laws in existence. The black lines represent countries that reference one or more other countries as part of their price approval process. Figure 1.8 does not, however, take into consideration that many pricing authorities engage in informal price comparisons, thus further adding to the mix. For example, national payers in Europe have many informal contacts, which give them a good lay of the land with respect to actual net prices in other countries.
Figure 1.7  International price referencing in some key countries

Figure 1.8  Global price referencing network
It may become clear from Figure 1.8, that local pricing decisions have regional and global implications. Forced price reductions or concessions in negotiations for launch can have far-reaching global implications and should be carefully assessed before implementation.

**PARALLEL TRADE/IMPORTATION**

In Europe, the Middle-East and parts of Asia, trading companies are actively purchasing pharmaceuticals in low-priced countries and shipping and selling them in higher-priced countries. When a prescription drug, for example Januvia, is €30 per pack cheaper in Greece, than it is in the UK, easy arbitrage opportunities are created for wholesalers. These wholesalers, parallel trading companies, file for a relatively simple to obtain approval for parallel import of a branded drug. In the European Union, parallel trading companies are authorized by law to re-package in a local language pack and print a local language package insert. Even small price differences between countries, frequently caused by currency exchange fluctuations over time or government forced price reductions, are sufficient to create a very profitable arbitrage opportunity for parallel traders. In the EU, pharmacists can substitute branded products with their parallel trade equivalent. In some countries, such as The Netherlands, pharmacists are actually incentivized to make the substitution by allowing them to pocket a substantial share of savings achieved.

Parallel trade is not unique to the pharmaceutical industry. In any other industry, a company can price its products across countries, best meeting local market conditions, without any interference by the government. Also, a company can adjust prices upward or downward to reflect cost changes or market conditions. When for example Toyota decides to sell its Corolla model at a higher price in Belgium than in Italy, an arbitrage opportunity is created for anybody, either for personal use or for financial gain, to purchase a vehicle in Italy and sell it in Belgium. Since the adoption of the Euro there is very little risk associated with this form of parallel trade. It is also simple to do as it essentially only requires financing and transportation. Now consider the same car situation with a price that is much higher in the UK than in Belgium, Italy and perhaps some other EU markets. The UK has not joined other EU markets in the common Euro currency. Currency exchange rate fluctuations between the British Pound and the Euro can impact relative price levels between the countries, which can further increase any existing price differences to a level where it becomes an attractive opportunity for a parallel trader. When deemed unacceptable to Toyota, they have the ability to adjust their prices in either of
the countries to eliminate price differences. In this case, Toyota may effectively be protected from trade due to the fact that British cars drive on the left side of the road, thus requiring a driver’s seat on the right side.

Let’s return to our pharmaceutical case. Even when a drug company is able to negotiate exactly the same price in all EU countries, currency changes between, say the British Pound and the Euro can cause substantial price differences between the UK and other EU markets. Since a drug company cannot increase prices in virtually every EU market, its only option is to reduce price in the UK or accept parallel trade. If subsequently the Swedish government mandates a price reduction or the Swedish Krone value slides relative to the Euro, a next round of price cascading is introduced.

Not only is parallel trade legal in Europe, it is actually illegal to engage in any preventive activities. As part of the efforts to eliminate trade barriers between EU markets, strict rules have been put into place limiting differentiation between countries on brand name, product form and other trade limiting features. Some “reasonable” supply restrictions based on local needs have been allowed. Through this mechanism, companies have been allowed to limit supply to lower-price countries to avoid shipping to other countries. Since it is hard to control whether drugs go to patients or to foreign warehouses, this mechanism of control has serious issues, as patients may be withheld access to much needed drugs when a wholesaler decides that he can make more money in trading it to a higher-priced country. In June 2009 an Opinion was issued that a “dual pricing” practice, charging wholesalers in a country more for an export drug than for domestically used drugs, is an infringement of the EC Treaty. This ruling is just another step in a long and complicated ongoing legal battle regarding parallel trade in the European Union.

How well allowing parallel trade has served society is debatable. Allowing parallel trade in the EU has been the result of a highly dogmatic implementation of the EU free trade principle. The combination of government price intervention and free trade simply doesn’t make any sense from any reasonable perspective. European bureaucracy has no doubt withheld useful drugs from patients in some lower-priced countries, as companies have been forced into all-or-nothing decisions on government set prices with relatively unrestricted arbitrage opportunities for parallel trade companies. It has also resulted in a proportion of the proceeds of patented pharmaceuticals going to parallel trade companies that essentially add no value, rather than funding new research for innovative drug treatments. It has had some impact on the
cost of drugs, but the question is at what price. Parallel trade causes the market to deal with imbalances between the separate EU markets, thus stimulating the creation of a single European market. However there are very few “markets” for prescription drugs in Europe as government have taken control of price either directly or indirectly.

The European Union has largely been unsympathetic to the industry’s complaints and has been very dogmatic in upholding its free trade principles. The fact that pricing freedom is blatantly absent in most European markets has not softened their position.

Discussions and legislative initiatives in the United States to allow wholesale importation of prescription drugs can have a substantial impact on the global drug market. Price differences between the US and Canada, caused by decades of Canadian government interference in drug marketing and compulsory licensing, favoring the local generics industry, are substantial for many drugs. A typical Canadian price may be 60 percent of the US price, although the difference is actually smaller when considering Medicaid and Federal Supply Schedule (FSS) prices. In some cases the differences are bigger. Many attribute the large price differences to the greedy behavior of pharmaceutical companies. In reality, prices in Canada are artificially low due to the lasting impact of a period of compulsory licensing in Canada, where Canada in effect enabled a now strong generics industry through the drug industry-wide government-forced licensing of their technology to these local generics companies. Upon the abolition of this practice, the industry was limited in its pricing through the establishment of the PMPRB agency, which ensured that prices could not easily exceed the prevailing generic price levels.

Over the last 10 to 15 years there have been many US bills to authorize wholesale importation of drugs into the US from Canada and other countries. In a number of bills, the number of authorized source countries is fairly large as it includes all EU countries, Switzerland, Canada, Australia, New Zealand and Japan. Safety concerns over imported drugs have withheld the implementation of previously approved legislation, but as the political pressure is high, this seems only a matter of time. Since October 16, 2013, Maine residents can directly buy imported prescription drugs from Canada, the United Kingdom, Australia or New Zealand in local retail pharmacies. Court battles are likely to endure for a while before the legality of this measure is clarified. Prior to this new broader (re-)importation initiative, Maine municipalities and companies were already
operating importation initiatives from Canada through organizations such as CanaRx.

The US name “re-importation” suggests that it is a US-manufactured drug that is imported back into the US after export to international markets. In some cases this may be true, but since the drug is sold in these international markets, it will have to comply with their requirements on for example excipients and dyes, not necessarily the US ones. Where the rules are different, this will certainly be importation rather than re-importation.

In this Chapter ...

It has been shown how drug pricing is uniquely different from pricing in other industries due to a number of reasons, including the “dinner for three” phenomenon and its competitive market implications. We learned that global drug pricing is highly complex as government controls and international trade aspects make for difficult trade-offs. The industry cost structure and humanistic considerations related to access to healthcare further add to sometimes emotional reactions to trade-off decisions.