

# Biopharmaceuticals: The Economic Equation

**As more biopharmaceuticals reach the market, more attention will be given to issues such as cost-effectiveness evaluations, biosimilars, and price controls. The value biologic therapies bring to the healthcare system may take years to appreciate in full—perhaps only when policy decisions allow for their economic effects to be understood.**

By Erwin A. Blackstone, PhD, and Joseph P. Fuhr Jr., PhD

The healthcare industry is taking an ever-growing share of the U.S. gross domestic product, even as health outcomes in the United States rank below those found in many other industrialized countries. Even though the United States has some of the most renowned medical facilities and offers some of the best and most sophisticated healthcare available anywhere, many people lack insurance coverage to pay for it. Meanwhile, biopharmaceuticals, in particular, and drugs, in general, are consuming a larger share of healthcare expenditures, with the former generating issues of cost and insurance cover-

*Erwin A. Blackstone, PhD, is a professor of economics at Temple University in Philadelphia. Joseph P. Fuhr Jr., PhD, is a professor of economics at Widener University, in Chester, Pa., and an adjunct research professor for the Department of Health Policy, Thomas Jefferson University, in Philadelphia.*

## CORRESPONDING AUTHOR

Joseph P. Fuhr Jr., PhD  
Widener University  
One University Place  
Chester, PA 19013  
(610) 499-1172  
joseph.p.fuhr.jr@widener.edu

age. This article discusses the complex issues that have already arisen and will become even more important.

Increased spending on pharmaceuticals has led to the current political and reimbursement issues facing the industry. This situation is likely to become even more acute for biopharmaceuticals, which are relatively costly to develop (about \$1.2 billion versus \$500 million to \$800 million for other pharmaceuticals) and to produce (Standard and Poor's 2006, Blackstone 2007).

Biologic therapies raise especially contentious issues in the current healthcare environment. Insurers and MCOs already have tried to reduce expenses for these drugs through the use of medical management, limited formularies, step therapy, prior authorization, and increased copayments, and are likely to employ additional efforts in the future.

To obtain authorization for coverage of biopharmaceuticals, a patient often must take the prescribed conventional therapies without suc-

cess. The physician must then provide substantial diagnostic information to obtain authorization from the patient's insurer for coverage (Robinson 2006). Requiring physicians to negotiate with insurance companies exacerbates the already high burden of administrative expenses on the U.S. healthcare system.

Private insurers already face rising biopharmaceutical expenses. Kaiser Permanente of California, for example, found that the share of total drug expenditures attributable to biopharmaceuticals grew from 10 percent in 2000 to 18 percent in 2005. Per-member, per-month expenses for biologic therapies increased 195 percent over the 5-year period ending in 2005 (Monroe 2006). Such increases can be attributed, in part, to biologics' comparably high acquisition costs. New biopharmaceuticals to treat rheumatoid arthritis (RA), for example, often result in annual per-patient expenses of \$12,000 or more, compared to a few hundred dollars for traditional treatments.

Biopharmaceuticals present



Erwin A. Blackstone, PhD



Joseph P. Fuhr Jr., PhD

some important issues. First, as the Economic Report of the President (2007) indicates, new technology often results in higher costs. The question is whether these costs come with commensurate benefits. If a biotech drug costs much more than a traditional pharmaceutical but provides only a slight improvement, is it worth the extra cost? One study showed a median survival gain in advanced lung cancer patients taking erlotinib (Tarceva) of only 2 months, from 4.7 to 6.7 months (Gillick 2006). This example is a strong argument for cost-effectiveness analyses, and we suspect that the rising expenditures for biopharmaceuticals will add to the pressure for policy change. Medicare has been explicitly forbidden from using such cost-effectiveness analyses (Robinson 2006). Private insurers can, of course, consider the cost-effectiveness of a new drug.

High biopharmaceutical prices raise the question of whether all insured individuals should be guaranteed access to these agents, and what the appropriate policy should be for the uninsured. Even for the insured, MCOs have raised copayments. For example, a cancer patient taking erlotinib in 2005 had annual drug expenses of \$31,000 and incurred a copayment of about \$6,000 (Berenson 2007).

## MEDICARE

Medicare is the largest purchaser of most drugs, including biopharmaceuticals, and as such, its coverage decisions can either facilitate or threaten the development of the biopharmaceutical sector. If Medicare becomes more cost-conscious

and selective about covering expensive biopharmaceuticals, drug development will be placed at greater risk. Increased scrutiny, however, may encourage companies to focus drug development efforts on medications that offer substantial improvement over existing therapies. With a competitive insurance market, consumers could choose an insurer based on drug coverage, including a particular biopharmaceutical. Unfortunately, in

## Medicare is explicitly forbidden from using cost-effectiveness analyses, but pressure to reverse that policy is expected to grow.

the case of Medicare, subscribers often have no direct choice.

Currently, biopharmaceuticals make up a small percentage of Medicare's expenditures, but their growing importance for patients with many difficult-to-treat illnesses, the expansion of pharmaceutical coverage under Medicare Part D, and the projected substantial increase in the aging population make the issues surrounding biopharmaceuticals increasingly contentious. These factors are expected to force an increase in total expenditures for biopharmaceuticals 20-fold over the next 10 years, by which time biopharmaceuticals will account for 30 percent of Part D expenditures (Gillick 2006).

Medicare generally covers biopharmaceuticals that meet its "reasonable and necessary" standard (Tunis 2006). It usually covers all

physician-administered cancer-treating biopharmaceuticals according to their U.S. Food and Drug Administration-approved label usage. These drugs are covered under Part B, not Part D. For off-label use, Medicare has discretion based on available scientific evidence and weighs the biopharmaceutical's benefits against its risks.

For most biopharmaceuticals, Medicare contractors follow the standard coverage decision of most insurers in their determination of reasonable and necessary, blurring the distinction between Medicare and private insurers. However, Medicare occasionally reviews evidence and makes national determinations about reasonableness and necessity (Carino 2006).

Biopharmaceuticals are covered under Part B if they are administered in a doctor's office or an outpatient hospital clinic. The top 5 biopharmaceuticals already account for about 30 percent of Part B spending (Engel & Novitt 2007). Under Part D, biopharmaceuticals probably will be covered substantially as well; their cost suggests that even agents that are obtained from a pharmacy and are self-administered will require out-of-pocket spending high enough to qualify a beneficiary for catastrophic coverage (in 2008, \$4,050 in out-of-pocket beneficiary spending or \$5,726.25 total covered pharmaceutical spending).

In addition, many patients must take biopharmaceuticals for extended periods for chronic conditions, such as RA. Further, biologics like epoetin alfa (Epogen) also are covered under the Medicare End Stage Renal Disease Program, a sep-

arate program from Parts B or D. Indeed, epoetin alfa has been the largest pharmaceutical expenditure under Medicare (Engel 2007).

The failure to consider the cost-effectiveness of cancer drugs is troubling and adds to the financial burden on Medicare. Illustrative of this situation is its reimbursement for darbepoetin alfa (Aranesp), a biopharmaceutical that, like epoetin alfa (Procrit, a similar but older drug), stimulates the growth of red blood cells from bone marrow (Keenan 2006). In 2003, Medicare found the drugs to be functionally equivalent and cut the reimbursement for darbepoetin alfa to the same rate as that of epoetin alfa. Congress responded by explicitly forbidding the use of functional equivalence. Again, the inability to consider cost is inconsistent with maintaining the financial viability of the Medicare system.

Providing pharmaceutical coverage for an eligible population while maintaining fiscal viability will be a substantial challenge for Medicare. Clearly, there will be a push toward allowing market access to generic or comparable biopharmaceuticals. The Access to Life-Saving Medicines Act, introduced last February, is probably a harbinger of what is to come. The act would establish an approval process for lower-cost copies of biotech drugs, and would authorize the FDA to determine, on a product-by-product basis, whether studies are needed to establish whether a new medication is clinically comparable to a brand-name agent. An argument in support of the act is the money that Medicare could accrue from allowing follow-on agents; it has been estimated that for Part B alone, aver-

age annual savings would be about \$1.5 billion (Engel & Novitt 2007).

### INTERNATIONAL

The international drug and biopharmaceutical markets differ greatly from those found in the United States. Most countries have some form of universal healthcare, with various types of price controls or profit regulation of pharmaceuticals. The United Kingdom regulates profit and, thus, indirectly the price, whereas all other European Union (EU) countries regulate prices directly. Many countries, especially EU members and Australia, use cost-effectiveness to determine the drug price, including for biopharmaceuticals (Maynard 2003). Most drugs in the EU require some form of copayment, which varies by country. Some nations issue no fees for essential medications, while others have no copayments for the poor and elderly.

Australia pioneered, and the United Kingdom has adopted, the requirement that companies submit evidence on both the costs and effects of new products. Some European Union members have begun developing requirements for basing price on cost-effectiveness. For example, in the United Kingdom, the National Institute for Clinical Excellence has determined that "On the balance of their chemical and cost-effectiveness, neither beta interferon nor glatiramer acetate is recommended for the treatment of multiple sclerosis in the NHS [National Health System] in England and Wales" (NICE 2002). Thus, the NHS will not provide any reimbursement for these treatments. In Australia, new drugs with no advantage over current medications are priced at

the same level as the existing drugs. Higher prices of superior drugs are reflective of their incremental cost-effectiveness (Gillick 2006).

The high prices of biopharmaceuticals may lead some countries to ignore patents. Less affluent nations may decide the high prices of biopharmaceuticals are too great a burden and try to find — or even fund — a generic producer even if the product is still patented. For example, Thailand and Brazil have threatened to bypass patents for an AIDS drug. The threat itself may lead manufacturers to offer sharply reduced prices to prevent such scenarios. Ignoring or bypassing patents is especially likely to occur with expensive biopharmaceuticals, and could make it difficult for manufacturers to recoup research and development (R&D) costs.

An interesting international situation may develop in the case of biopharmaceuticals. If biosimilars arise quickly in Europe, and if their prices are substantially below the cost of the innovator drugs in the United States, a strong incentive would exist for Americans to try to purchase them abroad and have them shipped, as has happened with drugs sold in Canada. Obviously, this incentive would be strongest for those individuals without insurance. Given the high prices for biopharmaceuticals, even a savings of around 30 percent could be significant (Blackstone 2007). Concerns would then arise about the drugs' safety and the FDA's authority over such activity.

### FOLLOW-ONS

High prices and expenditures for biopharmaceuticals are likely to lead to strong pressure for the pro-

duction of follow-on biologic products. Currently, the FDA has no explicit legislative authority to permit generic biopharmaceuticals — a void that would be filled by the Access to Life-Saving Medicines Act. In a March 8 hearing by the Senate Health, Education, Labor, and Pensions Committee, New York Sen. Charles Schumer, a cosponsor of the bill, recognized one primary concern about follow-on biologics: safety. The production process of biologics made from living organisms is riskier than that of chemical-based drugs. Another concern, from an economic point of view, is the importance of maintaining the delicate balance between encouraging innovation and permitting access to generics after patent protection has expired (Blackstone 2007).

The safety issue is complex because biopharmaceuticals, produced through living organisms, are much more difficult to characterize (U.S. Senate 2007a). Nevertheless, the European Economic Community (EEC) permitted the marketing of two biosimilar growth hormones — somatropin (Omnitrope) and somatropin injection (Valtropin) — in April 2006, and, as an EEC official notes, the ability to characterize biologics should improve over time, and the approval process should become more exact (U.S. Senate 2007b). The battles over permitting follow-on biopharmaceuticals will be no less intense, given the economic interests of the parties involved. Even so, society must be careful not to discourage costly innovation activities through the prevention of full-patent exploitation.

Even if follow-on biopharmaceuticals were permitted, their manufacturers would still face substantial barriers to entry. The characteristics of a biopharmaceutical are heavily dependent upon the manufacturing process, but that process typically is protected as a trade secret (Schacht 2007). The manufacturing process is far more extensive for biopharmaceuticals

### Biopharmaceutical costs will add pressure to impose price controls — pressure that is “unlikely to go away,” says one.

than chemical drugs because small changes in manufacturing can cause substantial differences in clinical properties (Schacht 2007). The FDA must approve both the biopharmaceutical itself and the process used to manufacture it. Indeed, a manufacturing facility — which typically costs between \$200 and \$400 million — must be built before FDA approval can be obtained.

Moreover, the materials used to manufacture biopharmaceuticals cost from 20 to 100 times more than those used for chemical drugs (Schacht 2007). More clinical trials are likely to be conducted for follow-on biopharmaceuticals than for chemical generics to prove their comparable safety and efficacy. Higher marketing costs for biosimilars may be incurred because of physician concerns about comparability. The results may be less generic competition in the biopharmaceutical market compared with that seen in the traditional

drug market and far smaller savings (10 to 20 percent among biologics versus 40 to 80 percent for chemical drugs) (Schacht 2007). Nevertheless, pressure to permit copies of biopharmaceuticals will be intense.

### PRICE CONTROLS

Rising expenditures for biopharmaceuticals will add pressure to impose price controls (Gillick 2006).

As Herrera (2006) notes, “The pressure in the United States for introducing prescription drug price controls is unlikely to go away.” It is difficult to justify discouraging biopharmaceutical research and development of what may be breakthrough drugs for incurable illnesses, but the burden of rising biopharmaceutical expenses within an overburdened healthcare system also poses difficult choices.

The danger is also great that price controls or regulations could discourage R&D in biopharmaceuticals. Firms assume the high cost of R&D because they expect to earn a profit (Scherer 2004). Though R&D expense as a percentage of sales in the biotechnology industry (excluding the major traditional pharmaceutical firms) has come down dramatically since its 80 percent level in the industry’s early days (Read 1994), R&D expense remains high relative to other industries, 38 percent (Ernst & Young 2007).

The potential for return on R&D spending also is quite risky. For example, despite substantial spending in this area, there were only four biologic license application approvals during 2006 (Engel & Novitt 2007). Moreover, only about 33 percent of new drugs enjoyed profits that were as high as the industry average R&D

cost (Schacht 2007). Although a few biotech companies have done exceedingly well, the sector as a whole lost \$2 billion in 2005, and the biotechnology sector has performed worse than the overall stock market; a \$1 investment in 1981 in a composite of biotechnology healthcare stocks would be worth \$8 now, compared to \$21 for the Dow Jones Industrial average (Pisano 2006).

In any event, biopharmaceutical companies have been able to raise substantial capital based on the expectation of future profit — \$27.9 billion in 2006 alone (Ernst & Young 2007). It is doubtful, however, that they can continue to raise such large amounts of capital in the face of mediocre returns. Investors may be willing to commit large sums of capital in the hope of finding another Amgen (Pisano 2006). In such a situation, the prospect of price controls on the few highly successful and profitable innovations could be especially problematic.

## CONCLUSION

Biopharmaceuticals will continue to be a large part of the healthcare industry, even as costs continue to rise. Although it spends a large percentage of its sales on R&D, the biotech industry as a whole is not yet profitable. The high cost of biopharmaceuticals will undoubtedly lead to many battles with insurance companies over coverage and reimbursement. Strong pressure is likely to be exerted to allow Medicare to use cost-effectiveness analyses. Price controls are apt to be advocated as a device to try to constrain costs. The risk-and-lottery nature of R&D and the low overall profit of the biopharmaceuti-

cal industry make such price controls problematic. The various threats to the biopharmaceutical industry could discourage innovation of potentially life-saving drugs, which must be weighed against the strong argument that biosimilars should be allowed if their safety and comparability can be assured. **BH**

## REFERENCES

- Berenson A. Costly cancer drugs bring hard decisions. *International Herald Tribune*. July 13, 2005. «<http://www.ihf.com/articles/2005/07/12/business/drugs.php>.» Accessed Nov. 16, 2007.
- Biotechnology. *Standard and Poor's Industry Surveys*. 2006:174:1–51.
- Blackstone EA, Fuhr JP. Generic biopharmaceutical drugs: an economic and policy analysis. *Biotechnol Healthcare*. 2007;4(1):43–48.
- Carino T, Williams RD II, Colbert AM, Bridges P. Medicare's coverage of colorectal cancer drugs: a case study in evidence development and policy. *Health Aff*. 2006;25:1231–1239.
- Economic Report of the President transmitted to Congress Feb. 2007. Washington: Government Printing Office. 2007.
- Engel & Novitt. Potential savings that might be realized by the Medicare program from enactment of legislation such as the Access to Life-Saving Medicine Act (H.R. 6257/S. 4016) that establishes a new CBLA pathway for follow-on biologics. Pharmaceutical Care Management Associates. January 2007.
- Ernst & Young. *Beyond Borders: Global Biotechnology Report 2007*. New York: Ernst & Young. April 2007.
- Gillick MR. Molecular medicine, the Medicare drug benefit, and the need for cost control. *J Am Geriatr Soc*. 2006;54:1442–1446.
- Herrera S. Price controls: preparing for the unthinkable. *Nat Biotechnol*. 2006;24:257–260.
- Keenan PS, Neumann PJ, Phillips KA. Biotechnology and Medicare's new technology policy: lessons from three case studies. *Health Aff*. 2006; 25:1260–1269.
- Maynard A, Bloor K. Dilemmas in regulation of the market for pharmaceuticals. *Health Aff*. 2003;22:31–41.
- Monroe DC, Potter L, Millares M, et al. Kaiser Permanente's evaluation and management of biotech drugs: assessing, measuring, and affecting use. *Health Aff*. 2006;25:1340–1346.
- National Institute for Clinical Evidence (NICE). Technology appraisal guidance no. 32, beta interferon and glatiramer acetate for the treatment of multiple sclerosis. January 2002. «<http://guidance.nice.org.uk/TA32>.» Accessed Nov. 16, 2007.
- Pisano GP. *Science Business: The Promise, The Reality, and the Future of Biotech*. Boston: Harvard Business School Press; 2006.
- Read JL, Lee KB. Health care innovation: Progress report and focus on biotechnology. *Health Aff*. 1994;13(3): 215–225.
- Robinson JC. Insurer strategies for managing use of and cost of biopharmaceuticals. *Health Aff*. 2006;25:1205–1217.
- Schacht W, Thomas JR. Follow-on Biologics: Intellectual Property and Innovation Issues. A Congressional Research Service Report for Congress, March 5, 2007. «[http://www.ipmall.info/hosted\\_resources/crs/RL33901\\_070604.pdf](http://www.ipmall.info/hosted_resources/crs/RL33901_070604.pdf).» Accessed Nov. 16, 2007.
- Scherer FM. The pharmaceutical industry: prices and progress. *NEJM*. 2004;351: 927–932.
- Tunis SR, Pearson SD. Coverage options for promising technologies: Medicare's coverage with evidence development. *Health Aff*. 2006;25: 1218–1230.
- U.S. Senate (Senate Committee on Health, Education, Labor, and Pensions). Testimony of Jay P. Siegel, MD, Group President, Biotechnology, Immunology and Oncology, Research and Development, Johnson & Johnson, before the Senate HELP Committee hearing on Follow-on Biologics, March 8, 2007a. «[http://help.senate.gov/Hearings/2007\\_03\\_08/2007\\_03\\_08.html](http://help.senate.gov/Hearings/2007_03_08/2007_03_08.html).» Accessed Nov. 16, 2007.
- U.S. Senate. Testimony of Nicholas Rossignol, Administrator, European Commission Pharmaceuticals Unit, Brussels, Belgium, before the Senate HELP Committee hearing on Follow-on Biologics, March 8, 2007b. «[http://help.senate.gov/Hearings/2007\\_03\\_08/2007\\_03\\_08.html](http://help.senate.gov/Hearings/2007_03_08/2007_03_08.html).» Accessed Nov. 16, 2007.

## DISCLOSURES

Erwin A. Blackstone, PhD, and Joseph P. Fuhr Jr., PhD, report that they have no financial arrangements or affiliations that might constitute a conflict of interest with respect to this article.