

# THE 5 STAGES OF BIOTECHNOLOGY MANAGEMENT

**T**he field of biotechnology and the area of specialty pharmacy management continue to garner substantial attention from manufacturers, payers, analysts, and providers. Much of this attention derives from the introduction of a series of innovative, expensive biotechnologies to treat comparatively more prevalent human diseases. Whereas biotechnology products once treated rare conditions like Gaucher's disease, hemophilia, and primary immune disease, many new therapies — and many in the pipeline — target larger populations. This shift is raising concerns among payers and population managers about the associated financial burdens (see figure, next page).

Over the last two years, The Zitter Group has been researching commercial payer strategies for managing biotechnology therapies. Commercial payers — principally MCOs — account for the most of the biotechnology utilization in the United States. Our research has included qualitative projects and a

**The biologics pipeline is flush with new technologies, many of which will come with high prices and treat more prevalent conditions. Payers will feel mounting pressure to manage costs effectively. To do this, more sophisticated economic models sensitive to unique and complex mechanisms of action are needed.**

**BY THOMAS BAKER**



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semiannual quantitative analysis of payer strategies and policies (see box, page 47). Additional findings from our consulting engagements augment the research. Our analysis identified a series of five distinct stages through which commercial payers will move as they seek to exert greater control over biotechnology expenditure (see table, page 49).

Each of these stages introduces new tools and strategies for reducing total biotechnology costs. As an organization moves from stage to stage, the complexity of the strategies grows, necessitating better management tools, diagnostics, and data to achieve desired objectives. More importantly, each stage increases the pressure on manufac-

turers to demonstrate the value of their products — or to make price concessions. Our research suggests that in several categories — particularly multiple sclerosis, rheumatoid arthritis, and hepatitis C — payers have reached the end of the second stage. Future savings will necessitate more complex strategies and will present manufacturers with some challenging questions.

## **Stage 1: Buy and bill** .....

Until only recently, most payers relied on their network or affiliated providers (physicians or specialty pharmacy vendors) to obtain specialty products, manage inventory, administer the product, and submit a claim. In return for managing the process, providers were able to bill at a premium above average wholesale price (AWP), ensuring a substantial revenue stream. By our research,

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some physician practices, particularly oncologists, relied on drugs to generate more than 65 percent of total practice revenue. The buy-and-bill model provided payers with little control of costs or utilization, and represented less a management strategy than a *de facto* abdication of oversight to providers.

### Stage 2: Specialty pharmacy, self-administration, and reimbursement changes

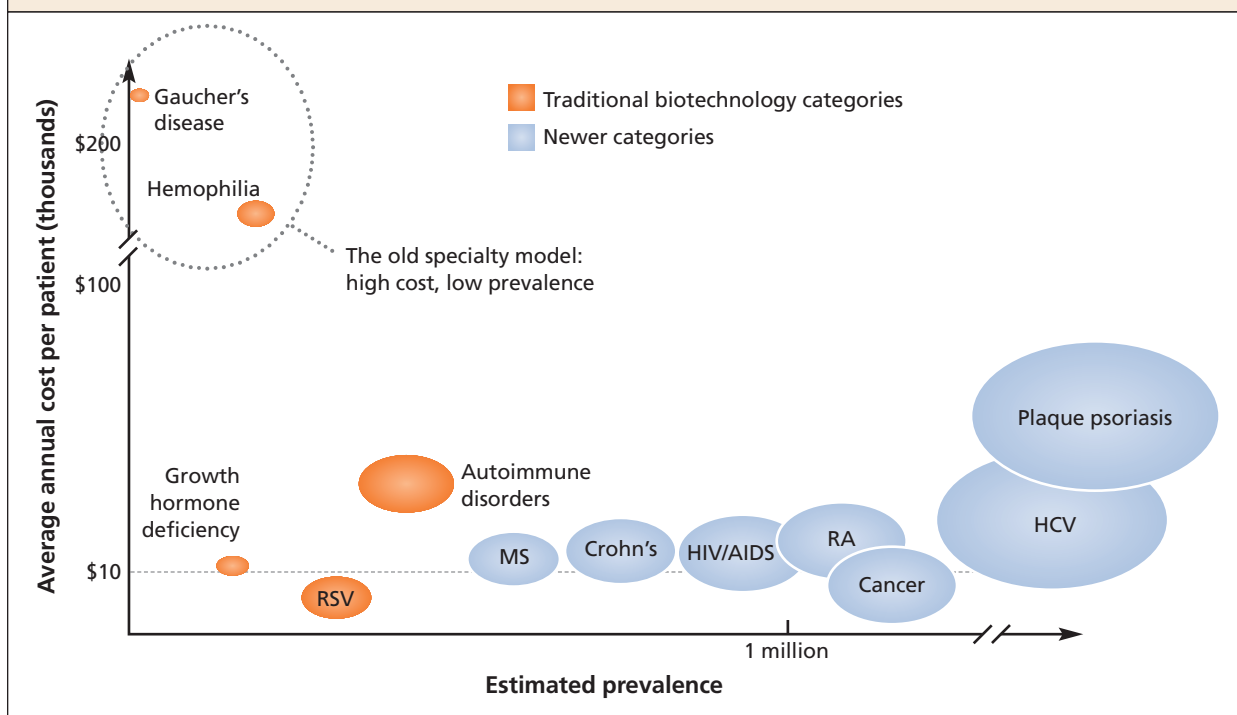
Faced with much greater costs compared to those associated with

small molecule products, payers have taken some preliminary steps to reduce their exposure to biotechnology costs. By signing contracts with specialty pharmacy providers (SPPs), payers have been able to eliminate physician drug mark-up and, in some cases, have negotiated favorable pricing. The emphasis on self-administered therapies similarly allows payers to eliminate payments to physicians for office visits and administration while fostering patient convenience. This preference for self-administered therapies places greater pressure on manufacturers of infused agents to justify their comparatively greater cost.

The penetration of SPPs into the commercial payer market — currently, 78 percent of payers use a specialty provider for all or some of their specialty products — has helped to drive acquisition costs down. At the same time, the passage of the Medicare Modernization Act (MMA) provides commercial payers with the cover needed to reduce payments to physicians still further. Our research shows that by mid 2004, the national buy-and-bill payment rate had quickly fallen to AWP minus 14.21 percent, effectively equal to the Medicare rate. As Medicare completes the transition from AWP-based reimbursement to average

**FIGURE** Changing cost and prevalence relationships in biotechnology

*The shift is toward targeting larger populations*



SOURCES: Raymond James & Associates Equity Research; AdvancePCS; Atlantic Information Services, *Specialty Pharmacy: Stakeholders, Strategies, and Markets*; William Blair & Company Equity Research; Jacobson 1997.

HCV=hepatitis C virus, MS=multiple sclerosis, RA=rheumatoid arthritis, RSV=respiratory syncytial virus.

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sales price (ASP) this year, most payers expect to follow Medicare's lead.

Though stage-2 strategies have been relatively effective in reducing payer expenditures, our analysis reveals that most of the savings generated to date have been captured from providers, mostly physician practices. Through a combination of reduced payments, mandatory vendor imposition, and patient self-administration, payers have lowered their costs by as much as 25 percent since early 2003. Significantly, little of this has come at manufacturers' expense.

### Stage 3: Category narrowing and preferred products

Our evidence indicates that opportunities to extract additional savings from providers have entered the area of diminishing returns, particularly as the MMA erodes practice profitability. As a consequence, payers will need to look elsewhere for savings opportunities, primarily by applying the lessons learned from small molecules to biotechnology and other specialty products.

Comparatively few payers have meaningful policies in place that are advantageous to a particular biotechnology agent or that narrow a category to only one or two effectively comparable therapies. Exceptions include Aetna, Cigna, and Keystone Mercy, which have moved to narrow their multiple sclerosis product choices, and Wellpoint, which recently narrowed the selection of TNF- $\alpha$  inhibitors on its formulary from three to two. In other cases — human growth hormone and intravenous immunoglobulin — the *de facto* commoditization of the category has prompted some

## About the methodology

Figures in this article derive from: Baker T, Rooney J. *The Spring 2004 Managed Care Injectables Index*. Millburn, N.J.: The Zitter Group. The *Managed Care Injectables Index* is a large, semiannual quantitative analysis of the management of biotech and specialty therapies by commercial payer organizations. The sample included 100 decision makers, split approximately evenly between pharmacy and medical directors. Organizations were drawn from across the United States and were a representative sample of organization types, sizes, demographics, and geography.

The study uses multiple techniques, including basic Likert scales, rank-ordering, and open-ended questions to collect information. Data are analyzed using SPSS version 9.0 (SPSS, Chicago).

manufacturers to contract for position and/or preferential status, albeit with uncertain results. To date, most payers have not successfully moved patients to a particular product, and the differences in patient cost-sharing between preferred and nonpreferred therapies have been minor or nonexistent.

Payers are exerting more pressure on manufacturers. Nearly 80 percent of payers agree that they would trade preferential position for a volume discount and, in many cases, nonpreferred agents may not have access at all. Thus, if questions remain about payers' ability to move share under a contract, few doubt their ability to block reimbursement or coverage for individual therapies. For biotech products whose annual costs exceed \$10,000, payers believe that narrowed categories are an attractive strategy to reduce biologic spending further.

### Stage 4: Benefit design and cost-sharing innovation

National data show clear evidence of rising patient cost-sharing

requirements, irrespective of how therapies are classified. Close to half of commercial payers now use tiered formularies to manage some or all biologics, generally placing these therapies in the highest tiers with copayments that average nearly \$40. Flat or nontiered copayments now average more than \$47, and cost-sharing requirements will continue to rise at a rate of 10 to 15 percent annually. As one HMO medical director told us, the "bottom line is: if costs continue to rise, copayments will continue to increase. In disorders where it's not life threatening, such as rheumatoid arthritis, cost-sharing will get to the point of the patients taking a 'longer look' to decide if they truly need the costly injectable or can 'survive' with other less costly therapies."

Herein lies the challenge for the future. As costs rise, payers will turn to more innovative benefit designs that increase patient cost-sharing burdens and provide employers with new coverage options (Vogenberg 2004a, 2004b). Payers consistently prioritize therapies that save lives, followed by those that spare disability. Other therapies, irrespec-

**TABLE** The five stages of biotechnology management

<b>1</b>	<b>Buy and bill</b>	<ul style="list-style-type: none"> <li>• Commercial reimbursement (AWP –14.21%) equivalent to Medicare rate</li> <li>• MMA provides cover and ensures consistency across payers</li> </ul>
<b>2</b>	<b>Specialty pharmacy, self-administration, and reimbursement changes</b>	<ul style="list-style-type: none"> <li>• 76% of payers report using SPP, up from 64%</li> <li>• 31% of SPP arrangements are semimandatory</li> <li>• 78% of payers seek to drive self-administration</li> </ul>
<b>3</b>	<b>Preferred products and narrowed categories</b>	<ul style="list-style-type: none"> <li>• Preferred status in some crowded categories</li> <li>• Contracts for Factor VIII, growth hormone, IVIG</li> <li>• Rapid growth in MS, RA necessitates action</li> </ul>
<b>4</b>	<b>Benefit design innovations and cost shifting</b>	<ul style="list-style-type: none"> <li>• Differentials expanding between tiers</li> <li>• Coinsurance still rare</li> <li>• Average nontiered copayment now exceeds \$40</li> <li>• Out-of-pocket maximums rising</li> </ul>
<b>5</b>	<b>Genomic diagnostics and genetic risk management</b>	<ul style="list-style-type: none"> <li>• Currently limited to antivirals, oncology, and rare diseases</li> <li>• HER2/<i>neu</i></li> <li>• Gefitinib (Iressa) as first-line therapy in NSCLC subpopulation?</li> <li>• Physician/system readiness?</li> </ul>

AWP=average wholesale price, IVIG=intravenous immunoglobulin, MMA=Medicare Modernization Act, MS=multiple sclerosis, NSCLC=non small cell lung cancer, RA=rheumatoid arthritis, SPP=specialty pharmacy provider.  
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tive of the innovative nature of their technology or the unmet medical need in the category, will be associated with more difficulties relative to providing justification for high prices. Biologic therapies for plaque psoriasis, for example, offer better outcomes for patients, but they are prescribed for a condition that is not life threatening and at costs so high as to make payers balk.

In other words, in a world of scarce resources, payers give the advantage to life-saving therapies. Other products face significant challenges with respect to communicating value that is sufficient to guarantee advantageous access.

Patients' willingness to pay increasingly must be integrated into market planning as payers pass more costs to patients. Evidence has shown not only an overall fall in utilization at higher cost-sharing levels but, increasingly, outcomes losses (Goldman 2004, Ozminkowski

2004). For payers, this raises difficult questions. For manufacturers, it means determining how to obtain favorable positioning relative to competing therapies and in absolute terms. Solo exclusive status means dramatically less when patients face a 25 percent coinsurance regime, particularly for non-life-saving or non-disability-sparing therapies. Similarly, preferred status has little value if the nonpreferred therapy has a comparable copayment.

A number of payers expect to introduce new benefit designs for specialty therapies in the next 6 to 18 months. Many already filed the necessary paperwork with state insurance commissioners and began selling the new designs in the market late last year so that the new models would take effect this year. Under these new models, intra-tier differentials widen, and coinsurance may apply to nonpreferred therapies. Although significant and difficult

questions remain about the equity of these designs — cost-sharing and, in particular, coinsurance, are highly regressive — they inevitably place greater pressure on manufacturers to demonstrate tangible (e.g., life-saving or disability-sparing) effect, to trade price for access, or to try some combination of both.

## Stage 5: Genomic diagnostics and genetic risk management

At a meeting in 2002, payers discussing the management of TNF- $\alpha$  inhibitors agreed that while the available agents might work differently in different patients, this theoretical allelic heterogeneity did not necessitate coverage of every available therapy (Baker 2003). In addition, payers indicate that the burden of proof actually lies with the manufacturers. If a case can be made for one agent over another at the mole-

cular or genetic level, then the manufacturers must demonstrate strong supportive data. Only 14 percent of payers believe "allelic heterogeneity necessitates keeping all biologic agents in a class on formulary."

On the other hand, payers cite individual products for which highly specific molecular diagnostics exist and to which access is contingent on a positive test. Perhaps most familiar is the Fluorescence in Situ Hybridization (FISH) test for HER2+ metastatic breast cancer, a positive result from which results in trastuzumab (Herceptin) therapy. While still relatively uncommon outside of oncology, virology, and a handful of rare diseases (e.g., cystic fibrosis), the flurry of merger and acquisition activity within the molecular diagnostic industry reinforces the importance of the trend.

Payers have raised questions about the overall value of costly molecular diagnostics, particularly where incumbent testing technologies may be more cost-effective (Farkas 2004). Faced with therapies that run into tens of thousands of dollars annually, molecular diagnostics increasingly represents a critical cost-saving strategy for payers.

For manufacturers, molecular gatekeeping will create new challenges, as well as greater incentives to harness the promise of pharmacogenomics. While some manufacturers view pharmacogenomics skeptically, fearing that it will unnecessarily limit sales growth, the converse may be closer to the truth. For example, although a large clinical trial failed to show that gefitinib (Iressa) confers a survival benefit for patients with non-small cell lung cancer at the population level, recently published data indicate that

patients with an extremely specific gain-of-function mutation may actually benefit from earlier, more aggressive use of the therapy (Lynch 2004). Additional analysis has identified a distinct subpopulation of likely gefitinib responders (Pao 2004), and suggests that specific somatic mutations in the tyrosine kinase domain of the epidermal growth factor receptor may predict sensitivity to gefitinib (Paez 2004). In other words, molecular diagnostics could serve to increase gefitinib utilization in patients expressing the mutation, while simultaneously providing payers with greater control over access.

#### WHAT'S NEXT?

The biologics pipeline remains flush with new technologies, many of which will carry significant price tags and treat comparatively more prevalent conditions than in the past. Concurrently, the population continues to age, placing more pressure on payers to manage cost growth more effectively. Continued double-digit premium growth cannot be sustained indefinitely, and employers and payers alike seek ways to rein in this trend. According to Medco Health Solutions, the pharmacy benefit management company, specialty spending will reach \$40 billion by the end of 2006, a growth rate twice that of the national average increase in drug spend (Medco 2004).

In this environment, payers will move along the management continuum, prioritizing therapies and placing more pressure on manufacturers to demonstrate tangible value. This will require developing more sophisticated economic models sensitive to unique and complex

mechanisms of action. It also will necessitate a more comprehensive approach to benefit design and cost-sharing. Many traditional approaches used with small molecules have significant limitations, such as high copayments. Yet, such approaches represent real constraints on producer pricing. For payers, the easy savings have been captured. Now comes the hard part. **BH**

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