Developing a successful, sustainable, and defensible international pricing strategy for pharmaceuticals has become an ever more complex challenge in a value-based world.

Multiple payers in multiple geographies, each with different ways of measuring value, make it very hard to realize the best price and maximize revenue everywhere.

Drug pricing is an increasingly high-stakes enterprise: price optimization of just 1% is equivalent to a 10% increase in profit, yet pharmaceutical companies award themselves an average score of just 56% for the effectiveness of their pricing function, according to a survey by Decision Resources, a global market research agency.¹

Healthcare systems worldwide have budgets that are not keeping pace with the rise in pharmaceutical research and development costs.

A 2014 report by the Tufts Center for the Study of Drug Development (TCSDD) estimates that the average cost of developing a new prescription medication is now $2.6 billion (in 2013 dollars), a 145% increase from $801 million in its 2003 analysis (TCSDD includes the estimated development costs of failed compounds in total expenditures per approved new drug).

As R&D costs go up, payers in many countries aggressively negotiate prices at launch. After that, stakeholders, such as regional governments, procurement groups, and hospitals throughout the value chain, further erode that public selling or “visible” price, bringing it all the way down to the “invisible” average selling price that is actually paid after all discounts and contracts have been negotiated. This price waterfall can result in an average selling price as much as 70% lower than the list price.

On top of that, the use of international reference pricing to control the costs of patent-protected drugs means that rolling out a drug in the wrong sequence can be a costly error.

To develop a global pricing strategy, companies must overhaul or discard outdated models and acquire new capabilities that will allow them to do the following:

- Integrate health economics early in the drug development process
- Generate evidence to demonstrate value and optimize price in multiple countries
- Anticipate and manage the “price waterfall”
- Devise the optimal launch sequence
- Monitor and respond to price fluctuations post-launch

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Unfortunately, too many companies are still using old models to guide their global pricing strategies. Traditional qualitative and quantitative research methods used to determine optimal, revenue-maximizing international pricing do not adequately account for these new complexities or for the increasing influence of health economics data in negotiations with payers.

Even innovative and effective drugs may falter or fail in this fast-changing environment. Last March, the U.K.’s National Institute for Health and Care Excellence (NICE) issued its final recommendation against using National Health Service (NHS) funds for Sanofi’s Zaltrap (ziv-aflibercept) for previously treated metastatic colorectal cancer (mCRC). Although NICE deemed the novel recombinant fusion protein “clinically effective,” it was not found to be cost-effective as compared with existing treatments. Zaltrap’s cost (even after Sanofi slashed the list price with deep discounts) as well as a label expansion for the competing angiogenesis inhibitor Avastin (bevacizumab), allowing Avastin’s use beyond first-line progression in mCRC, has complicated Zaltrap’s uptake across the globe.

INTEGRATE HEALTH ECONOMICS EARLY IN THE DRUG DEVELOPMENT PROCESS

The influence of increasingly sophisticated health economics data on international payer decisions has grown exponentially in many countries over the past five years. That makes it important for developers to integrate health economics into their pricing strategies as early as Phase I and II trials, if possible, to allow pricing scenarios to be understood early.

For example, one PAREXEL client was recently prioritizing its Phase I diabetes portfolio. This was a new therapeutic area for the company, and it had pharmacometrics data from a number of candidate compounds. Response was measured by traditional surrogate endpoints, such as changes in blood sugar levels (HbA1C), which are typical of randomized controlled trials (RCTs). Similar data was available for comparator drugs from a meta-analysis of published clinical literature.

The challenge was to link the surrogate endpoints to outcomes that were clinically meaningful for patients—such as death and quality of life (morbidity, pain, function)—and then to estimate the economic value associated with a given change in the surrogate. In a value-based system, the pricing of new diabetes drugs will be determined by payers according to value delivered in the “real world” of clinical practice, not by performance on RCT surrogate endpoints.

PAREXEL’s analysis identified which endpoints were associated with the highest utility gains on patient-reported outcomes, enabling the company to conserve its development dollars by terminating weaker candidates, advancing only those with the greatest potential economic and patient value. The research also led the firm to revise its trial designs and its target product profile before it began Phase II trials, giving its future diabetes treatments a greater chance of gaining market access to help those patients that need it, along with achieving optimal pricing for the company.

GENERATE EVIDENCE OF VALUE THAT SUPPORTS PRICING IN MULTIPLE COUNTRIES

Companies must engage stakeholders that influence product value and pricing/reimbursement policy decisions by constructing and communicating a compelling, data-driven value proposition at the earliest possible stage. Local affiliates should practice communicating and refining the value story in mock negotiations—and that narrative must be fine-tuned country by country.

For example, although there is free pricing in the U.K., NICE, in its watchdog role, may recommend against access regardless of regulatory approval. NICE makes decisions with a heavy emphasis on the
quality-adjusted life-year (QALY) cost utility analysis. Thus, drug developers in the U.K. must be prepared with a formal cost-effectiveness dossier in advance of regulatory approval. Extensive review of NICE submission histories, and published rulings for comparable compounds/therapeutic areas, shows that meeting the cost-effectiveness thresholds under existing pricing models is increasingly difficult.

In contrast, national pricing and reimbursement processes in Italy are combined post-registration. Prices are negotiated with manufacturers and cost-effectiveness data may be reviewed, but the Italian Medicines Agency’s Technical Commission and Pricing and Reimbursement Committee work in tandem and often utilize risk-sharing agreements to hold down costs, particularly in the area of oncology. Partial regional autonomy in Italy adds a further layer of complexity: subnational contracts for formulary access are commonplace and may also involve additional health technology assessments.

As a result, companies hoping to develop an effective global strategy are forced to evaluate comparative price benchmarks on a product-by-product, therapeutic-class-by-therapeutic-class, and country-by-country basis, including in-line and pipeline products. This can be a research- and resource-intensive undertaking.

In terms of modeling, mixing direct techniques and indirect techniques—so as not to over- or undersensitize the pricing analysis—will provide payers and prescribers with the context they need to make rational decisions. Use of newer techniques, such as self-explicated conjoint methodologies, can reduce research costs and increase the robustness of qualitative pricing analyses.

Another key to estimating the profit potential of an asset is to understand the uptake trajectory in light of anticipated pricing, reimbursement, and access restrictions by payers in disparate healthcare systems across the globe. Price is only one side of the

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**Figure 1: Pricing Waterfall for an Oncology Product, Italian Example**

*Companies must fully understand the effect that each interaction will have on their drug’s price and profit potential in the immediate and longer term, while determining the initial prices for each country and projecting the potential magnitude of the waterfall effect.*
equation. Risk sharing and contracting arrangements, such as “alternative” outcome or financial-based discounts, are common in certain countries, and may significantly impact both price and volume.

**ANTICIPATE THE “PRICE WATERFALL”**

The average selling price can be more than 70% lower than list because the price within a country is eroded all the way down the value chain (see Figure 1, page 3).

**OPTIMIZE THE LAUNCH SEQUENCE**

With due diligence, drug developers can determine a country-by-country launch sequence that accounts for international reference pricing policies and pricing/reimbursement policies that may vary by therapeutic area and molecule type.

PAREXEL recently advised a company on how to order the European launch sequence for its new biosimilar product in order to maximize revenue. The lack of established regulation of biosimilars in Europe presents unique opportunities as well as challenges. Because timing is critical—delays translate directly to lost revenue—PAREXEL was faced with a tight project deadline of about four weeks.

First, PAREXEL conducted primary research across all countries in the launch plan, including some that were off the beaten path. The result was a collection of key data points, including originator price, ex-manufacturing price, discounts, average selling price, and the expected volume of sales of the new entrant on a country-by-country basis.

Next, the data was entered into PAREXEL’s proprietary model that uses an optimization algorithm to order a revenue-maximizing launch sequence.

**Figure 2: EU Biosimilar Launch Sequence**

The chart above shows a typical revenue-maximizing launch sequence across 24 European countries that could be generated after detailed, country-specific data on price and volume are run through PAREXEL’s optimization algorithm. The gap between the upper “visible” list price (shown by the red or blue circles) and the lower “invisible” average selling price (shown in yellow) depicts the anticipated variation within the international price corridor across Europe.
sequence. The one factor that clearly has the greatest impact on revenue is launching as soon as possible. Therefore, companies need to understand how long the regulatory process will take in each country and build those timelines into the model.

Figure 2 (page 4) shows a typical optimized launch sequence. Despite uncertainties associated with recent changes in the German pricing/reimbursement landscape, Germany remains an absolute standard as the number one launch country due to its free pricing policies for setting the “list” [originator] price that is used as a starting reference point.

MONITOR AND RESPOND TO PRICE FLUCTUATIONS POST-LAUNCH

Once a product is available in all markets, a price change anywhere can create a domino effect on other countries and regions. As a result, companies need to monitor price (and currency) fluctuations on a daily basis across the globe and react swiftly to government requests and price changes.

Pharmaceutical prices will always be an easy target for countries looking to weather periods of economic difficulty. Big budget therapy segments, especially those with high prices and low product differentiation, inevitably will find themselves in the crosshairs.

As shown above, any effective price-management system must be supported both by internal procedures (such as alerts generated automatically when prices change, triggering review) and by external, real-time data from local affiliates.
Once a country affiliate is notified of a government-mandated price cut, it will need to choose a strategic response: acquiesce, make a formal challenge, or even withdraw the product from the market. Therefore, global strategy teams need to be able to simulate the impact of local pricing changes before making a decision.

The solution is to develop an integrated and data-rich in-house pricing management system to monitor international price fluctuations and enable effective, revenue-maximizing decisions on a real-time basis (see Figure 3, page 5).

Local marketing organizations/affiliates should be able to implement pricing strategy on a country-by-country basis. An effective global strategy by definition enables local agility: it provides local operating companies a framework within which to work, along with the ability to react to their specific market conditions. Traditionally, countries have been armed only with:

- A well-researched opening price point to kick off negotiations
- A commercially viable fallback price
- A “walk-away” price under which no deal can be cut

EFFECTIVE PRICING CAN MAKE OR BREAK NOT JUST AN ASSET, BUT A COMPANY

A corporate structure that separates pricing and health economics functions creates a barrier to achieving an optimal pricing strategy. Getting to the right price in multiple markets, each of which measures and perceives value differently and has a different willingness or ability to pay, demands close coordination of development, regulatory, and pricing functions within a firm.

It is critical to bring the people generating health economics data together with those who are developing the pricing hypotheses and early modeling. This gives the firm the best chance of making informed and efficient development decisions. Wasteful development efforts represent a huge lost opportunity cost and depress both profit margins and productivity for companies and the pharmaceutical industry.

Maximizing revenue across the globe allows companies to reinvest in new drug discovery, safeguarding short-term shareholder value and delivering healthcare value to patients. This has become far more complicated in the past decade, as pressure on healthcare systems has forced payers to increase the pricing pressure on the industry.

Effective pricing has the ability to make or break not just an asset, but also a company. Appropriate investment in pricing strategies, including the conduct of deep, technical analyses, is required for success in this new value-based world. Companies that are early adopters of an integrated, international approach to optimized pricing will see bottom-line benefits almost immediately. Those that do not will suffer.


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