CHAPTER 5

Medicare payment systems and follow-on biologics

CHAPTER 5

Medicare payment systems and follow-on biologics

Chapter summary

Medicare spending on biologics—drug products derived from living organisms—totaled about $13 billion in 2007. Medicare pays for drugs, which includes biologics and chemically synthesized small-molecule drugs, under Part B and Part D. The top six biologics account for 43 percent of spending on separately billed drugs in Medicare Part B alone. Biologics account for a relatively small—but rapidly growing—share of Part D spending. The Food and Drug Administration (FDA) does not have an expedited approval process for follow-on versions of most biologics, so the price of these products has not fallen over time. If FDA had a process to approve follow-on biologics (FOBs), Medicare drug spending could be reduced. In December 2008, the Congressional Budget Office estimated that if the Congress established an approval pathway for FOBs, the federal government could save between $9 billion and $12 billion, depending on assumptions, over the next 10 years. Much of that savings would accrue to Medicare.

Given that Medicare spending on biologics is substantial and is expected to grow significantly, the establishment of a process to

In this chapter

approve FOBs has important implications for Medicare. We describe the issues policymakers must confront in designing a regulatory pathway for approval of FOBs. Of course, FDA would have jurisdiction over approval of FOBs. However, as a large payer for biologics, Medicare has a strong incentive to ensure that it gets value for the money it spends on these products. Thus, this chapter focuses on how the entrance of FOBs into the market could affect Medicare spending and whether changes to the Medicare payment systems would be needed to capture savings from FOBs.

Stakeholders disagree on how to design a pathway for FOBs. For example, there is debate about what data exclusivity period—the period of time after FDA approval before a follow-on competitor can submit an application for approval based on the innovator's data on safety and efficacy—would most appropriately balance the goals of achieving cost savings and maintaining incentives for innovation. Other issues raised in establishing an FOB regulatory pathway include the FDA testing requirements to determine whether an FOB is highly similar to—with the same safety and efficacy profile as—the innovator reference product and whether the agency should have the authority to determine if an FOB and an innovator product are interchangeable, signifying that the same patient could switch back and forth between the two products indefinitely with no adverse effect.

Biologics play a substantial role in Medicare Part B, with the top six biologics accounting for more than $7 billion of Medicare spending on Part B drugs in 2007. A regulatory approval process for FOBs is needed to provide more competition among biologics and generate cost savings for Medicare Part B. The amount of savings would depend in part on how biologics are treated under the Medicare Part B payment system. This chapter discusses coding and payment strategies that could be pursued to ensure that Medicare Part B benefits fully from competition between FOBs and innovator biologics. In particular, we describe three approaches that could be considered for assigning FOBs and innovator biologics to the same

billing code and authority that could be given to the Secretary to make such determinations.

In 2007, Medicare Part D spending on biologics totaled approximately $3.9 billion, or about 6 percent of Part D spending. Spending on Part D biologics has increased more rapidly than overall drug spending. Between 2006 and 2007, Part D spending on biologics grew by about 36 percent, whereas total Part D spending grew by 22 percent. Increased spending reflects, in part, higher Part D enrollment in 2007. However, prices for biologics compared with prices for small-molecule drugs also increased rapidly.

Biologics covered under Part D fall into two broad categories. The first group includes older, simpler molecules such as insulin and human growth hormone. These products may have larger markets than many of the newer biologics and are less costly for consumers, as multiple brand-name products are often available. Alternatively, newer, more complex biologics often have more limited markets and high launch prices. The commonly used newer biologics covered under Part D have seen sharp price increases since 2006. Most Part D plans list all these products on their formularies with significant beneficiary coinsurance requirements.

An approval process for FOBs is necessary but not sufficient in and of itself to generate Part D savings; the Part D benefit would also need to be structured to take advantage of the potential savings offered by FOBs. While Medicare should achieve savings on FOBs for older biologics, the current benefit structure is likely to limit savings for newer products. Biologics are generally expensive and can result in the beneficiary quickly entering the coverage gap and reaching the catastrophic limit. Plans have no risk during the coverage gap but they do have limited risk during catastrophic coverage. They may have an incentive to manage the use of these biologics but few tools with which to do so. However, Medicare would have a strong interest in reducing the government's costs of covering biologics by encouraging use of lower cost follow-on products.

Implementing a process to approve FOBs may increase competition among manufacturers of biologics, which is expected to lead to some savings for Medicare. However, given the magnitude and growth of spending for drugs, including biologics, policymakers may want to look at other ways for Medicare to achieve savings. To help improve the value of Medicare spending, we discuss three pricing strategies that use information about a drug's clinical effectiveness when paying for it under Part B and Part D:

- ***Reference pricing:*** Set a drug's payment rate no higher than the cost of currently available treatments unless evidence shows that the drug improves beneficiaries' outcomes.
- ***Payment for results:*** Link a drug's payment to beneficiaries' outcomes through risk-sharing agreements with manufacturers.
- ***Bundling:*** Create payment bundles for groups of clinically associated products and services. ■

Many high-priced new medications are biologics—that is, drug products derived from living organisms (see text box). Biologics encompass a wide range of products, including vaccines, blood and blood products, gene therapy, and recombinant therapeutic proteins. They come from a variety of natural sources and may be produced through biotechnology and other innovative methods. Medicare spending on biologics is substantial, totaling about $13 billion in 2007.[1]

Medicare Part B drug expenditures are already concentrated in biologic products, and the development of biologics covered under Part D is increasing.[2] These products generally have high launch prices and neither public nor private payers have had much leverage negotiating lower prices with manufacturers. Policymakers have proposed giving the Food and Drug Administration (FDA) the authority to approve generic or follow-on versions of biologic products that were licensed under the Public Health Service Act (PHSA). If FDA had a process to approve follow-on biologics (FOBs), Medicare drug spending could be reduced. In December 2008, the Congressional Budget Office estimated that if the Congress established an approval pathway for FOBs, the federal government could save between $9 billion and $12 billion (depending on assumptions) over the next 10 years. Much of that savings would accrue to Medicare.

In January 2009, the Commission convened a technical panel on FOBs to discuss issues related to designing a regulatory pathway for approval of FOBs. Researchers from NORC at the University of Chicago and Georgetown University conducted the meeting. Ten individuals participated in the panel, including physicians, economists, health plan executives, attorneys, a scientist, experts on Medicare payments, and consultants to brand-name and generic pharmaceutical manufacturers. Participants were selected to provide a wide range of viewpoints. They discussed the requirements for an approval pathway and how FOBs would affect the market for these products.

This chapter provides information on the issues policymakers must confront in designing a regulatory pathway for approval of FOBs. We present information on the role of the patent process administered by the U.S. Patent and Trademark Office (USPTO) and the FDA approval process in bringing FOBs to market. We describe differences between similarity and interchangeability in the FDA approval process and discuss the findings from our technical panel. We also review the literature on FOBs and the perspectives of other relevant stakeholders.

Glossary of relevant terms

Biologic: A virus, therapeutic serum, toxin, antitoxin, vaccine, blood component or derivative, allergenic product, or analogous product … applicable to the prevention, treatment, or cure of a disease or condition of human beings (PHSA § 351(ii), 42 U.S.C. § 262 (i)).

Biotechnology: Any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.

Data exclusivity: Period during which generic manufacturers are prohibited from using innovator test data submitted to the Food and Drug Administration to demonstrate the safety and efficacy of a drug to seek approval of a generic version of that drug.

Evergreening: A method by which producers of technology keep their products updated, with the intent of maintaining patent protection for longer periods of time than normally would be permissible under the law.

Highly similar: Lacking meaningful differences in terms of safety, purity, and potency.

Immunogenicity: The property enabling a substance to provoke an immune response or the degree to which a substance possesses this property.

Interchangeable: Comparable to the reference product and expected to produce the same clinical result as the reference product in a given patient.

Patent: The grant of a property right to the inventor, issued by the Patent and Trademark Office.

Reference product: Brand-name product with which a generic or follow-on product is compared to ensure safety and efficacy. ■

Policymakers must make decisions on both the requirements for approval of these products and ways to ensure that Medicare payment systems can capture savings from competition between innovators and FOBs. Of course, FDA has jurisdiction over approval of FOBs. However, Medicare is a large payer for biologics and it has a strong incentive to ensure that it gets value for the money it spends on these products. Thus, we focus on how the entrance of FOBs into the market could affect Medicare spending. We analyze Part B and Part D drug claims and consider changes to Medicare payment systems that might increase Medicare's ability to achieve savings with FOBs. Finally, we look at other ways Medicare can take value into account when setting payment rates.

Biologics, patents, and FDA approval process

Biologics and small-molecule drugs differ in many significant ways. Because of these differences, FDA faces scientific and regulatory challenges in developing an approval pathway for FOBs. Challenges include:

- balancing incentives for innovation with encouraging competition
- ensuring product safety
- developing standards for product similarity

How biologics are different

Unlike chemically synthesized (or small-molecule) drugs, biologics are large, complex molecules derived from living organisms. The Public Health Service Act defines a biologic as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood component or derivative, allergenic product, or analogous product … applicable to the prevention, treatment, or cure of a disease or condition of human beings."[3] Typically, biologics are provided as injections or are infused directly into a patient's bloodstream. They often require special handling such as refrigeration. They may be more costly to produce than synthetically produced drugs, and they are more difficult to assess for a high degree of similarity after they have been produced.

Physicians have been using biologics—such as vaccines, blood products, and hormones—for many years. However, advances in science over the last 30 years have resulted in the development of more complex biologics produced through the use of biotechnology. In 1982, Eli Lilly marketed the first artificially produced human insulin product. As technology evolved, more complex molecules have been produced to treat diseases like cancer, anemia, chronic kidney disease, rheumatoid arthritis, and multiple sclerosis. More than 400 biologic drug products and vaccines are in clinical trials, accounting for more than one-third of all medicines in development (BIO 2009, Novartis 2008).

Biologics, like all medications, have safety issues associated with them. For example, most biologics have some immunogenicity—the ability of a substance to stimulate the body's immune response, generating antibodies. For many products, immunogenicity does not result in any clinically relevant effects, but, in rare cases, it can cause severe adverse reactions including life-threatening side effects (Siegel 2007). For example, FDA recently notified the public that several patients contracted a rare brain infection after taking efalizumab, a biologic used to treat psoriasis. Any FOB should have to meet standards for immunogenicity. However, severe adverse reactions may be very rare and even large-scale clinical trials may not uncover a problem before a product is approved for sale. Some analysts have suggested that postmarketing surveillance for all new biologics, including FOBs, may be warranted.

On the other hand, some have argued that the differences between biologics and small-molecule drugs are exaggerated. For example, brand-name products and their generic counterparts may differ, within an acceptable range, in how quickly the body absorbs them. Additionally, safety risks are associated with all pharmaceuticals. For this reason, some policymakers advocate wider postmarketing surveillance of all drugs.

Because of the large size and complexity of biologics, some stakeholders argue that manufacturers cannot produce a follow-on product that is identical to the original or reference product. FDA has identified a number of potential sources of variability among biologic products:

- Biologic proteins are often composed of mixtures of molecules that can vary slightly in their structure.
- Artificially engineered products can vary slightly from lot to lot even when the same manufacturing process is used.

- Natural biologics can also vary depending on the variability of the source material and the process used to extract and purify the product (Woodcock et al. 2007).

Other stakeholders argue that the extent to which manufacturers can produce a biologic that is identical to a reference product must be determined on a case-by-case basis. In some cases, current analytical techniques can measure beyond the molecule to the nanoparticle level, potentially allowing manufacturers to demonstrate that two biologics are identical.

Small differences in products can affect the intellectual property rights of the innovator because biologic development leads to different kinds of patents than those obtained for small-molecule drugs. Depending on the properties of the molecule and the production process, patent protection can provide more protection to innovators or no protection at all. Thus, some stakeholders assert that a regulatory pathway for biologics should differ from that applied to small-molecule drugs in terms of intellectual property rights, data exclusivity, and similarity of products.

Intellectual property protection: Data exclusivity and patents

Different organizations have responsibility for drug approvals and patent rights. FDA approves drugs but patents are awarded under the Patent Act and administered by the USPTO. These processes have different requirements and provide different protections. FDA approves drugs that meet standards for safety, effectiveness, and quality. For most new products, manufacturers must support their application with clinical data, safety reports, manufacturing standards, and other relevant information.[4] Manufacturers may market their products after they receive FDA approval. Examiners at the USPTO award patents on the basis of utility, novelty, and nonobviousness. Patent applications must include specifications that describe the invention so that skilled artisans can produce it without undue experimentation (Schacht and Thomas 2008). Patent holders can exclude competitors from the market for 20 years from the date the application was filed. In the case of drugs, the inventor generally files for patent protection before FDA approves a product.

The Drug Price Competition and Patent Term Restoration Act of 1984 amended FDA law to protect new drugs and to encourage generic competition. For example, manufacturers of new drugs, including biologics, receive patent term extensions for a portion of the time spent seeking FDA approval. (See text box, pp. 110–111, for more information about the 1984 law.) In addition, the innovator company is granted five years of data exclusivity—the period of time after approval before FDA can rely on an abbreviated regulatory filing based on the innovator's evidence of safety and efficacy in evaluating a follow-on product. Stakeholders disagree about how these issues may affect biologics given the potential dynamics of this market and the different nature of patent protection for these products.

Grabowski estimates that manufacturers require between 13 and 16 years to recoup the development costs of a new biologic, and the Biotechnology Industry Organization has used that estimate to assert that at least 14 years of data exclusivity are essential to provide adequate incentive for new investments (Grabowski 2008). They argue that innovators must attract investment capital to pay for the development costs and that investors will be reluctant to enter this market without the guarantee of a sufficient period of data exclusivity.

Brill presents an alternative case (Brill 2008). Depending on assumptions, he estimates a break-even point of less than nine years and suggests that "seven years of data exclusivity would be sufficient in maintaining strong incentives to innovate while fostering a competitive marketplace." Kotlikoff makes a similar argument, stating that lengthy exclusivity provisions would delay entry of low-cost alternatives and discourage competition (Kotlikoff 2008). Brand-name companies have little incentive to improve their products without the threat of imminent competition.

At issue is how long a period of data exclusivity is necessary to promote innovation and foster competition. There was a range of opinions among members of the Commission's technical panel on an appropriate time frame. The panel did not reach consensus on this issue.

Some panelists argued that the uncertainty surrounding patents complicates the entry of follow-on products. Biologic products tend to have more patents than small-molecule drugs, and the patents may be filed over several years. Patents may be held by multiple parties including research institutes and academic institutions. Patents may cover not just the product but also the production process and even the research tools used to develop it (Harbour 2007). Yet the product itself, as a naturally occurring entity, may not always be patentable in the same way as a small-molecule drug.[5] Additionally, innovators may not

The Drug Price Competition and Patent Term Restoration Act of 1984 created a streamlined process for generic drug approvals and extended patent protections to innovator drugs

The Drug Price Competition and Patent Term Restoration Act of 1984 sought to balance incentives for innovation by research-based pharmaceutical companies and opportunities for market entry by generic drug manufacturers. Key provisions of the law include:

- Creating an abbreviated approval process for generic drugs and testing generic drugs before the innovators' patents expire.
- Extending the patent protection of a brand-name drug to provide incentives to develop new drugs. It also compensates for delays that might occur as a result of regulatory review.

Changes to the approval process for generic drugs

Before 1984, generic drugs were subject to the same approval requirements as innovator drugs. The Food and Drug Administration (FDA) did not have a streamlined process by which to approve generic products of brand-name drugs whose patents had expired. By 1984, there were approximately 150 brand-name drugs whose patents had expired that had no generic equivalent (FTC 2002).

The Drug Price Competition and Patent Term Restoration Act of 1984 removed the duplicative testing requirements for generic drugs. Generic manufacturers can rely on the innovator company's data to demonstrate that their drug is bioequivalent to the innovator drug. It also gives a 180-day marketing exclusivity period to the first generic manufacturer to file an application with FDA.[6]

In addition, the law reversed a 1984 court ruling and allowed generic manufacturers to initiate the clinical tests required for FDA approval of their product before the reference innovator drug's patent expires. Before the Drug Price Competition and Patent Term Restoration Act of 1984, a generic company could not begin the required FDA approval process until after the patents on the innovator drug had expired. To begin the process earlier would have infringed the brand-name company's patents.

Thus, the law increased the probability that a generic copy would become available after patent expiration. It also reduced the average delay between patent expiration and generic entry from more than three years to less than three months (CBO 1998).

Changes to the length of patents for innovator drugs

Before passage of the Drug Price Competition and Patent Term Restoration Act of 1984, the effective terms of many drug patents were shortened because of the time required to conduct clinical trials and FDA's review of the information submitted by the

(continued next page)

provide sufficient information so that a "skilled artisan" can create the product. For example, they may not be willing to provide functional cell lines as part of their patent disclosure materials (Noonan 2008). Courts have invalidated patents for these reasons.

Some panelists were concerned that approval of FOBs could also result in practices by brand-name manufacturers to extend data exclusivity or patent rights. For example, manufacturers might increase their use of "evergreening"—a term used for the practice of making marginal improvements to existing drugs. They reported that the practice is common in the small-molecule market. Biologic manufacturers have had little need to use this practice because they have not faced any competition from FOBs.

For any given product, patent length or data exclusivity may provider longer protection. Extensive litigation around patents—particularly patents filed at different

The Drug Price Competition and Patent Term Restoration Act of 1984 created a streamlined process for generic drug approvals and extended patent protections to innovator drugs (cont.)

manufacturer about a drug's safety and efficacy. Under this law, drugs that contain a chemical entity never approved by FDA can qualify for an extension of the patent. These extensions, granted after the drug is approved, equal half of the time the drug spent in clinical testing (usually six to eight years) plus all the time associated with FDA review (usually about two years). The patent extension cannot be longer than 5 years and cannot exceed 14 years after the drug is approved. This provision of the 1984 law also applies to biologics.

The Drug Price Competition and Patent Term Restoration Act of 1984 includes other provisions that postpone generic competition. One provision—referred to as data exclusivity—is the requirement that competitors wait five years after an innovator drug is approved before filing an application to sell a generic copy. This requirement benefits drugs that have no patent or that have very little time left under patent when they are approved. That exclusivity provision, together with the patent-term extensions, postpones generic entry by an average of 2.8 years for all drugs approved that contain a new chemical entity (CBO 1998).

The Drug Price Competition and Patent Term Restoration Act of 1984 also grants innovator companies a 30-month stay (postponement) if they file suit for patent infringement when a generic manufacturer submits its application to FDA. This 30-month stay allows the patent holder the opportunity to assert its rights in court before the generic competitor is permitted to enter the market.

Other exclusivity provisions that may postpone generic competition include:

- the Orphan Drug Act of 1983, which grants a 7-year marketing exclusivity period to drugs that treat diseases affecting fewer than 200,000 people;
- the FDA Modernization Act of 1997, which provides a research incentive of six months of additional marketing exclusivity for manufacturers that conducted studies of drugs commonly used to treat children; and
- a three-year period of exclusivity granted by FDA for new indications or dosage forms of a previously approved drug. ■

points in time, with different expiration dates—can last longer than a data exclusivity period. On the other hand, if a new biologic is not patentable, a manufacturer's data exclusivity is the innovator's only protection against immediate competition.

Some panelists argued that data exclusivity and patent issues are not the most important considerations in creating market competition, despite the attention these issues receive in the public debate. Instead, they argued, the design of FDA's approval process, and whether drugs will be considered highly similar or interchangeable, will be the key to making the market attractive to follow-on manufacturers. That is, FDA's decisions will determine how successfully the manufacturers will be able to compete with the innovator products they are challenging.

FDA's role determining product safety, similarity, and interchangeability

As with all drugs, safety risks are associated with biologics, and FDA must ensure that FOBs meet the safety and efficacy profile of their reference product. Any proposed regulatory pathway would require FDA to make a determination of a high degree of similarity or comparability. FDA defines comparability as "the comparison by the manufacturer of a biological product before and after a manufacturing change to demonstrate that the safety, identity, purity, and potency remain unchanged" (Behrman 2008). Assessing comparability (or, in the case of FOBs, a high degree of similarity) requires more sophisticated tools than are needed to approve generic drugs.

Before the mid-1990s, FDA required the licensing of specific manufacturing sites when manufacturers of innovator biologics made any changes to their product or production processes. Because of the time and expense involved in meeting FDA requirements, manufacturers were reluctant to make even small improvements. However, scientific advances in manufacturing techniques and comparability testing have ameliorated this situation. In 1996, FDA, working with the biotechnology industry, introduced comparability protocols to support product changes. The protocols outline a series of laboratory tests required on a case-by-case basis to ensure that manufacturing changes have not compromised the safety and efficacy of the product. Products produced under different manufacturing conditions are analyzed for structural, chemical, and biological differences. FDA determines whether differences between the products are significant enough to require additional testing. In some circumstances, it will require clinical testing in the sense of assessing how the product affects blood levels in various tissues or the short-term impact of the product in animals or humans. These tests, although clinical, are not equivalent to long-term clinical outcome studies. At any stage of this process, FDA may determine that the two products are not comparable and end the testing (Novartis 2008, Schwieterman 2007).

Testifying before the Congress in 2007, former FDA scientist William Schwieterman said: "These scientific principles [comparability protocols] not only allow for insignificant postapproval brand-name product changes, but also very significant manufacturing changes, such as cell-line replacements, manufacturing facility site changes and the like."

Using these protocols, FDA approved a follow-on version of human growth hormone, a biologic that—for unique historical reasons—was originally approved through a new drug application (NDA) and regulated under the Drug Price Competition and Patent Term Restoration Act of 1984, which gave the agency authority to approve generic or follow-on products that were originally approved through NDAs. This product is now on the market in the United States as well as in Europe. With congressional authority, FDA could use the same protocols to decide that other FOBs and their reference products are highly similar, meaning that there are no clinically meaningful differences in terms of safety, purity, and potency. The extent of the testing required for this determination will affect the incentives for innovation and competition as innovator firms and their competitors both seek to introduce follow-on products.

With congressional authority, the agency could also determine that an FOB is interchangeable with its reference product.[7] Interchangeable products are expected to have exactly the same clinical result in the same patient—that is, the patient could switch back and forth between the two products indefinitely with no effect. If FDA designates two products as interchangeable, it will have implications for costs and competition. For example, in the small-molecule drug market, most states have instituted rules that allow pharmacies to substitute with the generic product without consulting with the prescriber.

There was some debate within our technical panel about whether the science exists to demonstrate interchangeability. Many believe advances in the methodology for assessing biologics will make this determination possible over time. They argued that the Congress needs to give FDA clear authority to make interchangeability determinations if they want to maximize the potential savings that could be created by competition from FOBs.

How FOBs will affect competition is not known

Analysts cannot yet determine how the entrance of FOBs into the market will affect competition and prices. Because the market has yet to develop, policymakers estimate impacts based on the effect generic small-molecule drugs have on competition and how that effect differs from current competition among biologics. In assessing the potential effect of FOBs, our panelists considered a number of factors including:

- the effect generic drugs have had on the small-molecule drug market,
- the size of the market for biologics,
- acceptance of FOBs by physicians,
- efforts by payers to promote the use of FOBs, and
- reactions of pharmaceutical manufacturers.

Generic drugs and the market for biologics

In the small-molecule drug market, manufacturers of generic products charge lower prices to capture market share. Prices fall most rapidly when a number of generic

versions of a brand-name product are on the market. Because generics are considered interchangeable, payers can negotiate with manufacturers with confidence that the lowest priced product is equivalent to the highest priced product. Charging FDA with determining that FOBs are interchangeable with their reference products could also lead to rapid price decreases in biologics.

For some biologics, however, the market is relatively small, which may be a barrier to entry: FOB manufacturers may be concerned that there are too few potential customers to recoup their costs if they have to charge lower prices to attract market share. In addition, the costs of manufacturing biologics may make companies without experience in this field more reluctant to enter the market. For these reasons, there may be a limited number of FOBs for a particular reference product, which could affect the potential savings for FOBs relative to the expense of generic drugs.

Price competition also occurs among brand-name manufacturers of competing but not interchangeable drugs in a therapeutic class. For example, health plans may negotiate lower prices for one statin and favor it on their formulary over another even though the two products are not identical. One panelist noted that, in biologic classes, this practice is less common. A certain percentage of people may have an adverse reaction to one biologic in a class and a certain percentage will not be helped by the product. This situation is more common with biologics than with other drugs—in part due to the characteristics of biologics, such as the risk of causing immune system reactions. However, some price competition does exist in Medicare Part B.

In their estimate of the extent of competition that could be expected as a result of one approach to follow-on legislation (S. 1695), the Congressional Budget Office assumed that a follow-on product would gain a 10 percent share of its market in the first year it becomes available and 35 percent by the fourth year on the market (CBO 2008a), resulting in price discounts of 20 percent to 25 percent in the first year and 40 percent in the fourth year.

Will doctors prescribe follow-on biologics?

The success of FOBs in the market depends on whether physicians trust the products and are willing to prescribe them for their patients. Physicians are likely to be influenced by the findings of FDA and the decisions of key opinion leaders in their specialty. Innovator companies, generic companies, patients, and payers are also likely to try to influence their decisions.

Physicians may be cautious about prescribing FOBs that have newly entered the market. Some members of our technical panel drew a clear distinction between prescribers' behavior. They may be willing to start patients on a new product but unwilling to switch patients who are stable on one product to another. If FDA does not determine that an FOB is interchangeable with the innovator product, this distinction could be important. In that case, follow-on products may be treated more like an additional product in the same class rather than the same product produced by a different manufacturer. Physicians are unlikely to switch existing patients to an FOB but may consider prescribing the new product for new patients. If the FOB is less expensive, patients may want to use it and get treatments that otherwise are unaffordable.

Several panelists noted the importance of manufacturers' direct marketing to physicians in maintaining physician prescribing for brand-name drugs. Just as they do with small-molecule drugs, manufacturers may make the case to physicians that FOBs are not truly similar to the innovator product. One panelist who has been watching the biosimilar process in Europe stated that manufacturers are pursuing this strategy there. They are saying "These drugs aren't the same, just similar." This marketing strategy could limit physician adoption of FOBs (see text box, pp. 114–115).

Payers may prefer follow-on biologics

Because new biologics tend to be expensive, payers have an incentive to encourage physicians to prescribe FOBs. For small-molecule drugs, public and private efforts have been made to counteract physicians' slow adoption of generics. Many states have laws that allow or require automatic substitution of the generic at the point of sale. Elsewhere, health plans may give pharmacists incentives to contact the physician's office for permission to fill a prescription with a generic alternative, including generics to replace competing brand-name drugs in the same class. Health plans also give enrollees an incentive to ask their physicians about generics. For example, the median cost sharing charged by stand-alone Medicare Part D plans for 2009 is $7 for a generic, compared with $38 for a preferred brand-name drug or $75 for a nonpreferred drug (Hoadley et al. 2008). Many plans also remove the brand-name version from their formularies when a generic becomes available. As one panel participant who works for a health plan described: "You start [the patient] on the generic so that they don't get started on the brand,

Follow-on biologics: The European experience

In 2005, the European Union (EU) adopted legislation that established the world's first explicit regulatory approval pathway for FOBs (called "similar biological medicinal products" or "biosimilars" in Europe) (EU Directive 2004/27/EC). The European Medicines Agency (EMEA) later released regulatory guidelines to govern the approval of biosimilars. In 2006, Omnitrope, a version of somatropin, became the first biosimilar to be authorized by the EMEA in accordance with the EU's legal framework (MIP 2008). As of June 18, 2008, the EMEA had approved more than 10 biosimilar products (MIP 2008).

The EU uses a case-by-case approach

According to EU law, the EMEA must review each biosimilar application individually to determine the degree and type of preclinical and clinical data required for the approval of each product. This case-by-case approach reflects the range of molecular complexity among biologic products. Depending on the product class-specific scientific determination made by the EMEA, any given biosimilar application could, in theory, require as few data as a generic small-molecule drug application or as many as a full, stand-alone application.

EU law grants manufacturers 10 to 11 years of market exclusivity for biologic products

European law applies the same data and market exclusivity periods to all medicinal product applications submitted to the EMEA. Manufacturers are granted eight years of data exclusivity for each product, which means that—during the first eight years after a drug is approved—disclosure of data to a competitor is prohibited, as is regulatory reliance on such data. Furthermore, during this time competitors are prohibited from entering the market, even if they submit original data. Once the eight-year period of data exclusivity expires, competitors may use innovator data to file biosimilar applications but cannot bring biosimilar products to market for another two years. An additional year of market exclusivity may be granted if a new indication is discovered during the initial eight-year data exclusivity period. This "8+2+1" exclusivity scheme allows for a maximum of 8 years of data exclusivity and 11 years of market exclusivity.[8] New combinations of old medicinal products are treated as new products eligible for 8+2+1 years of exclusivity.

European law does not treat biosimilars as biogenerics

Under European law, biosimilars are distinct from generic products. Consequently, biosimilars are not seen as universally interchangeable with innovator products, as generics are, and decisions about substituting a biosimilar for its reference product are made at the national level (EMEA 2005). Nearly all EU member states limit substitution to some degree, but specific provisions governing substitutability vary. Several countries prohibit automatic substitution of

(continued next page)

and prescribing physicians get used to that very quickly, because they know they'll get back [from us] that the generic is covered."

Medicare also has the power to steer physician prescribing within Part B by using financial incentives. Whether states, plans, and the federal government are willing to make these policies to require or encourage the substitution of an FOB for the innovator product will likely depend heavily on what FDA says about similarity.

Biologics and Part B

While the development of a regulatory pathway for FOBs clearly lies within FDA's jurisdiction, Medicare has a strong interest in the potential outcome of such a pathway. Medicare Part B spending on biologics is substantial. In 2007, the top six drugs that accounted for the most Medicare Part B spending were biologics. By themselves, these 6 biologics accounted for more than $7 billion of nearly $17 billion in total Medicare Part B spending on the

Follow-on biologics: The European experience (cont.)

biosimilars (e.g., France, Germany, Spain), others have guidelines that caution against substitution (e.g., Denmark, Norway), and still others require that physicians prescribe medicines by brand name to ensure that patients receive the appropriate product (e.g., Austria, Greece, United Kingdom). In nearly all EU nations, the responsibility to determine the appropriateness of substitution rests in the hands of physicians.

Although European biosimilars are not treated as biogenerics, EU law does allow for an eventual shift in this paradigm, pending scientific advancement.

The EMEA takes steps to maximize patient safety

The EMEA requires that every manufacturer of medicinal products for human use develop a plan for continuous postmarketing pharmacovigilance to ensure that its products do not exhibit immunogenicity problems or provoke other adverse reactions once on the market. This stipulation is particularly important in the case of biosimilars, as they are more likely than small-molecule drugs to react to slight manufacturing changes that may not be detected in clinical trials.

In addition to the manufacturer-based system, each member state has implemented its own national pharmacovigilance system for collecting and evaluating information relevant to the risk–benefit balance of medicinal products in its territory. Furthermore, the EMEA has developed a centralized computer database called EudraVigilance to be used for data collection, management, and sharing among member states.

Biosimilars in Europe have launched at lower prices than their reference products

The EMEA has approved more than 10 biosimilars and has denied authorization to 2. Approved substances include human growth hormone, epoetin, and filgrastim. These biosimilars have entered the market at prices that are, overall, 15 percent to 25 percent lower than those of their reference products (Towse 2008).

Developments elsewhere

New regulatory frameworks and biosimilar guidelines are in development in Canada and Japan. Additionally, the World Health Organization has issued draft guidelines to be used by countries that may not have the capacity to develop their own legal frameworks. ■

roughly 650 Medicare Part B separately paid drugs (Table 5-1, p. 116). If a regulatory approval process for FOBs is established, FOBs would likely provide competition for innovator biologics, generating cost savings to Medicare Part B and beneficiaries. Lowering the cost of expensive biologics could also increase access to these products for some beneficiaries. The amount of savings Medicare Part B would realize from FOBs would depend on a variety of factors, including the way FOBs are treated under the Medicare Part B payment system.

How biologics and small-molecule drugs are paid and coded under Medicare Part B and the effect of price competition among products can be instructive with regard to Medicare payment for FOBs. The level of potential program savings resulting from FOBs would depend, in part, on the approach used to code and pay for these products. This section discusses coding and payment strategies that could be pursued to ensure that Medicare Part B benefits fully from competition between FOBs and innovator biologics. Changes to the Medicare statute may be needed for Medicare to adopt these approaches.

How Medicare pays for and codes Part B drugs

Most drugs covered by Medicare Part B are physician-administered drugs. Physicians purchase them in the marketplace and administer them to patients. In accord with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), the Medicare program pays physicians for drugs covered by Medicare

TABLE 5–1

The top six biologics account for more than $7 billion in Medicare Part B drug spending in 2007

Biologic	Primary indication(s)	Medicare Part B spending, 2007 (in billions)
Epoetin alfa	Anemia	$2.6
Darbepoetin alfa	Anemia	1.3
Rituximab	Cancer, rheumatoid arthritis	1.1
Bevacizumab	Cancer	0.8
Infliximab	Rheumatoid arthritis, Crohn's disease	0.8
Pegfilgrastim	Cancer	0.8
Total		7.3

Note: Figures do not sum to total due to rounding.

Source: MedPAC analysis of Medicare Part B claims data for physicians and suppliers, hospital outpatient departments, and end-stage renal disease facilities.

Part B at a payment rate equal to the average sales price (ASP) plus 6 percent.[9,10] The ASP reflects the manufacturer's average price for sales to all purchasers (with certain exceptions) net of all rebates, discounts, and price concessions.[11] Regardless of the price the physician pays a wholesaler or distributor for the drug, Medicare pays the physician 106 percent of ASP, which gives the physician a financial incentive to seek the lowest available price for the product.

In establishing payment rates for drugs, Medicare assigns drugs to billing codes. Typically, each billing code refers to a unique form and strength of a biological or chemical entity. All products assigned to the same billing code receive the same payment rate. For a multiple source drug (i.e., a small-molecule drug that has both brand-name and generic versions), the brand-name and generic products are included in the same billing code and receive a payment rate equal to 106 percent of the volume-weighted average ASP for all manufacturers' products. The MMA requires that biologics and single-source drugs (i.e., brand-name small-molecule drugs without a generic version) be paid based on their own ASP and not averaged with other products. Consequently, these products receive their own billing code. Before the MMA, CMS had grouped a small number of closely related single-source drugs and biologics in the same billing code and paid all products in the billing code the same rate. The MMA grandfathered any billing codes that grouped different manufacturers' single-source drugs and biologics together as of October 1, 2003, and continued to pay these products at the same rate, now based on the average ASP for all products assigned to the code. Any new single-source drug or biologic that enters the market after October 1, 2003, is required to receive its own payment rate. Once a small-molecule generic drug enters the market, the single-source drug becomes a multiple-source drug and receives a payment rate based on the average ASP for the brand-name and generic products.

Competition among Part B biologics

Competition among Medicare Part B biologics has been quite limited because of the lack of clinically similar products on the market. However, erythropoiesis-stimulating agents (ESAs) are an example of an area where price competition has occurred in Part B. ESAs are used to treat anemia in cancer patients as well as patients with end-stage renal disease and certain other conditions. Two different ESAs marketed in the United States are used for cancer patients. In our site visits to oncologists in 2005 for our report to the Congress on the impact of the ASP payment system, we heard from oncologists that the two ESA manufacturers engaged in significant price competition to encourage oncologists to choose their product over their competitor's. During 2005, the first year of the ASP payment system, the Medicare payment rates for the two ESA products declined steadily each quarter, with total decreases in 2005 of 13 percent and 14 percent, respectively, likely reflecting this competition. The ASPs for these products later oscillated but overall trended downward, until mid-2008 when the prices of both products began to increase moderately.

Competition among Part B small-molecule drugs

Competition among small-molecule drugs covered under Medicare Part B is more common, particularly among products with generic alternatives. Medicare assigns generic and brand-name versions of the same drug to the same billing code, which fosters competition. Because all brand-name and generic versions of a particular drug receive the same payment rate based on the average ASP for all products, physicians have a financial incentive to seek the lowest priced product available. A two-quarter lag in the ASP payment rates further promotes competition among brand-name and generic versions of a drug. For example, the Medicare payment rate for the third quarter of the year is based on the ASP for the first quarter of that year. As a result of the lag, during the first two quarters generic drugs are on the market, they are paid based on the higher ASP for the brand-name product. Therefore, the Medicare payment rate typically is substantially higher than the physician's acquisition costs for a generic drug during the first two quarters generic drugs are on the market, creating a substantial incentive for physicians to purchase it. After generics have been on the market for two quarters, their prices are represented in the ASP data used to calculate the product's ASP payment rate, typically resulting in a substantial decline in Medicare's payment rate for the product. This situation creates further incentives for use of the generic product and spurs additional price competition among manufacturers to obtain market share.

The savings can be substantial when generic drugs come on the market. For example, a major chemotherapeutic drug, which accounted for more than $100 million in Medicare Part B spending in 2007, became generic in 2008. Between 2008 and 2009, the Medicare payment rate for the product declined by more than 85 percent. As another example, since generic versions of an intravenous antibiotic drug were introduced in 2006, the Medicare payment rate has declined by nearly 80 percent.

When several brand-name drugs exist to treat a condition, the entry of generic versions of one brand-name drug can generate competition for all brand-name drugs in the class. An example of this situation is a class of intravenous drugs to prevent or treat chemotherapy-induced nausea and vomiting. There are four brand-name drugs in this class; each is a different chemical entity and has its own billing code: dolasetron, granisetron, ondansetron, and palonosetron (Figure 5-1, p. 118). After generic versions of ondansetron became available, Medicare's payment rate for it dropped substantially (as that payment rate is based on the volume-weighted ASP for the brand-name and generic versions of that drug). The other three drugs in that therapeutic class each continued to receive separate payment rates based on each one's ASP.[12] Since the availability of generic versions of ondansetron, the ASPs for the other three drugs in the class have declined, although not nearly as much as the ASP for ondansetron.

The percentage savings from the entry of FOBs would not be expected to be as great as the savings obtained from generic drugs. Nonetheless, the generic drug examples illustrate some of the same market forces that are likely to be present with FOBs. The example of nausea drugs shows that when a generic product has the same billing code as the brand-name product, large decreases occur in the Medicare payment rate for that drug, and more moderate price decreases often result for other products in the same therapeutic class that have different billing codes, because of the effects of competition. The degree to which products are viewed as clinically similar affects how much price competition is likely to take place throughout the therapeutic class.

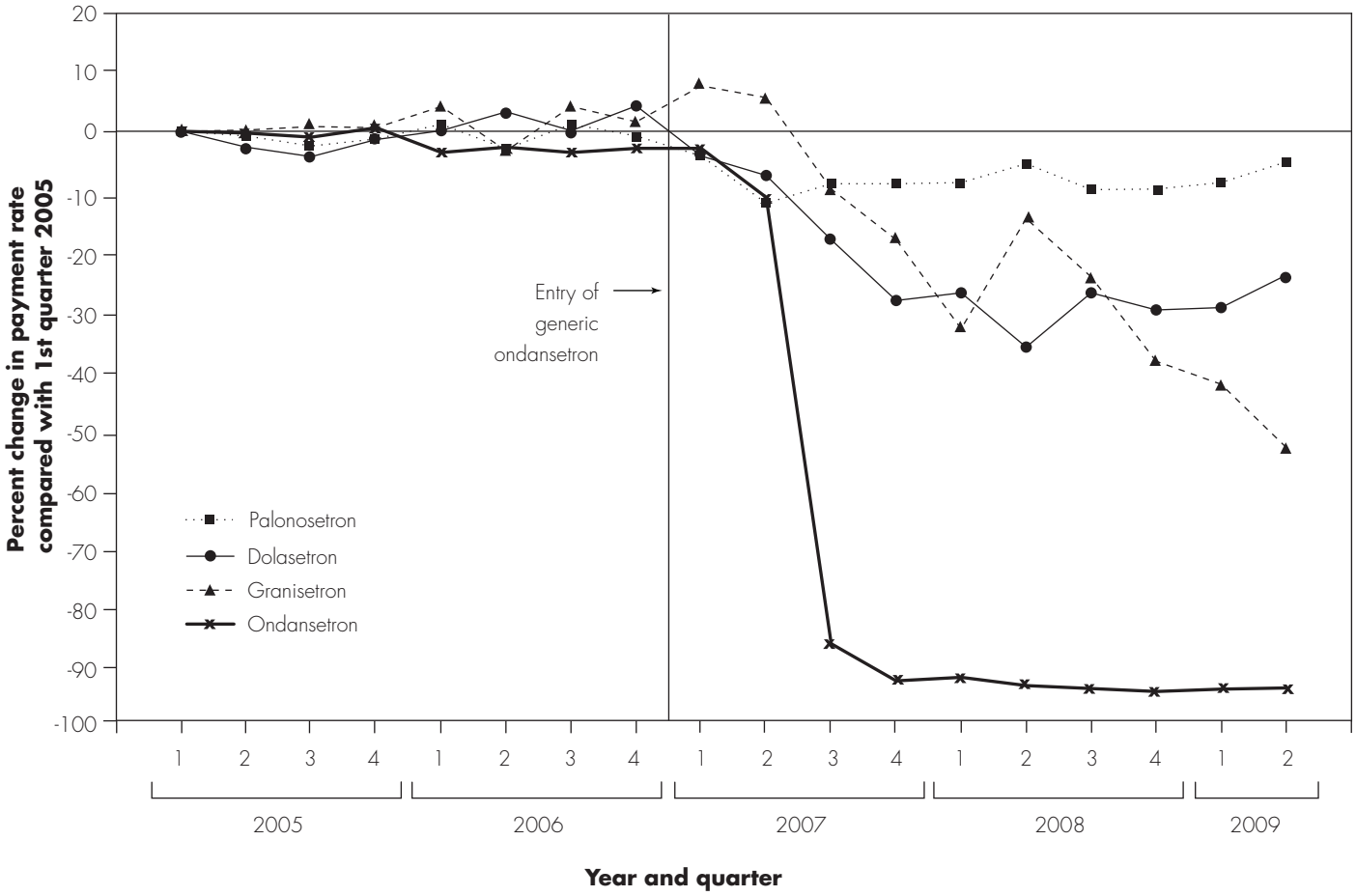
Potential for additional savings from coding changes

The extent to which a regulatory pathway for FOBs could achieve savings in Medicare Part B would depend in part on how these products are coded and paid under the Medicare Part B payment system. Currently, the statute requires that each biologic paid for under Part B receive a separate payment rate based on the product's ASP; consequently, each biologic has its own billing code.

Overall, assigning FOBs and innovator biologics to the same billing code would be expected to generate more competition among products and yield greater savings than assigning them to separate billing codes. Putting an FOB in the same Medicare Part B billing code as the innovator biologic would create incentives to use the lower priced product. Conversely, FOBs and innovator biologics assigned to separate codes and paid based on their individual ASPs in some cases may create financial incentives to use the more expensive product, as the 6 percent paid by Medicare in excess of ASP is larger for a more expensive product.[13] (In the aggregate, some savings would be expected to occur, however, since FOBs are expected to cost less than the innovator biologic). The Congressional Budget Office estimated that over the 2010–2019 period, an abbreviated FOB approval process would lead to federal savings of $9 billion if FOBs were

FIGURE 5–1

Example of generic entry causing a sharp decline in the Medicare payment rate for a drug, with moderate decreases among other drugs in the class



Source: MedPAC analysis of the quarterly average sales price drug pricing files. http://www.cms.hhs.gov/McPartBDrugAvgSalesPrice/.

assigned to separate Medicare Part B billing codes and $12 billion if they were assigned to the same billing code as the innovator biologic (CBO 2008b).

The clinical appropriateness of coding and payment of FOBs is an important consideration. FDA approval of an FOB would reflect the agency's judgment that any differences between the FOB and innovator biologic do not affect the safety and efficacy of the product. However, it would not necessarily mean that an individual patient could switch back and forth between the FOB and innovator biologic. Thus, placing FOBs and innovator biologics in the same billing code may raise concerns about the incentives for switching an individual patient from one product to another. As mentioned previously, members of our technical panel indicated that physicians would be more likely to start new patients on FOBs than to switch existing patients who are stable on one product to another one.

If policymakers choose to assign an FOB to the same billing code as the innovator biologic, one question would be what criteria should be used to assign an FOB and an innovator biologic to the same billing code. Arguments can be made for a standard based on interchangeability or a high degree of similarity. As noted previously, requiring an FDA interchangeability determination would signify that FDA has determined that an individual patient could switch back and forth between the FOB and innovator biologic multiple times without adverse effects. Any

clinical concerns about Medicare coding and payment policy influencing the use of one product versus another would be alleviated by such an interchangeability determination. However, interchangeability is a higher standard than similarity and may not necessarily be the appropriate threshold for determining whether FOBs should be assigned to the same billing code as innovator biologics.

Alternatively, one could argue that an FOB and an innovator biologic, which have been determined by FDA to be highly similar, should be treated similarly under the Medicare payment system and paid the same rate. As noted previously, there is precedent for putting closely related single-source drugs and biologics in the same billing code. Before the MMA, certain closely related single-source drugs and biologics, such as clotting factors and viscosupplements, were assigned the same billing code. The MMA grandfathered these preexisting coding decisions and required the grandfathered products to receive a payment rate based on the average ASP for the related products. These "grandfathered products" have not been subject to a determination of similarity by FDA—in contrast to FOBs, which FDA would have determined to be highly similar to the innovator product to receive approval.

Several different approaches could be considered for placing FOBs and innovator biologics in the same billing code depending on whether interchangeability or a high degree of similarity was the criterion used. A statutory change may be required to adopt any of these approaches. Three approaches include:

- ***FDA interchangeability determination.*** Under this approach, an FOB would be assigned to the same billing code as the innovator biologic if FDA determined that the products were interchangeable. Stakeholders disagree about whether the science currently exists to permit a determination that an FOB and innovator biologic are interchangeable. For this reason, it is unclear in the short run whether FDA would exercise the authority to make an interchangeability determination if given the statutory authority to do so. Thus, tying Medicare coding and payment to an FDA determination of interchangeability might lead to few, if any, follow-on products being included in the innovator product's billing code in the short run. However, this approach could have a more significant impact over time as the science evolves for determining interchangeability.
- ***Secretary's determination based on input from an advisory committee or a public comment process.*** This approach would give the Secretary authority to make a determination about assigning an FOB to the same billing code as the innovator product after obtaining input from a special advisory committee of medical and scientific experts developed for this purpose or from a public comment process. While generally relying on a standard of similarity, the Secretary would have the flexibility to base the decision on all available information about a particular biologic. Stakeholders' interest in such decisions could lead to a lengthy decision-making process before an FOB could be assigned to the same billing code as an innovator product. To partially mitigate the length of this process, a two-pronged approach could be considered where: (1) an FDA interchangeability determination results in automatic assignment of the FOB and innovator product to the same billing code, and (2) the Secretary has authority to assign an FOB and an innovator biologic that do not have an FDA interchangeability determination to the same billing code after input from an advisory committee or a public comment process.
- ***Require FOBs to be assigned to the same billing code as the innovator product.*** The Congress could require that FOBs be assigned to the same billing code as the innovator product. Underlying this approach would be the premise that a high degree of similarity is an appropriate standard for assigning FOBs and innovator biologics to the same billing code. If there were concerns that this standard might not be appropriate in all instances, the Secretary could be given the authority to exempt products from being grouped together if there is evidence that it is not clinically appropriate for a particular product. This approach would likely achieve greater savings than the other options outlined above because it would likely result in FOBs and innovator biologics being placed in the same billing code more quickly and more often.

Assigning FOBs and innovator products to the same billing code is not the only way to achieve equivalent payment rates for the two products. Payment rates equivalent to those resulting from the above approaches could be achieved by using separate billing codes if payment rates for biologics were based on the average ASP calculated across FOB and innovator product codes (based on an interchangeability or a high-degree-of-similarity standard).[14] Other innovative pricing

mechanisms could also be considered for payment of drugs, such as not paying a higher price for a product than the price of a similar product, unless there is evidence to suggest that it is clinically superior, as discussed in more detail later.

Biologics and Part D

Because most biologics are injected or infused directly into the patient, they are more likely to be covered under Medicare Part B. Consequently, biologics account for a relatively small share of gross Part D spending.[15] In 2007, spending on biologics totaled approximately $3.9 billion, or about 6 percent of Part D spending.[16] However, spending on Part D biologics has increased more rapidly than overall drug spending. Between 2006 and 2007, spending grew by about 36 percent compared with total Part D spending, which grew by 22 percent. Increased spending reflects, in part, higher enrollment in Part D in 2007. However, prices for biologics compared with prices of small-molecule drugs also increased rapidly. As more biologics enter the market, Part D is likely to see increased use of them.

Biologics covered under Part D fall into two broad categories. The first group includes older, simpler molecules such as insulin and human growth hormone. These products may have larger markets than many of the newer biologics but are less costly for consumers. Although there are no generic versions of older biologics, multiple brand-name products are often available.[17] Alternatively, newer, more complex biologics may have more limited markets. They tend to have high launch prices and many face high cost-sharing requirements.

Since Part D was implemented, biologics experienced faster price growth than other covered drugs. The Commission contracted with researchers at Acumen, LLC, to analyze price trends under Part D. They used claims data to construct a volume-weighted price index.[18] The index does not reflect rebates that plans may have received from manufacturers after the fact. It does reflect transaction prices. Measured by individual drug names, Part D drug prices rose by 7 percent from January 2006 through December 2007. However, prices declined by 6 percent when the index controlled for generic substitution. On the other hand, prices for biologics increased by 14 percent over the same period (or 10 percent when substitution is taken into account).[19]

How Medicare pays for Part D drugs

The Part D benefit is a much broader benefit than Part B. Part D covers most prescriptions that do not fall under the Part B coverage rules—particularly those filled at a retail pharmacy or in a long-term care facility. The benefit is administered by competing private plans, following a basic structure but with a great deal of flexibility and variety from plan to plan.

For 2009, the defined standard benefit includes:

- a $295 deductible,
- 25 percent coinsurance until the enrollee reaches $2,700 in total covered drug spending,
- a coverage gap in which the enrollee is responsible for the full discounted price of covered drugs until true out-of-pocket spending reaches $4,350, and
- about 5 percent coinsurance for drug spending above the catastrophic limit.

Plans can and often do offer alternative benefit structures. For example, a plan can offer a deductible lower than $295 or use tiered copayments rather than coinsurance—provided that the alternative benefit meets certain tests of actuarial equivalence. Plans place drugs on different cost-sharing tiers to encourage beneficiaries to use specific drugs in a therapeutic class that are both clinically appropriate and cost the plan less. Typically, plans' formularies include a generic tier, a preferred brand-name tier, and a nonpreferred brand-name tier.

Most plans also have a specialty tier where they list particularly high-cost drugs. In 2008 and 2009, plans could place drugs with prices that exceed $600 per month on their specialty tier. Specialty tiers have high cost sharing and beneficiaries may not appeal the level of coinsurance charged. For 2009, the median Part D enrollee in a plan with a specialty tier faces 33 percent coinsurance for drugs listed on that tier. Beneficiaries who regularly use drugs on a specialty tier are likely to reach the coverage gap in a short time and face 100 percent coinsurance until their drug spending reaches the catastrophic limit (MedPAC 2009).

For each Medicare enrollee in a Part D plan, Medicare provides plans with a subsidy that averages 74.5 percent of basic coverage, including a per capita subsidy to the plans and individual reinsurance. Under reinsurance, when an enrollee has drug expenditures over the catastrophic limit, Medicare subsidizes 80 percent of additional drug

TABLE 5–2

The top six Part D biologics that were eligible for specialty tier status, 2006–2007

Biologic	Primary indication	Total spending (in millions) 2006	Total spending (in millions) 2007	Percent change in spending, 2006–2007
Etanercept	Rheumatoid arthritis	$180	$262	45.8%
Epoetin alfa	Anemia	253	250	–1.6
Interferon beta-1a	Multiple sclerosis	169	223	32.4
Adalimumab	Rheumatoid arthritis	157	219	40.0
Teriparatide	Osteoporosis	123	179	44.6
Interferon beta-1b	Multiple sclerosis	74	87	17.3

Source: MedPAC analysis of prescription drug event data.

spending, the enrollee pays 5 percent, and the plan is at risk for the remaining 15 percent (MedPAC 2008).

In addition, Medicare subsidizes coverage for individuals eligible for a low-income subsidy (LIS), including beneficiaries dually eligible for Medicare and Medicaid. Individuals receiving the full subsidy have no deductibles, nominal copays, and no coverage gap. As of January 2008, about 9.4 million beneficiaries were receiving the subsidy, out of about 25 million Part D enrollees (MedPAC 2009). LIS recipients account for most spending on new biologics.

Of an estimated $50.7 billion total spending on Part D in 2008, enrollees paid $5 billion in premiums, and Medicare paid $18 billion in direct subsidies, $18 billion for LIS, and $6.5 billion in reinsurance payments. Medicare also paid $3.6 billion in subsidies to employers who provide drug coverage to their retirees (Boards of Trustees 2008).

Competition among Part D biologics

There is some price competition among the older biologic products for which alternatives are available. There are often multiple manufacturers producing older biologics like insulin, human growth hormone, and other hormones. Competition among these brands can result in lower prices. An entire vial of the most expensive insulin analog, for example, costs less than a single dose of many newer biologic products. There are at least three rapid-acting insulin brands, three regular or short-acting brands, three intermediate brands, and two long-acting brands. The competition in the insulin market results in relatively low Medicare expenditures, despite the widespread use of insulin. Although insulin made up more than 76 percent of Part D biologic prescriptions dispensed in 2007, it accounted for only about 17 percent of total spending on Part D biologics.

However, we see little sign of price competition among the newer biologics covered under Part D, even when several products are available in the same therapeutic class (e.g., rheumatoid arthritis). Of the top 20 Part D drugs by spending that were eligible for specialty tier status in 2007, 6 were biologics (Table 5-2). These six products include treatments for rheumatoid arthritis, anemia, multiple sclerosis, and osteoporosis.

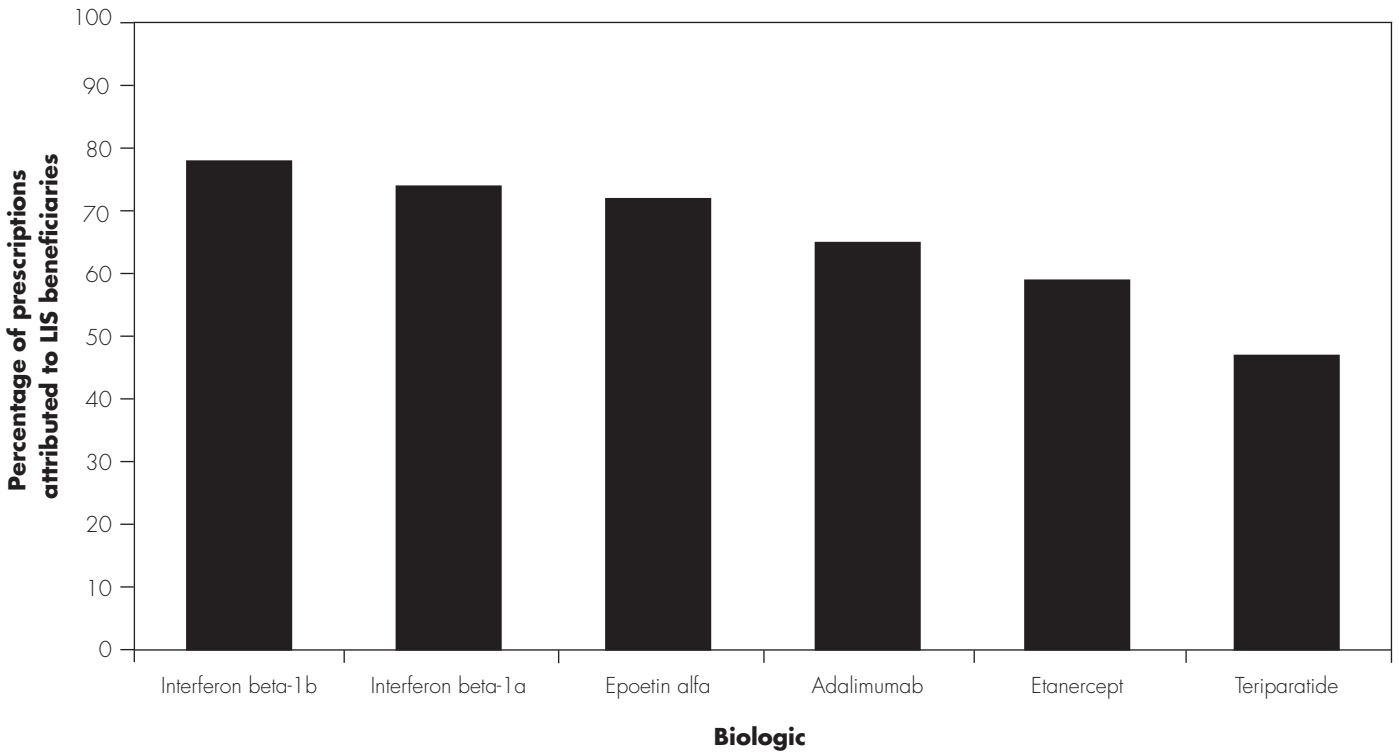
Prices for a volume-weighted market basket of these six drugs increased by 16 percent from January 2006 to December 2007. Most plans list all these products on their formularies at very similar prices (adjusted for dosage) with 25 percent to 33 percent beneficiary coinsurance requirements.

Plan risk for high-cost biologics is limited

New biologics are among the most expensive products covered under Part D. For example, Walsh estimates the average annual cost of biologics that treat multiple sclerosis at around $30,000 while biologics that treat rheumatoid arthritis can exceed $20,000 (Walsh 2009). A beneficiary taking one of these products will reach Part D's $2,700 initial coverage limit within a few months. At this point, the plan bears none of the cost of continued coverage until a beneficiary reaches the catastrophic limit. If the beneficiary is able to continue paying for the drug during the coverage gap, he or she will receive

FIGURE 5–2

LIS beneficiaries account for a large proportion of prescriptions for many high-cost biologics, 2007



Note: LIS (low-income subsidy).

Source: MedPAC analysis of 2007 prescription drug event records.

catastrophic coverage for several months of the year. At this point, plan liability is limited to 15 percent of all covered drug spending for the rest of the year.[20]

FOBs will be less expensive but may still be expensive. For example, the Congressional Budget Office estimates that in the initial year of competition, prices for FOBs would be about 20 percent below the prices of their reference products (CBO 2008c). Many will likely cost enough to result in catastrophic coverage if a beneficiary uses them for a full year. Because plans have no risk during the coverage gap and risk is limited during catastrophic coverage, they may have little incentive to tightly manage the use of the biologics or create incentives for beneficiaries to use FOBs. Plans may also have few tools to manage use of these products.

Many new biologics are covered on all formularies

Part D plans have the flexibility to establish a formulary that covers some drugs and not others. However, Part D rules require formularies to cover drugs in every therapeutic class and "key drug type." This policy protects some drugs that are the only drug available for treating a certain condition, while encouraging competition in most classes with multiple products. If a biologic is the only drug of its type, CMS generally requires Part D plans to cover it. For six drug classes in which access to a particular product may be especially important, Part D plans must cover "all or substantially all" drugs in the class. Those classes are: antineoplastics, antidepressants, antipsychotics, antiretrovirals, anticonvulsants, and immunosuppressants used by transplant patients. Although most drugs in the protected classes are not biologics, new biologics tend to be in small therapeutic classes where all or most products must be covered.

Plan representatives at our panel noted that they were unable to negotiate lower prices when manufacturers knew the plans would have to cover the manufacturers' products on the plans' formularies. Plans negotiate rebates

or other price concessions with manufacturers based on their ability to encourage enrollees to use one drug and not another. In the case of the protected classes or classes with few products, plans have little ability to steer utilization. In a few cases, drugs in different therapeutic classes may be used to treat the same medical condition. In those cases, plans may steer beneficiaries toward lower cost alternatives through differential cost sharing.

This situation may not change with the advent of FOBs. Unless an FOB is determined to be interchangeable with its reference product, plans may cover both products on their formularies. Unless a number of FOBs are introduced for the same product (an unlikely possibility initially), FOBs may not be substantially lower in price than innovator products for Part D beneficiaries. If more than one FOB for a reference product is introduced, plans may limit coverage to FOBs and savings may be greater.

LIS recipients are most likely to use new biologics

LIS beneficiaries make up a disproportionately large share of the market for biologics under Part D. In fact, LIS beneficiaries accounted for the majority of prescriptions for many high-cost biologics such as adalimumab, epoetin alfa, and etanercept in 2006 and 2007 (Figure 5-2).

As noted earlier, LIS beneficiaries have nominal cost sharing and no coverage gap. As a result, cost-sharing differences among products are less likely to affect their use.

For the same reason, beneficiaries receiving LIS would have little incentive to ask their physicians to prescribe FOBs. Because plans have limited ability to use cost-sharing differences to steer LIS recipients to FOBs, they may have few tools to influence use even though they may have incentives to do so. Other forms of drug management such as prior authorization also involve considerable administrative expense for plans. Further, if LIS beneficiaries' use of biologics resulted in losses in a given year, plans would raise their premiums the following year. Premiums could rise above the low-income threshold and beneficiaries would be reassigned to other plans.

Plans may experience selection bias if they provide more generous coverage of new biologics

In a few instances, plans may choose among more than one new biologic in a therapeutic class that is not one of the protected classes. For example, tumor necrosis factor inhibitors are used to treat several autoimmune disorders, especially rheumatoid arthritis. There are three drugs in this class. For Medicare patients, one (infliximab) is typically covered as a Part B drug, while the other two (adalimumab and etanercept) are generally Part D drugs. Plans have the option of favoring one drug on a preferred tier and negotiating for lower prices with the manufacturer.

In 2006, plans experimented with a range of formulary designs to cover drugs in this class. Some plans treated the drugs uniformly but others preferred one over the other and instituted wide cost-sharing differences between products to negotiate better prices with manufacturers. For example, one national plan charged a flat $17 copayment for one product and required 75 percent coinsurance for another. However, by 2009, plan treatment of these products was much more homogeneous. Part D formularies tend to list all three drugs (even though infliximab is not commonly paid under Part D), and plans with specialty tiers place all three on the specialty tier. Prices, adjusted for dosage, are also similar (Hoadley 2009).

Plans may have had multiple reasons for changing the way they cover this class of drugs. However, cost-sharing differences from 2006 to 2009 suggest that plans may be concerned that lower cost sharing for new biologics may lead beneficiaries with high-cost medical conditions to enroll in their plan. If that is the case, plans may be reluctant to offer FOBs at lower cost-sharing tiers if they believe it will increase selection into their plans.

FOBs may produce limited savings for Medicare Part D

While Medicare should achieve savings on FOBs for older biologics, the current benefit structure is likely to limit savings for FOBs for newer products. Because plans have no risk during the coverage gap and risk is dampened during catastrophic coverage, they may have limited incentive and few tools to tightly manage the use of these biologics. However, Medicare would have a strong interest in reducing the government's costs of catastrophic coverage by encouraging use of lower cost follow-on products.

If FDA determines that an FOB is interchangeable with its reference product, Part D could achieve significant savings from FOBs. Under current Part D policy, in classes in which plans must cover all drugs, or in small classes in which plans must cover at least two drugs, this rule is applied at the chemical level; plans can choose to cover the generic version of a drug and leave the brand name uncovered. Thus, plans could have the option of covering the innovator or the FOB or covering both products. No matter what decision the plan made, plan representatives would have more leverage negotiating with manufacturers.

However, most analysts do not expect FDA to determine that FOBs are interchangeable with their reference products in the near future.

In the more likely case that FOBs are not designated as interchangeable, opportunities for savings may be limited. Policymakers might need to consider changes to Part D to increase use of FOBs. Some potential options include:

- Modify the current Part D risk adjusters in a budget-neutral way to take into account drug utilization. In general, this practice would increase payments for LIS beneficiaries, who tend to take more drugs than other beneficiaries, and could increase plan willingness to enroll LIS beneficiaries and manage their use of high-cost biologics. If the risk adjuster were based on an indication of drug use within specific therapeutic classes rather than drug spending, plans would have more incentive to steer beneficiaries toward lower cost alternatives in a therapeutic class. In this case, plans might then create incentives for beneficiaries to use FOBs. However, it is not clear what tools would be available for them to use.
- Increase plan risk for coverage of drugs over the catastrophic limit. For example, Medicare could pay 80 percent of the lowest cost drug in a therapeutic class. Like the previous strategy, this situation could lead plans to design incentives to increase the use of FOBs.

Even if Medicare implemented one or both of these strategies, plans might still have difficulty convincing physicians and beneficiaries to use FOBs initially. If utilization of FOBs is minimal, plans would continue to have difficulty negotiating lower prices with innovator companies.

Any consideration of these options would require considerably more analysis. The Commission may want to look further into these issues. Alternatively, policymakers may want to focus more broadly on mechanisms to control costs for high-priced drugs.

Innovative ways to pay for biologics under Part B and Part D

Implementing a process to approve FOBs is one way to increase competition, put downward pressure on prices, and help lower expenditures on biologics. Given the magnitude and growth of Medicare's spending on biologics under Part B and the substantial increase in spending for biologics under Part D, policymakers could also consider adopting innovative pricing strategies to help alleviate rising expenditures for these products.

Some experts support pricing strategies in which Medicare takes into account a product's clinical effectiveness when setting reimbursement rates (Orszag 2008, Wilensky 2008). Whether paid for under Part B or Part D, a biologic's price does not usually account for the benefit of the product to beneficiaries or whether the product is a substantial improvement over existing treatments. This lack of flexibility leads to instances in which Medicare and Part D plans pay different rates for products that are clinically comparable and pay more for a new product without evidence that it is any better than currently available treatments.

In addition, Medicare's fee-for-service payment system lacks the flexibility to group—bundle—clinically associated products and services provided during an episode of care or to treat an illness or disease. For example, the program does not bundle drugs and doctor visits in the treatment of chronic illnesses. Paying for individual products and services fuels economic incentives for providers to increase the volume of medical services they furnish. This volume growth increases costs for beneficiaries and taxpayers, but in the aggregate there appears to be no correlation between higher spending and higher quality of care or improved health outcomes; in fact, the opposite may be true (Baicker and Chandra 2004, CBO 2008b, Fisher et al. 2003a, Fisher et al. 2003b, MedPAC 2003).

We have examined three payment strategies that, by considering information about a drug's clinical effectiveness, have the potential to improve the value of Medicare spending on drugs:

- ***Reference pricing:*** Set a product's payment rate no higher than that for currently available products unless evidence shows that the service improves beneficiaries' outcomes.
- ***Payment for results:*** Link a drug's payment to beneficiaries' outcomes through risk-sharing agreements with manufacturers.
- ***Bundling:*** Create payment bundles for groups of clinically associated products and services.

These approaches aim to improve the value of Medicare spending for drugs, including biologics, by making providers and patients more sensitive to the relative prices of treatments, reducing financial incentives for providers to furnish services that may have limited clinical benefits regardless of cost, and offsetting the efforts by manufacturers to market their products to providers and consumers. These policies can also be used to improve the value of Medicare spending for other products, items, and services that the program pays for. However, a statutory change would likely be necessary for widespread implementation of these pricing strategies. As discussed by Jost, the ability of Medicare to move to value purchasing strategies is greatly limited by the nature, structure, and terms of the Medicare statute (Jost 2009).

Reference pricing

Under reference pricing strategies, a single payment rate is set for a group of clinically comparable drugs; patients can pay the difference if they and their provider decide on a higher priced item. The rationale is that Medicare, beneficiaries, and taxpayers should not reimburse more for a product when a similar product can be used to treat the same condition and produce the same outcome but at a lower cost. Reference pricing policies do not control the price that manufacturers charge providers for their products.

A key aspect of reference pricing policies is determining the method for setting the reference price for each group of clinically comparable drugs. Alternative ways to calculate a reference price include basing it on the average price of the drugs within the group, the lowest cost drug within the group, the median, or the drug considered to be the most cost effective within the group.

Another key aspect of reference pricing policies is determining how to group drugs for the purpose of pricing. Reference pricing strategies rely on the ability to conclude that products are clinically comparable. A group could be narrowly defined to include all drugs with a similar substance—that is, an innovator small-molecule drug and its generics or an innovator biologic and its FOBs. Alternatively, a group could be more broadly defined based on drugs' pharmacologic equivalence. For example, such a group might consist of the biologics used to treat anemia—ESAs. An even broader definition would be to group drugs that are neither chemically similar nor pharmacologically equivalent but have similar therapeutic indications. For example, for payment purposes, the Canadian Patented Medicine Prices Review Board groups together five biologics (which have different active substances) used to treat rheumatoid arthritis.

Reference pricing strategies generally have not been used in the United States, although Medicare has some limited experience as we describe in the text box (p. 127) (Huskamp et al. 2000). Under the least costly alternative (LCA) policy, Medicare sets the payment rate for a group of clinically comparable products based on the least costly product within the group. However, a recent court decision may limit the widespread use of LCA payment policies for drugs.

The Congressional Budget Office (CBO) estimated that expanded use of reference pricing policies would result in savings for the Medicare program. In its 2008 report on reducing federal spending on health care, CBO included as a policy option use of the LCA approach to pricing for five products that physicians use to treat osteoarthritis of the knee. Although each product differs slightly, they are all approved by FDA for the same indication—osteoarthritis—and they work through the same mechanism of clinical action. Therefore, it could be argued that Medicare should not pay more for one product than for another if both are likely to have the same effect in a patient when prescribed for the same condition. CBO estimated savings of about $200 million between 2010 and 2014 and almost $500 million between 2010 and 2019 if Medicare set the payment for these five products based on the lowest priced product (CBO 2008c).

First implemented in Germany in 1989, the use of reference pricing for drugs including biologics is common internationally. Nearly all the 30 member countries of the Organisation for Economic Co-operation and Development (OECD) use some type of reference pricing strategy. Most OECD countries (24 of them) use some type of external reference pricing, in which the payer sets the price based on drug prices in other countries (OECD 2008a). However, there are differences across countries in the products paid for and the methods used to calculate prices. Table 5-3 (p. 126) highlights some of these differences for six selected OECD countries—Australia, Canada, Germany, Italy, the Netherlands, and Spain. For example, some countries (Australia, Canada, Germany, and the Netherlands) use reference pricing policies to set the price of patented and off-patent drugs, while other countries use such policies to set the price of only off-patent drugs (Italy and Spain).

TABLE 5–3 **Features of reference pricing policies vary across OECD countries**

Country	Method used to set the price	International comparison	Includes patented drugs
Australia	Lowest price of the drugs in the therapeutic group	New Zealand and U.K.	Yes
Canada	Prices generally cannot exceed cost of existing drugs in the therapeutic group	Cannot exceed France, Germany, Italy, Sweden, Switzerland, U.K., U.S.	Yes
Germany	Statistically derived from regression analysis; price set at the lowest third of the price in the therapeutic group	No	Yes
Italy	Lowest priced product in the group	Other European Union countries, particularly France and Spain	No
Netherlands	Price of the drug equal to or directly below the average of the prices in the therapeutic group	Maximum price cannot exceed average wholesale price in Belgium, France, Germany, and the U.K.	Yes
Spain	Mean of the three lowest cost drugs in the group	Selected countries within the European Union	No

Note: OECD (Organisation for Economic Co-operation and Development), U.K. (United Kingdom), U.S. (United States). Patented drugs include small-molecule drugs and biologics.

Source: Australian Government Department of Health and Ageing 2009; Kanavos and Reinhardt 2003; Österreichisches Bundesinstitut Für Gesundheitswesen 2006; OECD 2008a; OECD 2008b; Patented Medicine Prices Review Board 2009.

Other strategies that are used internationally to control drug expenditures include implementing price freezes, price cuts, and mandatory rebates; creating formularies; implementing coverage policies that set forth the indications, settings, and populations for which the payer will pay for the product; using pharmacoeconomic evaluations to determine launch prices; and determining reasonable limits for the profits to be made from innovator products.

These pricing policies generally result in lower prices for biologics and small-molecule drugs internationally than in the United States. Danzon and Furukawa used data from IMS Health, Inc. (which include data from all payers) to compare the prices of biologics in the United States with prices in Australia, Canada, France, Germany, Italy, Japan, Mexico, Spain, and the United Kingdom (Danzon and Furukawa 2006). Compared with the United States, biologics launched after 1996 were more costly in Mexico, while biologics launched before 1996 were more costly in Canada and France. Also using IMS data, the U.S. Department of Commerce reported that in 2003 prices for all patented drugs (small-molecule drugs and biologics) were 18 percent to 60 percent lower in Australia, Canada, France, Germany, Greece, Japan, Poland, Switzerland, and the United Kingdom than in the United States (DOC 2004). Several factors can affect the international comparison of drugs, including changes in currency rates between the year the data were published and 2009.

Proponents of reference pricing argue that it makes patients and their providers more sensitive to the relative prices of different services and more likely to consider cost when choosing among treatment options (Commonwealth Fund 2003). The Commission noted that LCA policies can stimulate price competition among alternative ways to treat a given illness (MedPAC 2007). Some observers argue that Medicare should not pay more for one product than another if both are likely to have the same effect in a patient when prescribed for the same condition (CBO 2008c).

Critics of reference pricing argue that these policies will negatively affect:

- patient outcomes
- patient access to new technology
- manufacturers' incentives to invest in research and development

Medicare has had some success in using reference pricing policies, but a recent court ruling discourages widespread use

Least costly alternative (LCA) policies, which are similar to reference pricing strategies, set the payment rate of a service based on the payment rate of a less costly, clinically comparable service. LCA policies are in place for: advanced prostate cancer drug regimens, alefacept therapy, nebulizers (inhalation drugs), manual wheelchair bases, power mobility devices, seat lift mechanisms, and supplies for tracheostomy care. Medicare's regional contractors establish such policies through the local coverage determination process.

In the Commission's January 2007 report, we stated our support for LCA policies (MedPAC 2007). We also noted that some providers have complained that LCA policies vary from region to region and that some contractors change their LCA policies frequently. We recognized that local coverage determinations promote innovation and flexibility but suggested that Medicare clarify the contractors' LCA policies when sufficient variation and inconsistency exist.

A 2008 ruling by the federal district court may affect the ability of Medicare's contractors to continue to apply LCA policies to drugs. The U.S. District Court for the District of Columbia ruled that Medicare can no longer use LCA policies to pay for Part B inhalation drugs. The court concluded that the statute's specific provision that sets the payment rate for Part B drugs (based on its average sales price) precludes Medicare from using LCA policies under the statute's broader authority of covering services that are reasonable and necessary (U.S. District Court for the District of Columbia 2008).

In addition to LCA policies, Medicare also has implemented a "functional equivalence" policy for two biologics (darbepoetin alfa and epoetin alfa) on a national level. The concept behind the functional equivalence policy is similar to the LCA policy; the payment rate of products that are considered to be close substitutes is based on the rate of the least expensive product. In 2003, Medicare set the payment rate for a new biologic at the same rate as that of an existing product after concluding that both products were clinically comparable because they used the same biological mechanism to produce the same clinical result—stimulation of the bone marrow to produce red blood cells. Medicare used the functional equivalence policy for these biologics in 2004 and 2005. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) limited the use of the functional equivalence standard. The Congress prohibited the use of this standard for other drugs and biologics in the hospital outpatient setting. However, the Congress did not preclude the agency from continuing to use the policy for the two biologics in the hospital outpatient setting or for setting the payment rate the same for other clinically comparable services in other settings. In response to passage of the MMA, the payment rate for each product was set based on its average sales price plus 6 percent beginning in 2006. ■

Some critics contend that physicians should be given discretion in selecting among clinically comparable services because the effectiveness of those services may vary among patients. The literature on the effect of reference pricing on patients' outcomes is mixed. One rigorous evaluation found that reference pricing for angiotensin-converting enzyme inhibitors for treatment of hypertension among patients 65 years or older did not result in patients (in British Columbia, Canada) discontinuing treatment or increasing the overall rate of physician visits or hospital admissions (Schneeweiss et al. 2002). By contrast, an uncontrolled study found an increase in complications when patients switched therapies under a system of reference pricing in New Zealand (Thomas and Mann 1998).

Some critics also contend that reference pricing policies may decrease access to innovations and may not encourage competition among clinically similar services. Danzon and Ketcham concluded that reference pricing policies of pharmaceuticals in New Zealand resulted in decreased availability of new compounds, particularly high-priced new products, and found no evidence that reference pricing encouraged competition, which they concluded is

consistent with the hypothesis that prices tend to converge to the reference price (Danzon and Ketcham 2003).

Critics of reference pricing also argue that grouping an innovator's product with other clinically similar products might change or reduce manufacturers' incentives to invest in research and development. Manufacturers might shift their research toward diseases not currently treated by multiple drug therapies or reduce investment in products that are incremental improvements of other products (Farkas and Henske 2006). Reference pricing might particularly discourage the development of incremental drugs and biologics. However, proponents of reference pricing policies counter that such policies might increase manufacturers' incentive to develop truly innovative products and to compare their product with other products in the clinical trials they sponsor. Kanavos and Reinhardt noted the lack of empirical evidence documenting the impact of reference pricing policies on the pace of innovation in the drug industry (Kanavos and Reinhardt 2003).

If the statute gave Medicare more flexibility to use reference pricing policies on a national level, the program would need to define the process that would be used to group clinically similar products. Ensuring transparency and stakeholder input would be key; establishing an advisory group to help Medicare's process might improve transparency and provide an opportunity for public input. Finally, the program could establish a process by which beneficiaries could petition to be reimbursed for using a higher priced product.

Payment for results

Another strategy is to explicitly link a drug's payment to patient outcomes through risk sharing with manufacturers. With performance-based pricing, the basis of risk is the quality of the drug's performance, as measured by agreed upon outcomes. For example, the manufacturer might guarantee clinically defined biomarker or surrogate outcomes, such as decreased low-density lipoprotein goals for a cholesterol drug.

Performance-based strategies might be particularly applicable for drugs that are costly and have different success rates among subgroups of patients. According to Garber and McClellan, payment by results represents an innovative approach to address a central dilemma in the allocation of drugs to patients (Garber and McClellan 2007). If the price of a product is uniform, patient access might be limited to those groups identified by clinical trial testing that showed substantial improvement in outcomes. In results-based payment, payers face less financial risk from treating groups that were either not included in clinical trial testing or did not show substantial improvement.

Challenges associated with performance-based pricing include defining objective measures of outcomes that are not heavily confounded by patient characteristics or by other treatments and developing and maintaining a mechanism to track patients' outcomes, such as via clinical registries or electronic medical records (Garber and McClellan 2007). The effects of providers' practice patterns and patients' adherence to the prescribed regimen are other variables that need to be considered when designing performance-based pricing strategies.

The United Kingdom uses performance-based pricing policies for several drugs. For example, in 2007, the British National Institute for Health and Clinical Excellence implemented an agreement with the manufacturer of bortezomib, an anticancer drug used to treat multiple myeloma. Under this agreement, the manufacturer rebates the full cost of the drug for patients who, after four cycles of treatment, have less than a partial response (i.e., less than 50 percent reduction in serum M-protein). Medicare pays for bortezomib under Part B using the ASP methodology; Medicare payment is estimated at about $4,500 for four cycles of treatment.[21]

Bristol-Myers Squibb offers a performance-based approach in the United States to patients with commercial insurance who are new users of the company's drug abatacept to treat rheumatoid arthritis. For the first six months, the company pays for patients' copayments for the product. For patients not satisfied with their outcomes after six months, the company will pay the first copayment of another rheumatoid arthritis medicine (up to $500). One study estimated the first-year costs of abatacept to be $19,000 (Vera-Llonch et al. 2008). Medicare pays for abatacept under Part B using the ASP methodology, but beneficiaries are not eligible for Bristol-Myers Squibb's program.

Bundling

Under a bundling strategy, providers are paid a prospectively set rate for a group—or bundle—of services they furnish during an episode of care. For Part B services that are currently paid for separately, a bundle could, for example, cover the Part B drugs, outpatient physician services, imaging tests, and laboratory tests associated with treating a chronic disease. Alternatively, a bundle could cover services associated with an event, such as

hospital and physician services during an inpatient hospital stay.

Creating a payment bundle for a group of associated items and services provided during an episode of care would encourage providers to operate efficiently, as they would retain the difference between the payment rate and their costs. Greater bundling of payments to cover all the services associated with a treatment or disease could reduce incentives to provide additional services that might be of low value. On the other hand, such approaches might raise concerns about the financial risk that providers face and their incentives to provide too little care (Orszag 2008).

Medicare's approach for paying for most services provided by institutional providers (and paid for under Part A)—including acute care hospitals, skilled nursing facilities, and home health agencies—is to pay for bundles of services using a prospectively set payment rate. The ultimate in bundled payments is a single capitated payment that covers all Medicare services, such as that used for Medicare Advantage plans.

With few exceptions, Medicare generally pays for each service physicians furnish under Part B. The exceptions include Medicare's monthly payment to physicians for the outpatient care of dialysis patients and the physician fee for major surgeries that encompasses the total physician inputs used during what is termed the global period, which includes the day of the surgery and postsurgery care. For example, the global period for a total hip replacement is 90 days.

Bundling is one option that might improve the value of Medicare spending. In our June 2008 report, the Commission recommended changes in fee-for-service payment for care provided around a hospitalization. The Commission noted that bundling Medicare payment to cover all services associated with an episode of care could improve incentives for providers to deliver the right mix of services at the right time.

Some researchers have suggested bundling physician services covered under Part B. Bach observed that Medicare might consider prospective payment for cancer care that stretches over the course of an episode of illness (Bach 2009). Under such a strategy, Medicare could pay a lump sum to cover all the costs of doctor visits, chemotherapy treatments, and the chemotherapy itself over a period of care. Wilensky recommended developing payments that cover all the services a single physician provides to a patient to treat one or more chronic diseases (Wilensky 2009). She also suggested bundling payments for high-cost high-volume stays to include, at a minimum, all physician services associated with the episode and the hospital payment.

Conclusions

This chapter summarized key issues that are being discussed as policymakers and stakeholders consider establishing a regulatory pathway for FDA to approve FOBs. While FDA has jurisdiction over approval of FOBs, Medicare is a major payer for biologics and has a strong incentive to ensure that it gets value for the money it spends on these products. Medicare spending on biologics is substantial and expected to grow significantly in future years. The lack of an expedited approval process for FOBs has kept the prices of innovator biologics high over time. Establishing an approval process for FOBs could put pressure on the prices of biologics, generating savings for Medicare. The Commission intends to continue to monitor the issues associated with implementing an expedited approval process for FOBs.

Because biologics have safety issues associated with their use, increased postmarketing surveillance to detect side effects of these products in a timely manner may be warranted. Some observers also argue for increased surveillance efforts to detect adverse events of small-molecule drugs. Existing postmarketing surveillance programs are unsystematic and rely on doctors, patients, and manufacturers to report adverse events. CMS is collaborating with FDA to use Medicare claims to create a postmarketing safety assessment program.

Changing Medicare's payment systems may be necessary to capture savings from FOBs. We described three approaches to the Part B payment system that could be considered for assigning FOBs and innovator biologics to the same billing code and authority that could be given to the Secretary to make such determinations. In addition, we explored ways to increase incentives to use FOBs under Part D. The chapter also examined three broader strategies to improve the value of Medicare spending on drugs—reference pricing, payment for results, and bundling. The Commission plans to continue to look at ways for Medicare to improve the value of spending for drugs. ■

Endnotes

1 The $13 billion in Medicare spending on biologics encompasses those biologics for which Medicare makes separate payment. It does not include biologics administered to hospital inpatients or a subset of biologics (low-cost biologics) administered in hospital outpatient departments that are subject to bundled payment.

2 The Food and Drug Administration defines drugs as encompassing both biologics and chemically synthesized, small-molecule drugs. This chapter uses the term "drug" to include biologics and other products and uses the term "small-molecule drug" to differentiate between biologics and other products.

3 PHSA § 351(ii), 42 U.S.C. § 262(i).

4 Technically, requirements for biologics approved under the Public Health Service Act may vary.

5 In the case of Diamond v. Chakrabarty (1980), the Supreme Court first ruled that a biologic could be patented. The product was a substance used for cleaning up oil spills.

6 During the 180-day marketing exclusivity period, FDA may not approve subsequent applications for the same drug product.

7 In Europe, determinations of comparability are made by the European Union but individual states have their own processes for determining interchangeability.

8 Article 14(11) of Regulation (EC) No. 726/2004.

9 Medicare also makes a separate payment for administration of the drug (e.g., injection or infusion).

10 In addition to drugs administered in physicians' offices, Medicare Part B also covers injectable drugs furnished in hospital outpatient departments, injectable drugs furnished in end-stage renal disease facilities, drugs used with durable medical equipment (e.g., inhalation drugs used with a nebulizer or infusion drugs furnished with an external pump), and a small number of oral drugs and other types of drugs. The Part B payment rates for separately paid drugs are 106 percent of ASP, with the exception of separately paid drugs furnished in hospital outpatient departments (104 percent of ASP in 2009), infusion drugs furnished with an external pump (95 percent of the October 1, 2003, average wholesale price), and certain vaccines and blood products other than clotting factor (95 percent of current average wholesale price).

11 The ASP calculation does not include sales at a nominal price and sales exempt from the calculation of Medicaid best price (e.g., sales to certain other federal programs, sales under the Federal Supply Schedule, sales at prices offered through state pharmaceutical assistance programs, depot or single contract sales to a government agency, and sales at prices negotiated by Medicare Part D plans and qualified retiree prescription drug plans).

12 Generic versions of intravenous granisetron have recently become available in the market and are reflected in the Medicare payment rates starting in late 2008. Thus far, we have seen steady quarterly declines in the payment rate for granisetron but little change in the payment rates for the other drugs in the therapeutic class. The minimal price changes among competitor products may reflect the effects of generic entry having already been realized with the earlier entry of generic ondansetron and differences in the degree to which the competitor products are considered substitutable.

13 Whether having separate codes creates a financial incentive for use of the more expensive product would depend on how an individual physician's acquisition cost compared with the ASP of each product and whether there were cash flow issues associated with stocking higher priced drug inventory.

14 CMS has adopted this type of approach for some of the grandfathered biologics and single-source drugs that were placed in the same billing code before the MMA. For programmatic reasons, CMS has established separate codes for some of the grandfathered products (e.g., certain skin substitutes) but maintained identical payment rates for the grandfathered products based on the ASP calculated across the codes. As a result, some of the products now have their own code for billing purposes, but they are paid a rate based on the ASP for the products that have been grandfathered together. A statutory change may be needed to apply this approach more broadly.

15 All spending estimates in this section were calculated using prescription drug event records and include dispensing fees, sales tax, and beneficiary cost sharing.

16 There is no single generally accepted list of approved biologics. These spending estimates are based on an amalgamation of several lists of biologic products, including lists from Pharmaceutical Research and Manufacturers of America, Biotechnology Industry Organization, Center for Biologics Evaluation and Research, and Center for Drug Evaluation and Research, as well as a list of drugs expected to cost more than $600 per month that we reviewed using the Orange Book, drugs@FDA, and DrugBank to identify

biologics. We used the combined lists to calculate spending based on 2006 and 2007 prescription drug event records, which include dispensing fees, sales tax, and beneficiary cost sharing.

17 As noted on p. 112, due to a historical quirk FDA has approved a follow-on version of one brand of human growth hormone.

18 For additional findings and discussion of methodology see MaCurdy and colleagues (2009, forthcoming).

19 Although there are no generic substitutes for biologics, this measure takes into account other kinds of substitution—for example, when a cheaper brand of insulin is substituted for a more expensive one.

20 If the annual cost of the drug is high enough, 15 percent of the total may still be a considerable sum.

21 Medicare payment is based on administering bortezomib twice weekly during the first six weeks of treatment to an individual with a body surface area of 1.6 square meters.

References

Australian Government Department of Health and Ageing. 2009. *Better health and active ageing for all Australians.* Canberra: Australian Government Department of Health and Ageing. http://www.health.gov.au.

Bach, P. B. 2009. Limits on Medicare's ability to control rising spending on cancer drugs. *New England Journal of Medicine* 360, no. 6: 626–633.

Baicker, K., and A. Chandra. 2004. Medicare spending, the physician workforce and beneficiaries' quality of care. *Health Affairs Web Exclusives* (April 7): W4-184–W4-197.

Behrman, R. 2008. Follow-on biologics: A brief overview. Presented to the Federal Trade Commission. November 2008.

Biotechnology Industry Organization. 2009. Biotechnology industry facts. Washington, DC: BIO. www.bio.org/speeches/pubs/er/statistics.asp?p=yes.

Boards of Trustees, Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds. 2008. *2008 annual report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds*. Washington, DC: Boards of Trustees.

Brill, A. 2008. *Proper duration of data exclusivity for generic biologics: A critique.* November. http://www.tevadc.com/Brill_Exclusivity_in_Biogenerics.pdf.

Commonwealth Fund. 2003. *Reference pricing for drugs: Is it compatible with U.S. health care?* New York: Commonwealth Fund.

Congressional Budget Office 2008a. *S. 1695: Biologics Price and Innovation Act of 2007*. Washington, DC: CBO. June 25.

Congressional Budget Office. 2008b. *Geographic variation in health care spending*. Washington, DC: CBO.

Congressional Budget Office. 2008c. *Budget options, volume one: Health care*. Washington, DC: CBO.

Congressional Budget Office. 1998. *How increased competition from generic drugs has affected prices and returns in the pharmaceutical industry*. Washington, DC: CBO.

Danzon, P. M., and M. F. Furukawa. 2006. Prices and availability of biopharmaceuticals: An international comparison. *Health Affairs* 25, no. 5: 1353–1362.

Danzon, P. M., and J. D. Ketcham. 2003. *Reference pricing of pharmaceuticals for Medicare: Evidence from Germany, the Netherlands, and New Zealand*. Cambridge, MA: National Bureau of Economic Research.

Department of Commerce. 2004. *Pharmaceutical price controls in OECD countries: Implications for U.S. consumers, pricing, research and development, and innovation.* Washington, DC: DOC. http://www.ita.doc.gov/td/chemicals/drugpricingstudy.pdf.

European Medicines Agency. 2005. *CHMP guideline on similar biological medicinal products*. CHMP/437/04. London: EMEA. October 30.

Farkas, C., and P. Henske. 2006. *Reference pricing for drugs.* http://www.forbes.com. April 14.

Federal Trade Commission. 2002. *Generic drug entry prior to patent expiration: An FTC study*. Washington, DC: FTC.

Fisher, E., D. Wennberg, T. Stukel, et al. 2003a. The implications of regional variations in Medicare spending. Part 1: The content, quality, and accessibility of care. *Annals of Internal Medicine* 138, no. 4 (February 18): 273–287.

Fisher, E., D. Wennberg, T. Stukel, et al. 2003b. The implications of regional variations in Medicare spending. Part 2: Health outcomes and satisfaction with care. *Annals of Internal Medicine* 138, no. 4 (February 18): 288–298.

Garber, A. M., and M. B. McClellan. 2007. Satisfaction guaranteed—"payment by results" for biologic agents. *New England Journal of Medicine* 357, no. 16: 1575–1577.

Grabowski, H. 2008. Follow-on biologics: Data exclusivity and the balance between innovation and competition. *Nature Reviews: Drug Discovery* 7 (June): 479–488.

Harbour, P. 2007. The competitive implications of generic biologics. Presented to the ABA Sections of Antitrust and Intellectual Property Law. June. http://www.ftc.gov/speeches/harbour/070614genbio.pdf.

Hoadley, H., E. Hargrave, K. Merrell, et al. 2008. Medicare Part D benefit designs and formularies, 2006–2009. Presented to MedPAC. December 5.

Hoadley, J. 2009. E-mail message to author, March 17.

Huskamp, H. A., M. B. Rosenthal, R. G. Frank, et al. 2000. The Medicare prescription drug benefit: How will the game be played? *Health Affairs* 19, no. 2: 8–23.

Jost, T. S. 2009. *Value-based purchasing: Laws and regulations.* http://www.newamerica.net/files/Jost-ppt.pdf.

Kanavos, P., and U. Reinhardt. 2003. Reference pricing for drugs: Is it compatible with U.S. health care? *Health Affairs* 22, no. 3: 16–30.

Kotlikoff, L. 2008. *Stimulating innovation in the biologics industry: A balanced approach to marketing exclusivity.* http://www.tevadc.com/Kotlikoff_Innovation_in_Biologics.pdf.

MaCurdy, T., N. Theobald, T. Lau, et al. 2009. *Price indices for Part D prescription drugs*. Prepared for MedPAC. Washington, DC: MedPAC. Forthcoming.

Managing Intellectual Property (MIP). 2008. Biosimilar debate heats up at BIO. *MIP Week*, June 18.

Medicare Payment Advisory Commission. 2009. *Report to the Congress: Medicare payment policy*. Washington, DC: MedPAC.

Medicare Payment Advisory Commission. 2008. *Payment basics: Part D payment system.* Washington, DC: MedPAC.

Medicare Payment Advisory Commission. 2007. *Report to the Congress: Impact of changes in Medicare payments for Part B drugs.* Washington, DC: MedPAC.

Medicare Payment Advisory Commission. 2003. *Report to the Congress: Variation and innovation in Medicare*. Washington, DC: MedPAC.

Noonan, K. 2008. Follow-on biologic drugs and patent law: A potential disconnect? *Snippets Review of Developments in Intellectual Property Law* 6, no. 1 (May):1–10 .

Novartis. 2008. Comments in response to Federal Trade Commission questions on follow-on biologics. Basel: Novartis. September 30.

Organisation for Economic Co-operation and Development. 2008a. *Pharmaceutical pricing policies in a global market*. Paris: OECD. http://www.oecd.org/document/36/0,3343,en_2649_33929_41000996_1_1_1_37407,00.html.

Organisation for Economic Co-operation and Development. 2008b. *Pharmaceutical pricing and reimbursement policies in Germany*. Paris: OECD. http://www.oecd.org/dataoecd/6/57/41586814.pdf.

Orszag, P. R., Congressional Budget Office. 2008. The long-term budget outlook and options for slowing the growth of health care costs. Written statement before the Committee on Finance, U.S. Senate. 110th Cong., 2nd sess. June 17. http://www.cbo.gov/ftpdocs/93xx/doc9385/06-17-LTBO_Testimony.pdf.

Österreichisches Bundesinstitut Für Gesundheitswesen. 2006. *Surveying, assessing, and analyzing the pharmaceutical sector in the 25 EU member states.* Luxembourg: European Communities. http://ec.europa.eu/competition/mergers/studies_reports/oebig.pdf.

Patented Medicine Prices Review Board. 2009. http://www.pmprb-cepmb.gc.ca/english/home.asp?x=1.

Schacht, W. H., and J. R. Thomas. 2008. *Follow-on biologics: Intellectual property and innovation issues*. Congressional Research Service Report for Congress. Washington, DC: Congressional Research Service. Updated May 21.

Schneeweiss, S, A. M. Walker, R. J. Glynn, et al. 2002. Outcomes of reference pricing for angiotensin-converting enzyme inhibitors. *New England Journal of Medicine* 346, no. 11: 822–829.

Schwieterman, W. 2007. Safe and affordable biotech drugs—the need for a generic pathway. Testimony before the Committee on Oversight and Government Reform, U.S. House of Representatives. 110th Cong., 1st sess. March 26.

Siegel, J. 2007. Follow-on biologics. Oral testimony before the Committee on Health, Education, Labor, and Pensions, U.S. Senate. 110th Cong., 1st sess. March 8.

Thomas, M., and J. Mann. 1998. Increased thrombotic vascular events after change of statin. *Lancet* 352, no. 9143: 1830–1831.

Towse, Adrian. 2008. Competition issues involving follow-on biologic drugs. Submission to the FTC. #537778–00049. December 31.

U.S. District Court for the District of Columbia. 2008. Ilene Hays and Dey, L.P., plantiffs, v. Michael O. Leavitt, Secretary of the United States Department of Health and Human Services, et al., defendants. Memorandum opinion. https://ecf.dcd.uscourts.gov/cgi-bin/show_public_doc?2008cv1032-22.

Vera-Llonch M., E. Massarotti, F. Wolfe, et al. 2008. Cost-effectiveness of abatacept in patients with moderately to severely active rheumatoid arthritis and inadequate response to methotrexate. *Rheumatology* 47: 535–541.

Walsh, B. 2009. *The tier 4 phenomenon: Shifting the high cost of drugs to consumers*. Research report. Washington, DC: AARP.

Wilensky, G. R. 2009. Reforming Medicare's physician payment system. *New England Journal of Medicine* 360, no. 7: 653–655.

Wilensky, G. R., Project HOPE. 2008. Comparative clinical effectiveness: Leveraging innovation to improve health care quality for all Americans. Written statement before the Committee on Finance, U.S. Senate. 110th Cong., 2nd sess. July 17. http://finance.senate.gov/hearings/testimony/2008test/071708gwtest.pdf.

Woodcock, J., J. Griffin, R. Behrman, et al. 2007. The FDA's assessment of follow-on protein products: A historical perspective. *Nature Reviews Drug Discovery*. April 13.