The SAGE Handbook of Healthcare

Global Policies • Business Opportunities • Scientific Developments

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Preface

Richard Frank

INTRODUCTION

Healthcare spending in the United States was over $2 trillion in 2006 and accounts for roughly 16% of Gross Domestic Product (GDP). In addition, the health sector directly employs nearly 14 million Americans. Many of these people are among the most educated and skilled people in the American society. While the United States spends more on healthcare than most other OECD (Organization for Economic Cooperation and Development) nations, other advanced economies spend between 8% and 12% of their GDP on healthcare. Growth in healthcare spending in the United States over the past 50 years has exceeded GDP growth by an average of about 2.5 percentage points. In Europe over the period 1995–2005 increases in healthcare spending has outpaced growth in GDP in nearly every nation. Accompanying these increases in the share of income devoted to healthcare are increases in longevity and declines in age-specific disability. Thus all advanced economies are struggling with the problem of how to control healthcare spending while continuing to enjoy the gains conferred by advances in modern medicine.

The consequences of nations trying to craft policies that balance a desire to limit the claims that healthcare makes on national income and public budgets is that each part of the health sector is scrutinized and determinations are made about the value of the activities taking place in the various subsectors. Making such judgments requires understanding science, the economic dynamics of the sector, and epidemiology and delivery of healthcare. *The Sage Handbook of Healthcare* offers up-to-date focused analysis of a number of key segments of the health sector in the United States and globally. The *Handbook* concentrates on the markets for pharmaceuticals and medical devices and addresses key developments in these areas in considerable depth.

Technology and Healthcare

Advances in medical technology have been blamed for cost growth and hailed for advancing the health and longevity of much of the world's population. Spending on biomedical research in the United States has grown steadily. Total

research and development in healthcare grew from $37 billion in 1994 to about $94 billion in 2003. The products of this research have frequently been dramatic including vaccines, prescription drugs, diagnostic instruments, and treatment devices that have saved millions of lives. Some have claimed that advances in medicine have improved welfare more than the sum of all other productivity improvements.

The manner in which medical technology is put to work has been pointed to as the most important driver of growth in healthcare spending.[1] For example, US healthcare spending growth has been decomposed into various underlying components. These include, economy-wide growth in prices; rises in medical prices, changes in the size and composition of the population, and changes in "intensity." Intensity is widely interpreted as representing changes in technology, know how, and capability of medical care. For the period 1960–2003, 32% of the growth in healthcare spending was attributed to changes in intensity. Moreover, if one considers the most recent part of that 44-year period, 2000–3, the portion of growth attributable to changes in intensity is 40%.[2]

As noted above drugs and devices are key elements of medical technology. Within those areas there have been important developments in the areas of biopharmaceuticals that now account for about 25% of new drugs; genomic tests, nanotechnologies, and new methods of diagnostic imaging.

The Market and Healthcare Technology

All OECD nations rely on markets to bring new medical products to doctors and patients. Private firms in the pharmaceutical industry, device manufacturers, and biotechnology enterprises make use of basic science (often conducted under government sponsorship), private capital, product development expertise, clinical research, and marketing know-how to bring new treatments to the medical market place. For the most part development of new drugs and devices is a long, costly, and risky process. Thus, the firms in this industry make investments in uncertain projects today that will frequently not begin to payoff until 8–10 years later. These are important industries accounting for over $260 billion dollars in spending in the United States alone. These industries are important both for the products they create and for the benefits they confer on their communities. These features serve to complicate both the economics and politics of policymaking towards this part of the healthcare sector.

Because healthcare is expensive, complicated, and so important to the lives and well-being of each nation's citizens, all countries regulate markets for healthcare products and their delivery. As the role of drugs and devices has expanded the policy attention given to this subsector has intensified. While each nation uses a somewhat different array of policy mechanisms to regulate markets for healthcare technology there are several sets of policy tools most countries have in common. These include law governing intellectual property

(e.g., patent law), regulation of market entry based on safety, efficacy, and sometimes cost-effectiveness; pricing (and purchasing arrangements); the regulation of product promotion and distribution channels (wholesaling, retail); and the role of public investments in each area.

The application of these policy levers results in a common set of policy debates. These focus on the tension between what economists refer to as static and dynamic efficiency. In the context of medical technology markets this means that there is a trade-off between getting "good deals" (low prices) today and a flow of new and innovative new treatments tomorrow. Getting low prices today means today's clients benefit from lower claims on their budgets and more money to devote to satisfying wants beyond healthcare. It also means that the returns to investment in innovative technology are reduced which may mean a reduced flow of innovative medical products in the future. Achieving balance in this policy arena is complicated by the fact that the politics of public budgets tend to make policymakers myopic about long-run gains from maintaining strong incentives to innovate. At the same time assessing the "true" economic costs and hence the economic return to investment in say pharmaceutical R&D is very difficult. Hence industry interests, knowing the tendency of policymakers to be myopic, will frequently offset those claims by suggesting that any attempts to rein in prices will drive investment in R&D to levels that are too low.

The *Handbook* covers a tremendous amount of ground aimed at informing these difficult policy debates. It touches on the science, policy toward intellectual property in the United States and Europe; payment policy in the United States, Canada, Europe, and Japan, the R&D process for specific clinical areas and the regulation of market entry in the United States, Europe, and Japan; and finally issues related to the delivery of care. The *Handbook* addresses long-standing debates such as the impact of reference pricing for prescription drugs. It also introduces a relatively new set of policy challenges related to the economics personalized medicine, and the development of policy towards price competition for "generic" or "follow-on" biologics. These are emerging as hotly debated policy issues that may profoundly shape the cost of care and the flow of new treatments. The authors of the *Handbook* have performed a valuable service by gathering such a comprehensive and informative set of materials in one place. For policymakers and researchers seeking to "get smart" about what is going on in the science, regulations, and economics of the healthcare technology this book represents an ideal starting place.

Notes

1 Newhouse, J.P. An iconoclastic view of health cost containment. *Health Affairs*, 1993;12:1524–31.
2 www.cms.hhs.gov/statistics/nhe/

Foreword

Gerard Wedig

INTRODUCTION

For every person involved in the business of healthcare, one of the most important challenges is the access to information. How does one gain a working knowledge of both the scientific and business sides of the industry? The problem is even more acute in the cases of the pharmaceutical and biotechnology industries, where the science and business models are arguably more complex. Many scientists, who understand the technical possibilities of new therapeutic approaches, still need to understand business models in order to gauge what innovations may be brought to fruition. Conversely, many individuals with business training still need to understand the current trends in medical technology, if only at a basic level.

The present volume lays out both the scientific and technology issues in a manner that enables the reader to gain insights into the industry's future. Each chapter in this book provides either a business or a scientific insight, and in many cases, both. For those with a technical orientation, the book provides a complementary business discussion of issues, including pricing and regulation. For those with primarily a business background, the book provides an effective overview in technical areas that include genomics, oncology, cardiovascular, and other therapeutic areas as well as emerging trends in diagnostics.

PHARMACOECONOMICS

One foundation for understanding what technologies will become commercially feasible is a firm grounding in pharmacoeconomics. Pharmacoeconomics is the study of the cost-benefit ratios of drugs with other therapies or with similar drugs, where costs include both financial and quality-of-life measures. It is a vitally important area of study because in many cases it forms the foundation of what third-party payers will pay for drugs. Third-party payment policy, in turn, is a key "driver" of which drugs will make it to the market and what the future "landscape" of the industry will look like.

The first section of this volume focuses generically on pharmacoeconomics, with a special focus on international pricing and regulatory climates.

Pharmaceutical pricing and reimbursement policy show a great deal of variability, worldwide. Most of these differences are driven by government policy. It is well-known, for example, that most governments in Europe use their own novel approaches to control drug costs, by regulating both the price and entry of drugs into the market place. In some cases, drugs that cannot demonstrate adequate efficacy are not covered at all. In cases where the drug is covered, a host of reimbursement mechanisms may be used, including the rate-of-return regulation, reference pricing, strict cost-plus reimbursement, plus other approaches. The result is that reimbursement levels vary a great deal.

One result of this is that European drug prices are (on average) only 50% of the price levels achieved in the United States. Furthermore, some analysts estimate that if US pharmaceutical companies were able to receive the same prices abroad as they receive in the United States, they would be able to increase their annual profitability by anywhere from 18 to 27 billion dollars. For this reason alone, it is important to understand the international differences in pricing and reimbursement. It is also well-known that in European countries, much of the profit from a drug must be made upon the drug's introduction. Thereafter, government policy frequently dictates that discounts must be granted. This contrasts with the United States, where, until recently, it has been normal for patented drugs' prices to enjoy year-over-year markups.

There are of course exceptions to these general findings. Drugs in certain areas that qualify as "niche" indications are one example. In the case of niche drugs, European prices are frequently closer to the US levels. For example, Roche indicated that the drug Avastin was introduced in Europe with only a 20% discount relative to US prices.

Of course, differences in international drug prices also have implications for the practice of parallel importation or drug reimportation, which represents the practice of arbitraging drug prices between two countries. The issue has been contentious in the United States, as some individuals have secured drugs from Canada. Moreover, pharmaceutical companies are generally concerned about the same practice originating from Europe, although recent legislative sentiment has been against this.

PHARMACOGENOMICS

Part 2 of this book focuses on pharmacogenomics. Genomics is the study of gene location, structure, regulation, and function. As a business enterprise it provides opportunities in at least two areas: (1) the discovery and marketing of new products and therapies; (2) the development of enabling platforms that consist of new technologies (e.g., equipment), information (e.g., mapping data bases) as well as research capabilities. This section of the volume provides several useful chapters on this topic, which range from discussions of genomics

more generally, to specific discussions of pharmacogenomics (e.g., efforts to improve individual responses to drugs), as well as proteomics and nanotechnology.

Genomics lies at the heart of the biotechnology industry. The completion of the human genome project, which provides a complete mapping of the human genome, provides a great opportunity for the development of new targets and clinical therapies. Most analysts, however, expect that the process of developing actual therapies will take a number of years. This is because disease processes and their relation to genes and gene expression is an enormously complex topic. For example, to date only a small percentage of diseases have actually been linked to genes. Still, the opportunities are tremendous. If the more than 1000 hypothesized "disease genes" can be identified, the potential exists for the development of 5,000–10,000 new disease "targets," representing the proteins expressed by these genes.

Pharmacogenomics uses genomics to study individual responses to drug therapies, based upon individual genetic differences and backgrounds. This increases the potential for the development of personalized medicine, which may increase both drug efficacy and guard against adverse events. Genomics-based "point of care" medicine aims to use genomics to make instant diagnoses of patient-specific immunities and other biological conditions to optimize treatments. One application is in the area of infectious disease. Although this approach has not been made operational, it may be so in the foreseeable future.

Proteomics studies the specific proteins that are expressed by genes. The proteins in turn are implicated in actual diseases and other abnormalities. Ultimately, proteomics allows scientists to understand how individual genes affect basic cellular processes that are at the heart of a disease. Clinical proteomics is the application of proteomics to clinical applications. Thus, it provides a new approach to the diagnosis and treatment of a disease.

The various chapters in this section of the volume combine both scientific discussions of developments in these areas, while simultaneously outlining the business opportunities and products that may follow from the scientific developments.

THERAPEUTICS: CASE STUDIES

Oncology

Prior to this century, in the period from 1950–99, virtually all approved cancer drugs could be classified as chemotherapeutic agents. A major drawback of chemotherapy is the associated side effects and toxicity of drugs used. Modern cancer treatments provide the promise of therapies that are more targeted to cancer cells and also less toxic. They do this by being more selective of targets that are located on cancer cells. The chapters in this section of the book

describe a wide range of clinical and business opportunities in this area, ranging from cancer-vaccine development to antiangiogenesis treatments as typified in the drug Avastin.

There are many cancer treatments in development that target the biological mechanisms underlying the disease. An important class of these is kinase inhibitors. Kinase inhibitors account for the majority of new cancer drugs in development. They work by impeding growth mechanisms in cancer cells, that is by inhibiting kinase, an important protein implicated in cell reproduction.

Another important class of drugs consists of monoclonal antibodies. Monoclonal antibody technology works through the design of antibodies that bind to cancer cells. Once the antibodies bind to cancer cells they effectively kill the cancer cells through a variety of mechanisms. Finally, cancer vaccines hold out the promise of preventing the occurrence or reoccurrence of cancers. They work by stimulating the body's immune system to identify and remove cancers, using cells and antigens.

This section of the book provides many insights into these developments. It also provides updates on reimbursements for cancer treatments as well as updates on novel ways to conduct clinical trials of these developments, through the development and tracking of biomarkers.

Cardiovascular and Other Therapies

This section of the book also includes several chapters that discuss new developments in the therapies for cardiovascular disease, diabetes, hypertension, and inflammatory diseases. Cardiovascular diseases are one of the leading causes of mortality and morbidity. One important treatment for cardiovascular disease is the use of stents and, more recently, drug-eluting stents. Recent years have witnessed significant advances in the technology of this market, with multiple competitors "leapfrogging" one another with their own version of a drug-eluting stent. In addition, there have been great strides in the development of new drugs which address cardiovascular disease, many of which are discussed in this chapter.

VLA-4 antagonist drugs are designed to treat inflammatory diseases, such as multiple sclerosis, Crohn's disease, and asthma. A key mechanism in these diseases is the body's inflammatory response. VLA-4 plays an important role in this response and hence presents an intriguing drug target that may be the basis of new therapies. For example, it may be possible to design monoclonal antibodies for this target. Recently, concerns have been raised about the safety of such drugs. These concerns and their likely impact on the treatment of various inflammatory diseases are also discussed in this section of the volume.

Type 2 diabetes is a chronic and progressive disease associated with several morbidities. The incidence of Type 2 diabetes has been increasing worldwide as it is associated with the growing incidence of obesity, among other factors.

A recent study, referred to as the PROactive study shows that certain antidiabetic drugs may have favorable effects on the risk of cardiovascular events that are frequently associated with Type 2 diabetes. Another recent development in the treatment of diabetes is the development of inhalable insulin. Inhaled insulin eliminates the need for painful injection as a delivery mechanism.

Recent developments in this delivery option are also described in this section.

DIAGNOSTICS

The emergence of genomics offers a new opportunity to combine diagnostics and treatments. Genomic tests may identify individuals who may best benefit from treatments. The same technology that forms the basis of treatment may also form the basis of an effective diagnostic test. Moreover, as it becomes important to personalize treatments, it may eventually be necessary to link diagnostics with treatment. This requires comarketing of diagnostics and therapy. The first two chapters of the final section of this volume describe the challenges of comarketing diagnostics and therapies. For example, the traditional marketing channels for marketing therapies and diagnostics are quite different. It will be important to develop new business models for the challenges associated with comarketing diagnostics and therapies.

The final section of this volume also discusses diagnostic markers for the detection of Alzheimer's disease. To administer effective treatments to Alzheimer's patients in a timely fashion, patients must be diagnosed before severe, cognitive symptoms are evident. Several Alzheimer's markers are presently in development. The chapters under this section review these potential markers.

PART I

Pharmacoeconomics

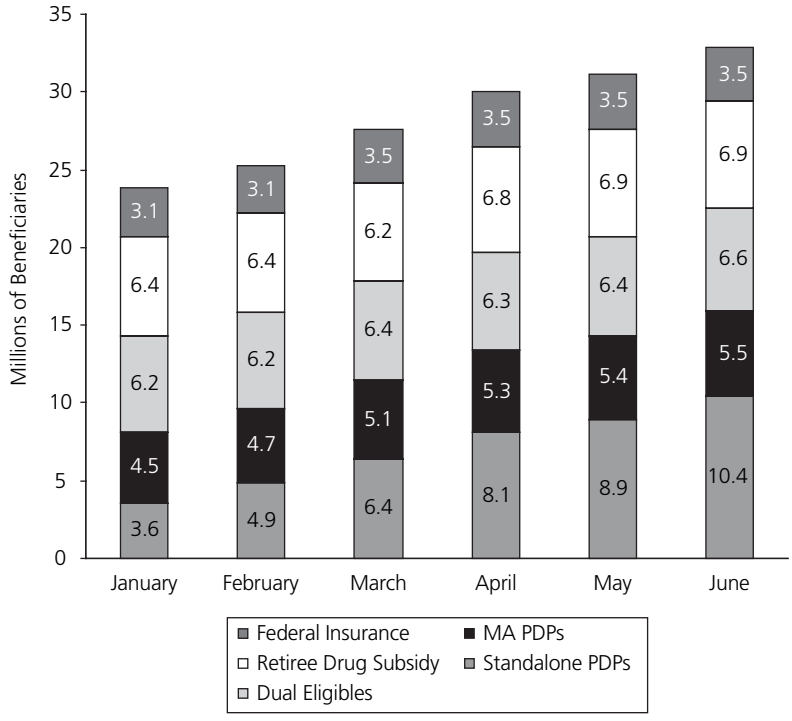
1 Medicare Part D: An Outlook

OVERVIEW

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (more commonly known as the Medicare Modernization Act or MMA) is widely recognized as the most radical reform in the long history of this insurance program. The MMA's most significant achievement is the introduction of Medicare Part D, a wide-ranging new outpatient prescription drug benefit. Yet, the debut of this important new venture was anything but auspicious. The program's launch in January 2006 was beset by problems: a bewildering choice of plans, slow initial enrollment, criticism of the benefit's design (especially the notorious coverage gap), refusal of coverage for some beneficiaries' medicines in the program's first few weeks, and long delays in the reimbursement of pharmacies.

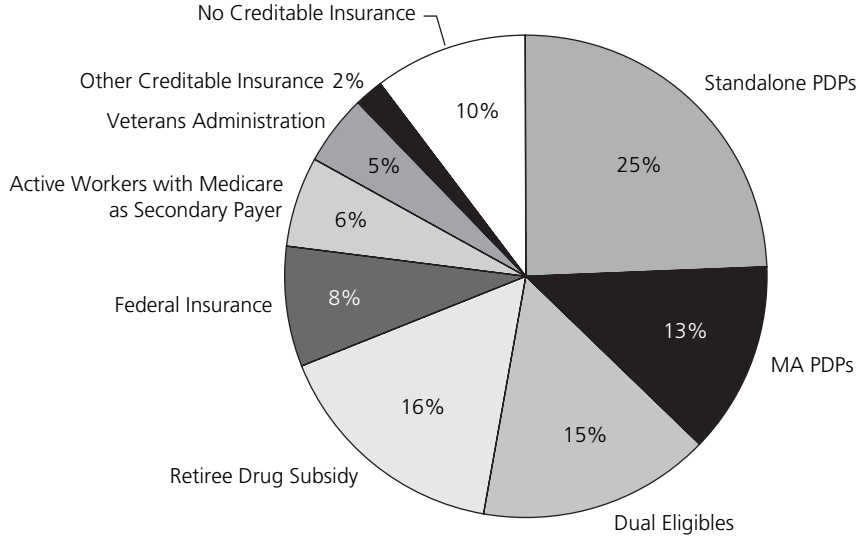
Despite these initial difficulties, the program has steadily gained momentum during the course of the year. Figure 1.1 traces the growth in Medicare Part D enrollment from January to June 2006. According to the Centers for Medicare and Medicaid Services (CMS), overall enrollment increased from 23.8 million in January 2006 to 32.9 million in June 2006, with by far the fastest growth occurring in standalone prescription drug plans (PDPs). Thus, in June 2006, 77% of the 42.5 million Medicare beneficiaries were benefiting from Part D funding in one form or another. In addition, most of the remaining Medicare beneficiaries had drug benefits from an alternative source (e.g., Veterans Administration in active employment with Medicare as the secondary payer, state pharmaceutical assistance programs, Indian Health Service). Figure 1.2 shows the main sources of drug coverage in the Medicare population in June 2006. Disturbingly, 4.4 million beneficiaries (10%) still lacked creditable drug benefits in June 2006. Many of these beneficiaries are younger, healthier seniors who calculated that the costs of membership were likely to exceed the benefits they would derive.

We begin this chapter with a review of key changes to the Medicare Part D plans offered in 2007. We then examine several areas that are likely to be the focus of particular attention from insurers: employer-sponsored health plans, dual-eligible beneficiaries (i.e., beneficiaries who qualify for both Medicare and Medicaid), special needs plans (SNPs), and disease management. We also consider Medicare medical savings accounts – a new provision that, although distinct from Part D, is likely to impact many Medicare beneficiaries. We conclude with a brief assessment of the outlook and implications for biopharmaceutical companies and insurers.



MA = Medicare advantage
PDP = Prescription drug plan

Figure 1.1 Enrollment in Medicare Part D-Related Plans, January to June 2006



MA = Medicare advantage
PDP = Prescription drug plan

Figure 1.2 Sources of Prescription Drug Coverage for Medicare Beneficiaries, June 2006

KEY CHANGES IN 2007

The number of companies that offer national PDPs will increase from 9 in 2006 to 17 in 2007 (the original number of national PDPs in 2006 was 10, but UnitedHealthcare and PacifiCare merged). The new national PDP organizations are EnvisionRx Plus, Express Scripts, Health Net, Longs Drug Stores, NewQuest Health Solutions, NMHC Systems, Humana, and Torchmark. The total number of standalone plans will increase from 2,183 (provided by 86 carriers) in 2006 to 2,844 (provided by 97 carriers) in 2007. The number of Medicare Advantage (MA) plans is set to grow even more dramatically – from 36,348 (provided by 316 carriers) in 2006 to 63,391 (provided by 271 carriers) in 2007 (unlike standalone PDPs, MA plans offer a much wider range of services than just the Part D drug benefit, including administration of care under Medicare Part A [inpatient treatment] and Medicare Part B [outpatient treatment]). Because the margins on MA plans are much more generous than on standalone PDPs, insurers that offer both of these plan types would generally like to maximize enrollment in their MA plans.

As required by the MMA, the basic parameters for the standard drug benefit design (e.g., standard deductible, initial coverage limit, threshold for catastrophic coverage) are adjusted annually in line with changes in drug expenses. In 2007, the parameters will be increased by 6.86%. The annual deductible will rise from $250 in 2006 to $265 in 2007. Thereafter, Medicare will cover 75% of the cost of prescription drugs up to an annual total of $2,400. Coverage will then cease until the beneficiary's annual drug costs reach a total of $5,451.25 (and out-of-pocket payments reach a total of $3,850) – a provision known as the "coverage gap" or "doughnut hole." Medicare will then cover 95% of drug costs in excess of the annual threshold of $5,451.25. Table 1.1 summarizes key changes in the standard benefit design from 2006 to 2007.

Table 1.1 Key Features of Standard Medicare Part D Drug Benefit, 2006 and 2007

	Payments ($)	
	2006	*2007*
Annual deductible	250.00	265.00
Initial coverage limit	2,250.00	2,400.00
Out-of-pocket threshold	3,600.00	3,850.00
Drug cost threshold for catastrophic coverage	5,100.00	5,451.25

The open enrollment period for 2007 runs from November 15 to December 31, 2006. Beneficiaries who are already enrolled in a Part D plan and who do not wish to change their plan need take no action. CMS reports that only 5% of beneficiaries who qualify for the low-income subsidy (LIS) will need to change plans to avoid losing this subsidy. Overall, premiums will average $24 per month if beneficiaries remain with their existing plans, but 83% of beneficiaries could reduce their premiums by switching plans. On average, premiums will be 10% lower in 2007 than in 2006. Lower premiums are obviously a competitive advantage, and plans that set their premiums below the benchmark level will benefit from the automatic assignment of dual-eligible beneficiaries.

The 2006 median monthly premium for standalone PDPs is $35.94, but the range is enormous – from a low of $1.87 to a high of $104.89. Seventy-seven percent of plans offer premiums in the range of $20.01–$50.00. In 2007, the median monthly premium will be $33.40, and the range will be $1.90–$135.70. Eighty-three percent of standalone PDPs will offer premiums in the range of $20.01–$50.00. Figure 1.3 compares the distribution of standalone PDPs' monthly premiums in 2006 and 2007.

With the advent of Medicare Part D, most MA plans have added the new drug benefit to their existing range of services. In 2006, most MA plans charged a monthly drug premium of $10.01–$40.00, but 25% of plans waived the drug premium. By comparison, in 2007, 52% of MA plans will waive the drug premium (Figure 1.4). The

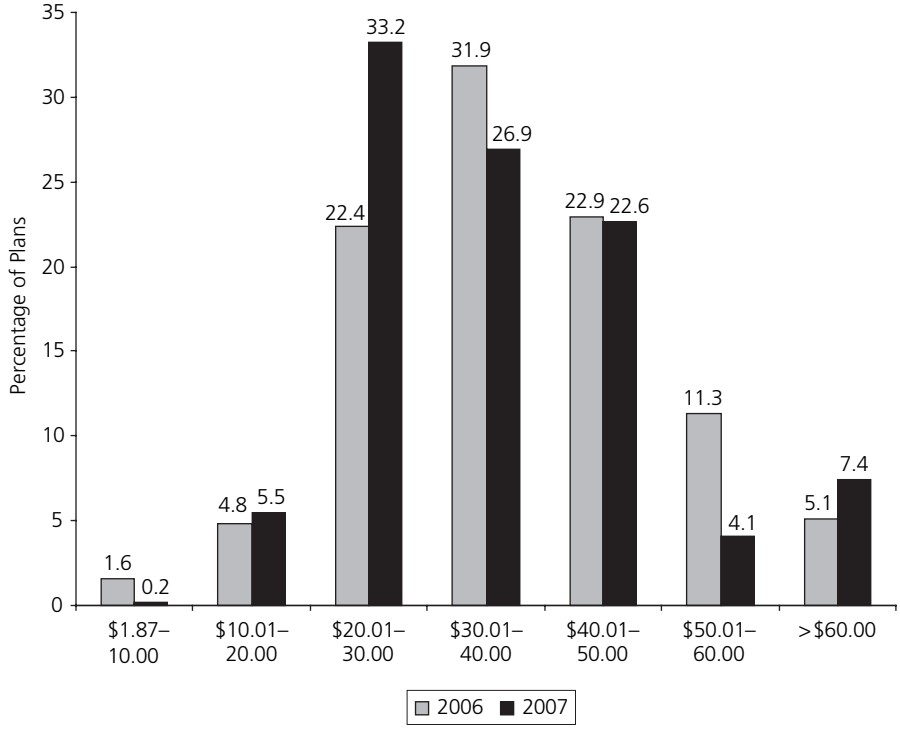


Figure 1.3 Percentage of Standalone Prescription Drug Plans Charging Various Monthly Premiums, 2006 and 2007

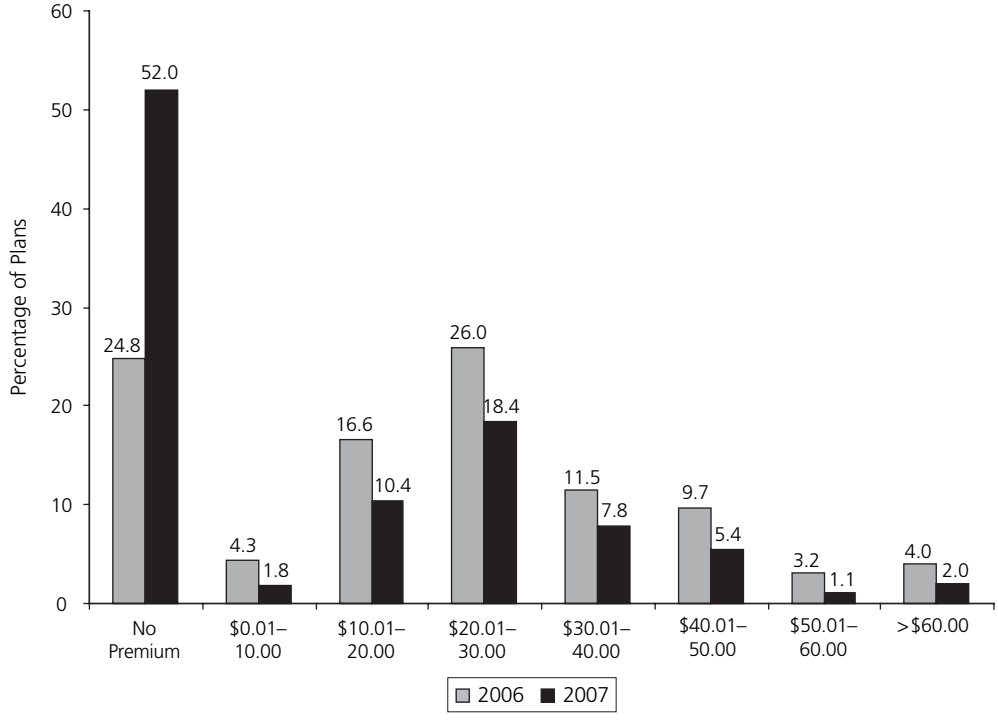


Figure 1.4 Percentage of Medicare Advantage Plans Charging Various Monthly Drug Premiums, 2006 and 2007

median drug premium will decrease from $40.00 in 2006 to $24.40 in 2007.

Most standalone PDPs forgo the annual deductible. Figure 1.5 shows that 58% of plans waived this charge in 2006, a figure that will increase to 60% in 2007. By comparison, only 31% of plans will charge the full deductible in 2007 – down from 34% in 2006. MA plans have been even more decisive in abandoning the annual deductible. Figure 1.6 shows that 91% of MA plans will waive the drug deductible in 2007 – a substantial increase on the 67% of plans that pursued this policy in 2006.

The coverage gap has been one of the most controversial aspects of the Medicare drug benefit – not least because relatively few carriers even offer the option of any form of reimbursement in the gap. At present, 85% of standalone PDPs and 86% of MA plans do not reimburse Part D drugs at all while patients are in the coverage gap, and only 3% of PDPs and 5% of MA plans cover both branded and generic drugs in the gap. However, Figure 1.7 shows signs of a change among PDPs in 2007: only 71% will offer no coverage in the gap, whereas 27% (compared with 13% in 2006) will cover generics. By comparison, MA plan providers are much less inclined to change their coverage gap policies in 2007 (Figure 1.8): 85% will continue to offer no coverage.

EMPLOYER-SPONSORED HEALTH PLANS

Employers that offer their retirees prescription drug benefits that at least match Medicare Part D (e.g., in terms of deductibles, coinsurance, and cost-sharing) can receive a subsidy for Medicare beneficiaries who do not choose to enroll in Part D. In 2006, the tax-free subsidy is equivalent to 28% of retirees' drug costs between $250 and $5,000, with a maximum subsidy per

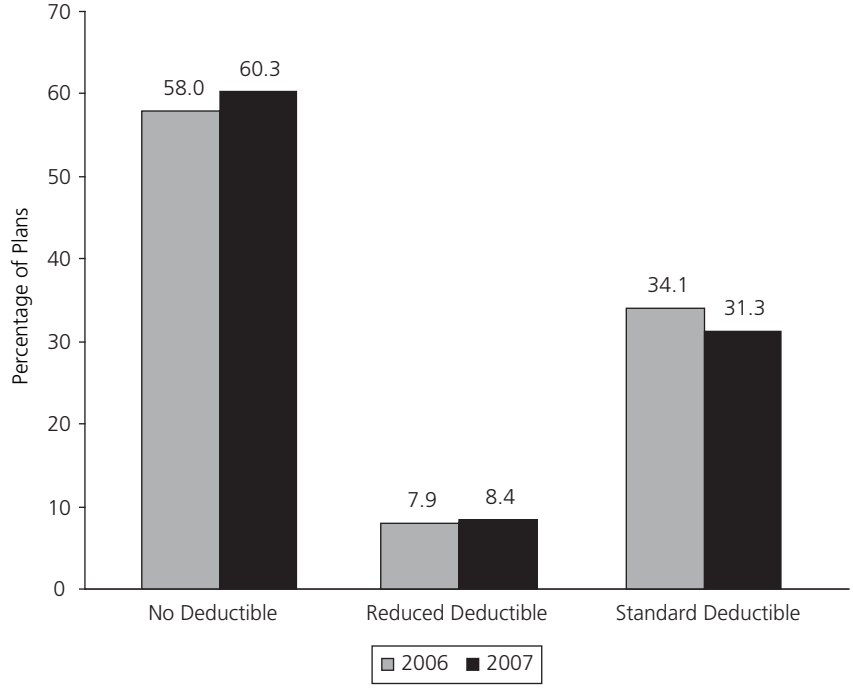


Figure 1.5 Percentage of Standalone Prescription Drug Plans Levying Various Drug Deductibles, 2006 and 2007

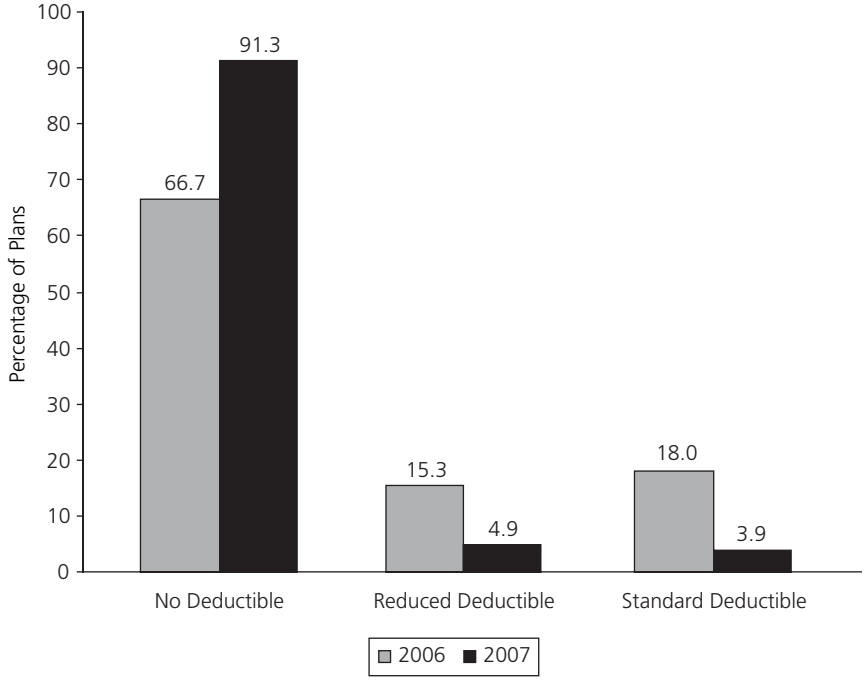


Figure 1.6 Percentage of Medicare Advantage Plans Levying Various Drug Deductibles, 2006 and 2007

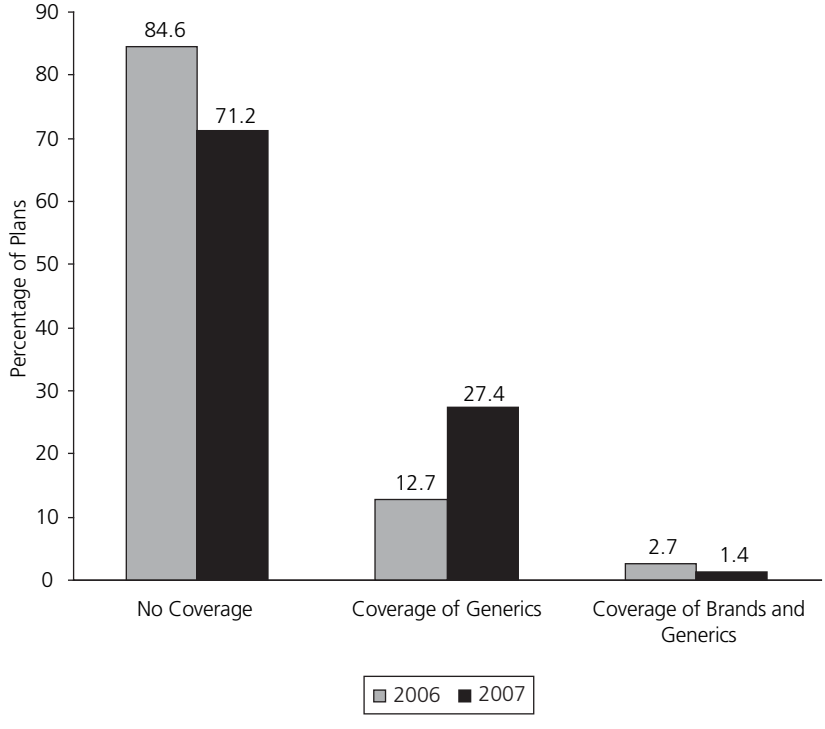


Figure 1.7 Percentage of Standalone Prescription Drug Plans Offering Various Levels of Drug Coverage in the Coverage Gap, 2006 and 2007

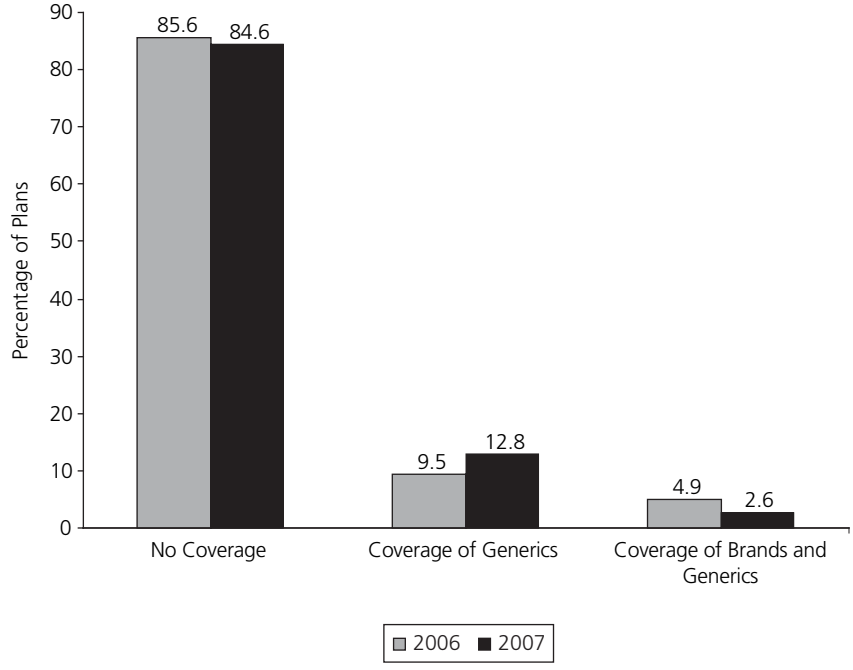


Figure 1.8 Percentage of Medicare Advantage Plans Offering Various Levels of Drug Coverage in the Coverage Gap, 2006 and 2007

beneficiary of $1,330. In 2007, the subsidy will apply to drug costs between $265 and $5,350. To qualify for a subsidy, employers' drug benefits must pass an actuarial equivalence test. Alternatively, companies may decide to pay part or all of the monthly premiums for PDPs or MA plans in which their retirees choose to enroll, contract with CMS to offer an officially approved PDP, or offer their retirees a "wraparound" drug benefit that supplements Medicare Part D.

Between June 21, 2005, and October 7, 2005, the Kaiser Family Foundation and Hewitt Associates conducted a survey of 300 large employers (i.e., companies that each have 1,000 or more employees) that currently offer health benefits to their retired former employees. *Prospects for Retiree Health Benefits as Medicare Prescription Drug Coverage Begins* found that 94% of participating employers believed that their drug benefits were actuarially equivalent or superior to the standard Medicare prescription drug benefit for 2006. Overall, 82% of these employers intended to maintain their prescription drug benefits and take the 28% Medicare subsidy in 2006. Fifteen percent planned to wrap their drug benefits around Medicare Part D, but 11% indicated that they were likely to discontinue drug coverage in 2006.

Beyond 2006, many companies that planned to take the Medicare subsidy for their own drug benefits would consider changing their policies on retiree drug coverage. Fifty percent of these companies considered it very likely and 32% somewhat likely that they would continue to offer their own benefits supported by the Medicare subsidy in 2007, but 3% were very unlikely and 4% somewhat unlikely to follow this course, and 11% did not know what they would do. Not surprisingly, employers' certainty about their intentions diminishes over time. In 2010, only 20% of these companies are very likely and 30% are somewhat likely

to continue to offer their own benefits supported by the Medicare subsidy, while 10% are very unlikely and 12% are somewhat unlikely to follow this course, and 28% did not know what they would do.

The Medicare subsidy has been a welcome innovation in the short term, but it is unlikely to have a significant long-term impact on the steady decline in employer-sponsored drug benefits for retirees. Many employers reportedly dislike the complexity and uncertainty associated with applications for the Medicare subsidy. In addition, government accounting standard rules on valuing retiree liabilities will make it more advantageous for employers to contract out their drug benefits.

The Segal Company, a benefits, compensation, and human resources consultancy, found that most of its clients received subsidies of $500–$600 per employee in 2006. However, transferring coverage to a PDP could deliver savings of more than $700 per employee in 2007 and reduce the actuarial and administrative burden and cost of operating a plan. Companies could then give their retirees more generous support (e.g., covering the deductible, paying a proportion of costs in the coverage gap).

In 2007, John Gorman, CEO of the Washington, DC-based Gorman Health Group, expects employers to begin a gradual shift away from the subsidy toward drug plans with private companies. He believes that more generous subsidies would be required to persuade many employers to continue sponsoring their own insurance. Gorman predicts that national and multistate MA plans that have dominant group businesses (e.g., WellPoint, UnitedHealthcare, Humana, Blue Cross/Blue Shield plans) will gain most from the migration from group insurance to PDPs. Public sector employers, labor unions, and tax-exempt and nonprofit organizations are likely to be at the forefront of this movement, a reflection of the relative unimportance of the subsidy to such employers.

Gorman expects many employers to turn to MA plans (e.g., PPOs, private fee-for-service plans, medical savings accounts), which offer retirees more flexible benefits than do HMOs. He believes the Blues plans' large share of the group insurance market among government employers will be a distinct advantage in converting members to PDPs. Midsize employers are expected to follow suit in coming years, followed by the large private-sector employers. Gorman believes that "it's only a matter of time before large employers are out of the retiree health business altogether, as it's becoming a competitive issue."

Pharmacy benefit management (PBM) companies will also benefit from the exodus from employer-sponsored retiree drug benefits. In 2007, four PBMs – EnvisionRx Plus, Express Scripts, Longs Drug Stores, and NMHC Systems – will join Caremark Rx and Medco Health Solutions in offering national standalone PDPs. Dan Mendelson, President of consulting firm Avalere Health, believes the PBMs launched national PDPs specifically to target the employer-sponsored insurance market. This migration is unlikely to be a rapid process. For example, Caremark expects limited change in the retiree market for the year 2007: most of its clients will continue to take the Medicare subsidy. However, two unnamed Caremark clients wrapped their drug benefits around a PDP in 2006.

DUAL-ELIGIBLE BENEFICIARIES

In 2006, an estimated 14.4 million Medicare beneficiaries who had incomes below 150% of the federal poverty level (FPL) qualified to have 85–98% of their prescription drug costs paid by Medicare. The US government laid particular emphasis on encouraging these beneficiaries to sign up for a Medicare PDP or MA plan. Effective January 1, 2006, 6.2 million residents who qualified for both Medicare and Medicaid (the health insurance program for low-income residents) and had an income at or below 100% of the FPL – so-called full-benefit dual-eligible beneficiaries – had their outpatient drug

benefits transferred from Medicaid to Medicare Part D. A small minority of these dual-eligible beneficiaries enrolled in a plan of their own choice, however, a majority of 5.9 million dual-eligible beneficiaries were automatically assigned to a plan.

CMS assigned dual-eligible beneficiaries to plans that did not exceed the benchmark for monthly premiums. Carriers that benefited significantly from this process included UnitedHealth (1.1 million automatically assigned beneficiaries), WellPoint (more than 600,000), Humana (595,000), WellCare (570,000), Universal American Financial (328,000), and MemberHealth (260,000). However, dual-eligible beneficiaries were free to switch to a different plan if they wished (e.g., if the automatically assigned plan did not offer generous coverage of their prescribed drugs). WellCare, for instance, expected to lose 20–30% of its automatically assigned beneficiaries to Blue Cross/Blue Shield plans, UnitedHealth, and Humana.

As noted earlier, CMS data indicate that 95% of the low-income beneficiaries will be able to remain with their existing plan and still receive the LIS in 2007. Similarly, Goldman Sachs predicts that more than 90% of dual eligibles will not change their plans in 2007. However, the National Senior Citizens Law Center (NSCLC), in Oakland, California, reports that some plans are leaving the market or no longer meet the benchmark. Jeanne Finberg, the NSCLC's directing attorney, predicts that as many as 30% of the nation's subsidized enrollees could need reassignment. She believes that many of these beneficiaries will stay with the same sponsor but may take on new identification numbers and different formularies.

Plans whose premiums do not exceed the low-income premium subsidy amount by more than $2 in 2007 will keep their LIS-eligible members. At the time of reenrollment, CMS will review plans that have premiums above the benchmark or that are terminating their coverage. CMS will reassign beneficiaries enrolled in such plans to other plans. If a carrier offers other plans in the same region that have premiums below the benchmark level, CMS will switch beneficiaries to such a plan. Otherwise, CMS will reassign beneficiaries randomly among PDP sponsors that offer eligible plans in a given region. Beneficiaries may elect to remain with their existing plan (if still available), but they will then face higher costs.

Following the reassignment process in mid-October 2006, CMS will provide the "losing" PDPs with a preliminary listing of members who will be switched effective January 1, 2007. PDPs gaining new members will also receive a reassignment notification file; by early December, they must send beneficiaries an acknowledgment that their enrollment has been accepted by CMS. According to CMS, 750 plans across the United States will offer a premium waiver to beneficiaries who qualify for the full LIS.

SPECIAL NEEDS PLANS

In preparation for the launch of the Medicare prescription drug benefit, CMS automatically enrolled more than 90% of dual-eligible beneficiaries in standalone PDPs. However, these beneficiaries – and others with special requirements – could benefit from a particular provision of the MMA: SNPs. These plans offer tailored coverage to dual-eligible beneficiaries, residents of long-term care facilities, and beneficiaries who have severe or disabling chronic conditions. Many of these beneficiaries have complex care needs, see multiple physicians, are uneducated, and receive little support from their communities. They could benefit from inclusion in a managed care organization (MCO) instead of being enrolled in plans dedicated solely to Medicare Part D.

Kevin "Kip" Piper, President of Health Results Group and Senior Counselor at Fleishman-Hillard, estimates that there are 3.5 million institutionalized beneficiaries and 7.5 million dual eligibles. CMS data show that 83% of Medicare beneficiaries have at least one chronic condition, but the 23% of beneficiaries who have 5 or more

chronic disorders account for 68% of total Medicare spending. According to the recently resigned CMS administrator, Mark McClellan, in the course of a year, these severely ill beneficiaries make an average of 37 physician-office visits, consult 14 different providers, spend 7 days in hospital, and fill 49 prescriptions. By comparison, the average Medicare beneficiary consults just 7 different physicians and fills approximately 20 prescriptions per year. Therefore, Piper believes that SNPs have the potential to exploit "an extraordinarily large, virtually untapped market. We are talking on the order of a quarter-trillion dollars." He added that, "if a plan wants to grow, especially a large plan, they have to get in this business."

In 2005, the first year of the SNP initiative, 125 plans were in operation – mainly managed care plans that had existing MA contracts with CMS. In 2006, the number of SNPs increased to 276. Most of these plans (226) focus on dual eligibles, but 37 care for institutionalized beneficiaries, and 13 address the needs of the chronically ill. Overall, these plans had 550,000 members as of August 1, 2006. According to CMS, the number of SNPs will increase again in 2007, to a total of 471. Piper expects enrollment to grow even faster, reaching 1 million by the end of 2007 and doubling again in 2008. This expected rapid growth is attributable to substantial increases in payments for managing patients with multiple chronic conditions. Plan sponsors have expressed interest in creating specialized SNPs for several chronic conditions, including cardiovascular diseases, osteoarthritis, obesity, mental disorders, end-stage renal disease, and HIV/AIDS.

Before 2005, Medicare beneficiaries with special needs were commonly regarded as an unwelcome liability for health plans. However, the MMA introduced a risk adjustment model that offers greater rewards for managing an increasing number of chronic disorders. The *New York Times* of October 21, 2006, noted that, before the introduction of risk adjustment, a health plan would have received $8,145 per year for the care of a 70-year-old woman. The payment would have varied only according to beneficiaries' age and sex, not their health profile. Under the new system, the basic payment is only $4,075 per year, but this amount increases to $6,197 if the patient is diabetic. If the beneficiary also has circulatory problems, the health plan receives $12,182 per year, and the payment would total $30,126 if the patient additionally had emphysema, congestive heart failure, and depression. These additional payments have made the sickest Medicare beneficiaries a financially attractive target for insurance companies. John Gorman told the *New York Times* that "the people these plans were running from five years ago now become the desirables. It's totally standing the economics of this industry on their head." Notwithstanding these sharp increases in payments for beneficiaries with multiple chronic conditions, some observers see the need for a "frailty adjuster" to cover plans' much higher expenses for the most infirm beneficiaries. CMS is reportedly considering the introduction of such a measure in the future.

SNPs promise to be profitable. Piper forecasts that start-up costs will limit early margins to 4–6%, but improving care and eliminating waste could increase margins to 6–10% in future years. However, government intervention and the need to increase benefits in response to growing competition could trim those margins in the long term.

In the past, differences between Medicare and Medicaid with regard to bidding, contracting, enrollment rate setting, and marketing deterred many plans from entering the special needs market. While Medicare is a federal program, Medicaid is administered at state level, with pronounced policy differences from one state to another. A review of SNPs in Boston (Massachusetts), Miami (Florida), and Phoenix (Arizona) conducted by Mathematica Policy Research found that the most successful plans generally have extensive experience working with both Medicare and Medicaid and can effectively

partner with state governments, which have input on the Medicaid business (see Medicare Advantage SNPs site visits, Mathematica Policy Research, June 2006, www.mathematica-mpr.com/publications/pdfs/medadspecial. pdf. Accessed November 15, 2007). The most astute and ambitious plans are creating their own SNPs to service the dual-eligible population. Meanwhile, federal and state governments appear to favor an integrated model for full dual-eligible beneficiaries. Many state governments express a desire for closer collaboration with Medicaid managed care providers in caring for their dual-eligible populations, but Mathematica found that plans were often forced to work primarily with CMS's central office instead of regional offices.

According to Mathematica, approximately a dozen states have passive enrollment in SNPs. In other states, plans must use marketing initiatives to reach out to potential members, but this strategy has had mixed results to date. Data limitations make it difficult for insurers to identify dual-eligible beneficiaries. The Medicare and Medicaid programs have separate enrollment lists, and eligibility for Medicaid changes in line with beneficiaries' income. Insurers do not have contact details for dual eligibles, with the obvious exception of beneficiaries who have been automatically enrolled in their SNPs. Plan sponsors may be able to obtain referrals from network physicians. In addition, MA plans can use claims data to identify members who have specific illnesses that they are targeting.

Aveta has become one of the largest SNP providers in the United States, with almost 100,000 enrollees in total (74,000 chronically ill patients and 23,000 dual-eligible beneficiaries). The Fort Lee, New Jersey-based company has had particular success with its SNPs in Puerto Rico, where it already had a strong presence in MA. In contrast, the company has struggled to raise awareness of its SNPs in Cook County, Illinois, where it has thus far recruited only around 100 members. Consequently, Aveta has requested help from CMS in educating Medicare beneficiaries about the SNP option. Overall, the company expects strong growth, particularly from SNPs for dual-eligible beneficiaries.

HealthSpring, an MCO headquartered in Nashville, Tennessee, was likewise forced to find potential enrollees in the community. However, Craig Schub, the company's senior vice president of marketing, confirms that many dual eligibles cannot be reached through normal marketing channels. Instead, HealthSpring has relied on a strategy of reaching Medicare beneficiaries through trusted organizations in the community, for example, government agencies, community outreach groups, churches and so on (for more information on HealthSpring's future growth strategy, see the sidebar, "Healthspring: A Regional Player Goes National").

Beginning in the 2008 contract year, CMS will allow SNPs to limit enrollment of dual eligibles to subsets (e.g., the disabled) who are receiving care under Medicaid. This change is intended to provide a more integrated delivery system. CMS will provide further guidance on acceptable subsets and the approval process.

The current legislation governing SNPs runs until December 2008, and Congress will review the impact of this initiative before deciding whether to renew it. However, few observers expect this program to be cancelled.

Healthspring: A Regional Player Goes National

HealthSpring, an MCO based in Nashville, Tennessee, initially chose to focus its Medicare Part D activities in a handful of regions in southern states – its well-established core market. The company considered it advisable to gain experience in the new program in familiar territory before contemplating nationwide expansion. According to Wendy Richey, the company's

vice president of government programs, "the legislative requirements are huge. We're now at a point where we can do national work." Joining the exclusive ranks of national players is a major step for HealthSpring.

At the beginning of 2006, the company received automatic assignments of approximately 90,000 PDP members in the states in which it was active, but many of these beneficiaries subsequently left for competing plans. On May 1, 2006, the company received another 20,000 PDP members, and enrollment in its standalone plan currently stands at 88,000. In 2007, the company hopes a strong focus on customer service will enable it to retain two-thirds to three-quarters of its new automatically assigned members.

Like many other plan sponsors, HealthSpring sees the second year of automatic assignment of dual-eligible beneficiaries as a way to add covered lives and expand into new regions. However, although the company is casting a wide net, it expects to catch far fewer new enrollees than the national companies did last year. Richey predicts that "the migration is not going to be what it was last year because ultimately CMS is going to try to keep duals with who they had this year as long as the premium is within $2 of the national benchmark." The company could benefit from automatic assignment of low-income beneficiaries who become eligible for Medicare in 2007 or whose former plans no longer qualify for the LIS, but this number is expected to be modest. Moreover, HealthSpring will have to contend with more competitive price points from Humana, UnitedHealthcare, and WellCare.

In preparation for the move to nationwide activity, HealthSpring has expanded its resources. The company has moved away from managing each PDP at the state level and will bring that work in-house to the corporate pharmacy. HealthSpring's PBM company has also had an important role to play in broadening the MCO's networks.

DISEASE MANAGEMENT

Historically, Medicare fee-for-service (FFS) enrollees generally lacked access to disease management (DM) programs, unless they had some form of supplementary health insurance. CMS officials have long acknowledged that this situation is a significant problem. In testimony before the House Committee on Ways and Means Subcommittee on Health on May 11, 2004, Mark McClellan offered the following explanation for the dearth of DM activities in the Medicare FFS system:

> The Medicare fee-for-service system is structured and financed to manage acute care episodes, not to manage and support individuals with progressive chronic diseases. Providers of care are organized and paid for services provided in discrete settings (for example, hospitals, physician offices, home health care, long-term care, or preventive services). Patient care can be fragmented and poorly coordinated and patient information difficult to integrate among settings. Providers may lack timely and complete patient clinical information to fully assess their patients' needs and to help prevent complications. Ongoing support to beneficiaries for managing their conditions outside their physicians' offices is rare.

In October 2004, the Congressional Budget Office (CBO) published what has since become a widely publicized review of the clinical effectiveness and cost-effectiveness of commercial DM initiatives. The report, entitled *An Analysis of the Literature on Disease Management Programs*, concluded that "the prevailing evidence appears to be that while disease management programs improve adherence to practice care guidelines and lead to better control of the disease, their net effects on health costs are not clear." The CBO suggested that it might prove difficult to translate the results of successful commercial DM programs to Medicare FFS beneficiaries – a population that is elderly, has multiple illnesses, and consults a wide range of medical providers. The fact that Medicare beneficiaries remain in the program much longer than most employees remain in the same employer-sponsored health plan should enhance the effectiveness of DM in the Medicare population. However, the CBO suggested that the clinical effectiveness of DM programs might actually

increase Medicare's total costs over a beneficiary's lifetime: "If beneficiaries ended up dying from diseases that are more expensive to treat (such as cancer), the total cost for the program could actually increase."

Section 721 of the MMA mandates by far the largest DM demonstration in history – a voluntary chronic care improvement program, now called Medicare Health Support, to improve the quality of care and life for approximately 180,000 Medicare beneficiaries who have multiple chronic illnesses (e.g., congestive heart failure [CHF], complex diabetes, chronic obstructive pulmonary disorder [COPD]). CMS reports that approximately 14% of Medicare beneficiaries have CHF, but they account for 43% of the program's spending. Similarly, the 18% of Medicare beneficiaries who have diabetes account for 32% of the program's expenditures. The Medicare Health Support Program must reduce health risks, improve participants' quality of life, and achieve savings for Medicare and its beneficiaries. Participating companies are paid monthly fees, but they have to refund some or all of these fees to the federal government if they do not meet agreed standards for quality improvement, save Medicare at least 5% of healthcare costs for enrollees, and improve beneficiary satisfaction.

The MMA made a provision for a wide range of enterprises (e.g., disease management organizations, health insurers, integrated delivery systems, physician group practices, consortia of such entities) to apply to serve as chronic care improvement organizations (CCIOs) in this demonstration project. In December 2004, CMS awarded contracts with a combined value estimated at $100–200 million to 9 CCIOs:

- American Healthways, Washington, DC and Maryland.
- LifeMasters Supported SelfCare, Oklahoma.
- Health Dialog Services, Western Pennsylvania.
- McKesson Health Solutions, Mississippi.
- CIGNA Healthcare, Northwest Georgia.
- Aetna Life Insurance, Chicago, Illinois.
- Humana, Central Florida.
- XLHealth, Tennessee.
- Visiting Nurse Service of New York and United HealthCare Services, Brooklyn/Queens, New York.

If it is apparent before three years have passed that any of the demonstration projects are clearly successful, Medicare will expedite the rollout of these programs to the wider Medicare population. CMS has high expectations for the Medicare Health Support Program. In his aforementioned testimony before the House Committee on Ways and Means Subcommittee on Health in May 2004, McClellan expressed the hope that the Chronic Care Improvement Program (CCIP, now renamed the Medicare Health Support Program) would provide an opportunity to reward disease prevention and health improvement in the Medicare FFS system:

> Currently, Medicare fee-for-service payments do not encourage prevention of diseases, good outcomes and performance. Instead, the payment system provides money for acute events, missing a potential opportunity to prevent these situations which could be beneficial from a cost standpoint, but, more importantly, from a health perspective. In a sense, payment incentives are the opposite of the way they should be. The CCIP seeks to address this problem, as well as others described above, by rewarding efforts to prevent acute episodes and improve health. Under CCIP, awardees will work to increase patient compliance, facilitate communication between patients and providers, and better coordinate care among providers caring for the same individual. In a much more direct way than ever before under fee-for-service Medicare, economic incentives will be directly lined up with prevention and performance. We hope to reward high quality care, rather than high volume and high intensity care.

The DM industry also hopes that the Medicare Health Support Program will give its members the opportunity to penetrate the potentially enormous and lucrative market for Medicare DM. Some analysts suggest that, if the Medicare Health Support Program is judged a success and opens the floodgates to DM, total revenues in this industry could ultimately increase from approximately

$1.2 billion per year at present to $10 billion or even $20 billion per year.

In an interview with the Commonwealth Fund in June 2005, Christobel Selecky, the CEO of LifeMasters Supported SelfCare and President of the Disease Management Association of America, articulated her hopes for this demonstration project:

> Should the Medicare Health Support pilots be successful, and I believe that most of them will be, it will open the door toward a significant expansion of disease management into an as-yet untapped population. Because most of these pilots are built on collaborative models that include disease management organizations, physician organizations, health plans, community organizations, and consumer groups, among others, I hope that their success will serve to more deeply embed disease management into the fabric of our health care system.
>
> Some of the companies involved in the new Medicare Health Support initiative will continue to concentrate on providing DM services in support of health insurers and employers. For example, American Healthways works with more than 50 carriers, including 16 that operate MA plans. On the other hand, some DM organizations have recently shown interest in setting up their own Medicare health plans. For instance, in October 2006, Visiting Nurse Service of New York (VNSNY) launched an MA plan and a standalone PDP under the banner of VNS CHOICE Select. The company plans to target the approximately 250,000 full-benefit dual eligible beneficiaries who live in the five boroughs of New York City. In addition to offering the usual range of MA services, including administration of Medicare Part A and B benefits, VNS CHOICE Select will build on the company's existing program of nurse visits to patients' homes.
>
> In 2006, XLHealth launched a chronic care SNP in its home state of Maryland. In 2007, the company plans to expand this operation to Texas, Arkansas, Missouri, Georgia, and South Carolina. XLHealth chose these states on account of their low overall health scores, lack of MA penetration, and physicians' receptivity to SNPs. The new plans will cover diabetes, COPD, heart failure, and end-stage renal disease. The company estimates the total number of potential enrollees in its target states at 1.2 million, but it would be pleased to sign up 25,000–30,000 members in 2007.

This diversification strategy is not without risks: the launch of the SNP could upset some of the more established plans for which XLHealth has long provided DM services. However, Paul Serini, Executive Vice President at XLHealth, believes "there's plenty of room, plenty of room for others to come in and it would increase awareness of [chronic-care] SNPs in the physician community and in the beneficiary community, and competition is always a good thing." The company has already agreed to form an SNP partnership with an MA plan in New York and is conducting negotiations with three or four major national plans that could lead to alliances in 2008.

MEDICARE MEDICAL SAVINGS ACCOUNTS

The MMA contained a little-known measure to encourage people under age 65 – and their employers – to save toward their current and future healthcare costs: health savings accounts (HSAs). Contributions to an HSA are tax-free if the beneficiary enrolls in a health plan that has a high deductible and a high cap on annual out-of-pocket expenses. Plan enrollees can use funds from their spending account to pay for medical expenses, including prescription and nonprescription medicines. If their spending accounts are exhausted, members must pay all their healthcare expenses out-of-pocket until they reach their plan's deductible. Any money in an HSA that is not spent in a given year may be carried over to the next year and will gain interest tax-free, thereby allowing savers to accumulate substantial funds to cover their healthcare expenses. Approximately 3.2 million US residents have HSAs, and one-fifth of companies (one-third of companies with more than 5,000 employees) offer this type of account to employees.

Under the terms of the MMA, current Medicare beneficiaries cannot sign up for new HSAs, but they can benefit from funds they saved in such accounts before they became eligible for Medicare. However,

CMS has been able to sidestep this ban by means of a demonstration project. Beginning in 2007, a provision similar to HSAs – Medicare medical savings accounts (MSAs) – will be offered in a total of 39 states. In addition, more flexible MSAs will be offered in two states. These more flexible accounts will cover preventive services during the deductible period, provide a deductible below the out-of-pocket maximum, impose cost-sharing up to the out-of-pocket maximum, and reduce out-of-pocket payments if enrollees use in-network services.

MSAs cover Medicare Part A and B benefits but exclude Part D: beneficiaries must sign up for a standalone PDP if they wish to receive outpatient drug benefits. Funds in an MSA cannot count as Internal Revenue Service (IRS)-qualified expenses if they are used to pay Part D premiums, but they can be used toward copayments, coinsurance, and deductibles for the Part D drugs. Plans may offer additional benefits for an increased fee, but no plans intend to take advantage of this provision in 2007.

At the beginning of each year, CMS will pay an annual deposit into an interest-bearing account to pay for medical services. After the enrollee has paid the deductible for the year (at least $2,000 in 2007 – far more than the typical Medicare PDP deductible of $265), the insurer will pay for any Medicare-covered services (enrollees whose expenses exceed their annual deductible may be required to share some of the subsequent costs, subject to an out-of-pocket maximum). As with HSAs, unused money in an MSA can be rolled over to the following year, allowing the beneficiary to accumulate money tax-free.

According to CMS, three companies will offer varied MSA plans in 2007:

Blue Cross of California will offer a regular MSA plantargeted at individual and employer group markets in California. Deductibles will range from $2,500 to $4,500, with no cost-sharing after the deductible is met and no coverage of preventive services before the deductible.

Unicare Life and Health Insurance is offering a productsimilar to that of Blue Cross of California but is focusing on individual and employer group markets in 38 states.

American Progressive, a subsidiary of Universal American Financial, is rolling out a demonstration MSA plan serving the individual market in New York and Pennsylvania, and all 50 states for the employer market. The plans feature a $4,000 deductible, a $4,800 out-of-pocket maximum, 29% cost-sharing after the deducible is met up to the out-of-pocket maximum, and some coverage of preventive services before the deductible.

CMS believes that MSAs will appeal particularly to beneficiaries who are healthier or have experience with HSAs. Federal officials present MSAs as one element in a portfolio of products, ranging from preferred provider organizations (PPOs) to private fee-for-service plans, intended to contain beneficiaries' costs. The National Association of Health Underwriters believes that introducing greater choice and competition into Medicare should foster innovative ideas for controlling costs and improving healthcare delivery.

Before his recent resignation, CMS administrator Mark McClellan predicted that enrollment in Medicare Part D overall and in the MSA demonstration project would grow substantially in 2007 and 2008. Industry observers believe the MSA plans could draw away beneficiaries from the extremely popular Medicare private fee-for-service offerings.

If the high-deductible model takes hold, companies that have long experience in the consumer-directed market (e.g., WellPoint, UnitedHealthcare) could take a substantial share of the market as it matures.

OUTLOOK AND IMPLICATIONS

The massive increase in the number of Medicare Part D plans – especially MA plans – in 2007 demonstrates the health insurance industry's commitment to this new program. Lower premiums, zero deductibles, and an expansion of coverage in the coverage gap are all good news for beneficiaries. However, these changes

reflect the intense struggle among insurers to gain an advantage in a highly competitive market.

The large insurers have quickly assumed a dominant position in the Medicare Part D market, leaving other companies to compete for a marginal share of regional markets. In a recent report, Deutsche Bank Securities noted the top-5 PDPs controlled nearly 70% of the Part D market by August 2006. Analysts predict that most of the smaller companies will eventually try to sell their Part D businesses to the large insurers. John Gorman expects smaller companies to reassess their competitive position around the second quarter of 2007, by which time the enrollment figures of all participating insurers will be known. Small companies will then be prime targets for acquisition, and extensive consolidation appears inevitable in the longer term.

With approximately 90% of the Medicare population already enrolled in a Part D plan or equivalent, insurers will need to redouble their efforts to persuade the 4.4 million beneficiaries who still lack drug benefits to sign up in 2007. In addition, successful PDP sponsors will increasingly seek to convert enrollees to MA plans. For example, Humana has stated its ambition to boost its current MA enrollment of close to 1 million by converting many of its 3.5 million PDP members. Almost 70% of Humana's PDP enrollees were not given the option of an MA plan in 2006: they were enrolled through the CMS Web site, Humana's State Farm partnership, or other channels that did not feature MA plans. Humana projects profit margins of 3–5% for its MA business, compared with just 1–3% for its standalone PDPs.

Employer-sponsored insurance for retirees has been in decline in the United States for many years. Research conducted by the Kaiser Family Foundation and the Health Research and Educational Trust found that, among large employers (i.e., companies with 200 or more employees) that offer health insurance to their active employees, the percentage that also offers such a benefit to their retirees has decreased from 66% in 1988 to just 35% in 2006. Medicare's retiree drug subsidy may arrest this decline temporarily, but it is unlikely to stop or reverse the trend in the long term. As noted earlier, many employers would require more generous subsidies to continue to offer these benefits to their former employees in years to come. Medicare Part D will be an invaluable safety net for senior citizens affected by such changes, but the overall quality of retiree drug benefits could be steadily eroded.

The increased emphasis on beneficiaries with special needs – especially chronic illness – will be a positive development. The biopharmaceutical industry could benefit from greater use of its products, particularly in disease prevention. Manufacturers need to look for opportunities to support and sponsor disease management programs linked to this new initiative.

The coverage gap will remain one of the most contentious features of Medicare Part D. The sharp increase in the number of PDPs that offer generics coverage in the gap offers some comfort to beneficiaries who have substantial drug costs, but critics maintain that this provision remains an imperfect solution to a serious problem. Monthly premiums are much higher for plans that offer any form of coverage in the coverage gap. For PDPs, the median monthly premium in 2007 will be $29.00 for plans that offer no gap coverage, $46.90 for plans that cover generics, and $103.20 for plans that cover all formulary drugs (effectively eliminating the gap). Beneficiaries who fell into the doughnut hole in 2006 will likely be interested in plans that fill the gap in future years, but the monthly premiums for plans that cover all formulary drugs may still be unaffordable for some beneficiaries. More significantly, only 38 PDPs will offer coverage of all formulary drugs in the coverage gap in 2007, and some beneficiaries may find that their medications are excluded from these plans' formularies.

The coverage gap presents multiple threats to manufacturers of branded drugs. Nonadherence is one potentially serious

problem: faced with a sudden large increase in their out-of-pocket payments, some beneficiaries may discontinue their drug therapy, miss doses, or reduce their dosage to save money. Other beneficiaries may conclude that it is no longer worthwhile to continue paying premiums for Medicare Part D and therefore drop out of the program, losing all drug benefits in the process. Beneficiaries who accept a switch from a branded medicine to a generic one will not necessarily revert to their original medication when they emerge from the coverage gap and are eligible for 95% reimbursement of their drug costs. Physicians may be reluctant to change a patient's medications twice in a year, particularly if the patient has been stabilized on the generic alternative. In that event, the coverage gap could cost manufacturers of branded medicines some of their patients on a permanent basis.

According to CMS, Medicare beneficiaries already rely more heavily on generics than does the US population overall. Prescribing data for the first two quarters of 2006 indicate that generics accounted for 51.9% of prescriptions in the pharmaceutical market as a whole, but 60.1% of prescriptions in the Medicare population. Recent initiatives by retail pharmacies to make inexpensive generics available to all customers – led by Wal-Mart's high-profile promise of generics for $4 per prescription – could reduce the need for generics coverage in the gap. However, the range of drugs included in these programs would need to be expanded substantially to meet the needs of most Medicare beneficiaries.

Most worrisome of all for the biopharmaceutical industry is the renewed focus on drug prices under Medicare Part D. The MMA precludes CMS from using its influence to negotiate price cuts, but many members of Congress remain highly critical of this fundamental aspect of the legislation. Some of the proponents of change cite a study by Dean Baker, an economist at the Center for Economic and Policy Research, which found that direct price negotiation by CMS could deliver total savings more than twice the size of the coverage gap. Following their victories in midterm elections for both the Senate and the House of Representatives, the Democrats have pledged to introduce legislation within the first 100 hours of the new legislative session to empower CMS to bargain for price cuts. The Republicans, led by the Bush administration, remain resolutely opposed to such a change, but it may be difficult for them to withstand the growing pressure for some form of government intervention in Medicare drug pricing.

2

Changes in US Oncology Drug Reimbursement: Medicare Sets the Pace

INTRODUCTION

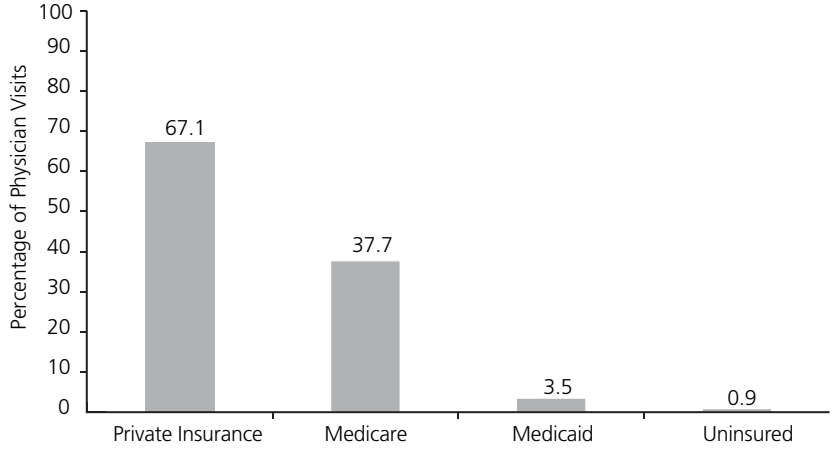
Cancer has a higher profile than almost any other disease. According to the American Cancer Society (ACS), 10.1 million US residents have been diagnosed with cancer at some time in their lives, and approximately 1.4 million US residents are expected to be diagnosed with some form of cancer in 2006. The lifetime risk of developing cancer is 1 in 2 for US men and 1 in 3 for US women. Cancer is also the second most common cause of death in the United States (after coronary heart disease), accounting for one-quarter of all deaths. The ACS forecasts that 564,830 US residents will die from cancer in 2006 (American Cancer Society, 2006).

Providing access to effective cancer therapies is a public health priority, but oncology drugs can cost tens of thousands of dollars per year. Because of the rarity of certain cancers, manufacturers have to recoup their R&D costs from a relatively small patient population. In addition, many of the most efficacious therapies are biologics – agents that have very substantial manufacturing costs. Furthermore, most cancer therapies are intravenous infusions that must be administered by medical professionals – a requirement that adds significantly to the overall treatment costs. Consequently, access to cancer drugs is subject to strict controls.

In most therapeutic areas, patients obtain their own medications from community pharmacies and are reimbursed by their third-party payer (if they have appropriate coverage). Oncology reimbursement in the United States is generally different, however. Approximately 84% of patients receive their cancer therapy in oncologists' offices, and these practices are responsible for collecting patients' out-of-pocket payments and claiming reimbursement for their drug and administrative costs from the relevant payers.

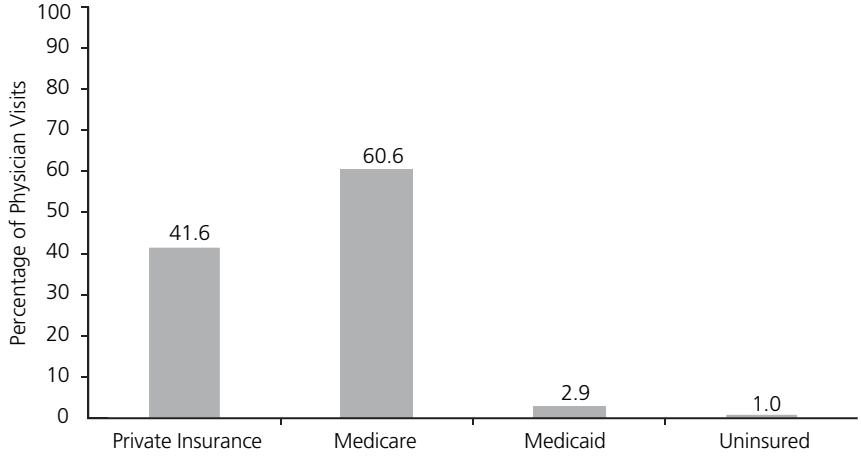
Cancer treatment in the United States is funded by a mixture of public payers (e.g., Medicare, Medicaid, the Department of Veterans Affairs) and commercial payers (e.g., indemnity insurance plans, managed care organizations [MCOs]). The ACS reports that 76% of cancer patients are aged 55 or older, including many Medicare beneficiaries. Data from Verispan's Physician Drug & Diagnosis Audit (PDDA) confirm the important role that Medicare plays in the treatment of cancer in the United States.

Figures 2.1–2.5 show the main sources of insurance coverage for patients who visited a physician for treatment for breast, skin, prostate, lung, and colorectal cancers in the first six months of 2006 (because some patients have more than one form of health insurance, percentages for each indication exceed 100). Medicare was the most common source of funding for all of these cancers except breast cancer, a disease that frequently has an earlier onset than most of the other highly prevalent cancers. Figure 2.6 shows that Medicare and private insurance were the dominant sources of insurance coverage for these five cancers overall. Therefore, our discussion focuses on the reimbursement environment in Medicare and commercial health plans.



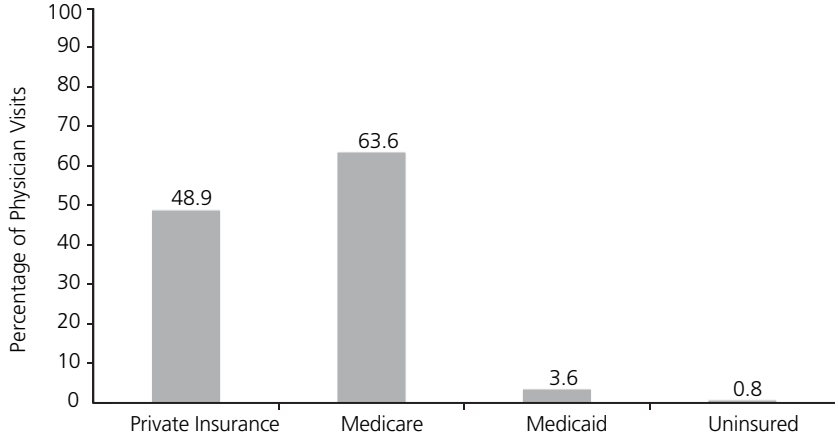
Note: Percentages total more than 100 because some patients have more than one form of insurance

Figure 2.1 Main Sources of Insurance Coverage for Breast Cancer Therapy, 2006



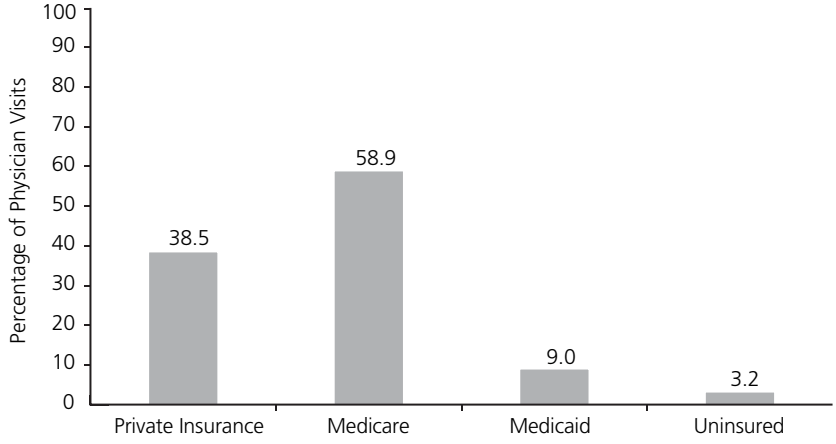
Note: Percentages total more than 100 because some patients have more than one form of insurance

Figure 2.2 Main Sources of Insurance Coverage for Skin Cancer Therapy, 2006



Note: Percentages total more than 100 because some patients have more than one form of insurance

Figure 2.3 Main Sources of Insurance Coverage for Prostate Cancer Therapy, 2006



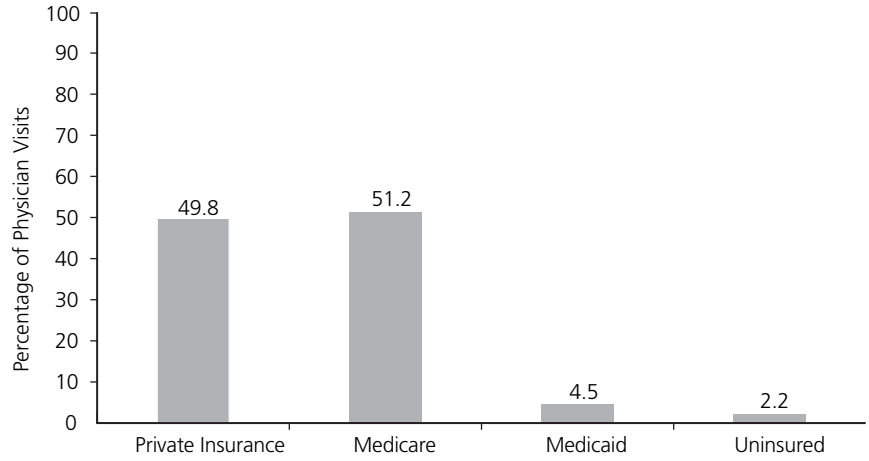
Note: Percentages total more than 100 because some patients have more than one form of insurance

Figure 2.4 Main Sources of Insurance Coverage for Lung Cancer Therapy, 2006

We begin this chapter with a detailed examination of Medicare's reimbursement procedures for office-based treatment, hospital outpatient therapy, hospital inpatient treatment, and self-administered drugs (under the new Medicare Part D prescription drug benefit). We then compare practice in the private sector and review policies on off-label prescribing. We conclude with a brief assessment of the outlook and implications for the pharmaceutical industry.

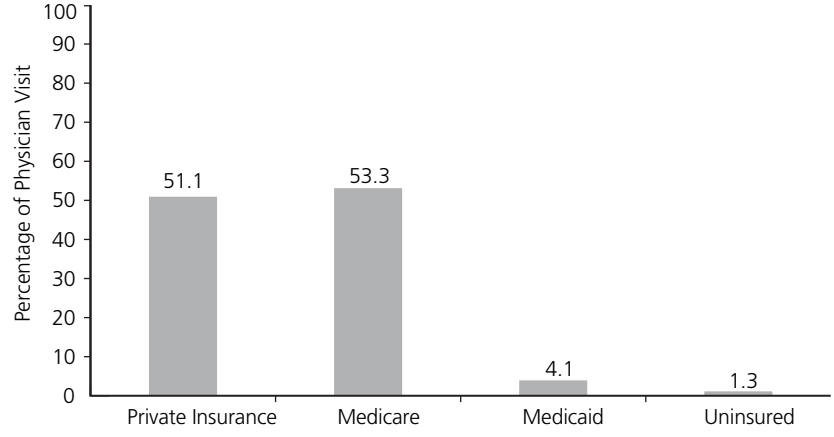
Medicare

Since its creation in 1965, the Medicare program has become a major source of



Note: Percentages total more than 100 because some patients have more than one form of insurance

Figure 2.5 Main Sources of Insurance Coverage for Colorectal Cancer Therapy, 2006



Note: Percentages total more than 100 because some patients have more than one form insurance

Figure 2.6 Main Sources of Insurance Coverage for Breast, Skin, Prostate, Lung, and Colorectal Cancer Therapy, 2006

healthcare coverage for seniors, the disabled, and patients with end-stage renal disease in the United States. In 2006, approximately 43 million US residents are recipients of at least basic Medicare benefits.

Historically, Medicare offered only limited coverage of prescription medicines: Part A covers inpatient drugs, and Part B (an optional program) covers outpatient drugs that are not usually self-administered (e.g., intravenous infusions, intramuscular injections) but generally excludes oral drugs. In addition, Medicare beneficiaries who can afford the premiums (typically around $140 per month at present) can purchase optional Medigap insurance to increase their level of benefits, including prescription drug

coverage. Beginning in 1999, Part C, commonly known as Medicare + Choice (renamed Medicare Advantage in 2004), offered additional services – including prescription drug benefits – through private fee-for-service plans or Medicare MCOs. However, inadequate government funding led to a rapid erosion of benefits and the contraction or closure of many Medicare + Choice plans. To improve beneficiaries' access to outpatient prescription medicines, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (commonly known as the Medicare Modernization Act [MMA]) introduced Medicare Part D – a new outpatient drug benefit that began operation on January 1, 2006.

Because most cancer therapies are administered in physician offices in the United States, Part B is currently the most important source of Medicare funding in oncology. However, the shift toward self-administered injections and oral dosage forms will increase the importance of Part D in the future.

In recent years, the US government has broadened Part B prescription drug coverage. The Medicare, Medicaid, State Children's Health Insurance Program (SCHIP), and Benefits Improvement Act of 2000 (BIPA) extended coverage from drugs that are not self-administered to drugs that are not usually self-administered. In May 2002, the Centers for Medicare and Medicaid Services (CMS) clarified this provision: drugs that are delivered by intramuscular injection are covered, but medicines administered by subcutaneous injection are not covered. Oral drugs are excluded from Part B coverage, with the exception of products that also have an injectable dosage form that would be reimbursed if it was administered by a physician. Consequently, innovative oral medicines (e.g., Novartis's Gleevec [imatinib] for chronic myeloid leukemia), which do not also have a dosage form requiring physician administration, are not eligible for reimbursement under Medicare Part B.

Office-Based Treatment

Oncology-related drugs account for the majority of Medicare Part B's pharmaceutical expenditures. Figure 2.7 traces the growth of

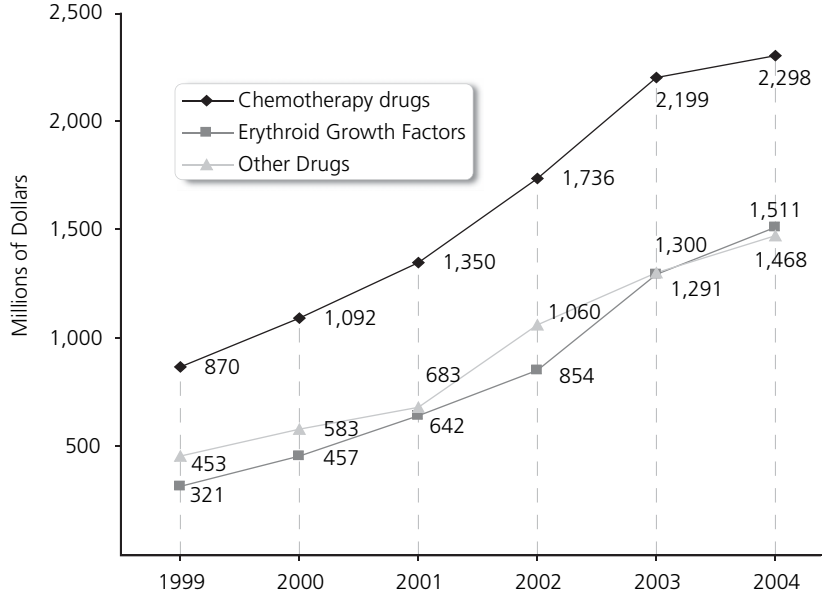


Figure 2.7 Evolution of Medicare Part B Spending on Oncology Drugs, 1999–2004

Medicare spending on oncology-related drugs from 1999 to 2004. Over that period, spending on chemotherapy drugs rose from $870 million to $2.3 billion, a 164% increase (equivalent to 21.4% per year). Spending on erythroid growth factors grew even faster, from $321 million in 1999 to $1.5 billion in 2004, a 371% increase (36.3% per year). Medicare Part B expenditures on other oncology-related drugs rose from $453 million in 1999 to $1.5 billion in 2004, a 224% increase (26.5% per year). Total expenditures on oncology-related drugs grew from $1.6 billion in 1999 to $5.3 billion in 2004, a 221% increase (26.5% per year). Payments for the administration of oncology-related drugs rose relatively slowly, from $180 million in 1999 to $288 million in 2003, but then leapt to $912 million in 2004, following radical changes to the Medicare Part B reimbursement structure (see the next section). Overall, Medicare Part B expenditures on oncology (including evaluation and management services, tests, imaging, and other procedures) grew from $2.5 billion in 1999 to $7.3 billion in 2004, a 191% increase (23.8% per year).

Physician Reimbursement

Historically, Medicare Part B reimbursed physicians for most drugs administered in their offices at 95% of average wholesale price (AWP) – the AWP is the average list price that a manufacturer suggests wholesalers charge pharmacies; in practice, this price is often heavily discounted, particularly for Health Maintanence Organizations (HMOs) and other large purchasers. But actual acquisition costs for most physician-administered drugs were much lower than reimbursement prices. A study conducted by the Government Accountability Office (GAO) found that providers' drug acquisition costs were actually 13–86% below AWP. The GAO and the Office of the Inspector General of the Department of Health and Human Services have independently estimated that the total difference between Medicare Part B drug acquisition costs and reimbursement payments was approximately $1 billion per year (in addition to reimbursing physicians for medications they supply under Medicare Part B, CMS pays these clinicians for providing drug administration services).

Oncologists were the main beneficiaries of the price differential between acquisition costs and reimbursement payments: CMS and the Congressional Budget Office (CBO) estimated that these physicians received $700 million in overpayments for Part B drugs each year. In their defense, physicians argued that overpayments on drug reimbursement offset underpayments by CMS for the cost of administering these drugs. Many oncologists asserted that, without generous reimbursement of drug costs, they could not afford to offer their Medicare patients office-based administration of cancer therapies. Office-based physicians argued that they used the "spread" – the differential between drugs' acquisition prices and their reimbursement prices – to offset the costs of administering these medicines and to subsidize other patient services. CMS estimated that, in 2003, oncologists derived an average of 70% of their Medicare income from the differential between drug acquisition and reimbursement prices.

The MMA mandated radical changes in the method for calculating reimbursement rates for Medicare Part B drugs that are administered in physicians' offices. In 2004, the standard reimbursement rate for office-administered drugs was reduced to 85% of the AWP on April 1, 2003. For certain drugs judged to be subject to particularly aggressive discounting, reimbursement was as low as 80% of AWP. Beginning January 1, 2005, Medicare introduced a new method for reimbursement calculations. Office-administered drugs are generally reimbursed at 106% of the manufacturer's average sales price (ASP). A drug's ASP is the manufacturer's total revenue from the drug divided by the number of units sold. CMS revises its list of ASPs on a quarterly basis. The switch from AWP- to ASP-based reimbursement of drug

costs substantially reduced the payments physicians received for providing pharmaceuticals under Medicare Part B.

To mitigate the impact of reduced drug reimbursement, CMS increased its payments for drug administration services (especially chemotherapy) by an average of 110% in 2004. In addition, providers benefited from transitional supplementary payments of 32% of standard drug administration payment rates in 2004 and 3% in 2005. The introduction of new drug administration codes in 2005 also enabled physicians to charge for more services during each session of chemotherapy than had been permitted previously.

CMS calculated that the move to ASP-based reimbursement would reduce oncologists' income from Medicare by an average of 8%. However, in September 2004, the American Society of Clinical Oncology (ASCO) predicted a much more severe impact on its members' incomes. Based on a survey of 93 oncology practices across the United States, ASCO estimated that the average reduction in drug reimbursement rates would be 15% in 2005. With the sharp reduction in the level of the transitional supplementary payment (from 32% to 3%) for drug administration services, ASCO forecast that overall Medicare funding for chemotherapy services would decline by 54%, a cut that would "certainly affect the way oncologists are able to deliver care in the United States."

Three reports published by federal agencies have challenged ASCO's assertions. In December 2004, the GAO published an analysis of Medicare Part B's new drug and administration fees for chemotherapy (Government Accountability Office, 2006). The study reviewed 2003, 2004, and preliminary 2005 acquisition costs and Medicare payments for 16 drugs that together accounted for 75% of Medicare payments to oncologists for physician-administered agents in 2003. Overall, payments for these 16 drugs exceeded acquisition costs by 22.4% in 2004 and 5.5% (projected) in 2005. Extrapolating these figures to the oncology market as a whole, the GAO estimated that Medicare Part B payments for cancer drugs exceeded oncologists' acquisition costs by a total of $790 million in 2004 and by a projected sum of $202 million in 2005.

In September 2005, the Office of Inspector General (OIG) of the Department of Health and Human Services published a report on the adequacy of Medicare Part B's new reimbursement rates, as mandated by the MMA (Office of Inspector General, 2006). The study examined data for 39 reimbursement codes that collectively accounted for more than 94% of Medicare's 2004 payments for hematology, hematology/oncology, and medical oncology. The authors estimated that, overall, Medicare reimbursement rates exceeded acquisition costs for 35 of the 39 codes.

In January 2006, the Medicare Payment Advisory Commission (MedPAC) published a wide-ranging review of the impact of Medicare reimbursement reforms on the practice of oncology in the United States (Medicare Payment Advisory Commission, 2006). The authors' analysis of Medicare Part B claims data showed a 33% increase in the number of chemotherapy drug administration services and a 182% increase in spending on these services in the first half of 2005 compared with the first six months of 2003. The study also reported a 13% increase in the number of chemotherapy sessions in the first half of 2005 compared with the first six months of 2004. However, spending on chemotherapy drugs was 14% lower in the first six months of 2005 than the first half of 2004.

As part of its investigation, mandated by the MMA, MedPAC visited oncology practices in Atlanta, Seattle, Iowa, New Jersey, and New Mexico in 2004, and conducted follow-up interviews in 2005. All physicians contacted in the course of MedPAC's research reported that, following the introduction of the payment reforms, they were devoting more time and resources to sourcing lower-priced drugs. Group purchasing organizations (GPOs) indicated that it had become more difficult to secure substantial discounts from manufacturers – a reflection of the fact that large price cuts would reduce a drug's ASP in subsequent quarters. The new

Table 2.1 Average Price Variations for Select Oncology Drugs Under Medicare Part B, December 2004 and June 2005

	Price Variation (%)	
	December 2004	*June 2005*
Branded drugs	15.6	6.8
Generic drugs	10.4	8.4
Chemotherapy agents	6.9	5.2
Nonchemotherapy agents	25.3	10.3

reimbursement system has significantly reduced the variation in the prices of Part B drugs. Table 2.1 compares price variations for branded and generic oncology drugs, and for chemotherapy and non-chemotherapy agents, in December 2004 and June 2005. The reductions in the price variation of non-chemotherapy agents (from 25.3% to 10.3%) and branded drugs (from 15.6% to 6.8%) are particularly striking.

MedPAC found that oncology practices were generally able to obtain drugs that have lost patent protection relatively recently (e.g., carboplatin, cisplatin) at prices substantially below Medicare's reimbursement rates, but purchasing older generics at prices below 106% of ASP was often more problematic. Price has become a particularly influential factor in the choice of ancillary drugs (e.g., antiemetics, erythroid growth factors), and many practices now tend to stock just one drug in each of these classes. By maintaining smaller drug inventories, practices tie up less capital, can respond quickly to price changes, and can benefit from discounts for prompt payment.

The leading oncology societies and their members are not convinced by the conclusions contained in the GAO, OIG, and MedPAC reports. In July 2006, at a hearing of the Subcommittee on Health of the House Committee on Ways and Means, spokespeople for ASCO and the Community Oncology Alliance (COA), as well as individual oncologists, gave evidence on the damaging effects of Medicare reimbursement reforms. Joseph S. Bailes, ASCO's executive vice president, offered the following assessment of the OIG's analysis:

> The OIG's conclusion that reimbursement was "generally adequate" and its analysis based on average drug costs to physicians do not appropriately consider the many situations faced by particular physicians in which the Medicare payment amount does not cover the cost of the drugs. Although the OIG's conclusions did not highlight this problem, the report shows that for 17 of the 39 drugs reviewed, at least 20 percent of physicians incurred an out-of-pocket loss. Only 3 of the 39 drugs could be obtained by all physicians at the Medicare payment amount or less. The OIG's conclusion fails to acknowledge that out-of-pocket losses are incurred by physicians in many circumstances, a situation that threatens access to care for some cancer patients. In some of those circumstances, practices are referring patients to hospital outpatient departments. We have received reports from ASCO members that, in some instances hospitals are not accepting those patients. This is a particular challenge to patients without secondary insurance.

Frederick M. Schnell, the COA's president, expressed a very similar opinion: "Analyzing a clinic's drug acquisition costs in comparison to ASP plus 6% reimbursement and concluding that reimbursement covers cost is a faulty analysis, which is the problem with studies completed by the [OIG] and the [GAO]." In particular, he noted that Medicare's new reimbursement methodology takes no account of patient out-of-pocket payments that are not collected. The COA estimates that such bad debts are, on average, equivalent to 5.3% of Medicare Part B payment rates. In addition, the alliance asserts that Medicare's effective payments are reduced further by a 2% prompt-pay discount that is factored into ASP calculations and by delays in adjusting ASPs to reflect market prices. As a result, the COA calculates that oncologists are effectively reimbursed at ASP minus 3.8%, rather than the headline rate of ASP plus 6%.

The implications of insufficient reimbursement are that community cancer clinics report sending more patients to the hospital for treatment, closing satellite facilities and practices, reducing staff, and being pressured to factor economic decisions into the cancer treatment plan in order for clinics to continue treating patients. In addition, clinics report considering dropping out of the Medicare

program. Already, in 2006, there are reports about access problems from community cancer clinics in over 37 states.

The COA's testimony also included several comments that it had received from some of its members. The clear consensus was that practices could no longer afford to treat Medicare patients who do not have a supplemental insurance. Some of the most disturbing of these quotations are as follows:

> On an average we are sending 25–30 patients to the hospital a month for their chemotherapy treatment and growth factor support due to an overwhelming percentage of 20% coinsurance turning into bad debt. Facilities, however, are providing a very limited number of open chairs for patients which means patients are being delayed a week or two waiting on an open chair.

- We are looking toward closing one of our offices. We can no longer cover the overhead of the practice due to the inadequate payments of ASP plus 6%. The other reimbursement schedules are grossly inadequate. We have already cut staff. Medicare D for oncology patients is a catastrophe. Most cannot afford the co-pays on these very expensive drugs. They are priced out of effective medications such as the [tyrosine kinase] inhibitors, Revlamid, etc. THERE IS A NEW WRINKLE! Medicare is now not denying our claims but "PENDING" all claims for Rituxan, Aranesp, and Herceptin – thus they delay payment for three to four months. This has wiped out all of our money. We cannot purchase any more drugs! We will now be sending all patients to the hospital 10 miles away for chemotherapy. Does Medicare wish to eliminate the private practice of medical oncology?
- We cannot afford to treat patients that cannot pay their 20%. Right now 26 of 64 drugs we commonly give are underwater (i.e., not fully reimbursed) at 100% of Medicare. Also, the hospitals are seeing more and more patients in their outpatient units. We are in a high competition area, and a lot of the oncologists in this area are sending patients to the hospital for treatment.

At the time the MMA was enacted, the CBO forecast that the act's reimbursement reforms would reduce Medicare spending on outpatient cancer therapy by a total of $4.2 billion from 2004 to 2013. However, a more recent study that the COA commissioned from PricewaterhouseCoopers (PwC) forecasts total savings at $13.7 billion over the 10-year period – a reduction in spending that would be a body blow to office-based oncologists.

Patients' Out-of-Pocket Payments

Patients are required to pay 20% of all costs incurred under Medicare Part B, with no limit on the level of out-of-pocket payments. Providers are responsible for collecting these coinsurance payments on CMS's behalf. Medigap covers these payments for beneficiaries who have opted for this form of supplemental insurance.

MedPAC estimates that 9% of Medicare beneficiaries have no form of supplemental insurance. In its investigation of the impact of the MMA on oncologists, the commission found that many oncology practices now employ advisers to check that new patients will be able to meet their out-of-pocket obligations. These advisers may notify patients who do not have supplemental insurance about alternative sources of funding (e.g., Medicaid, manufacturer-sponsored patient assistance programs [PAPs]). However, many physicians have reservations about the value of PAPs in oncology. Because cancer patients frequently require polytherapy, it may be necessary to apply to multiple manufacturers for enrollment in their respective assistance programs. The choice of therapies might then be dictated by the companies that approve the patient for enrollment in their PAPs, a far-from-ideal situation. Furthermore, many physicians dislike the fact that PAPs generally do not cover the cost of medications but replace drugs that have been used. This form of compensation is of little value if a physician has only one patient who requires a particular drug.

Patients who are not eligible for assistance and cannot meet the 20% coinsurance payments are increasingly likely to be referred to hospital outpatient departments or "safety-net facilities" for therapy. From the patients' perspective, treatment in hospital outpatient departments has two major disadvantages compared with

therapy in physician offices: it is much more time-consuming (in some cases, 5 to 6 hours instead of the 1 to 2 hours required in the office setting) and incurs larger out-of-pocket payments. However, hospital outpatient departments are better placed than office-based practices to accept patients who cannot afford their out-of-pocket payments. Unlike physician offices, hospitals can recover 70% of bad debts on out-of-pocket payments from CMS. Nevertheless, some hospitals have stopped treating Medicare patients without the supplemental insurance, or have even discontinued outpatient chemotherapy altogether.

Competitive Acquisition Program

The MMA called for the creation of a competitive acquisition program (CAP) as an alternative method of supplying providers with Part B drugs. Office-based physicians who did not want to purchase medicines and claim reimbursement from CMS would be able to delegate these responsibilities to Medicare-approved vendors (e.g., pharmaceutical wholesalers, specialty pharmacies). These vendors would buy Part B drugs, deliver required supplies to physician offices, collect patient coinsurance payments, and submit reimbursement claims to CMS.

This initiative was originally scheduled to take effect on January 1, 2006, but implementation was delayed by widespread criticism from both the medical community and potential vendors. The program eventually began operation on July 1, 2006, despite a continued lack of enthusiasm from physicians, wholesalers, and specialty pharmacies. Indeed, only one company – BioScrip – has thus far been registered as a CAP vendor. Other possible applicants have been deterred by the perception that this program offers limited potential for profit. For two main reasons, manufacturers would be reluctant to offer CAP vendors substantial discounts: these discounts would be included in future ASP calculations, and vendors have to supply the drugs prescribed by physicians and cannot promote a switch to an alternative drug.

MedPAC found that physicians had several fundamental reservations about CAP:

- Vendors would be able to discontinue the supply of drugs to patients who did not make their coinsurance payments.
- The administrative burden would increase.
- Practices would have to keep separate drug inventories for each patient treated under the CAP program.
- Practices would not be able to change their vendor mid-year.
- Physicians would be required to appeal all denied claims.
- In rural areas, satellite offices that cannot receive drug deliveries or that mix drugs would be excluded from the program.

Demonstration Projects

In 2005, CMS undertook a one-year demonstration project to assess the side effects of chemotherapy. Oncologists could receive $130 per patient per day (including a 20% coinsurance payment from each patient) in return for asking three questions on patients' levels of fatigue, nausea, and pain. These payments have been a welcome source of additional income for many practices, but critics question the value of the data gathered in this exercise.

In 2006, CMS launched a new demonstration project. Hematologists and medical oncologists can receive $23 per patient per day for collecting data on how various cancers are treated at different stages. Participating physicians use new payment codes to indicate the stage of the patient's disease, the purpose of each visit (e.g., disease evaluation, supervision of therapy, disease monitoring, end-of-life care), and the degree of compliance with clinical guidelines (where applicable).

Hospital Outpatient Treatment

When it was established in 1965, Medicare relied entirely on retrospective payment systems for all services – reimbursing providers on the basis of costs incurred. As time passed, the Healthcare Financing

Administration (now CMS) began to realize that this system encouraged inefficiency and undesirable variations in healthcare practice. The Balanced Budget Act of 1997 mandated the introduction of a Medicare outpatient prospective payment system (OPPS), which began operation on August 1, 2000. MedPAC reports that, in 2004, 47% of Medicare beneficiaries received at least one OPPS service, from a total of approximately 4,300 hospitals. The OPPS does not cover beneficiaries who are enrolled in Medicare managed care plans, HMOs, preferred provider organizations (PPOs), or Medicare private fee-for-service plans.

According to CMS, the new payment system is "designed to ensure that Medicare and its beneficiaries pay appropriately for services and to encourage more efficient delivery of care." Under the old cost-based reimbursement system, Medicare payments for outpatient services did not keep pace with prices, with the result that patients' out-of-pocket expenses increased sharply. Prior to the introduction of OPPS, Medicare beneficiaries paid approximately 50% of the total cost of outpatient services. By 2004, this figure had declined to 34%, and it is eventually expected to stabilize at 20%. In addition, Congress has ruled that the patient copayment for a procedure must not exceed the annual inpatient deductible (i.e., $952 in 2006).

The OPPS uses the healthcare common procedure coding system (HCPCS) to assign services to one of approximately 600 ambulatory payment classification (APC) groups. Each group consists of services that are clinically comparable and require similar resources. CMS calculates the national median cost for services and procedures within each group, then adjusts the labor-related proportion of this sum (60% of the national total) to reflect the geographic variations in labor costs. Drugs with median daily costs of less than $50 per day (i.e., the great majority of medicines), along with many other incidental items and services, are bundled into the APC payments. CMS reviews APC payment rates in the fall of each year and makes adjustments, as necessary, to take account of increased costs from new technologies.

New technologies that cannot be readily accommodated within an existing APC group can qualify for reimbursement by one of two other methods: inclusion in a new technology APC group or to be granted transitional pass-through payment status (see further on). A new technology APC is created only for procedures or services that can neither be included in an existing APC group nor meet the conditions for pass-through drugs. Once sufficient time has passed to gather data on hospitals' actual expenditures on these new services and procedures, CMS reassigns these new technologies to standard APC groups as part of its annual review process. Because new technology APC groups are not budget-neutral, they could substantially increase hospitals' treatment costs.

Transitional pass-through payments apply to new drugs, biologics, and medical devices that complement an existing service but are too expensive to be included in existing APC groups. For example, a pass-through payment for a costly new monoclonal antibody may be used to supplement the established base payment that covers the administration of chemotherapy. Table 2.2 lists the technologies that have pass-through status in 2006. To qualify for this status, a new technology must have been on the market for no more than two to three years and must be more expensive than existing therapies. In addition, medical devices (as opposed to drugs) must offer a substantial clinical advantage over established treatments – the same standard that is a condition for add-on payments in the Medicare inpatient prospective payment system (IPPS) that is discussed in the following section. In November 2001, CMS published the following characteristics of a new technology that offers "substantial clinical improvement":

- It offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
- It offers the ability to diagnose a medical condition in a patient population whose medical condition is currently undetectable or to

Table 2.2 Technologies with Pass-Through Status in the Medicare Outpatient Prospective Payment System, 2006

HCPCS Code	*APC Code*	*Product*
C9220	9220	Sodium hyaluronate
C9221	9221	Graftjacket regular matrix
C9222	9222	Graftjacket soft tissue
C9225	9225	Fluocinolone acetonide
J0128	9216	Abarelix injection
J0878	9124	Daptomycin injection
J2278	1694	Ziconotide injection
J2357	9300	Omalizumab injection
J2503	1697	Pegaptanib sodium injection
J2783	0738	Rasburicase
J2794	9125	Risperidone, long-acting
J7518	9219	Mycophenolic acid
J8501	0868	Oral aprepitant
J9027	1710	Clofarabine injection
J9035	9214	Bevacizumab injection
J9055	9215	Cetuximab injection
J9264	1712	Paclitaxel injection
J9305	9213	Pemetrexed injection
Q4079	9126	Natalizumab injection (1 mg)

HCPCS = Healthcare common procedure coding system (HCPCS)
APC = Ambulatory payment classification

diagnose a medical condition earlier in a patient population than is allowed by currently available methods. There must also be evidence that the use of the technology to make a diagnosis affects the management of the patient.

- Use of the technology significantly improves clinical outcomes for a patient population as compared with currently available treatments. For example, improvements might include the following:

  1. Reduced mortality rate.
  2. Reduced rate of complications.
  3. Reduced rate of subsequent diagnostic or therapeutic interventions (e.g., due to reduced rate of recurrence of the disease process).
  4. Decreased number of future hospitalizations or physician visits.
  5. More rapid beneficial resolution of the disease process.
  6. Less pain, bleeding, or other quantifiable symptom.
  7. Reduced recovery time.

Table 2.3 summarizes the similarities and differences of the new technology payment mechanisms in Medicare's prospective payment systems. Critics deplore the inconsistencies of these mechanisms. In a report to Congress published in March 2003, MedPAC made the following assertion:

> The treatment of drugs and devices is inconsistent, in that only newness and cost criteria are applied to pass-through drugs. This difference in the criteria represents unequal treatment between types of technology within the outpatient payment system. It also leads to a discrepancy between the treatment of drugs under the inpatient and outpatient payment systems since the clinical criteria are applied to all technologies, including drugs, on the inpatient side. Furthermore, without considering clinical benefit, the criteria applied to pass-through drugs may overemphasize the goal of paying adequately for new technologies at the expense of prudent purchasing.

Furthermore, MedPAC suggested that "it is appropriate to reserve additional payments for technologies that provide clinical benefit and do not have clinical substitutes. It may even be appropriate to limit payments to technologies that provide additional benefits commensurate with their costs."

Hospital Inpatient Treatment

Medicare Part A provides funding for inpatient hospital treatment. Beneficiaries pay a deductible ($952 in 2006) when first admitted to hospital, but this sum is the only out-of-pocket payment during the first

Table 2.3 Key Features of Medicare Inpatient and Outpatient New Technology Payment Mechanisms

	Inpatient Add-On Payments	*Outpatient Pass-Through Payments*		*Outpatient New Technology APCs*
		Medical Devices	*Drugs and Biologics*	
New technologies eligible for additional payments	New technologies that offer a new procedure or are san input to an existing DRG	New technologies that are an input to an existing DRG	New technologies that are an input to an existing DRG	New technologies that offer a new service
Criteria used by CMS	Clinical benefit, novelty, cost	Clinical benefit, novelty, cost	Novelty, cost	Novelty
Funding method	Budget-neutral	Budget-neutral	Budget-neutral	New expenditures
Unit of payment	Additional costs of treating a case using new technology	Cost of new technology	Cost of new technology	Cost of service
Method of determining payments	Payment = 50% of additional costs (capped at 50% of estimated cost of new technology)	Payment = 100% of reported costs minus device costs already built into base payment rate	Payment = 95% of average wholesale price	Payment = midpoint of payment range for new technology APC group

APC = Ambulatory payment classification
CMS = Centers for Medicare and Medicaid Services
DRG = Diagnosis-related group

60 days of inpatient treatment in a given benefit period. Thereafter, beneficiaries pay an additional $238 per day from day 61 to 90, and $476 per day beyond the 90th day of hospitalization in a benefit period.

In 1983, CMS established the Medicare IPPS, a reimbursement system that pays hospitals according to a patient's diagnosis-related group (DRG) coding at the time of inpatient discharge. DRGs group patients on the basis of factors such as their primary or secondary diagnosis, complications and comorbidities, procedures, age, and sex.

The DRG system that forms the foundation of Medicare's IPPS has been refined repeatedly. The current version is based on the *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) and comprises a total of 25 major diagnostic categories (MDCs) subdivided into 526 DRGs. Each case is assigned to a particular patient cluster, based on factors such as principal and secondary diagnoses, principal procedures, sex, and discharge status. CMS updates the DRGs, and the related diagnostic and procedural codes, annually, but critics assert that the system is too slow in reflecting changes in medical technology. In April 2006, CMS published proposals for further reform of the IPPS. Among other measures, in fiscal year 2008, the agency plans to introduce a revised version of 3M's All-Patient Refined DRG (APR-DRG) system to take better account of variations in disease severity. CMS intends to consolidate the APR-DRG's 1,258 DRGs into a new system of 861 severity-adjusted DRGs.

The IPPS bundles the costs of most drugs and medical devices into the DRG payment system. New technologies can be added to the standard DRG system through one of three methods:

- A technical advisory panel assigns the new technology an ICD-9-CM code.
- CMS can alter DRG assignments to ensure that a costly new technology is covered by a higher-paying DRG.
- The annual review of DRG case weights is used to adjust payments so that they cover the cost of the new technology.

Particularly expensive new technologies are initially reimbursed by a different method: add-on payments. This procedure applies to drugs and devices that would increase the cost of a case substantially beyond the relevant base DRG payment. In addition, to qualify for add-on payments, technologies must be new (i.e., on the market for less than two to three years) and must offer Medicare beneficiaries a significant clinical advantage over existing therapies. To encourage the prudent use of new technologies, CMS does not reimburse the full cost of these products. Rather, the add-on payment amounts to only 50% of a hospital's costs in excess of the standard DRG payment, to a maximum of 50% of the estimated cost of the new drug or device. Add-on payments are budget-neutral (i.e., they are offset by reductions in base payment rates) and cannot exceed 1% of total operating payments.

The appendix to this chapter shows spending in 2004 on the 46 oncology-related DRGs in the IPPS. Medicare reimbursement for these DRGs totaled $3.2 billion. Surgical costs likely account for the overwhelming majority of Medicare Part A oncology spending.

Self-Administered Drugs (Medicare Part D)

As of June 11, 2006, 38.2 million out of a total of 42.6 million Medicare beneficiaries enrolled in a Part D program or equivalent, including 6.1 million Medicare-Medicaid dual-eligible beneficiaries who were automatically enrolled in a Medicare prescription drug plan (PDP). At present, Medicare Part D plays a relatively minor role in oncology, but its significance will grow as this program becomes more established and the number of self-administered cancer therapies (e.g., oral dosage forms, subcutaneous injections) increases.

The standard benefit design for Part D requires beneficiaries to pay an average premium of $24 per month and an annual deductible of $250. Thereafter, Medicare covers 75% of the cost of prescription drugs up to an annual total of $2,250. Coverage then ceases until the beneficiary's annual drug costs reach a total of $5,100 (and out-of-pocket payments reach a total of $3,600) – a provision known as the "coverage gap" or, more colloquially, the "doughnut hole." Medicare then covers 95% of drug costs in excess of the annual threshold of $5,100. Variations on the standard benefit design are available, including plans that charge reduced premiums, waive or reduce the annual deductible, or cover drugs (typically generics only) while patients are in the coverage gap. In a recent survey, CMS found that Medicare PDP enrollees who signed up for the lowest-cost plan in their area could save an average of 59%, and a maximum of 72%, on their drug costs (compared with cash prices to patients who have no drug coverage). However, some beneficiaries face the prospect of losing access to PAPs.

PDPs are generally required to cover at least two drugs in each therapeutic category and pharmacological class. CMS expects PDPs to "provide adequate access to medically necessary treatments for Part D enrollees." In particular, plans must cover "all or substantially all" drugs in six classes, including antineoplastic agents. However, relatively few cancer therapies fall within the scope of Part D, a program that focuses primarily on self-administered drugs. CMS notes that "the definition of a covered Part D drug excludes any drug for which, as prescribed and dispensed or administered to an individual, payments would be available under Parts A or B of Medicare for that individual, even though a deductible may apply."

Plans cover an average of 75% of Part D oncology drugs. PDPs are not obliged to cover off-label prescribing, and they are permitted to use utilization management controls such as multitier formularies, prior authorization, step therapy protocols, generics substitution, and quantity limits to contain pharmacy costs. However, plans make limited use of these measures in oncology: only 10% of Part D cancer drugs are subject to prior authorization and 4% to quantity limits.

PDPs also exercise restraint in the out-of-pocket payments they impose on cancer patients. The majority of plans levy flat-rate copayments, rather than a percentage coinsurance charge, on most Part D oncology drugs. Moreover, the copayments are generally relatively modest – $30 or less, in most cases. Genentech/OSI Pharmaceuticals' Tarceva (erlotinib) and Gleevec (imatinib) are notable exceptions to this rule: the majority of PDPs require a percentage coinsurance payment for both these drugs.

PRIVATE SECTOR

Physician Reimbursement

Because most oncology drugs are administered by healthcare professionals, private insurers have generally covered these treatments as a medical, rather than a pharmacy, benefit. In their claims for reimbursement, physicians use J codes, a subcategory of HCPCS. These five-digit codes indicate the name and quantity of a prescribed drug, but not the manufacturer, formulation, or strength. CMS updates the HCPCS list annually, but drugs are frequently on the market for 12 to 18 months before they are assigned a HCPCS code. In the meantime, physicians use a miscellaneous J code in their reimbursement claims. The relatively imprecise nature of HCPCS codes prevents insurers from accurately monitoring the use of these therapies. In addition, covering drugs as a medical benefit makes it difficult to distinguish drug costs and administration fees.

To improve the utilization management and control costs, health plans are increasingly moving oncology drugs from the medical benefit to the pharmacy benefit. In the process, they are replacing HCPCS codes with National Drug Center (NDC) codes. These more detailed 10-digit codes specify a prescribed drug's manufacturer, strength, dosage form, formulation, and pack size. In 2003, Express Scripts, a leading pharmacy benefit management (PBM) company, reported that adoption of NDC coding and stricter biologic formulary control had reduced its medical costs by 10–20%. Covering drugs as a pharmacy benefit enables payers to adjudicate reimbursement claims electronically and to compile long-term data on how these agents are used. In the future, plans will be able to use these data in comparing the cost effectiveness of different therapies. However, the shift to pharmacy benefit coverage of oncology drugs is far from complete: most plans still cover the majority of these agents in their medical benefit.

Private insurers have long followed Medicare's AWP-based model for reimbursing office-based physicians' drug costs – albeit with slightly more generous rates. To determine reimbursement levels in the private sector, MedPAC commissioned a survey of health plans. Between October and December 2002, Dyckman & Associates interviewed representatives of 33 health plans on their use of AWP calculations in setting reimbursement rates for physician-administered drugs. Most health plans paid physicians 90–100% of AWP, and the average reimbursement rate was 98% of AWP. Note, however, that some health plans varied their AWP reimbursement formula by drug class or provider. Respondents were aware that physicians' actual drug acquisition costs were often far below AWP. Some participating health plans were thinking of changing their reimbursement methodology for physician-administered drugs, but many indicated that they would consider increasing fees for drug administration to offset reduced drug reimbursement payments.

MedPAC commissioned a separate study on distribution and payment issues for physician-administered drugs in the private sector from NORC at the University of Chicago. The authors conducted 16 structured interviews with a range of stakeholders, including oncologists, health plans, PBMs, specialty pharmacy companies, consultants, a wholesaler, and a GPO. Representatives of insurers and PBMs believed that the "spread" between acquisition costs and reimbursement payments for physician-administered drugs was a significant source of profit for physicians. Some respondents suggested that cancer therapy reimbursement accounted for 50–60% of oncologists' income. Oncologists, on the other hand, maintained that the spread barely covered their rapidly rising drug administration costs and that they lost money on many chemotherapy procedures. They also insisted that neither a drug's price nor its spread had any influence on their prescribing decisions.

In recognition of the substantial disparities between AWP and drug acquisition prices, many plans have reduced their reimbursement rates as a percentage of AWP. According to the Zitter Group's Managed Care Injectables Index, health plans' average reimbursement rate for specialty pharmaceuticals was 85.8% of AWP in fall 2004 and 84.3% of AWP in fall 2005. Slightly higher rates were available if physicians accepted specialty pharmacy services (Figure 2.8).

Relatively few insurers have yet followed Medicare's move to ASP-based reimbursement. However, the June 2006 issue of *Biotechnology Healthcare* reported that 39.5% of payers that operate Medicare plans intend to adopt ASP-based reimbursement by the end of the year. Some observers believe that oncology drugs will be among the last products to be subjected to ASP-based reimbursement in the private sector. Insurers may be concerned that reduced reimbursement could prompt office-based oncologists to refer more patients to hospital outpatient departments – a more costly situation for the administration of chemotherapy.

Distribution Controls

In most cases, oncologists decide how to obtain the medicines they need. They may buy directly from manufacturers, use general

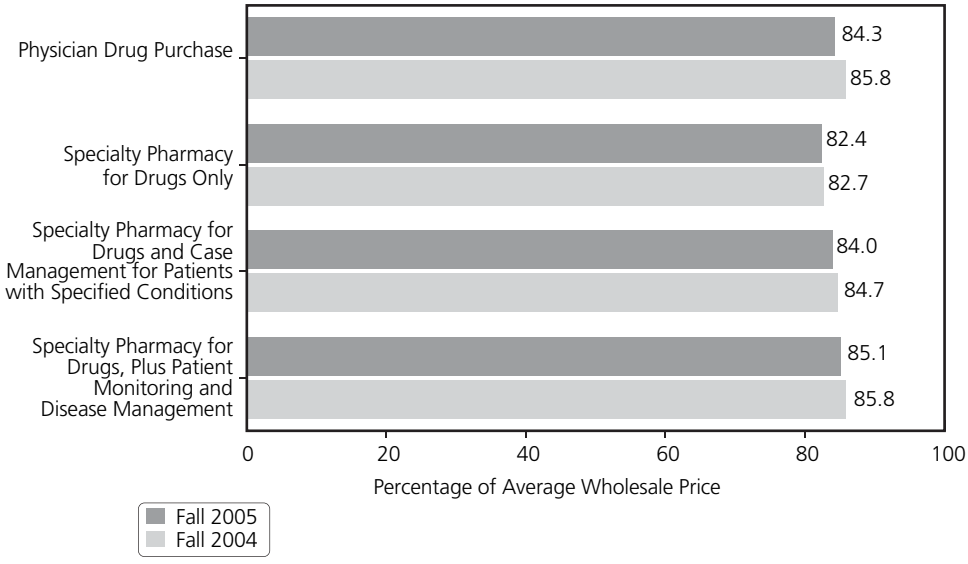
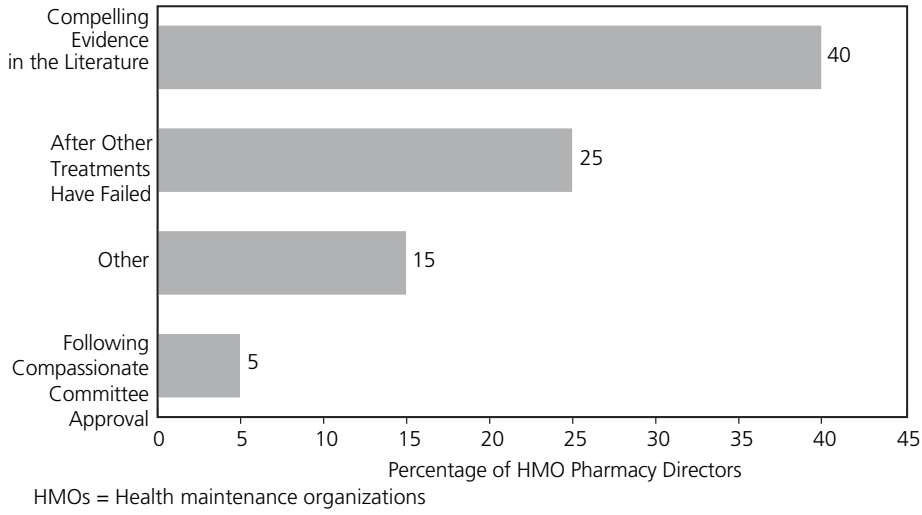


Figure 2.8 Private Health Plans' Average Reimbursement Rates for Onclolgy Drugs, Fall 2004 and 2005



AQ: Please provide in-text cross-reference for Figure 2.9.

Figure 2.9 Circumstances in which HMO Pharmacy Directors Would Authorize Off-Label Use of Oral Chemotherapeutic Agents, 2005

wholesalers or one of several specialist oncology wholesalers, contract with GPOs, or purchase pharmaceuticals from a local retail pharmacy. Recently, however, some health plans and PBMs have introduced a policy of mandatory vendor imposition, requiring oncologists to use particular distribution channels – typically a specialty pharmacy company.

The origins of specialty pharmacy can be traced back to the mid-1990s, when relatively inexperienced biotechnology companies were looking for assistance in marketing their new products (the term "specialty pharmaceuticals" has various definitions but typically includes drugs that are injected subcutaneously or infused intravenously, as well as oral cancer chemotherapeutics: many of the most widely prescribed specialty pharmaceuticals are biologics). Specialty pharmacy companies acted as intermediaries between biotechnology companies and physicians, patients, insurers, and pharmacies. Over time, many health plans began to contract with specialty pharmacy companies to reduce the health plans' costs for specialty pharmaceuticals. Leading PBMs have also established their own specialty pharmacy services.

Some health plans have adopted a policy known as "brown bagging," requiring patients to take their own medications to their physician's office for administration. Health plans that find an inexpensive wholesaler for specialty pharmaceuticals may insist that patients who are prescribed these drugs have their medications mailed either to their home or to a local retail pharmacy for collection. Patients then carry their medicines to the physician's office in the "brown bag."

Brown bagging may save health plans money, but it has many potential disadvantages for patients and their physicians. Specialty pharmaceuticals (especially biologics) may be temperature sensitive or have other special handling requirements, but some couriers may lack the knowledge or equipment needed to comply with these requirements. Medicines may be damaged in transit or left in unsuitable conditions (e.g., outside the patient's house). Patients may not know how to store their medicines correctly and may, out of embarrassment, mislead their physician about how the drugs have been stored. One or more of these events could render certain drugs useless and thereby compromise patients' treatment. Besides the risks of

inappropriate storage, brown bagging is likely to entail some additional inconvenience for seriously ill patients. They may have to make an extra visit to their physician's office for a blood count to ensure that they can tolerate chemotherapy; the physician then orders the drugs for delivery to the patients' home or a nearby pharmacy. If medicines are delivered to the pharmacy, patients have to make an extra journey to collect their drugs prior to administration.

Critics of brown bagging within the medical community argue that this practice is inefficient and imposes a significant burden on their practices. Physicians have to keep separate accounts and other records for each health plan. In some cases, physicians may store brown-bagged drugs in their offices, but these drugs must be kept separate from the practice's regular stock of drugs. Maintaining multiple inventories increases a practice's workload. In addition, high-priced drugs are often wasted: if a patient does not require the full contents of a vial or all the vials in a multivial pack, the remaining medication may not be used to treat another patient.

Cost Sharing

Cancer therapy in the private sector can incur substantial out-of-pocket costs. A recent analysis of 2003 and 2004 pharmacy and medical claims data from 55 employer-sponsored health plans with a combined total of 1.5 million covered lives found that cancer patients had median out-of-pocket expenditures of $1,509 per year, including $336 for medications. In some cases, expenses can be much higher. This survey found that more than 10% of cancer patients had out-of-pocket spending in excess of $18,585, and 5% spent more than $35,660 on their treatment (Goldman, 2006).

For drugs that are covered as medical benefits, insurers generally levy a percentage coinsurance payment – typically 20%. Drugs covered as pharmacy benefits are included in plan formularies. Three-tier formularies are currently the norm, with generic drugs generally assigned to tier 1, preferred brands to tier 2, and nonpreferred brands to tier 3. Plans generally impose flat-rate copayments that increase with each of these tiers. Recently, some health plans have added one or more additional tiers to their formulary designs. Biologics and other high-priced agents, including some cancer therapies, are assigned to a specialty pharmacy tier. Plans frequently levy a percentage coinsurance charge for drugs in the specialty pharmacy tier. Caps on out-of-pocket payments are generally used to protect patients against hardship.

The move from medical to pharmacy benefit coverage of cancer drugs will make it easier for health plans to implement cost-containment strategies. Many plans and/or their PBMs encourage pharmacists to substitute generics for branded versions of off-patent drugs, and some plans and PBMs even promote therapeutic substitution (i.e., switching a patient to a different [and less expensive] compound from the one prescribed). Prior authorization policies exclude certain drugs from reimbursement unless the prescriber justifies the need for these medications and the plan or PBM approves the prescription. Quantity limits restrict the pack size of prescriptions and the frequency of refills. Step therapy protocols reimburse costly drugs only if the patient has first tried, and failed to respond adequately to, less expensive therapies. The Zitter Group's spring 2005 Managed Care Injectables Index found that 64% of payers had increased their use of prior authorization for specialty pharmaceuticals, 42% limited access to these drugs, 33% had increased out-of-pocket payments by more than $20, 30% used differential prior authorization rules to promote the prescription of particular agents, 27% offered higher reimbursement rates for drugs sourced through a particular distribution channel, and 26% had a policy of strict prior authorization with limited cost sharing. It is unclear, however, to what extent such measures are applied specifically to oncology drugs. Given the

limited choice of drugs for some cancers and the life-threatening nature of this disease, it is more difficult to impose restrictions on cancer therapies than most other drug classes.

OFF-LABEL PRESCRIBING

In 1991, the GAO published a report titled *Off-Label Drugs: Reimbursement Policies Constraints Physicians in Their Choice of Cancer Therapies*. The authors noted that, "although respondents reported reimbursement problems with many third-party payers, the insurer most frequently cited was Medicare." In an attempt to remedy this situation, the Omnibus Budget Reconciliation Act of 1993 introduced a legal requirement for Medicare to reimburse off-label prescribing that is supported by citations in any of three compendia: *American Hospital Formulary Service Drug Information* (AHFSDI), *United States Pharmacopoeia Drug Information* (USPDI), or the American Medical Association's *Drug Evaluation* (merged into USPDI in 1996). In addition, the act allows Medicare carriers to make local coverage decisions on off-label reimbursement based on supportive clinical evidence published in peer-reviewed medical journals. Data from at least two Phase II clinical trials conducted in different centers are required to support off-label use, but Phase III trial results carry greater weight.

To determine how coverage of off-label usage by both Medicare and private payers affects US oncologists' prescribing behavior, in 2005, the Association of Community Cancer Centers (ACCC), the Biotechnology Industry Organization (BIO), and the Pharmaceutical Research and Manufacturers of America (PhRMA) jointly commissioned a survey from Covance, a leading drug development service company (Covance Market Access Services, Inc., 2006). Covance interviewed 28 oncologists and 12 oncology practice managers. Respondents identified more than 50 physician-administered therapies that are used off-label. For guidance in off-label prescribing, physicians rely most heavily on peer-reviewed literature (cited by 25 of 28 oncologists), drug compendia (mentioned by 17 oncologists), and manufacturer hot lines and case reports (each cited by seven oncologists). However, reimbursement restrictions deter many oncologists from prescribing cancer therapies off-label, particularly to Medicare patients. Fifteen oncologists (54%) stated that Medicare policies on off-label usage frequently or very frequently interfered with their clinical decision making. By comparison, just eight oncologists (29%) indicated that private payers' policies on off-label usage frequently or very frequently interfered with their clinical decision making.

One participant in Covance's survey commented that "Medicare will deny every off-label indication that is not listed in the two compendia [i.e., AHFSDI, USPDI]. So, at this point, I am only using those products off-label for those indications that are listed in the compendia." The study notes that "listings in recognized compendia are outdated, incomplete, and may not include references to potential off-label uses of new drugs that may be supported by other published clinical evidence." Coverage of off-label prescribing is more restrictive under Part D than Part B. Off-label uses are eligible for reimbursement under Medicare Part D only if they are supported by one or more of three compendia (i.e., AHFSDI, USPDI, and Drugdex); evidence from peer-reviewed literature alone is not adequate for Medicare Part D coverage of off-label prescribing.

Private insurers vary enormously in their policies on reimbursement of off-label prescribing, and published research on this subject is extremely limited. Coverage of off-label usage may be subject to one or more of the following conditions:

- The prescribed drug is Food and Drug Administration (FDA) approved and listed on the payer's formulary.
- The patient is diagnosed with a life threatening or otherwise very serious disease.

- The risk-benefit ratio of prescribing the drug for an unlicensed indication justifies this usage.
- Evidence of efficacy is available in designated compendia (e.g., AHFSDI, USPDI) or peer-reviewed journals.
- Therapies approved for the indicated disease are not available, are deemed inappropriate for the patient, or have been tried and found ineffective.
- The payer's medical director approves the off-label usage.

OUTLOOK AND IMPLICATIONS FOR THE PHARMACEUTICAL INDUSTRY

Medicare's recent reimbursement reforms have had a seismic impact on the landscape of oncology in the United States. One immediate effect has been a sharp increase in the number of office-based oncology practices referring Medicare patients who lack supplemental insurance to hospital outpatient departments. Worse still, the reimbursement cuts have reportedly undermined the viability of some office-based oncology practices – especially smaller rural practices. Their problems could be compounded in 2007, if CMS follows through on recently announced proposals to cut physician reimbursement for Part B services by 5.1% and to change the formula for Part B drug reimbursement from ASP plus 6% to ASP plus 5%. If implemented, these changes would be a severe blow to beleaguered oncologists. The CAP was meant to reduce oncologists' financial exposure, but this program appears doomed to failure unless CMS can persuade more companies to become vendors – and more oncologists to use this service.

Other repercussions of the Medicare reforms may take longer to emerge. The MMA explicitly forbids CMS from setting drug prices within Medicare Part D, but CMS has a very powerful influence over prices in Part B – a far more significant factor in the US oncology market. In his testimony to the Subcommittee on Health of the House Committee on Ways and Means, Frederick Schnell of the COA asserted that "Medicare, with its considerable market clout, has set reimbursement rates artificially low for private payers to follow." ASP-based reimbursement has introduced an unprecedented price sensitivity into the US oncology market – a trend that is unlikely to be reversed. Thus far, relatively few private insurers have adopted ASP-based reimbursement, but past experience (and recent surveys) suggests that they will eventually follow CMS's example.

CMS may also set a lead for private insurers in the adoption of health technology assessment and evidence-based medicine. As noted earlier, in its report on the OPPS, MedPAC suggested that "it is appropriate to reserve additional payments for technologies that provide clinical benefit and do not have clinical substitutes. It may even be appropriate to limit payments to technologies that provide additional benefits commensurate with their costs." It will be interesting to see if CMS makes cost effectiveness a condition of reimbursement in the future.

Private payers will continue the recent trend of moving physician-administered drugs from the medical benefit to the pharmacy benefit. The launch of increased numbers of oral or self-injectable drugs will facilitate this migration to the pharmacy benefit. This shift will make it easier to impose cost-containment measures, such as multitier formularies, variable copayments or coinsurance, and prior authorization. However, because of the very specific demands of cancer therapy, oncology drugs will probably be spared from certain forms of cost containment (e.g., generics and/or therapeutic substitution, quantity limits). The adoption of NDC coding will enable health plans to adjudicate claims electronically, perform drug utilization review, and evaluate the long-term impact of drug therapies.

This rapidly changing environment presents manufacturers of oncology drugs with considerable challenges. Companies may need to exercise greater restraint in their pricing policies: when they increase their prices, hard-pressed oncology practices will be penalized by CMS's delay in updating the ASPs that determine reimbursement payments. On the other hand, manufacturers

need to be cautious about offering discounts, given that these reductions will be factored into the following quarter's ASP calculations, thereby lowering Medicare reimbursement levels. Companies may find that they experience a significant increase in the number of applications for their PAPs in the future.

The United States has long led the world in terms of the adoption of the most modern cancer therapies. However, unless office-based oncologists receive additional funding by some means as a matter of urgency, innovative medical oncology in the United States could be in jeopardy.

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3

Prospective Payment Systems: Opportunities and Threats for the Pharmaceutical Industry

OVERVIEW

In recent years, cost-containment initiatives in the pharmaceutical market have focused primarily on the retail sector. This trend is hardly surprising, given the size and high profile of the retail pharmacy market. In contrast, the hospital sector has received relatively little attention. Indeed, within the constraints of their overall budgets, hospitals have been largely left to their own devices, to define their reimbursement policies and decide how best to control their costs. Today, the climate in the hospital sector is undergoing a marked change. Governments are becoming increasingly concerned about runaway costs and ballooning deficits in their hospitals, a problem that is usually attributed to a combination of inefficiency, waste, inequality, and lack of transparency.

In an attempt to reduce costs and raise the general standard of secondary care, governments in many countries have begun to move from cost-based reimbursement for services rendered to prospective payment systems that pay providers a predetermined amount according to specific definitions. Prospective payment systems are typically based on diagnosis-related groups (DRGs), a system that groups patients on the basis of factors such as their primary or secondary diagnosis, complications and comorbidities, procedures, age, and sex.

Drug manufacturers will need to change in response to this shift from cost-based reimbursement to prospective payment. The high degree of complexity of prospective payment systems precludes an analysis of the intricacies of each system. Rather, this chapter provides an overview of the growth of prospective payment systems in major pharmaceutical markets (the United States, France, Germany, the United Kingdom, and Japan) and assesses the outlook and implications for the pharmaceutical industry.

UNITED STATES

Healthcare in the United States has three main sources of funding: the federal Medicare program for seniors, registered disabled persons, and patients with end-stage renal disease; joint federal/state Medicaid programs for low-income residents; and commercial health plans (sponsored primarily by employers). The use of prospective payment systems varies enormously among these insurance programs.

Medicare

The Medicare program has been the dominant driver of prospective payment systems in the United States. When it was established in 1965, Medicare relied entirely on retrospective payment systems for all services – reimbursing providers on the basis of costs incurred. As time passed, the Healthcare Financing Administration (HCFA; renamed the Centers for Medicare and Medicaid Services [CMS] in 2001) began to realize that this system encouraged inefficiency and undesirable variations in healthcare practice.

Inpatient Prospective Payment System

In an attempt to tackle the deficiencies of cost-based reimbursement, the Omnibus Budget Reconciliation Act (OBRA) of 1980 introduced the ambulatory surgery center benefit. The act stated that "this overhead factor is expected to be calculated on a prospective basis utilizing sample survey and similar techniques to establish reasonable estimated overhead allowances for each of the listed procedures which take account of volume (within reasonable limits)." In 1982, the Tax Equity and Fiscal Responsibility Act introduced measures to calculate Medicare inpatient reimbursement by means of a case-mix system based on DRGs. The following year, Congress revised this act to establish the Medicare inpatient prospective payment system (IPPS). Payments are based on the DRG coding at the time of inpatient discharge.

The DRG system that forms the foundation of Medicare's IPPS has been refined repeatedly. The current version is based on the *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) and comprises a total of 25 major diagnostic categories (MDCs) subdivided into 1,258 all-patient refined DRGs. Each case is assigned to a particular patient cluster, based on factors such as principal and secondary diagnoses, principal procedures, sex, and discharge status. CMS updates the DRGs, and the related diagnostic and procedural codes, annually, but critics assert that the system is too slow in reflecting changes in medical technology. In April 2006, CMS published proposals for further reform of the IPPS. Among other measures, in fiscal year 2008, the agency plans to replace the 1,258 existing DRGs with 861 severity-adjusted DRGs to take better account of variations in disease severity.

The IPPS bundles the costs of most drugs and medical devices into the DRG payment system. New technologies can be added to the standard DRG system through one of three methods:

- A technical advisory panel assigns the new technology an ICD-9-CM code.
- CMS can alter DRG assignments to ensure that a costly new technology is covered by a higher-paying DRG.
- The annual review of DRG case weights is used to adjust payments so that they cover the cost of the new technology.

Particularly expensive new technologies are initially reimbursed by a different method: add-on payments. This procedure applies to drugs and devices that would increase the cost of a case substantially beyond the relevant base DRG payment. In addition, to qualify for add-on payments, technologies must be new (i.e., on the market for less than two to three years) and must offer Medicare beneficiaries a significant clinical advantage over existing therapies. To encourage the prudent use of new technologies, CMS does not reimburse the full cost of these products. Rather, the add-on payment amounts to only 50% of a hospital's costs in excess of the standard DRG payment, to a maximum of 50% of the estimated cost of the new drug or device. Add-on payments are budget-neutral (i.e., they are offset by reductions in base payment rates) and cannot exceed 1% of total operating payments.

Outpatient Prospective Payment System

Encouraged by the success of the IPPS, in 1988, the HCFA commissioned 3M Health Information Systems to design a prospective payment system for outpatient treatment. The company published the first version of its ambulatory patient group (APG) system

in 1990, and a revised version followed in 1995. Medicare and Medicaid carriers in some states adopted one or the other version of the APG system, but the HCFA decided not to use this system.

The Balanced Budget Act of 1997 mandated the introduction of an outpatient prospective payment system (OPPS), which began operation on August 1, 2000. The Medicare Payment Advisory Commission (MedPAC) reports that, in 2004, 47% of Medicare beneficiaries received at least one OPPS service, from a total of approximately 4,300 hospitals. The OPPS does not cover beneficiaries who are enrolled in Medicare managed care plans – HMOs, preferred provider organizations (PPOs), or Medicare private fee-for-service plans.

According to CMS, the new payment system is "designed to ensure that Medicare and its beneficiaries pay appropriately for services and to encourage more efficient delivery of care." Under the old cost-based reimbursement system, Medicare payments for outpatient services did not keep pace with prices, with the result that patients' out-of-pocket expenses increased sharply. Prior to the introduction of OPPS, Medicare beneficiaries paid approximately 50% of the total cost of outpatient services. By 2004, this figure had declined to 34%, and it is eventually expected to stabilize at 20%. In addition, Congress has ruled that the patient copayment for a procedure must not exceed the annual inpatient deductible (i.e., $952 in 2006).

The OPPS uses the healthcare common procedure coding system (HCPCS) to assign services to one of approximately 600 ambulatory payment classification (APC) groups. Each group consists of services that are clinically comparable and require similar resources. CMS calculates the national median cost for services and procedures within each group, then adjusts the labor-related proportion of this sum (60% of the national total) to reflect geographic variations in labor costs. Drugs with median daily costs of less than $50 per day (i.e., the great majority of medicines), along with many other incidental items and services, are bundled into the APC payments. CMS reviews APC payment rates in the fall of each year and makes adjustments, as necessary, to take account of increased costs from new technologies.

New technologies that cannot be readily accommodated within an existing APC group can qualify for reimbursement by one of two other methods: inclusion in a new technology APC group or to be granted transitional pass-through payment status (see further on). A new technology APC is created only for procedures or services that can neither be included in an existing APC group nor meet the conditions for pass-through drugs. Once sufficient time has passed to gather data on hospitals' actual expenditures on these new services and procedures, CMS reassigns these new technologies to standard APC groups as part of its annual review process. Unlike the aforementioned add-on payments under Medicare IPPS, new technology APC groups are not budget-neutral and could therefore substantially increase hospitals' treatment costs.

Transitional pass-through payments apply to new drugs, biologics, and medical devices that complement an existing service but are too expensive to be included in existing APC groups. For example, a pass-through payment for a costly new monoclonal antibody may be used to supplement the established base payment that covers the administration of chemotherapy. Table 3.1 lists the technologies that have pass-through status in 2006. To qualify for this status, a new technology must have been on the market for no more than two to three years and must be more expensive than existing therapies. In addition, medical devices (as opposed to drugs) must offer a substantial clinical advantage over established treatments – the same standard that is a condition for add-on payments in the Medicare IPPS system. In November 2001, CMS published the following characteristics of a new technology that offers "substantial clinical improvement":

- It offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
- It offers the ability to diagnose a medical condition in a patient population in which their medical condition is currently undetectable or to diagnose a medical condition earlier in a patient

Table 3.1 Technologies with Pass-Through Status in the Medicare Outpatient Prospective Payment System, 2006

HCPCS Code	*APC Code*	*Product*
C9220	9220	Sodium hyaluronate
C9221	9221	Graftjacket Regular Matrix
C9222	9222	Graftjacket Soft Tissue
C9225	9225	Fluocinolone acetonide
J0128	9216	Abarelix injection
J0878	9124	Daptomycin injection
J2278	1694	Ziconotide injection
J2357	9300	Omalizumab injection
J2503	1697	Pegaptanib sodium injection
J2783	0738	Rasburicase
J2794	9125	Risperidone, long acting
J7518	9219	Mycophenolic acid
J8501	0868	Oral aprepitant
J9027	1710	Clofarabine injection
J9035	9214	Bevacizumab injection
J9055	9215	Cetuximab injection
J9264	1712	Paclitaxel injection
J9305	9213	Pemetrexed injection
Q4079	9126	Natalizumab injection (1 mg)

APC = Ambulatory payment classification
HCPCS = Healthcare common procedure coding system

population than allowed by currently available methods. There must also be evidence that the use of the technology to make a diagnosis affects the management of the patient.

- Use of the technology significantly improves clinical outcomes for a patient population as compared with currently available treatments. For example, improvements might include:

  1. Reduced mortality rate.
  2. Reduced rate of complications.
  3. Reduced rate of subsequent diagnostic or therapeutic interventions (e.g., due to reduced rate of recurrence of the disease process).
  4. Decreased number of future hospitalizations or physician visits.
  5. More rapid beneficial resolution of the disease process.
  6. Less pain, bleeding, or other quantifiable symptom.
  7. Reduced recovery time.

Table 3.2 summarizes the similarities and differences of the new technology payment mechanisms in Medicare's prospective payment systems. Critics deplore the inconsistencies of these mechanisms. In a report to Congress, which was published in March 2003, MedPAC made the following assertion:

> The treatment of drugs and devices is inconsistent, in that only newness and cost criteria are applied to pass-through drugs. This difference in the criteria represents unequal treatment between types of technology within the outpatient payment system. It also leads to a discrepancy between the treatment of drugs under the inpatient and outpatient payment systems since the clinical criteria are applied to all technologies, including drugs, on the inpatient side. Furthermore, without considering clinical benefit, the criteria applied to pass-through drugs may overemphasize the goal of paying adequately for new technologies at the expense of prudent purchasing.

Furthermore, MedPAC suggested that "it is appropriate to reserve additional payments for technologies that provide clinical benefit and do not have clinical substitutes. It may even be appropriate to limit payments to technologies that provide additional benefits commensurate with their costs."

Medicaid

The Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA) opened the way for state Medicaid administrations to establish prospective payment systems for their

Table 3.2 Key Features of Medicare Inpatient and Outpatient New Technology Payment Mechanisms

	Inpatient Add-On Payments	*Outpatient Pass-Through Payments*		*Outpatient New Technology APCs*
		Medical Devices	*Drugs and Biologics*	
New technologies eligible for additional payments	New technologies that offer a new procedure or are an input to an existing DRG	New technologies that are an input are to an existing DRG	New technologies that an input to an existing DRG	New technologies that offer a new service
Criteria used by CMS	Clinical benefit, novelty, cost	Clinical benefit, novelty, cost	Novelty, cost	Novelty
Funding method	Budget-neutral	Budget-neutral	Budget-neutral	New expenditures
Unit of payment	Additional costs of treating a case using new technology	Cost of new technology	Cost of new technology	Cost of service
Method of determining payments	Payment = 50% of additional costs (capped at 50% of estimated cost of new technology)	Payment = 100% of reported costs minus device costs already built into base payment rate	Payment = 95% of average wholesale price	Payment = midpoint of payment range for new technology APC group

APC = Ambulatory payment classification
CMS = Centers for Medicare and Medicaid Services
DRG = Diagnosis-related group

payments to federally qualified health clinics and rural health clinics. Beginning January 1, 2001, states could switch from the established cost-reimbursement system to prospective payment. However, a recent study conducted by the Government Accountability Office (GAO) suggests that many states were slow to embrace prospective payment. On average, states took slightly more than a year to implement Medicaid prospective payment systems, and the GAO found that some states still had not completed this exercise as of June 1, 2004. A survey conducted by the National Association of Community Health Centers (NACHC), assisted by George Washington University, found that 23 of the 42 states that responded excluded pharmacy benefits from their Medicaid prospective payment systems in 2005, compared with just seven states in 2004.

Commercial Health Plans

Commercial insurers observe Medicare's reimbursement practices very closely and often follow CMS's lead (e.g., historically reimbursing office-based clinicians 95% of the average wholesale price of physician-administered drugs). In the matter of prospective payment, however, commercial health plans have generally been reluctant to copy Medicare's example. Adopting a DRG-based IPPS similar to the Medicare model is relatively simple, and some plans have developed such systems in recent years. However, copying Medicare's OPSS would be more challenging. For instance, some APCs are based not on clinical factors but on Medicare reimbursement policies. CMS updates its APC system each quarter, a cycle that would require more frequent changes than many plans would like.

FRANCE

France has traditionally operated a bimodal system of hospital funding. Public and private hospitals working in the public sector receive a *dotation globale* (global budget) that is divided among various areas of expenditure, whereas private hospitals receive

per diem or activity-based payment. However, as part of its *Plan Hôpital 2007* (Hospital Plan 2007) reform program, the French government wants all hospitals engaged in medicine, surgery, or obstetrics in that country to adopt a system known as *tarification à l'activité* (T2A; activity-based pricing). This new approach to hospital funding in France is based on *groupes homogènes de séjour* (GHSs; uniform hospitalization groups), a system similar to DRGs. The government expects to realize the following key benefits from the T2A system:

- Greater role for clinical factors in funding.
- More responsible behavior by leading players and an incentive for them to change.
- Greater equality of treatment between the (public and private) sectors.
- The development of health economic steering mechanisms (management controls) at the heart of public and private hospitals.

The timetable for the T2A program calls for a steady migration from cost-based reimbursement to activity-based funding. Figure 3.1 shows the government's targets for the percentage of total spending in public and private hospitals working in the public sector that will be derived from activity-based funding in select years from 2004 to 2010, the year when the transition is scheduled for completion.

As a general rule, medicines are included in the GHSs. However, the French government recognizes that certain drugs and other technologies (notably medical devices) are too expensive to fit within the GHSs; therefore, these products will be funded separately. The Ministry of Health and the *Agence Technique de l'Information sur l'Hospitalisation* (ATIH; Technical Agency for Information on Hospitalization) have compiled a list of approximately 80 products that qualify for supplementary reimbursement (Table 3.3). Almost half of these products are oncology-related medicines. The Ministry of Health will update the list annually.

To control spending on drugs that qualify for supplementary reimbursement, ceiling prices will be determined either through negotiations between the manufacturers and the *Comité Economique des Produits de Santé* (CEPS; Economic Committee for Healthcare Products), the organization responsible for setting reimbursement prices

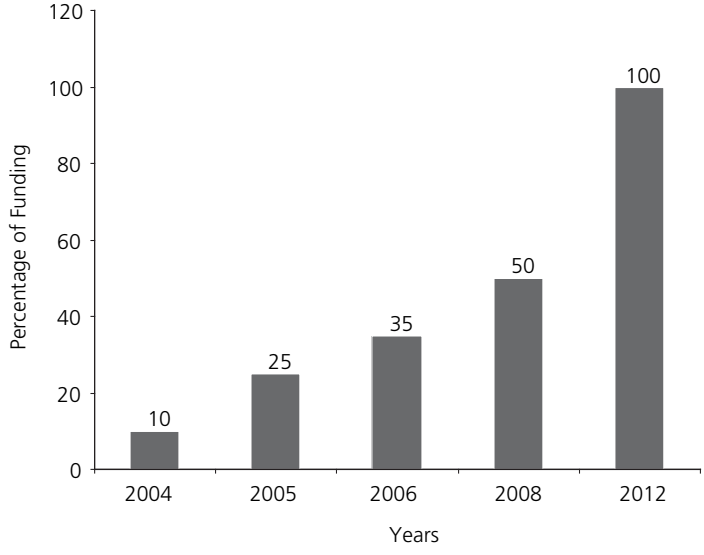

Figure 3.1 Activity-Based Funding in France: Projected Share of Total Budget for Public and Private Hospitals Working in the Public Sector in Selected Years, 2004–12

Table 3.3 Drugs Eligible for Supplementary Reimbursement in France, 2005

Drug Class/International Nonproprietary Name	*Brand Name*	*Manufacturer*
Antineoplastic drugs		
Aldesleukin	Proleukin	Chiron
Alemtuzumab	Mabcampath	Schering
Arsenic trioxide	Trisenox	Cell Therapeutics
Bortezomib	Velcade	Janssen-Cilag
Busulfan	Busilvex	Pierre Fabre
Carmustine	Bicnu	Bristol-Myers Squibb
Cladribine	Leustatin	Janssen-Cilag
Daunorubicin	Daunoxome	Gilead Sciences
Docetaxel	Taxotère	Sanofi-Aventis
Doxorubicin	Caelyx, Myocet	Schering-Plough, Elan Pharma
Epirubicin	Farmorubicin	Pharmacia (Pfizer)
Fludarabine	Fludara	Schering
Fotemustine	Muphoran	Servier
Gemcitabine	Gemzar	Lilly France
Ibritumomab-tiuxetan	Zevalin	Schering
Idarubicin	Zavedos	Pfizer
Irinotecan	Campto	Sanofi-Aventis
Oxaliplatin	Eloxatin	Sanofi-Aventis
Paclitaxel	Taxol	Bristol-Myers Squibb
Pemetrexed	Alimta	Lilly France
Pentostatin	Nipent	Wyeth-Lederle
Pirarubicin	Theprubicine	Sanofi-Aventis
Raltitrexed	Tomudex	AstraZeneca
Rituximab	Mabthera	Roche
Tasonermine	Beromun	Boehringer Ingelheim
Topotecan	Hycamtin	GlaxoSmithKline
Trastuzumab	Herceptin	Roche
Vinorelbine	Navelbine	Pierre Fabre
Other oncology-related drugs		
153Sm-samarium-acid	Quadramet	Cis Bio International
89Sr-strontium chloride	Metastron	Amersham Health
Amifostine	Ethyol	Schering-Plough
Darbepoetin alfa	Aranesp	Amgen
Dexrazoxane	Cardioxane	Chiron France
Erythropoietin alfa	Eprex	Janssen-Cilag
Erythropoietin beta	Neorecormon	Roche
Iodine-131 lipiodil	Lipiocis	Cis Bio international
Rasburicase	Fasturtec	Sanofi-Aventis
Porfimer sodium	Photofrin	Isotec
Thyrotrophine	Thyrogen	Genzyme
Yttrium chloride	Ytracis	Cis Bio International
Antifungals		
Amphotericin	Abelcet	Elan Pharma
Amphotericin B	Ambisome	Gilead Sciences
Caspofungin	Cancidas	Merck Sharp & Dohme
Voriconazole	Vfend	Pfizer
Coagulation factors		
Eptacog	Alfa Novoseven	Novo Nordisk
Antihemophilic factor (recombinant)	Advate	Baxter
Factor VII	Factor VII LFB	LFB
Factor VIII	Factane	LFB

(continued)

Table 3.3 Continued

Drug Class/International Nonproprietary Name	*Brand Name*	*Manufacturer*
	Helixate Nexgen	Aventis-Behring
	Hemofilm M	Baxter
	Recombinate	Baxter
	Refacto	Wyeth-Lederle
	Monoclate	Aventis-Behring
	Kogenate Bayer	Bayer Pharma
Factor IX	Betafact	LFB
	Mononine	Aventis-Behring
Factor XI	Hemoleven	LFB
Nonacog	Alfa Benefix	Baxter
von Willebrand factor	Wilfactin	LFB
von Willebrand factor and factor VIII in combination	Willebrand LFB, Innobranduo	LFB LFB
Other blood derivatives		
Activated prothrombic complex	Feiba	Baxter
Antithrombin III	Aclotin	LFB
Factors IX, II, VII, and X in combination	Kaskadil	LFB
Inhibitor C1	Esterasine	Baxter
Protein C	Ceprotin,	Baxter
	Protexel	LFB
Orphan drugs		
Agalsidase alfa	Replagal	TKT Europe 5S
Agalsidase beta	Fabrazyme	Genzyme
Bosentan	Tracleer	Actelion
Carglutamic acid	Carbaglu	Orphan Europe
Epoprostenol	Flolan	GlaxoSmithKline
Iloprost	Ventavis	Schering
Imiglucerase	Cerezyme	Genzyme
Laronidase	Aldurazyme	Genzyme
Miglustat	Zavesca	Actelion
Sodium phenylbutyrate	Ammonaps	Orphan Europe
Treatments for rheumatoid arthritis		
Etanercept	Enbrel	Wyeth-Lederle
Infliximab	Remicade	Schering-Plough
Immunoglobulins		
Antilymphocyte immunoglobulin	Lymphoglobulin	Imtix-Sangstat
Antithymocyte immunoglobulin	Thymoglobulin	Imtix-Sangstat
Immunoglobulin antihepatitis B	Ivhebex	LFB
Polyvalent human immunoglobulins for intravenous administration	Endobulin	Baxter
	Gammagard	Baxter
	Octagam	Octapharma
	Sandoglobulin	OTL Pharma
	Tegelin	LFB
Treatments for severe septicemia		
Drotrecogin	Xigris	Lilly

LFB = Laboratoire FranÁais du Fractionnement et des Biotechnologies

in France, or through a decree from the ministers of health and social security. Manufacturers will also be subject to price/volume constraints, whereby prices will be reduced if sales volume is judged to have grown excessively.

High-priced new drugs can be added to this list as soon as they receive marketing authorization in France. After 12 months on the market, a drug will either be approved to remain on this list, in which case it will become subject to a ceiling price, or it will be removed from the

supplementary reimbursement list and covered by the relevant GHS tariff.

Hospitals will be reimbursed for medicines on the supplementary reimbursement list at the level of a drug's ceiling price. To encourage hospital pharmacies to negotiate manufacturer discounts on these medicines, hospitals will be permitted to keep a proportion of any price difference they secure between the ceiling price and their actual purchase price.

Hospitals will also be required to sign a contract for the good use of medicines. Institutions that fail to sign this contract will have their reimbursement rate for drugs on the supplementary reimbursement list reduced to just 70%, leaving them out of pocket. Similarly, if a hospital fails to comply with the terms of its contract for the good use of medicines, the local *agence régionale d'hospitalisation* (ARH; regional hospitalization agency) can call on the health insurance funds to cut the reimbursement rate to 70%.

GERMANY

The German hospital sector has come under intense pressure in recent years. With the exception of Japan, Germany has proportionally more acute hospital beds than any other member of the Organization for Economic Cooperation and Development (OECD): 6.6 per 1,000 population in Germany in 2002, compared with an OECD average of 4.2. Furthermore, hospital stays are longer in Germany than in any other OECD member state except South Korea: an average of 9.2 days in Germany in 2002, compared with an OECD average of 6.7. Not surprisingly, the German healthcare system has struggled to fund this level of hospital care. Healthcare expenditures have risen faster than budgets, with the result that the statutory health insurance system has had deficits in many years since the early 1990s. The implementation of a DRG system is intended to promote greater efficiency in the hospital sector in Germany.

In April 2002, the German Parliament passed the *Gesetz zur Einführung des diagnoseorientierten Fallpauschalensystems* (Act for the Introduction of a Diagnosis-Related Group System). The introduction of this new DRG system began in 2004 and was originally scheduled for completion in 2007, but the government was persuaded to agree that this timetable was too aggressive. The *Zweites Fallpauschalenänderungsgesetz* (second Diagnosis-Related Group Modification Act), enacted in December 2004, extended the deadline for the full implementation of the DRG system to January 1, 2009, with the possibility of a further one-year extension, if necessary (Figure 3.2). As of October 2005, approximately 1,720 acute-care hospitals (94% of the national total) had begun the process of implementing the new DRG system. These hospitals had a total of 494,000 beds, managed 15.3 million cases, and had combined expenditures of €45 billion ($56 billion); for the sake of uniformity of the analysis, the US dollar-to-euro exchange rate used in this chapter is the 2005 average rate, that is, $1 = €0.80453.

Germany's DRG system is an adaptation of the Australian Refined Diagnosis-Related Group (AR-DRG) system. However, the two systems differ significantly in their applications. The Australian system is used essentially as an instrument to manage the supply of healthcare services, but the German system was created as a budgetary control mechanism.

The *Fallpauschalenkatalog* (DRG Catalogue) is updated annually by the *Deutsches Institut für Medizinische Dokumentation und Information* (DIMDI; German Institute for Medical Documentation and Information) and the *Institut für das Entgeltsystem im Krankenhaus* (InEK; Institute for Hospital Reimbursement), in consultation with specialist societies. The total number of DRGs has increased from 664 in 2003 to 954 in 2006 (Figure 3.3). This total is substantially larger than in most other DRG systems and reflects the demand for more nuanced grouping in Germany. Similarly, the number of categories for disease severity was recently increased, from five to eight.

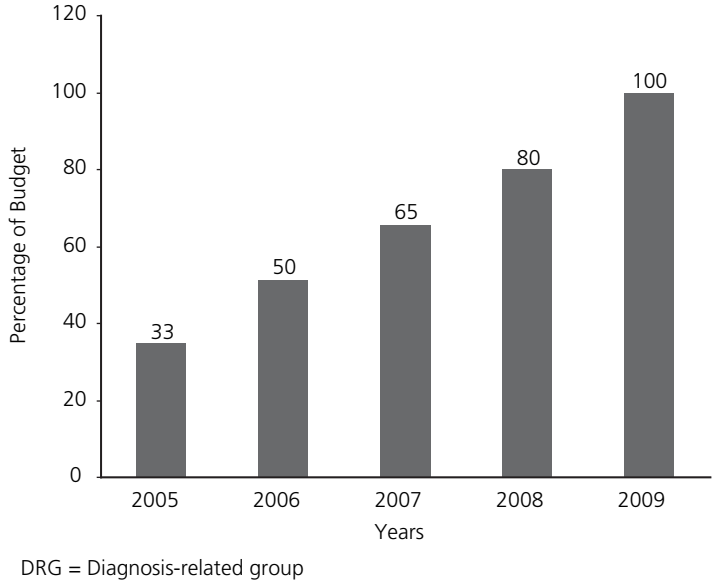

Figure 3.2 Percentage of German Hospitals' Budgets to Be Derived from DRG-Based Funding 2005–9

DRG rates vary from state to state. By 2009, payments to all hospitals will be expected to converge on their relevant state rates. High-priced hospitals will lose from this exercise, whereas low-priced hospitals will gain.

A key objective of DRG-based reimbursement is to shorten the length of hospital stays. New cost management systems will measure how effectively a given treatment reduces overall therapy costs while achieving the same clinical outcomes. Product evaluations will need to take account of the following factors:

- Therapy costs that correlate duration of treatment with length of stay.
- Cost of managing side effects.
- Administration and disposal costs.
- Cost of treating therapy failures.

At present, DRGs apply only to inpatient procedures, with the exception of two semi-ambulatory groups related to renal dialysis. However, the government has had plans to introduce DRGs for office-based specialists, a step that is in keeping with the administration's policy of *integrierte Versorgung* (integrated care). Family physicians, specialists, and medical and nonmedical healthcare practitioners in both the primary care and hospital sectors are encouraged to work together to improve the quality of patient care. Hospitals may offer ambulatory care for certain indications and highly specialized services and become involved in disease management programs and the provision of ambulatory care where there is a shortage of office-based specialists. This provision is expected to reduce the need for patients to visit both office- and hospital-based physicians.

In a position statement published in March 2004, the *Verband Forschender Arzneimittelhersteller* (VFA; German Association of Research-Based Pharmaceutical Companies) described the introduction of the new DRG system as "the greatest structural reform in the [German] hospital sector in the last 30 years." The new system presents the pharmaceutical industry with both opportunities and challenges. Drug costs are generally included in the standard DRG rates, but additional funding is available

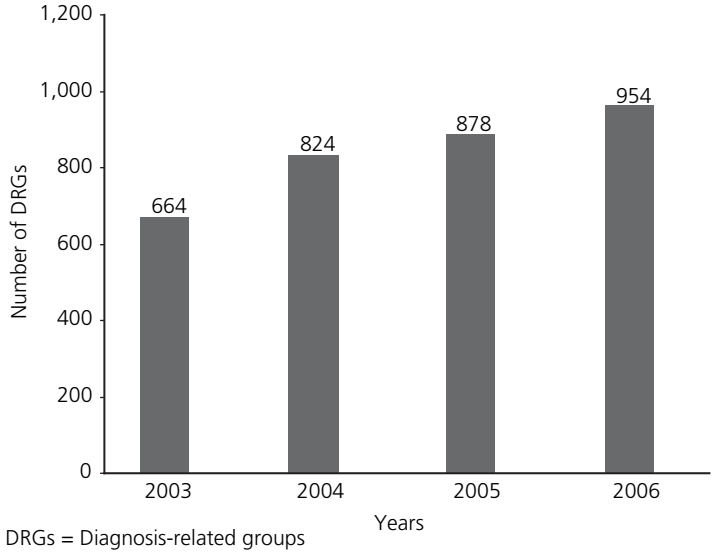

Figure 3.3 Total Number of Diagnosis-Related Groups in Germany, 2003–6

for new therapies in specific circumstances. Hospitals can apply for a *Zusatzentgelt* (supplementary payment) for drugs or devices that are not yet covered by DRGs. Supplementary payments are available for technologies that meet any of the following conditions:

- Insufficient data available for inclusion in a DRG.
- Use in multiple DRGs.
- Potentially significant impact on the cost of a given DRG or on the hospital's overall expenditures.

Table 3.4 lists the drugs that are eligible for supplementary payments in 2006. Payments are dose dependent.

Supplementary payments, along with DRGs and days of treatment, are used to set a hospital's revenue budget. The full amount of the supplementary payment is available if hospitals submit their applications to statutory health insurance funds in advance of treatment, but retroactive submissions qualify for only 75% reimbursement. If a hospital exceeds its revenue budget, it must generally repay 65% of the surplus to the statutory health insurance

Table 3.4 Drugs Eligible for Supplementary Payments in Germany, 2006

Code	*Drug*
ZE13	Alemtuzumab
ZE15	Docetaxel
ZE17	Gemcitabine
ZE19	Irinotecan
ZE23	Oxaliplatin
ZE24	Paclitaxel
ZE25	Rituximab
ZE27	Trastuzumab
ZE30	Prothrombin complex
ZE38	Human immunoglobulin for cytomegalovirus
ZE39	Caspofungin
ZE40	Filgrastim
ZE41	Polyvalent human immunoglobulin
ZE42	Lenograstim
ZE43	Liposomal amphotericin B
ZE44	Topotecan
ZE45	Voriconazole (oral)
ZE46	Voriconazole
ZE47	Antithrombin III
ZE48	Aldesleukin
ZE49	Bortezomib
ZE50	Cetuximab
ZE51	Human immunoglobulin for hepatitis B surface antigen
ZE52	Liposomal doxorubicin
ZE53	Pemetrexed

Unless otherwise indicated, coverage relates to parenteral administration

funds, but this rate is reduced to 25% for excess revenues derived from supplementary payments for drugs and devices. On the other hand, if a hospital earns less than its revenue budget, it generally receives 40% of the shortfall from the statutory health insurance funds – but nothing for a shortfall in revenues from supplementary payments for drugs and devices. Supplementary payments are a budget-neutral measure – in other words, monies allocated to supplementary payments reduce funding for other areas of the overall budget.

UNITED KINGDOM

The infrastructure of the U.K. National Health Service (NHS) has undergone many changes in recent years. In April 2002, the 95 regional health authorities in England were merged to form 28 new strategic health authorities (SHAs). These SHAs are responsible for strategic development of healthcare services within their areas and for managing the performance of 303 primary care trusts (PCTs) and more than 300 NHS hospital trusts. The SHAs distribute unified budget allocations to the PCTs, the organizations that are now the dominant fund holders in the U.K. healthcare system, managing 75% of the entire NHS budget and 100% of local funds. PCTs have three main roles: (1) to improve the health of the community; (2) to develop primary and community health services; and (3) to commission hospital care for their patients. As the main source of funding for public hospitals, PCTs have enormous influence over the finances and policies of these hospitals. In the spring of 2006, the U.K. government announced plans for further reform of the NHS, reducing the number of SHAs in England to 10 and PCTs to 152.

The government has also made radical changes to hospital funding in England. Until very recently, hospital budgets were set on the basis of historical expenditures. In October 2002, however, the Department of Health published *Reforming NHS Financial Flows*, a blueprint for a new patient-centered funding system known as Payment by Results (PbR). This system gives NHS patients the freedom to choose when and where they receive hospital treatment, a right they had never previously enjoyed. The mechanism has been summarized with the motto "the money follows the patient." Specifically, PbR has the following key objectives:

- Promoting choice and competition.
- Increasing efficiency and value for money.
- Facilitating therapeutic innovation.
- Cutting waiting times and inpatient length of stay.
- Improving equity and transparency in the healthcare system.

The implementation of this new system began on a limited scale in 2004 and was then expanded in 2005 to include all elective inpatients. From 2006 to 2008, the system will be extended to nonelective inpatients, emergency room admissions, and outpatients. Beginning in 2008, PbR will be introduced into the primary care sector.

PbR is based on healthcare resource groups (HRGs), a form of DRG that groups patients who have similar clinical conditions and similar consumption of healthcare resources. The HRG system has been refined repeatedly to make it more discriminating, and a further review is in progress, with the objective of identifying all disease complications and comorbidities. HRGs provide the data that underpin the national tariff for services provided within the PbR system. Efficient hospitals that can provide services for less than national tariff prices will be permitted to keep the surplus. By reinvesting the money saved in their organizations, these hospitals can improve the quality of their services and attract patients away from less-efficient hospitals.

The national tariff does not include procedures that are highly specialized, rarely performed, or subject to price volatility. Furthermore, high-cost drugs (e.g.,

antiretrovirals, tumor necrosis factor-alpha inhibitors, beta interferons, treatments for hepatitis C, therapies for pulmonary hypertension, some chemotherapy drugs) and devices (e.g., aortic stents, insulin pumps) are excluded from the PbR national tariff. Table 3.5 lists excluded drugs for the 2006–7 financial year. Hospitals that wish to use these drugs have to commission supplementary funding from local PCTs. In addition, new technologies, as well as some existing drugs and devices that have a high price or uneven distribution, may qualify for pass-through status for a maximum of two years. PCTs must notify the Department of Health if they grant pass-through status to drugs used by hospitals in their respective catchment areas.

Since January 1, 2002, PCTs have a statutory obligation to provide funding for therapies endorsed by the National Institute for Health and Clinical Excellence (NICE)

Table 3.5 Drugs Eligible for Supplementary Reimbursement in the United Kingdom, 2006

Drug Class	*Examples*
Cytokine inhibitors	Infliximab (Schering-Plough's Remicade)
Treatments for primary pulmonary hypertension	Bosentan (Actelion's Tracleer), iloprost (Schering's Ventavis), epoprostenol (GlaxoSmithKline's Flolan), phosphodiesterase-5 inhibitors
Antifibrinolytic drugs/hemostatics	Factor VIIa, factor VIII, factor IX, antithrombin III, prothrombin, fibrinogen, factor XI, protein C, von Willebrand factor, factor VIII bypassing products, prothrombin complex, porcine factor VIII, fibrin sealants, thrombin (for topical use only)
Treatments for torsion dystonia and other involuntary movements	Riluzole
Antifungals	Amphotericin (lipid formulations), caspofungin (Merck Sharp & Dohme's Cancidas), voriconazole (Pfizer's Vfend)
AIDS/HIV antiretrovirals	Abacivir with lamivudine and zidovudine (GlaxoSmithKline's Trizivir)
Treatments for viral hepatitis (B and C) and respiratory syncytial virus	Palivizumab (Abbott's Synagis)
Growth hormones and growth hormone receptor antagonists	Somatropin (multisource)
Drugs affecting bone metabolism	Teriparatide (Lilly's Forsteo)
Treatments for multiple sclerosis	Interferon alpha and beta
Somatostatin analogues	Octreotide acetate (Novartis's Sandostatin), lanreotide acetate (Ipsen's Sometuline LA)
Treatments for neutropenia	Filgrastim (Amgen's Neupogen), pegfilgrastim (Amgen's Neulasta)
Drugs used in metabolic disorders	Treatments for carnitine deficiency, Fabry's disease, Gaucher's disease, mucopolysaccharidosis I, nephropathic cystinosis
Treatments for hyperuricemia associated with cytotoxic drugs	Rasburicase (Sanofi-Aventis's Fasturtec)
Dermatological drugs that modify the immune response	Efalizumab (Serono's Raptiva)
Intravenous/subcutaneous human normal immunoglobulins	Baxter BioScience's Subcuvia, ZLB (Behring's Vivaglobin

within three months of the institute's publication of its decision. To provide funding for these treatments, the PbR budget was increased by £304 million ($553 million [0.7%]) in financial year 2004–5 and by £328 million ($596 million [0.7%]) in financial year 2005–6 (for the sake of uniformity of the analysis, the U.S. dollar-to-pound sterling exchange rate used in this chapter is the 2005 average rate, that is, $1 = £0.55004). The 0.7% increase was based on national averages and may not have been sufficient to cover increased expenditures in hospitals that had an above-average usage of NICE-endorsed technologies.

A performance assessment known as the annual health check will determine whether hospitals and PCTs are meeting their PbR obligations. These organizations will be required to declare whether they are conforming to NICE's technology appraisals and taking the institute's clinical guidelines into account in the delivery of healthcare. To make such a declaration, hospitals and PCTs must have robust systems to assess, plan for, and monitor the financial impact of implementing NICE's guidance.

JAPAN

In April 2003, the Japanese government introduced a new flat-sum reimbursement system, based on diagnosis-procedure combinations (DPCs), for acute care of inpatients at 82 special-function hospitals and other hospitals that provide advanced medical treatment. The mean fee-per-day determined for each diagnosis group is adjusted according to the mean length of stay at individual hospitals. By fiscal year 2005, 144 Japanese hospitals had adopted the DPC system and 145 other hospitals had introduced it on a trial basis, with more expected to follow in the future. The pharmaceutical industry is concerned that DPC reimbursement might lead to inappropriate prescribing behavior. In an analysis published in June 2004, the Healthcare System Subcommittee of the Federation of Pharmaceutical Manufacturers' Associations of Japan (FPMAJ) suggested that "the expansion of the DPC system is acceptable only to the extent that it does not affect the proper use of drugs." The authors predicted that the DPC system will expand and warned that this trend "will necessarily make medical institutions more strongly concerned about the use of drugs." The DPC system is likely to prompt hospitals to increase their use of generics in order to reduce their drug acquisition costs. To this end, hospitals are introducing electronic prescribing systems that facilitate prescribing by international nonproprietary names.

The Ministry of Health, Labor, and Welfare (MHLW) has ruled that, from July 2005, some expensive therapies (e.g., rituximab for non-Hodgkin's lymphoma) must be excluded from the DPC system and reimbursed on a fee-for-service basis. This decision was prompted by a sizable gap between the treatment costs as calculated in the DPC and fee-for-service systems. Drugs that are more expensive than the DPC cost are funded by medical institutions, a situation that defeats the objective of the DPC system (i.e., cutting the costs of acute inpatient care). The MHLW suggests that such a situation is exceptional and transient, but it has not offered a clear solution to this problem. Therefore, it may be necessary to reserve some expensive therapies for use in the outpatient setting (where the DPC system is not used).

OUTLOOK AND IMPLICATIONS FOR THE PHARMACEUTICAL INDUSTRY

The expansion of prospective payment systems in the world's major pharmaceutical markets appears to offer limited new opportunities for manufacturers of branded medicines. Such systems are meant to improve access to high-quality healthcare and to eliminate geographic inequalities in treatment, but they are also clearly intended to reduce costs – potentially including pharmaceutical expenditures.

Hospitals that can cut their costs below prospective payment system reimbursement levels frequently derive a dual benefit: they

can keep part or all of the money they save, and increased resources enable them to improve the quality of their service and attract more patients. This environment increases the pressure on hospitals to use generics wherever possible and to negotiate substantial discounts on branded medicines. On the other hand, hospitals that make above-average use of innovative technologies – in many cases, university hospitals in the vanguard of medical practice – could find themselves penalized for their high costs.

Governments would insist that their measures are not intended to hinder innovation, and all of the prospective payment systems reviewed in this report allow for exceptional coverage of new and/or costly therapies. However, exploiting this provision is not always easy in practice. Hospitals must typically overcome administrative barriers to secure coverage of these therapies. Precise advance planning may be needed to obtain maximum reimbursement – no easy task when new and relatively unfamiliar technologies are involved. Given these obstacles, some hospitals may be deterred from pursuing exceptional coverage of innovative therapies, but such a decision could actually have the effect of delaying the inclusion of these treatments in standard DRGs. Moreover, the fact that funding for new technologies is often diverted from more established products – to ensure a budget-neutral impact – is bad news for both hospitals and pharmaceutical companies.

It will be interesting to observe the growing impact of health economics and health technology assessment on prospective payment systems in the future. NICE is certainly one of the best-known exponents of such research, and many other countries are following suit. Indeed, NICE recently agreed on a triangular collaboration with Germany's *Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* (IQWiG; Institute for Quality and Economy in the Healthcare System) and France's *Haute Autorité de la Santé* (HAS; High Authority on Health), in addition to an earlier agreement to exchange information with the Food and Drug Administration (FDA). After largely ignoring health economics and health technology assessment for many years, the United States is slowly beginning to embrace these disciplines. In fact, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) calls on the Agency for Healthcare Research and Quality (AHRQ) to conduct trials to compare the clinical effectiveness and cost-effectiveness of branded medicines that compete within a given drug class. The act directs that cost-effectiveness studies may include "high-cost" healthcare products and services "as well as those which may be underutilized and overutilized and which may significantly improve the prevention, treatment, or cure of diseases and conditions (including chronic conditions) which impose high direct or indirect costs on patients or society." It remains to be seen to what extent the AHRQ's research will influence CMS's decisions on Medicare prospective payment. Furthermore, MedPAC's recommendation that additional payments should be restricted "to technologies that provide additional benefits commensurate with their costs" echoes statements made in some highly cost-conscious European countries.

Continued expansion of prospective payment systems appears very likely. With the steady growth of consumer-directed healthcare, U.S. residents are becoming increasingly aware of opportunities to curb healthcare spending. Commercial health plans may soon decide that the time is right to follow Medicare's lead in establishing prospective payment systems for hospital treatment. European countries look set to overtake the United States in their implementation of prospective payment. Germany plans to extend this system to office-based specialists, and the United Kingdom has an even more radical ambition – to introduce prospective payment in primary care. The trend for closer integration of primary and secondary care may prompt other countries to consider a similar expansion of prospective payment.

If the pharmaceutical industry is to derive some benefit from the growth of prospective

payment, it needs to demonstrate clearly and cogently how innovative prescription drugs can add substantial value in such a system. In the past, hospitals had a financial (though not necessarily clinical) incentive to extend a patient's length of stay, but prospective payment essentially inverts this proposition: it is more lucrative to discharge a patient at the earliest appropriate opportunity. If pharmaceutical companies can demonstrate that their products can shorten a patient's length of stay or reduce treatment costs in other ways, their products will surely find a place in even the toughest prospective payment systems.

4

Off-label Prescribing: Overcoming the Reimbursement Barrier

OVERVIEW

Off-label prescribing is the practice of using a medicine for a purpose other than that for which it has been officially approved. Off-label usage takes a variety of forms: departing from the dosing range or duration of therapy, using a medicine in an unapproved combination with another agent, prescribing a drug to patients who belong to populations for which the agent is not approved (notably children), and using the product for unlicensed indications.

A drug's initial label is often very narrow, and gaining approval for additional indications can take a long time. Manufacturers are understandably reluctant to conduct expensive clinical trials for new indications on drugs that have lost or will soon lose their patent protection. Furthermore, physicians are often quick to deviate from a new drug's labeling restrictions. Off-label prescribing is frequently prompted by a dearth of effective licensed drugs with which to treat patients. Nevertheless, physicians may expose themselves to an increased risk of litigation if they prescribe medicines off-label. In addition, payers may refuse to reimburse physicians and/or their patients for off-label usage of medicines that does not meet strict conditions.

Anecdotal evidence suggests that off-label prescribing accounts for the majority of uses of certain drugs. Reportedly, this practice is particularly common in oncology, cardiology, neurology, and psychiatry, but few studies have actually measured the frequency of off-label usage. One recent study analyzed prescribing patterns by diagnosis for 160 commonly prescribed drugs in the United States (Radley et al. 2006). The authors found that, of a surveyed total of approximately 725 million prescriptions dispensed in 2001, about 150 million (21%) were for unapproved indications. Off-label prescribing accounted for 46% of prescriptions for cardiac therapies (excluding antihyperlipidemics and antihypertensives) and anticonvulsants, 42% of prescriptions for antiasthmatics, 34% of prescriptions for allergy therapies, 31% of prescriptions for psychiatric therapies (i.e., antidepressants, anxiolytics, antipsychotics), and 30% of prescriptions for peptic ulcer and dyspepsia therapies. Gabapentin was the drug most frequently prescribed off-label: 83% of uses were for unlicensed indications.

Other investigations of off-label prescribing have generally focused on particular drug classes. For example, an analysis of claims data from the Georgia Medicaid program in 1999 and 2000 found that 71% of uses of anticonvulsants were off-label (Chen et al. 2005). An analysis of atypical antipsychotic usage in North Staffordshire, England, from 1994 to 2001 found that 41% of uses of these drugs

were for indications that were not approved at the time (Hodgson and Belgamwar 2006). A 2003 study of atypical antipsychotic usage in 7 Italian psychiatric outpatient services found that 52% of prescriptions for these drugs were for off-label indications (Barbui et al. 2002).

Given the time, effort, and cost involved in securing approval for multiple indications, it can be tempting to drug manufacturers to promote off-label prescribing of their products. However, unless carefully controlled, this practice may prove illegal, provoking potentially costly litigation.

This chapter examines the reimbursement barriers to off-label prescribing in the world's six largest pharmaceutical markets: the United States, France, Germany, Italy, the United Kingdom, and Japan. We begin with an analysis of the scale of off-label usage in the United States of four key drug classes: antineoplastic drugs, antidepressants, antipsychotics, and anticonvulsants. We then review the hazards that manufacturers may face when they engage in off-label marketing and explore the reimbursement environment in the United States, focusing on Medicare, Medicaid, and private insurance. Next, we consider the reimbursement challenges in each of the other countries covered in this chapter. We conclude with a brief assessment of the outlook and implications for the pharmaceutical industry.

UNITED STATES

Scale of Off-label Prescribing

To assess the current scale of off-label prescribing in the United States, we analyzed 2005 claims data from Verispan's Physician Drug & Diagnosis Audit (PDDA) database for leading oncology, neurology, and psychiatry drugs. The results of this analysis are presented in the sections that follow. We focused on off-label usage in the form of prescriptions for unlicensed indications and did not examine off-label prescribing by patient age (i.e., the prescription to children of drugs that are not approved for pediatric use). The indications for which drugs were prescribed were based on four-digit codes in the *International Classification of Diseases*, 9th Revision (ICD-9). We deemed prescriptions to be on label in cases where diagnostic codes were more general than, but related to, the approved indication. For example, we considered a diagnosis of "anxiety states" to be compliant with the label for drugs approved for generalized anxiety disorder, social anxiety disorder, or cognate disorders. The PDDA database did not allow us to determine if prescriptions met all of the conditions specified on a given drug's label (e.g., cancer staging, failure to respond to other therapies, use in combination with other agents).

Antineoplastic Drugs

Table 4.1 lists the approved indications in the United States for 14 antineoplastic drugs included in our analysis. Figure 4.1 shows the level of off-label usage for each of these agents. The dearth of effective therapies for some life-threatening cancers is a powerful stimulus to off-label prescribing.

Carboplatin was the antineoplastic drug most frequently prescribed off-label – in 77% of cases. Although this drug is approved for initial and secondary treatment of advanced ovarian cancer, less than 23% of uses were for this indication, compared with 52% for lung cancer, an unlicensed indication. Vinorelbine was also widely prescribed off-label: only 36% of uses were for the approved indication of lung cancer, compared with 47% for breast cancer. The age of these two drugs and the fact that both are off-patent and subject to generics competition may contribute to their very extensive off-label use. At the other end of the spectrum of off-label usage, trastuzumab, oxaliplatin, imatinib, rituximab, and erlotinib were used for unlicensed indications in less than 10% of cases.

Antidepressants

Table 4.2 shows the approved indications in the United States for 10 antidepressants, and

Table 4.1 Approved Indications for Select Antineoplastic Drugs in the United States

INN	*Brand Name*	*Manufacturers*	*Year of First Approval*	*Approved Indications*
Bevacizumab	Avastin	Roche	2004	Metastatic colorectal cancer
Capecitabine	Xeloda	Roche	1998	Colorectal cancer; breast cancer
Carboplatin	Paraplatin; generics	Multisource	1989	Advanced ovarian cancer
Cetuximab	Erbitux	Bristol-Myers Squibb	2004	Metastatic colorectal cancer
Docetaxel	Taxotere	Sanofi-Aventis	1996	Breast cancer; nonsmall-cell lung cancer; prostate cancer; gastric adenocarcinoma
Erlotinib	Tarceva	Genentech/OSI Pharmaceuticals	2004	Nonsmall-cell lung cancer; pancreatic cancer
Gemcitabine	Gemzar	Eli Lilly	1996	Breast cancer; nonsmall-cell lung cancer; pancreatic cancer
Imatinib	Gleevec	Novartis	2001	Chronic myeloid leukemia
Irinotecan	Camptosar	Pfizer	1996	Metastatic colorectal cancer
Oxaliplatin	Eloxatin	Sanofi-Aventis	2002	Colorectal cancer
Paclitaxel	Taxol; generics	Multisource	1992	Advanced ovarian cancer
Rituximab	Rituxan	Genentech/ Biogen Idec	1997	Non-Hodgkin's lymphoma; rheumatoid arthritis
Trastuzumab	Herceptin	Roche	1998	Metastatic HER2-positive breast cancer
Vinorelbine	Navelbine; generics	Multisource	1994	Advanced nonsmall-cell lung cancer

HER2 = Human epidermal growth factor receptor 2
INN = International nonproprietary name

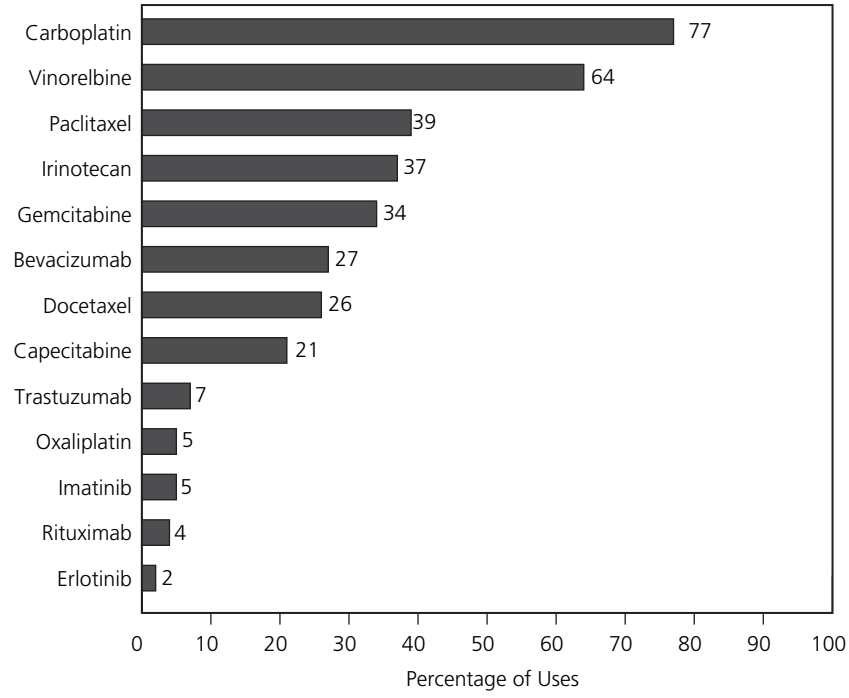

Figure 4.1 Percentage of Off-Label Uses for Select Antineoplastic Drugs in the United States, 2005