Original Article

Pricing biologics: Issues, strategic priorities and a conceptual model

Received (in revised form): 28th October 2010

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ABSTRACT **The advent of complex and often expensive biologics raises critical commercial challenges – the most important of which pertains to developing a viable pricing, distribution and reimbursement model that is intrinsically geared to the special characteristics of biologic products and the expectations of a diverse customer population. Idiosyncratic differences in health-care systems, their philosophical motivations and preferred methods of controlling access to expensive biologic treatments pose additional challenges. This article discusses key issues about pricing biologics from the primary viewpoint of biologic manufacturers and marketers, focusing on the inseparable relationship between price, distribution, access and reimbursement. Specific priorities are explicated for streamlining biologic pricing and access strategies to meet upcoming challenges. A conceptual model for developing viable biologic pricing strategy is presented. Insights from the author's work implementing key aspects of the model in the real world are discussed. The article concludes by presenting an overview of a pricing decision support system that has proven invaluable in formulating and managing biologic pricing strategies over a finite time horizon.**

Journal of Commercial Biotechnology (2011) **17,** 7–23. doi:10.1057/jcb.2010.30;
published online 14 December 2010

Keywords: biologics; pricing; strategy; access; commercial; conceptual model

BACKGROUND

Much has been written and discussed recently about the paucity of pipelines responsible for introducing new treatments to the commercial marketplace for medicines. By one estimate, bio/pharmaceutical R&D expenditures in 2014 are expected to rise 400 per cent over levels in 2000, while the number of new molecules coming to market as a result is likely to halve. Pending widespread adoption of new drug discovery paradigms, this trend demands changes to existing models of drug development and commercialization.[1]

A silver lining in the ominous cloud of thinning pipelines is the rising number of

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biologic product approvals. In 2009, 16 new biologic drugs were approved by the FDA, compared to 11 in 2008 and nine in 2007.[2] Although small compared to the number of new product approvals of chemical-based pharmaceuticals, the trend is significant in that it is likely to persist into the next decade, justifying the ubiquitous investment interest in the relatively modern field of protein-based biotechnology. By all accounts, global utilization of biologics will likely quadruple by 2014. One out of every three dollars spent on bio/pharmaceuticals will be due to the use of a biologic medication. In 2011, the US government will spend upwards of US$100 billion on biologics.[3]

BIOLOGIC PRICING

Trends portending more approvals and utilization of biologics are tainted by widespread perceptions that biologic prices are exorbitant relative to chemical-based pharmaceuticals. More often than not, biologics aim to treat hitherto untreated conditions that have irrevocable consequences on morbidity and mortality. Development timelines stretch into decades contributing in no small measure to sunk costs that cannot be recovered in ways other than through higher prices of commercialized products. Not inconsequentially, several biologics are novel, first-in-class entities that enjoy virtual monopolies with the ability to command high prices. In-market, monoclonal antibodies (MABs) – one of the more common categories of biologic medications – typically cost upward of $15 000 a year. Biologic treatments for cancer or rare, life-threatening diseases can cost anywhere from $50 000 to $400 000 per year.

The promise of biologics to address hitherto incurable afflictions is threatened by the apparent lack of a conceptual model that allows its manufacturers to price their products such that they benefit patients – regardless of their ability to afford them – while generating sufficient returns on their investments. There is mounting evidence, for example, that even for those patients covered by some form of health insurance, high out-of-pocket costs reduce the use of biologics. According to one study of 8500 newly diagnosed Rheumatoid Arthritis (RA) patients covered by employer-sponsored health insurance, patients who had to pay more for common MAB drugs were less likely to start using them and were less likely to continue once they start. Only one in two patients with RA is currently receiving treatment for it.[4] Further, estimated compliance rates for RA patients is between 30 and 50 per cent.[5] As shown in numerous studies of patients with chronic diseases, those who are not adherent have a higher risk of complications, hospitalizations and ER visits, exhibit worse outcomes and incur higher condition-related costs than adherent patients.[6] In other words, the very population of patients meant to be served by novel, biologic treatments is deprived of their promise primarily because of cost; with added, undesirable societal burden fraught with economic consequences.

INSURING PATIENTS AGAINST HIGH BIOLOGIC COSTS

The triple threat of high biologic costs, lack of consequent widespread access and the paucity of effective biologic pricing models has been cause for serious rethinking among a few leading health-care insurers. There is no consensus on what may be an appropriate approach to balancing the enormous promise of biologic products with the costs of insuring plan members, in addition to fulfilling supply conditions that ensure proper storage, delivery and ongoing patient compliance with relatively complex modes of drug intake. There has been some debate asking for a rethinking on whether the current model of delivering medicines through a pharmacy is the right one for biologics. Another logical argument raises an ethical question – should private insurers be required to cover the cost of potentially high priced benefits promised by biologics?[7] Even if they did, could a private insurer sustain such coverage over the

next two decades when demand for a wide variety of biologics is expected to rise manifold? No matter what the philosophical question, however, it is fast becoming clear that under the existing model of insuring patients for the cost of approved medicines, biologics will be evaluated for coverage on the basis of evidence even more stringently than may be the standard for considerably less expensive small molecules. The need for expensive biologics to proactively provide hard outcomes data, preferably in a comparative context corresponding to real-world settings, has never been more vital. A commonly held view that has received considerable attention in this vein suggests that company-sponsored clinical trial data filed to support regulatory approval is not adequate by itself to pass an insurer's muster about a new biologic's ability to fulfill its mandate. The burden of proof to justify biologic price tags of ~$100 000 per treatment cycle is fast hinging on the availability of post-approval outcomes data, preferably in comparison to the prevailing standard of therapy.

Until comparative, real-world outcomes data are freely available to bolster coverage decisions, insurers will continue to focus on issues of controlling biologic utilization as the preferred means of balancing costs with expected benefits. Key questions driving biologic product insurance decisions will continue to revolve around rationing utilization to meet the needs of those in dire need subject to available resources until substantive outcomes-based data are available to justify wider coverage. As such, changes to the current model of insuring patients – devised primarily for relatively low-cost small molecule pills – reflect the desire to better manage biologic utilization and ensuing costs.

Examples of such evolutionary changes include –

- *Classifying the biologic as providing a pharmacy benefit, and adding a fourth tier (to the customary three-tier formulary structure) in the existing formulary requiring the beneficiary to pay a percentage of the total cost of the biologic upon purchase*. In 2007, patients in the United States purchasing biologics under such an adjustment paid an average of 36 per cent of the biologic's total cost. According to data from the 2007 Kaiser/HRET employer survey, an RA patient purchasing a popular MAB costing $23 000 a year paid $8424 out of pocket for a full year's purchase.[8]
- *Exploring new ways of classifying medicines (including biologics) into co-payment tiers*. For example, the insurer Humana created a program called RxImpact in which Tier 1 would include drugs designed for treating chronic, long-term conditions such as cancer or AIDS. Tier 2 would cover drugs the use of which offset other medical events such as hospitalizations. Tier 3 would cover drugs that may not have a medical tradeoff but which improved daily functioning, such as a pill for allergies. The fourth group of drugs may not offer any medical payback, but would instead have life style improvement benefits. Depending upon approved indications, a new biologic may fall into one such tier. An employer offering coverage to its employees would decide which tier(s) it would support, based on its own criteria including costs.
- *Advocating heightened use of specialty pharmacies through contracting or acquisitions*. Among other benefits, this model relies on high-touch, high-expertise skills and technological infrastructure provided by specialty pharmacies staffed with specialist pharmacists and nurses to purchase, store, deliver and closely monitor patient utilization of biologics from multiple manufacturers so that measureable savings in total costs and improvement in adherence result. Such savings, it is believed, can find their way into lower total coverage costs, somewhat mitigating the proportionately high cost of biologic utilization in a large member population. One other oft-mentioned benefit of specialty pharmacies is the ability to measure real outcomes of taking specific biologics in true care settings,

provided such a process is duly implemented. Such outcomes data, it is hoped, would help insurers make better-informed decisions about the cost-effectiveness of specific biologics, which in turn, would provide enough rationale for making efficient formulary inclusion and benefit design decisions.

- *In single payer systems as is widely prevalent outside the United States, relying heavily on health technology assessments of biologics provided by autonomous research bodies, such as NICE (in the United Kingdom) or ANAES (in France).* Such assessments focus on answering questions about a biologic's efficacy, its appropriateness for intended patients, its suggested cost relative to its benefits, and comparisons of such assessments with alternatives as may exist. While the main purpose of biologic HTAs is to inform policy-making decisions,[9] an equally important consequence is their ability to impact biologic utilization either positively or adversely (depending upon the assessment) inasmuch as the recommendations are implemented within a payer system. Such impact is usually quite substantial in single or dual payer systems where the ability of a high-priced biologic to generate reasonable market share outside the dominant payer system is minimal.

BIOLOGIC REIMBURSEMENT IN FLUX

While insurers devise fixes to existing models of coverage to fit the advent of biologics, reimbursement methods covering purchase and use of a large number of biologic medications are also in a state of flux. The structure of many biologic medications currently precludes the possibility of delivering them in modes other than through an injection or an infusion, usually requiring oversight by a medical professional (such as a nurse or a physician). As such, additional administrative costs are associated with the list price of a biologic, not to mention demands on storage space and strict temperature and product-handling requirements. As an example, for every $100 that a US-based community cancer clinic spends on purchasing cancer drugs, an additional $12 is spent on costs associated with billing and reimbursement, storage and inventory, pharmacy, documentation and overhead.[10] Unlike small molecules, this radically changes the *de facto* pricing model for biologics – in addition to managing margins associated with selling products to wholesalers and other types of distributors, manufacturers and insurers are tasked with effectively managing the process and costs of selling product to private medical professionals and infusion centers which administer biologics to patients. As evidenced by developments in the past decade, no one model of biologic product reimbursement has found widespread acceptance largely due to this. In the US health-care system, for example, Medicare originally reimbursed private clinics purchasing and utilizing biologics under a formula based on the average wholesale price charged by manufacturers to wholesalers, who in turn offered discounts off a marked-up price to purchasers of the biologic. Over time, this resulted in inefficient use of Medicare funds, often resulting in disproportionate profit-taking by private clinics based on the difference between the stated and actual price paid for purchase of a biologic. Other less than desirable consequences of this method of reimbursement included the disproportionately high influence of product price and profit potential on prescribing and utilization decisions. In other words, patients were likely to receive a biologic as much for the profit potential it represented to the clinic as to its clinical efficacy. In 2005 Medicare switched to a system whereby biologic manufacturers were required by law to report biologic selling prices on a quarterly basis, so that an average sales price (ASP) could be used as a basis for reimbursing clinics that bought and used biologics. A standard formula of ASP + 6 per cent is currently in place to control for

  1462-8732 **Journal of Commercial Biotechnology** Vol. 17, 1, 7–23

some of the discrepancies stemming from the previous reimbursement model. But as is well known, the current model is far from solving the issues it set out to address. For example, there is concern that the (ASP + 6 per cent) formula is less than adequate to cover ancillary costs associated with the purchase and utilization of a cancer treating biologic (estimated in citation 9 at ~12 per cent of the list price). In other words, stand-alone community cancer clinics purchasing a typical biologic to treat cancer would tend to lose an average of ~6 per cent off the purchase price on every unit purchased. This is in stark contrast to their ability to make a profit with every biologic administration under the previous AWP-based formula. For the same reason, private insurers desirous of following Medicare's example (while at the same time mindful of the costs incurred by their network of physicians) have offered their physicians reimbursement rates that range from ASP + 6 per cent to ASP + (9 per cent–18 per cent).[11] There are a variety of other issues outlined in anecdotal evidence and published literature which tend to make the overarching point that a fair and equitable biologic purchase and reimbursement model is a goal yet to be attained, and that with the advent of more biologics with higher price tags and complex modes of administration in the coming years, current models are destined for radical change.

EXPERIMENTS IN BIOLOGIC PRICING

The lack of a rational framework for setting an equitable price for a biologic that works well for patients, manufacturers, physicians and private and public insurers is a key reason why governments and agencies in single or dual payer systems continue to experiment with rules and regulations for controlling the apparently uncontrollable prices of bio/pharmaceuticals. For a good part of the last two decades, arbitrary price and profit controls were accepted models for determining prices of bio/pharmaceutical products, especially high-priced biologics in much of the world outside the United States. Even in markets such as the G5 in the EU, manufacturers were free to set a price launch, but only for a limited time after which price and profit controls would kick in. As of April 2010, the German health-care system was debating new proposals for placing a three-year block on price rises for prescription drugs, and requiring drug-makers to refund money earned on the sales of 'overpriced' drugs. Further, manufacturers would be required to submit dossiers that provided cost/benefit analyses justifying product prices compared to existing alternatives. Such evidence would form the basis of negotiations with insurers who covered ~70 per cent of the population. If the negotiations failed, insurers could impose a mandatory short-term rebate of 16 per cent off the manufacturer's price, instead of the current 6 per cent. If no evidence of additional benefit provided by the drug could be shown, it would immediately be placed on the existing fixed-price scheme for patented drugs.[12] The greatest cause for concern for German insurers over the next four years is the costs of patented drugs to treat cancer, rheumatology and multiple sclerosis, that is, categories where biologics are predominantly utilized.[13]

STRATEGIC PRIORITIES FOR BIOLOGICS

Analysis of the current pricing, insurance coverage and reimbursement landscape for biologics indicates that manufacturers of biologics would do better by refocusing strategic priorities so that the full promise of future biologic therapies can be realized. Pending such change, it will become increasingly hard to justify current trends in biologic pricing, and even harder to settle on an effective conceptual model that guides pricing decisions at launch and thereafter. Key elements of such re-alignment would include the following.

Crafting biologic product value propositions for multiple customer segments well ahead of launch

By all accounts, resistance to high biologic prices on the part of customers is indicative of a failure to establish convincing rationales for their purchase and use. That such resistance manifests in a variety of alternative modes in distinct segments such as government agencies, private payers, patients or specialist physicians points to the need for customizing such rationale as may exist. Further, it is no secret to those who concern themselves with issues of marketing strategy that changing opinion on the basis of clinical data is an ongoing process that evolves with time, especially in the face of unfavorable *status quo*. As such, an important precursor to the launch of a new biologic that could command higher than expected pricing is the development of product value propositions customized to the expectations of distinct customer segments such as specialist physicians, private and public payers (including government agencies), employers or patients. Rather than aiming to build or change perceptions, such propositions strive to align themselves early with clinical trial designs under the rubric of an overarching pre-launch positioning strategy,[14] which serves as a beacon for impactful trials and resulting data that find their way into customer-specific value propositions.

Designing studies that meet the rising demand for outcomes data, preferably in a head-to-head context

Given the expected advent of a large number of high-priced biologic products in the near future, the need for an integrated clinical program spanning pre- and post-launch time-frames has never been more acute. In the pre-launch phase, conducting multiple-armed trials powered to test variations against existing standards of treatment, dosage, patient populations and geographies are rising in importance. More stratification and randomization to reflect real-world representation will go a long way in generating clinical data which can be relied upon as a matter of course in day-to-day clinical practice. A pre-launch clinical trial program can only benefit by a careful consideration of the type of results that could conceivably be generated by a structured patient and/or prescriber registry and a program of claims-based analyses after launch, when sales and marketing efforts are underway. A careful consideration of what may be required for approval versus what may be necessary to justify an appropriate price at launch is well worth the effort during the process of developing a clinical program. In this context, the importance of developing an REMS initiative well ahead of finalizing launch pricing strategy needs to be emphasized. Current, heightened emphasis on safety data coupled with an apparent lack of adequate information about the risks of taking a relatively complex medication can have an adverse impact on the perception of value delivered by a biologic, especially relative to its cost. Proactive assessments of potential REMS requirements for a biologic can only serve to mitigate adverse demands after launch. Recent thinking about how best to prepare for REMS advocates the collection and analysis of appropriate safety data as early as Phase 1.[15]

Expanding the notion of proof for approval and adoption to include data on clinical effectiveness, quality of life, cost effectiveness and budgetary impact

The ubiquitous debate about the true worth of high priced bio/pharmaceutical products has brought into sharp focus the demarcation between the type of proof that secures regulatory approval and the kind of evidence that enables wide access to them. With each passing year, the number of approved biologics that fail to get recommended by agencies such as NICE (in the United Kingdom) has only increased. Even in purported free markets for bio/pharmaceuticals such as the United States,

there is hardly any approved biologic that is accorded a preferred, unrestricted position on the formularies of commercial plans. It is quite the norm that when supported on formularies, expensive biologics are subject to strict management controls that regulate utilization as well as force its users to assume a relatively higher burden of the product's cost. What determines wide access are measures such as (a) clinical effectiveness, that is, evidence that the product is effective in a wide variety of diagnosed patients, not limited to the type under study in a clinical trial and (b) cost effectiveness of the product in terms such as a quantifiable increase in quality-adjusted life years, especially in the case of indications have proven links to mortality. It is no longer a stretch to recommend that a smart biologic pricing strategy incorporate analyses which explore the impact of a range of prices on specific cost effectiveness measures, so that approved products are launched at a price which can assure wider access and faster market penetration.

Emphasizing the critical importance of ensuring patient adherence in drug development, commercialization and in-market management of biologics

It is well documented that less than one in two patients receiving a biologic for the treatment of their RA or Multiple Sclerosis are compliant.[16] The relatively high cost of co-payment or co-insurance to obtain a biologic has a lot to do with it. Anecdotal cases reported in the media[17] reiterate the impact that high patient out-of-pocket costs for biologics have on adherence, as well as on systemic costs downstream by increasing hospitalization rates, emergency room visits, workplace absenteeism and presenteeism. According to one study, patients whose families had high health-care expenses were less than half as likely to start biotech drugs as were those from households with average costs.[18] What is less documented is the relatively high impact lack of adherence can have on biologic revenues, given their high unit costs and limited target patient populations. With the imminent increase in the availability of biologics for the treatment of orphan diseases and expensive cancer vaccines, for example, non-adherence will become even more of an issue than currently. Clearly, radically improving or re-envisioning reimbursement systems and benefit designs specifically developed for biologics is a strong imperative. In parallel, technological improvements in biologic drug delivery and absorption methods which reduce unit costs, make for easier administration, facilitate patient convenience and affordability and thus, collectively, improve biologic adherence are called for.[19] Offering patient co-payment assistance through direct or indirect channels to ease the burden of high cost is an obvious, even necessary, step; but hardly the panacea to solve the burgeoning problem.

Investing in product distribution channels that specifically optimize biologic adoption and related, operational efficiencies

The preponderance of evidence about market reactions to current biologic pricing and access indicates a crying need for channels of distribution that are fine-tuned to their unique characteristics. Failing that, fundamental inefficiencies in the current distribution model will continue to generate unnecessary costs, providing every stakeholder in the supply chain little option but to raise its price. For example, considerable evidence suggests that the buy and bill model for administering biologics can lead to excessive utilization, waste and reimbursement. Routing biologics to the specialist through specialty pharmacies – specifically geared to handle purchase, storage, insurance, reimbursement, supply and maintenance requirements of biologics – would eliminate such inefficiencies. Manufacturers would be able to develop preferred vendor relationships with specialty pharmacies, generating possible savings which could be passed on to payers

and patients in the form of lower prices. In parallel, changing patient insurance structure to cover a biologic under the pharmacy benefit (rather than a medical benefit) would lead to more transparency in recording costs and dose utilization patterns,[20] as distinct from costs grouped with that incurred for product administration and office visits. This would also enable manufacturers to better control access through, among other means, attractive product pricing via payer-specific contracting. The downside to such a restructuring of biologic distribution is not trivial. For example, attempts to eliminate buy and bill in the United States almost always equate to reducing (or sometimes eliminating) the profits specialists take through purchase and administration of biologics. Although the larger specialist practices are able to wither such impact, cases of small specialist offices shutting down, merging or selling themselves to larger groups because of reduced reimbursement are not uncommon.

Emphasizing payer targeting and relationship development

It is but axiomatic to believe that the promise of expensive biologics cannot be fully realized without the cooperation, endorsement and support of payers responsible for enabling vital provider and patient access to them. And yet, as more patients obtain insurance, and more specialty products (biologics, specialty vaccines or chemical entities) vie for payer support in a highly competitive marketplace, it is increasingly harder for manufacturers to develop strong working relationships with payers. That the payer population in a multi-payer market such as the United States is heterogeneous makes it all the more challenging. In lieu of highly customized relationships with distinct segments of payers (that may differ on the basis of geography, patient profile, provider network structure, preferred approaches to controlling utilization and financial goals, for example), setting prices for inherently expensive biologics can become a dicey exercise at best, with the manufacturer attempting to unilaterally maximize its perceived gain. In such cases, it is not surprising to note autonomous agencies (such as NICE) wielding considerable influence in bringing prices down indirectly by applying the yardstick of cost-effectiveness. A key precursor to convincing payers of the true value inherent in an expensive biologic consists in understanding the specific needs of a payer, its relevant patient population and its provider network such that required value-establishing information is communicated appropriately and in advance of product launch. In multi-payer environments such as the United States, it is very much the norm that distinct segments of payers exist, each of which has distinct sets of needs. Understanding the full spectrum of payer needs, motivations and expectations can also help jump start advance contracting negotiations to maximize product access. The notion of implementing a Key Account Management (KAM) Model[21] to customize payer marketing and relationship development is fast gaining ground as a means to this end. When implemented with specific, custom goals and in tandem with all concerned stakeholders such as key payer accounts, providers, hospitals, academia and government agencies, KAM models can lead to significantly better access, better perceptions, strong stakeholder satisfaction and significant profits. Of late, sporadic examples of large pharmaceutical companies working in collaboration with agencies such as NICE to achieve mutually beneficial goals have been reported.

Adapting existing sales-force models to fit the specific demands of biologics

The traditional share-of-voice, face-to-face, physician-focused, sales-rep model is *prima facie* not suited to selling biologics.[1] For one, physician offices do not represent the most important points-of-purchase decisions impacting expensive biologics. Larger customers such as public and private payers,

government agencies, specialty pharmacies, hospitals or group-purchasing-organizations purchase such products for their formularies on the basis of expectations requiring a selling model distinct from the traditional detailing/sampling model. Specialists in general are gravitating toward online avenues for obtaining clinical information, on-demand samples, promotional materials and product support. In the event that a personal sales pitch is called for, the nature of the specialist-rep interaction demands diverse skill sets spanning in-depth scientific knowledge, ability to discuss elements of a contract or facilitating further, customized dialogue through virtual means. The increasing influence on physicians of patients interacting with each other in social media can only be expected to rise with time. If the sales-force is to be relied upon to communicate the value inherent in high priced biologics (or even to mitigate negative perceptions of less than desirable cost-effectiveness), it needs to be highly trained, possibly encompassing skill sets consisting of deep medical knowledge, contracting savvy, product utilization economics and expertise in facilitating on-demand electronic interactions.

BIOLOGIC PRICING: A CONCEPTUAL MODEL

If there is one common thread in the strategies discussed in the previous section, it is the overwhelming need to establish and communicate a biologic's true value to its disparate customer segments. Unless a manufacturer proactively takes upon itself the task of specifying a biologic's value structure, the accompanying value proposition and its impact on customers' profits and profitability, perceptions of cost, comparability and lack of differentiation are bound to influence purchase and utilization decisions in rampant ways. That value means different things to different customers can only complicate the selling space even more.

Much of the burden in establishing biologic value lies on the shoulders of an effective biologic pricing model. A viable pricing model developed specifically for new biologics would have desirable characteristics such as:

1. an ability to communicate the full value of the product instead of drawing disproportionately biased attention to its price;
2. a propensity to reflect the expectations and assessments of every customer segment involved in decisions impacting its purchase, access and utilization;
3. clear, customer-derived explications of how individual product components contribute to the overall price of the biologic, accounting for the all too real possibility that such explications may differ from one customer segment to another;
4. reflective of the links between product price, its mode of distribution and key elements of its marketing mix (including promotional spend and positioning strategy and tactics) which together contribute to top-line performance;
5. cognizant of the impact of price on profits and profitability attributable to the biologic, after considering key elements of the cost structure necessary to support its launch and life-cycle management;
6. success in standing up to rigorous cost-benefit tradeoff analyses at the level of every customer segment influencing its purchase, access and utilization;
7. in systems where moderating forces such as reference pricing and parallel trade are en vogue, the ability to estimate and factor their impact so as to generate a realistic, transparent and viable price;
8. ability of the model to enable pricing recommendations even as fundamental assumptions change: such as with the availability of new clinical data, the results of outcomes research, the launch of competing biologics; evidence, price or promotion-based competition, the availability of new forms of drug delivery or policy and regulatory changes.

Aligning biologic pricing on value percepts offers manufacturers the opportunity to engage in rational dialogue with a wide variety of stakeholders, including payers and organizations that influence payer product coverage decisions on the basis of cost effectiveness, specialist physicians who make purchase and utilization decisions or large institutions such as hospitals or group-purchasing organizations who are concerned about making tradeoffs between costs and effectiveness. The value approach to pricing[22] biologics is philosophically distinct from pricing them to recover high sunk costs or to conform to price controls or profit regulations that may be in effect in any given market. Additionally, it offers opportunities to present biologic price not in isolation as a cost to be borne, but as an integral element of the marketing mix[23] that works in synergy with specific, tangible benefits offered by the product to serve its patients, providers and payers.

When developing and implementing biologic pricing strategies on the basis of value, four important challenges need to be addressed.

1. ascertaining with a high degree of accuracy the disparate and often latent value structures relied upon by each stakeholder segment to make biologic product purchase decisions;
2. integrating such customer-specific value structures across all involved customer segments to develop a working notion of customer value imputed to the product;
3. determining a range of possible product prices that adequately reflect value estimates; and
4. assessing the net impact of value-based prices on market performance in the context of market and marketing forces as may realistically exist.

KEY CONSTRUCTS: ASSESSING BIOLOGIC VALUE

The task of ascertaining disparate customer value structures is made less daunting by seeking recourse to theoretical work in marketing science which suggests that three critical constructs are central to understanding customer assessments of value offered by a product. These constructs are abstract enough to be applicable to every stakeholder, and specific enough to be practical, measureable and actionable. Measuring these constructs at the level of each customer and predicting the nature and magnitude of their relationship with price establishes the foundation for a sound, market-level value-based pricing strategy.

Preference is the first key construct. It is a measure of customer affinity for a feature of a product, such as a biologic. It is important to understand a customer's strength of preference for each feature of a biologic, given that it is made up of a variety of features of varying interest to customers such as payers, specialists, government agencies or patients. Equally important to the process is to answer questions such as – 'if the customer had to pay a desired price to obtain benefits offered by the biologic, how much of a feature (such as safety or convenience) will he or she be willing to give up to receive more of another feature (such as efficacy)?

Choice is another key construct vital to understanding value and determining a range of prices reflective of a biologic's value. Given a collection of possibly competing treatment alternatives, each made up of distinct features, what will influence a customer to select a biologic over other possible alternatives? And, of equal importance, to understand what is the role of price in influencing such choices. To the extent that customers make choices based on price alone or in conjunction with perceptions of benefits offered by other elements of the biologic, quantifying such a linkage is vital to setting a price that accurately reflects its value to the customer.

Share of relevant market likely to be achieved by the biologic under key market assumptions is yet another construct vital to understanding imputed value. Whereas preference and choice are individual

constructs, market share is an aggregate construct reflecting market behavior inherently integrated over individual customer proclivities. Critical to the notion of market share are the considerable influences on market performance of sales, marketing, medical and payer-related commercial activities. Setting a value-based price can become a practical, realistic effort only after accounting for such influences inasmuch as they serve to communicate product value and attenuate negative perceptions associated with higher than expected price.

Significant strides made in the realm of marketing science and econometrics over the past decade have led to the development of methods that accurately measure and predict key constructs vital to assessing customer perceptions of biologic value. Methods, when duly contextualized, also exist to integrate constructs across relevant customer segments so that accurate market level estimates of value and its drivers can be made, opening the door, as it were, to set a value-based price in sync with desired manufacturer goals.

For example, if the goal is to assess preferences and value for specific features of a biologic from the point of view of specialist physicians and hospital pharmacists, one can use conjoint analysis or its adaptive or hybrid variants.

If the number of biologic features is large (as in promising compounds that may be in early clinical trials, with a number of development options contingent on trial results), one may use a more recently developed methodology called the Maximum Difference Method, applicable in principle to any type of customer.

If the goal is to ascertain realistic market shares likely to be obtained by a biologic under varying scenarios represented by alternative levels of sales and marketing effort, possible competitive reactions and other incidental market events, one can build a system of simultaneous equations for estimation on a database using methods such as SUR (Seemingly Unrelated Regressions).

DEVELOPING BIOLOGIC PRICING STRATEGY: INSIGHTS

As a marketing scientist goes about the process of understanding, modeling, recommending and predicting the impact of alternative value based pricing strategies, key insights vital to a deeper understanding of a biologic's customers come to the fore. While important in themselves to the development of a rational, value-driven pricing strategy, they lend themselves well to the design of smart, actionable brand strategies that are bound to impact disparate customer segments in desirable ways.

Table 1 is one output from an experiment to assess the value imputed by Rheumatologists to a proposed value proposition describing a new biologic likely to be indicated for the treatment of RA. Data for the experiment were collected under a design constructed according to principles of double-blinding and randomization. Data thus collected were used to develop a choice-based hybrid conjoint (CBHC) model of preferences for elements of the value proposition. Column 1 shows what elements comprised the product's value proposition. Column 2 shows Rheumatologists' self-explication of the relative value of each element in influencing product selection. Note that Rheumatologists believe almost every feature is about equally important. Column 3 presents estimates of relative value predicted by the CBHC model. Note the difference between Columns 2 and 3 – when faced with real prescribing situations as represented by randomized scenarios used in a CBHC experiment, Rheumatologists place more importance on biologic access as well as its cost to patients. Also note that this value structure is a function of the type of patient under consideration. Columns 4 and 5 present results of the same experiment for biologic-naïve patients, that is, patients who have never received a biologic before. Note that for such patients, Rheumatologists place more value on efficacy. For patients who are already on some biologic (Columns 2 and 3),

Table 1: Estimating the relative importance specialists impute to elements of the product's value proposition reveal insights that help shape value based product-pricing decisions

Preference driver	*Preference for switch candidates*		*Preference for biologic naïve patients*	
	Self explicated importance (%)	*Derived* importance (%)*	*Self explicated importance (%)*	*Derived* importance (%)*
Efficacy (total)	13	13	14	26***
Safety	12	15	13	12
Labeled indication	10	5	10	2
MOA	11	4	10	2
Mode of administration	10	4	10	9
Dosing frequency	10	3	10	15***
Sub-Q dosing amount	9	5	9	4
Patient co-pay	13	22	13	17
Access restrictions	13	30**	13	13
Total	100	100	100	100

*Based on multi-attribute preference models.

**Significantly more important in terms of impacting biologic preference for switch candidates than for biologic naïve patients, at a confidence level of 95%.

***Significantly more important in terms of impacting biologic preference for biologic naïve patients than for switch candidates, at a confidence level of 95%.

the new biologic under consideration is likely to represent a switch to a second or third line treatment. It is almost invariably the case that such treatments are more expensive. Payer formularies tend to restrict use of such treatments contingent on the use of first line (usually less expensive) medications. As such, the results of the value assessment experiment indicate more consideration of access and cost for patients likely to be switched from one drug to another.

Figure 1 illustrates valuable insights derived from a value-based pricing experiment with private payers in the United States. As part of the experiment, a sample of payers representing the private payer population was randomly exposed to a set of alternative value propositions, each differing on the basis of net product price to the payer. The X axis represents price to payer, increasing in magnitude from left to right. The Y axis represents the impact of payers' decisions as a result of the indicated price, in terms of the size of the patient population likely to be covered by the product at the indicated price. In other words, the Y axis represents a measure of access to the product at the prices shown on the X axis. Note that at relatively low prices (say @$2 per day), payers will gladly require that the product under study is about the only one that should be prescribed to all of its member-patients. At higher prices (say @$10 or more per day), fewer patients will have broad access to the product on an exclusive basis, because more payers are likely to believe that at such prices, the product is less valuable compared to other options. As price to payer increases, less and less number of payers will prefer recommending the product on an exclusive basis, in effect reducing the number of patients who might receive the drug. With experiments and models of possible behavior such as this, astute marketers can gauge – well ahead of launch – the impact of a range of possible pricing options (including ranges of possible discounts or rebates) on market behaviors.

Figure 2 presents results from a value assessment experiment with patients. Such experiments are especially valuable in health-care systems such as the United States where patients can buy private insurance, or in systems (such as in France or Germany) where patients can privately buy supplemental insurance to augment public insurance, as a

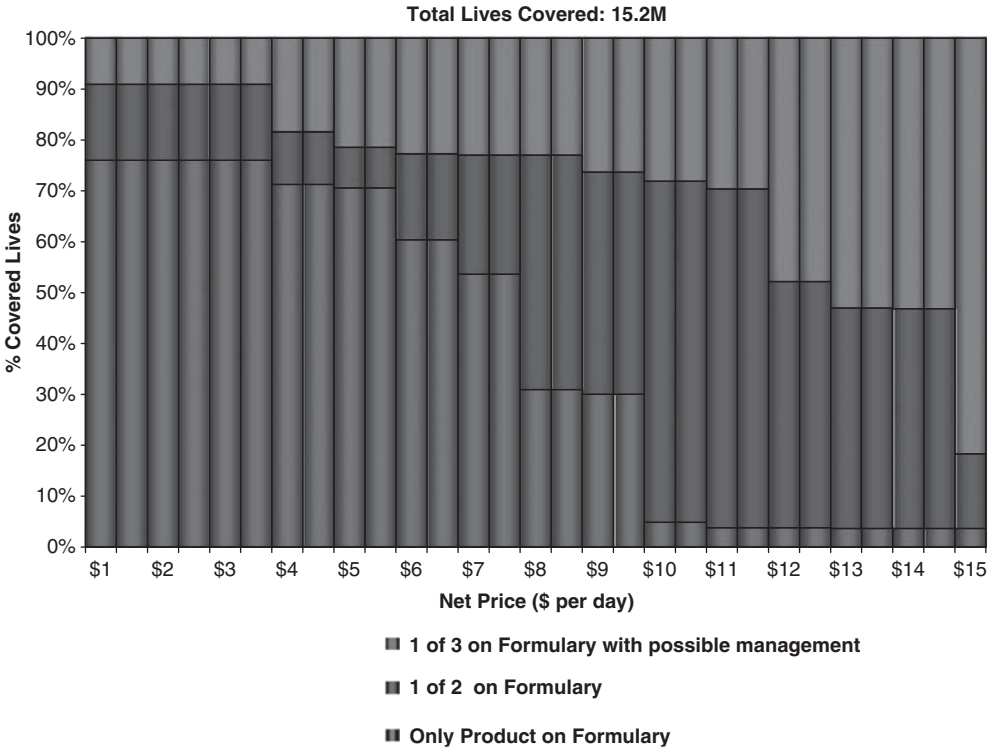

Figure 1: Price-value experiments with payers provide useful information about possible formulary placement as a function of product price.

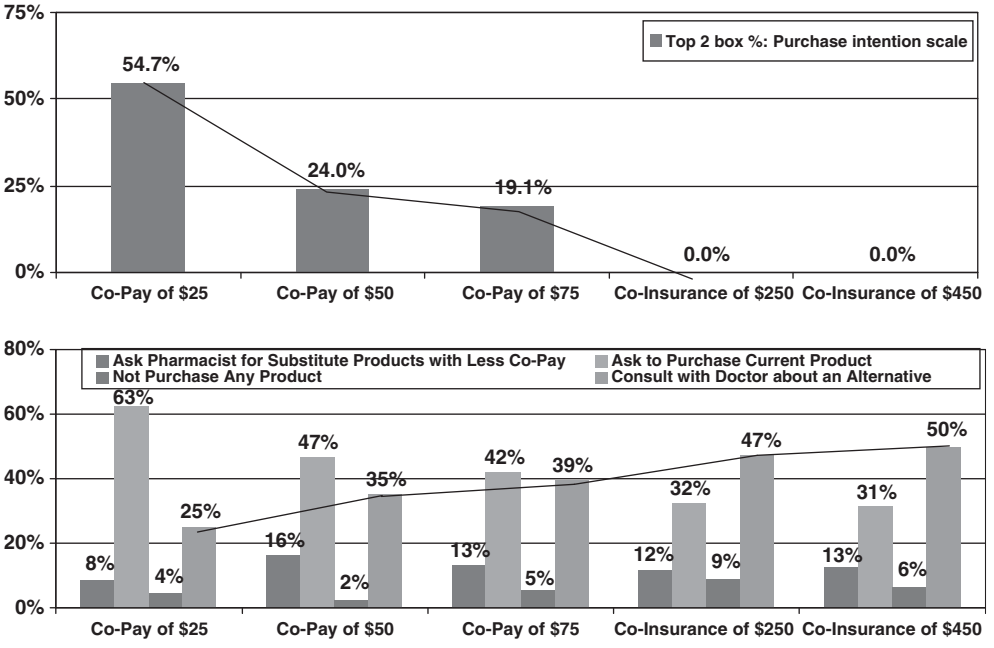

Figure 2: Co-payment sensitivity experiments with patients reveal patient value assessments and consequent future behaviors.

consequence of which they incur a non-trivial co-payment for purchasing some bio/pharmaceutical products. The top half of the figure shows how sensitive patients are to increases in co-payment for a new, yet to be launched product. As the co-payment increases from $25 to $50, the number of patients who intend to purchase it drops by half. The bottom half shows other behaviors patients may engage in as a result of an increase in co-payment. Note that for the same increase in co-payment (from $25 to $50), the number of patients who will ask the pharmacist for a less expensive substitute will likely double.

Figure 3 illustrates one result from an effort to understand the relative importance of product price and other elements of the sales and marketing mix on product performance as measured by new patients started on a drug. Conducted before the launch of a new product, the analysis was based on a database of analogous products containing time-based information on product performance (such as measures of revenue, market share, new and total patient starts, new and total prescriptions) as well as the full matrix of sales and marketing activities supporting each product during the time under consideration. A system of simultaneous equations was set up to represent hypotheses that described cause and effect relationships, including self and cross-product effects. Among other inferences, the results in the figure indicate the relative value of product price in the context of other elements of the marketing mix. For instance, this category appears to be highly sensitive to direct-to-consumer promotions, which appear to have a relatively high impact on new patient starts. Order of product entry into the market (as modeled by product age) is the most important influencer of new patient starts – perhaps attesting the fact that in the category under consideration, being first in class with a novel product continues to have a lasting impact on physician choices.

BIOLOGIC PRICING STRATEGY: DECISION SUPPORT SYSTEMS

Models of stakeholder behaviors as a function of the full range of possible strategic options – including self and competitor prices seen by respective customer segments, clinical trial information, macro market variables such as order of entry or the impact of sales and marketing activities – are best used after integrating them upward to represent a market level view of a product's expected performance. A Marketing Decision Support

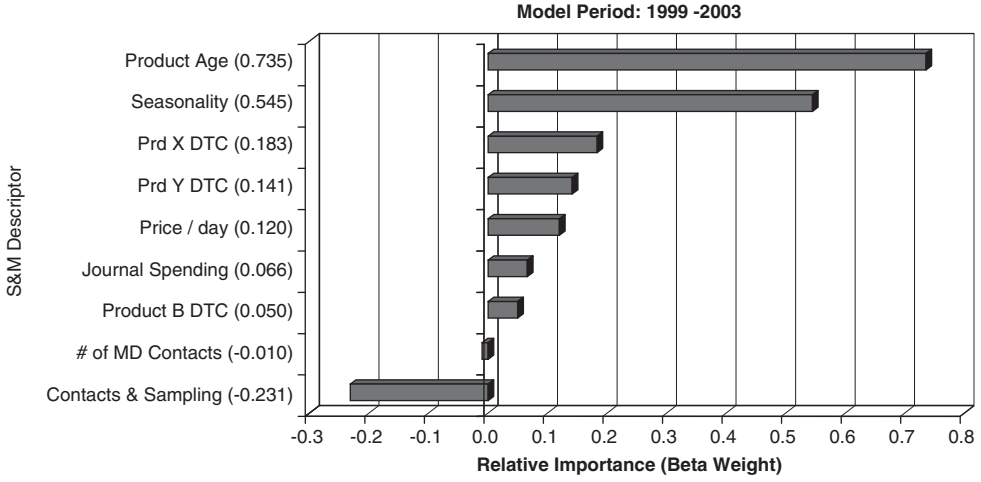

Figure 3: Marketing science model-based analyses of relevant analogue product performance reveal the relative importance of sales and marketing activities in impacting future product trial.

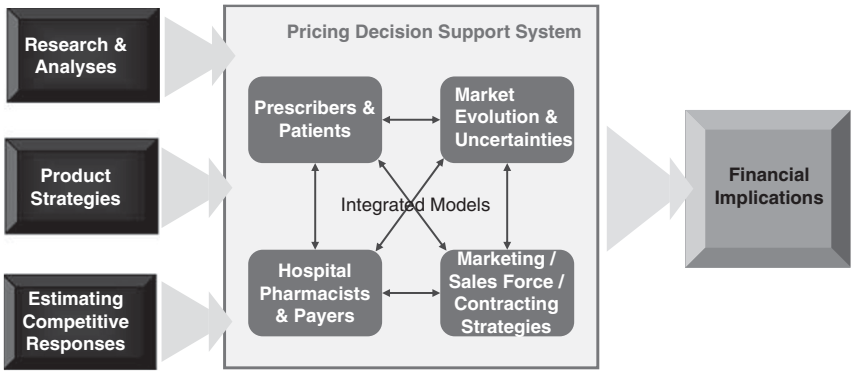

Figure 4: Marketing research, existing strategies and baseline information provide critical inputs to developing a decision support system involving multiple stakeholders, influences and market uncertainties.

System[24] (MDSS) for developing and implementing value-based pricing strategy provides the necessary interface to enable this. Figure 4 presents a schematic of an MDSS used by the author and his colleagues in several engagements meant to recommend realistic pricing strategies for novel products, including biologics. A custom decision support system can be built and used to forecast the market value of alternative pricing strategy options based on financial implications. Marketing research, existing strategies and baseline information provide critical inputs to developing a decision support system involving multiple stakeholders, influences and market uncertainties. A user-friendly decision support system for pricing strategy supported on a desktop help commercial teams build pricing strategy by iterative, scenario simulations. A well-designed decision support system for value-based pricing strategy offers key abilities to assess –

- variations in product features, and clinical and/or outcomes data in the real context of current and anticipated changes in the marketplace;
- impact of alternative list and net prices, and possible variations in self and competitor market access status simultaneously in terms of measureable impact on product performance;
- the extent and influence on market performance of product sales and marketing expenditures;
- the impact of key market events that have direct influence on product performance, such as order of product entry, introduction of new products or changes in product class definitions;
- the evolutionary impact, over a pre-defined time horizon, of customer segments such as target patients, physician specialties, payer types and structures and institutional mix;
- the impact of cost structures supporting commercialization activities, including expenditures for clinical trials, depreciation, various capital expenses, taxes and milestone/royalty payments, if any.

Figure 5 summarizes one result of assessing, modeling and predicting the impact of value-based pricing on market performance, after integration of value-constructs across disparate stakeholders, such as payers, specialist physicians, patients and pharmacists. Note that the X axis represents a realistic range of possible prices that a product may command. The Y axis to the left presents predicted market share at each price point considered. The Y axis to the right predicts the corresponding revenue generated. Such information is obviously invaluable in

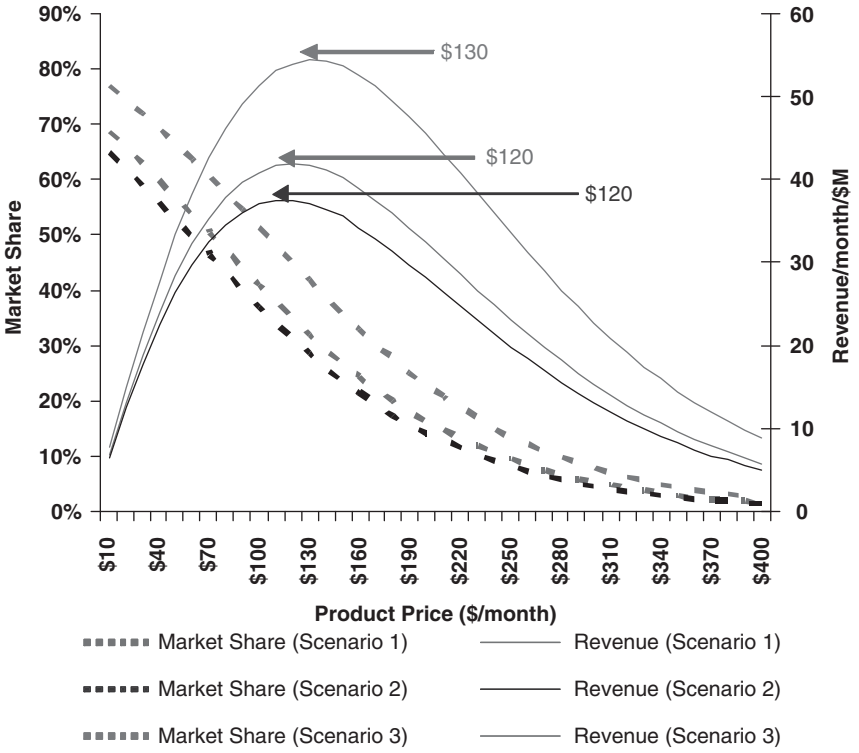

Figure 5: Value-based pricing strategy is best developed by simulating the impact of price on market share and revenue derived by integrating over customers and constructs.

contemplating all available options to craft an impactful pricing strategy. For instance, the graph is useful in determining the price which would maximize market share as quickly as possible, or the price which would maximize revenue. In some engagements, the author has incorporated in the pricing MDSS the modeling of uncertain inputs by embedding a Monte Carlo algorithm, which provides a range of desired outputs contingent on combinations of input uncertainties. If appropriate numerical optimization procedures are built into the pricing MDSS, decisions can be made contingent on the stipulation of constraints, such as manufacturing capacity limitations and availability of clinical data. If a forecasting framework is overlaid on cross-sectional data (and supported with updated research that informs its inputs), the pricing MDSS can also be used to recommend price management strategies over a finite time horizon after launch.

CONCLUSION

Investments made over the past 25 years in the field of protein-based biotechnology are bearing fruit as a rising number of biologic medications are currently receiving approval in the United States and other geographies. The trend is only expected to strengthen in the future. In 2011, for example, the US government will spend upward of $100 billion on the purchase of biologics. The advent of biologics raises critical commercial challenges, the most important of which pertains to developing a viable pricing, distribution and reimbursement model that is intrinsically geared to the special characteristics of biologic products and the expectations of a diverse customer population. Idiosyncratic differences in health-care systems, their philosophical motivations and preferred methods of controlling access to expensive biologic treatments pose additional challenges. This article discusses key issues

about pricing biologics from the primary viewpoint of biologic manufacturers and marketers, focusing on the inseparable relationship between price, distribution, access and reimbursement. Specific priorities are explicated for streamlining biologic pricing and access strategies to meet upcoming challenges. A conceptual model for developing viable biologic pricing strategy is presented. Insights from the author's work implementing key aspects of the model in the real world are discussed. The article concludes by presenting an overview of a pricing decision support system which is invaluable in formulating and managing biologic pricing strategies over a finite time horizon.

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