



# Value-Based Oncology **BENEFIT DESIGN**<sup>TM</sup>

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## *Breast Cancer, Multiple Myeloma, and Prostate Cancer*

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Benefit Design** ~ page 12

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### Target Audience

This activity was developed for pharmacy directors, P&T Committee members, managed care pharmacists, oncology pharmacists, and other key stakeholders who wish to enhance their knowledge concerning the implementation of a value-based benefit design for cancer care.

### Learning Objectives

At the completion of this educational activity, participants should be able to:

- Identify the intersection of epidemiologic shifts in the American cancer patient population, new cancer drug costs, and new diagnostic measures, on achieving value-based clinical treatment
- Recognize the role of value (cost, quality, access) in the new value-based healthcare system and the incentives of payers and purchasers to meet each of these 3 aspects of value in cancer care
- Discuss how NCCN clinical practice treatment guidelines are aiding all stakeholders in attaining value-based cancer care amidst rising new product costs
- Incorporate value-based principles in the treatment of cancer

### Commercial Support Acknowledgment


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Dr Kavita V. Nair is a consultant for Centocor Inc.

Dr Gary M. Owens is a consultant for Encysive Pharmaceuticals, Endo Pharmaceuticals, Patton Medical, and a speaker for Wyeth Pharmaceuticals.

Dr Al B. Benson, III is a scientific adviser for and receives research support from Amgen Inc., Bristol-Myers Squibb Company, Genentech, Inc., ImClone Systems Inc., MDS Nordion, Pfizer Inc., Roche Laboratories Inc., sanofi-aventis, Taiho Pharmaceutical Co., Ltd.

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*Estimated time to complete activity: 1.5 hours*

*Initial Release Date: February 20, 2009.*

*Expiration Date: February 20, 2010.*



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*This publication has been supported by educational grants from Amgen, Inc., Biogen Idec, and Millennium Pharmaceuticals, Inc.*

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## Mission Statement

*Value-Based Oncology Benefit Design™* provides payers and others involved in overall healthcare resource allocation with the information they need to make competent formulary and benefit design decisions. The sharp escalation in the cost of cancer care is threatening the financial stability of the healthcare system and has become a major area of strategic focus for payers, purchasers, government, and other stakeholders. New cancer therapies must meet a triad of qualities to find acceptance by payers: *cost, quality, access*—the value proposition for all healthcare interventions.

# Value-Based Benefit Design in Cancer Management

Kavita V. Nair, PhD

In 2008, approximately 745,180 men and 692,000 women were diagnosed with some form of cancer.<sup>1</sup> Despite the growing prevalence of the disease, survival rates have improved tremendously over the last several decades, increasing by 16% from 1977 to 2003.<sup>2</sup> For specific cancers, improvements in survival rates during this period have been particularly notable. For prostate cancer, survival rates increased by 30%, and for breast and colorectal cancer, the rates increased by 14%.<sup>2</sup> Improved survival rates can be attributed to the effectiveness of newer drug therapy technologies, along with the benefits of increased screenings, better patient education, and reductions in tobacco use.<sup>3</sup>



## The Cost Burden of Cancer Treatment Cancer Drugs

Cancer drugs fall into 2 broad categories: chemotherapy drugs (which can be further divided into cytotoxic agents and biologic/biotechnology agents) and drugs used to treat the adverse effects of therapy (eg, erythropoietin-stimulating agents used to counter anemia that results from chemotherapy treatments).<sup>4</sup> Forecasts from IMS Health project that global sales of cancer drugs will grow at an annual rate of 12% to 15%, reaching \$75 billion to \$80 billion by 2012.<sup>5</sup> The 2007 Drug Trend Report by Express Scripts showed that utilization of cancer drugs increased by 24% in 2008 and is expected to increase by 34% in 2009.<sup>6</sup>

Several of the new cancer drugs recently approved by the US Food and Drug Administration (FDA) have changed the face of cancer treatment. In March 2007, the FDA approved lapatinib (Tykerb), a dual kinase inhibitor for the treatment of breast cancer. Sales of this drug are projected to reach \$1 billion by 2010. Darbepoetin alfa (Aranesp) is an erythropoietin product that was approved for a new indication in the treatment of anemia in 2007. Similarly, in 2008, the FDA approved intravenous degarelix for advanced prostate cancer and oral imatinib mesylate (Gleevec) for a new indication in the treatment of gastrointestinal stromal tumor. Also in 2008, intravenous bendamustine hydrochloride (Treanda) was approved for the treatment of chronic lymphocytic leukemia, and injectable bortezomib (Velcade) was approved for the initial treatment of multiple myeloma.<sup>7</sup>

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The Medicare population bears the highest burden for cancer treatments. The Medicare Payment Advisory Commission estimated that in 2005, Medicare spent \$7.3 billion on medical care for cancer services, of which \$5.2 billion was for cancer drugs and related drug products used to treat the adverse effects of chemotherapy.<sup>4</sup> The 2007 Drug Trend Report estimated that the average cost for a prescription drug used to treat cancer was \$1816 in 2007, although some drugs, such as imatinib mesylate, cost as much as \$3109 per prescription.<sup>6</sup> In 2006, several cancer drugs were among the top 50 drugs for nationwide retail sales for all brand-name prescription drugs.<sup>8</sup> These included rituximab (Rituxan), used to treat non-Hodgkin's lymphoma (\$3861 million); trastuzumab (Herceptin), used in breast cancer (\$3314 million); imatinib mesylate, used in leukemia (\$2554 million); bevacizumab (Avastin), used in colorectal cancer (\$2364 million); and docetaxel (Taxotere), used to treat several types of cancer (\$2021 million).<sup>8</sup>

## Out-of-Pocket Expenses

Patients also face significant out-of-pocket costs for cancer treatments. Using claims data from 55 nationwide employers covering 1.5 million lives from 2003 to 2004, Goldman and colleagues estimated that more than 10% of patients with cancer had out-of-pocket expenses that exceeded \$18,585 in 1 year, and 5% had costs that exceeded \$35,000 per year.<sup>9</sup> Trastuzumab is a good example of how expensive out-of-pocket costs can be. Trastuzumab is a new intravenous drug used in the treatment of metastatic breast cancer. The recommended initial dose is 4 mg/kg administered as a 90-minute infusion; the weekly maintenance dose is 2 mg/kg administered as a 30-minute infusion. Patients generally receive the drug for 1 year. Assuming that a patient weighs 150 pounds, an initial dose would be 272.16 mg, and subsequent doses would be 136.08 mg per week. The manufacturer sells trastuzumab in a 440-mg multidose vial that costs approximately \$2400. A multidose vial of trastuzumab could be used for 3 weekly infusions for a patient after the first vial, which would be sufficient for 1 initial and 1 weekly dose. In 1 year, this would result in the use of 17 vials for a total cost of \$40,800. Under Medicare, patients are responsible for 20% of the costs of any drugs under the Part B benefit. A patient's annual cost share could therefore be \$8160 if the drug was covered under the medical benefit.

### Formulary Coverage

Formulary coverage for cancer drugs also has an impact on the cost of cancer treatments. An analysis of Part D plan formularies in 2006 showed that both prescription-only drug plans and Medicare Advantage plans covered 75% of selected oncology drugs. Generic drugs were covered more frequently than brand-name drugs.<sup>10</sup> However, a recent analysis by the American Cancer Society Action Network and Avalere Health found that in 2009, most brand-name oral cancer drugs, including imatinib mesylate, lapatinib, sunitinib malate (Sutent), erlotinib (Tarceva), and thalidomide (Thalomid) for the Medicare Part D population were placed in the fourth or specialty tier in prescription-only drug plans. Under these plans, patients would face cost-sharing portions ranging from 26% to 35% of the cost of the drug.<sup>11</sup> Using the trastuzumab example above, under a pharmacy benefit, a patient's cost-sharing burden could be as high as \$13,464 (33%).

### Oncologists' Reimbursement for Cancer Drugs

Since Medicare reimburses more than 50% of the cancer population, the history of Medicare reimbursement under the Centers for Medicare & Medicaid Services (CMS) policies set the stage for current payment methods for cancer drugs. Prior to 1997, CMS reimbursed the cost of outpatient chemotherapeutic drugs based on 100% of the average wholesale price (AWP) under Medicare Part B. Since the AWP did not reflect the actual prices charged to the physicians, the use of this metric resulted in payments that were well above the actual acquisition costs of the drugs, which was very profitable for oncologists.<sup>12</sup> In 1997, however, under pressure from health plans and pharmacy benefit managers, CMS reduced the reimbursement rates to 95% of the AWP. Even with this reduction, oncologists were still able to maintain strong revenues from the chemotherapeutic drugs they administered. The passage of the Medicare Modernization Act in 2003 resulted in more changes in the reimbursement of chemotherapeutic drugs, instituting reductions of 85% of the AWP in 2004.

In 2005, CMS developed a new reimbursement pricing method using the average sales price (ASP), which reflects the average of actual transaction prices between the manufacturer and the purchaser and is set prospectively based on data from 2 previous quarters.<sup>12</sup> Under the ASP methodology, Medicare Part B drugs are reimbursed at 106% of the ASP. However, oncologists are concerned that the ASP pricing method will substantially reduce the reimbursement rates for the drugs they procure and administer in their office. The ASP is based on actual prices and represents the net price that manufacturers charge after discounts, rebates, and other concessions and therefore can be lower than the price that oncologists actually pay for these drugs.<sup>4</sup> In addition, the ASP method does not reflect changes in market pricing. Updates to the ASP occur quarterly, but drug prices

may change more frequently than every quarter. Thus, oncologists may lose money on a quarterly basis if they buy a drug in the first quarter and the ASP for that drug decreases in the second quarter.

A report by the Office of Inspector General (OIG) in 2005 analyzed acquisition costs for oncology drugs during the first quarter of 2005 after the introduction of the ASP methodology.<sup>13</sup> The OIG analysis found that the reimbursement rates for some chemotherapeutic drugs declined from 72% to 38%, and for some drugs, Medicare reimbursement was inadequate to meet oncologists' costs of acquiring them.

The Medicare Modernization Act also mandated the Competitive Acquisition Program, or CAP, which accommodates oncologists who do not want to buy drugs themselves and submit for reimbursement under the current CMS methodology. Participation in this program is voluntary, and oncologists can work with authorized CAP vendors to obtain cancer drugs without having to pay for them. It is the responsibility of the CAP vendor to bill CMS for reimbursement of the drugs.<sup>12</sup> However, an oncologist who signs up for CAP must obtain all drugs on the CAP list from the CAP vendor. Participation in CAP has been low, because of concerns about low onsite inventory, the likelihood of treatment delays resulting from the "middleman" approach, and the additional administrative burdens on practices.<sup>12</sup> CMS has suspended CAP for 2009 and is in the process of collecting feedback from physicians and vendors before moving forward with the program.

### Designing a Value-Based Benefit in Cancer Management

The oncology landscape is complex, presenting many challenges to the design of a value-based benefit program. These challenges include (a) the unique role of the oncologist historically as the payer, provider, and administrator of cancer drugs, (b) the high patient cost-sharing amounts due to the placement of most cancer drugs in specialty tiers, for which a coinsurance fee is charged, and (c) a rapidly growing cancer pipeline that includes new oral cancer drugs.

A benefit for cancer drugs defines the terms and limits of drug coverage, the categories of drugs that are covered, the patient's share of the drug costs, the nature of the reimbursement for the drug, and other controls for utilization, such as prior authorization and step therapy.<sup>14</sup> The coverage of cancer drugs solely under the medical or pharmacy benefit can lead to a misalignment of financial incentives among oncologists, patients, and specialty providers.

### The Medical Benefit Approach

Historically, cancer drugs were included in the oncologists' professional responsibility and were part of the medical benefit for intravenous drugs that were administered in the office. Oncologists were financially responsible for the procurement and provision of these drugs. Under the medical benefit, oncologists have been able to enjoy a revenue

stream, but newer reimbursement methods such as the adoption of the ASP pricing may have limited that ability. In addition, coding ambiguities associated with the use of J codes in medical claims, which lack specific information such as the patient's dosage that payers require for reimbursement, and the administrative burden of the "buy and bill" approach, present new challenges with this type of benefit coverage for cancer drugs.

Under the medical benefit, the selection of cancer drugs is determined by the oncologists, and payers have little influence on drug selection and utilization. Although patients face a 20% coinsurance under the medical benefit, these out-of-pocket payments were often waived by the oncologists because the amounts were offset by the high revenues they received under AWP methods of reimbursement. However, introduction of the ASP methodology has reduced the reimbursement rates for oncology practices. As a result, oncologists may be less willing to waive the coinsurance costs for patients, thereby subjecting them to high out-of-pocket costs for drugs that they traditionally received for "free."

### ***The Pharmacy Benefit Approach***

In contrast, under the pharmacy benefit, the procurement and provision of the drugs are not the direct responsibility of the oncologist but are handled by the health plan and a network of pharmacies, which deliver the drugs directly to the patient. The selection of cancer drugs is the responsibility of the Pharmacy and Therapeutics Committee, the specialty pharmacy vendor, or both. The physician's involvement in the choice of drugs and influence over the selection are determined by a formulary and not tied to any financial incentives; payers thus have more control over drug selection and utilization. In addition, the convenience of home delivery and other services offered by specialty pharmacies, whose growth has exploded in the last decade, could improve a patient's ability to procure these drugs.<sup>15</sup> Under the pharmacy benefit, however, patients may still face high cost-sharing amounts, between 25% and 33% of the cost of an expensive cancer drug, which may limit their ability to purchase the medications they need.

### ***The Restructured Pharmacy Benefit***

The insurance industry's current approach to designing a more value-based benefit program is to move as many of the specialty or high-cost biologics, including cancer drugs, from the medical benefit to the pharmacy benefit. The pharmacy benefit is then restructured to accommodate these agents, often with the addition of a fourth, or specialty, tier that involves cost-sharing in the form of coinsurance. A specialty pharmacy vendor may also be used to administer this portion of the pharmacy benefit. Whether this approach is a true attempt at creating a value-based benefit design or merely a cost-shifting strategy needs to be evalu-

ated. One example of recreating this pharmacy benefit for cancer drugs in order to provide more "value" to the patient is the creation of multiple "specialty tiers" in which established cancer drugs are placed in tiers that have lower out-of-pocket costs and newer cancer drugs are placed in tiers with higher out-of-pocket costs.

### ***The Unified Benefit Approach***

The creation of a unified benefit would require a significant commitment from oncologists, pharmacy services, medical management, specialty pharmacies, and patients.<sup>14</sup> Such a benefit has yet to be designed and adopted by payers. Advantages would include (a) uniformity of coding systems, permitting measurement of outcomes associated with the use of cancer drugs, (b) delinking of financial incentives with prescribing decisions, (c) less administrative burden for oncologists' offices, (d) development of clinically appropriate guidelines for the use of cancer drugs, and (e) reduction in the cost-sharing burden for patients.

## **Current Innovations in Benefit Design**

### ***Limitations on Out-of-Pocket Costs***

Payers nationwide have started to adopt some of the elements of a unified benefit in the last 5 years, the most popular being an effort to reduce the extent of patient cost-sharing for cancer drugs. For example, some payers have chosen to limit the out-of-pocket costs on a monthly basis for patients receiving an intravenous drug or a self-injectable drug. Employers have imposed an out-of-pocket limit of \$150 per prescription per month in exchange for the employee's paying higher premiums; or, when there is a 20% coinsurance rate, some have established a maximum out-of-pocket limit of \$100 per prescription per month. Patients can also pay a fixed copay amount ranging from \$50 to \$75 rather than a coinsurance for drugs they obtain from network oncologists and specialty pharmacies but pay a coinsurance rate per drug for drugs obtained elsewhere.<sup>16</sup>

### ***Adjusted Reimbursement for Oncologists***

United Healthcare chose to alter their method of reimbursement for oncologists by increasing their rates for professional services and other fees paid to them to mitigate some of the lost revenue from use of the ASP method for reimbursement.<sup>17</sup>

### ***Tailored Plans for Types of Employees***

Other discussions of creating a value-based benefit design have considered the type of employee population. For example, for employers who typically retain long-term employees (10–20 years of job tenure) and experience little turnover, creation of a benefit that provides generous coverage for cancer and other biologic drugs may be a worthwhile investment. This type of plan might be less advantageous for an employer who experiences high turnover rates.<sup>18</sup>

### Inclusion of Clinically Relevant Practice Guidelines

Another approach to a value-based benefit design in oncology involves the adoption of clinically relevant practice guidelines that would provide for the cost-effective utilization of cancer drugs. Both payers and providers agree that successful outcomes for oncology patients include overall survival, disease-free survival, and progression-free survival.<sup>19</sup> However, with regard to the use of cancer drug therapies, different stakeholders may place a different value on specific end points. Payers, for example, are interested in the total cost of a cancer regimen and in ensuring its appropriate use, whereas providers are interested in quality of life and the impact of cancer drugs on survival rates.

### Oral Cancer Drugs in Benefit Design

Complicating the issues in value-based benefit design is the increased use of oral cancer drugs. According to a recent estimate, oral cancer drugs currently represent about 20% of a health plan's overall spending in cancer treatments, but their utilization is expected to grow by 250% annually.<sup>20</sup> This projected expansion in the use of oral cancer drugs is attributed to their demonstrated efficacy coupled with strong patient preference for the convenience of oral drugs and aversion to the discomfort associated with intravenous treatments.<sup>21</sup>

The use of these drugs presents an interesting challenge for oncologists. Although some oral agents represent new formulations of existing intravenous cancer treatments (eg, cyclophosphamide, 6-mercaptopurine, methotrexate, and busulphan for leukemia and lymphoma), newer oral drugs represent "smart drugs" or "targeted therapies" directed at components of intracellular signaling pathways such as protein kinases.<sup>22</sup> Therefore, patients may experience fewer adverse effects compared with older intravenous treatments. However, because of the "newness" of the oral cancer treatments, strategies for insurance coverage are still developing. In the meantime, patients may be denied coverage for these agents, experience higher cost-sharing amounts, or have trouble obtaining the drugs from local pharmacies due to low inventory. In addition, the prescribing of oral drugs may be influenced by the potential for lost revenue. Oncologists may be less likely to consider an oral medication that they do not procure and for which they receive no reimbursement.

The adoption of clinical guidelines, such as those of the National Comprehensive Cancer Network (NCCN), may alleviate the concerns felt by payers and oncologists alike about the utility of newer oral cancer drugs.<sup>23</sup> The NCCN, founded in 1995, established panels of oncology researchers and clinicians to develop recommendations for each type of cancer based on the best available evidence. A formal adoption of these guidelines by payers, as a basis for guiding oncologists on the appropriate treatments, may align the needs of both payers and providers and continue the evolution of a value-based benefit design in oncology. ■

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# Biologics for Cancer Care: Raising the Stakes in the Value Equation

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The current decade has seen a remarkable increase in the number of agents and therapeutic options available to treat cancer. As a result, tremendous strides have been made in the treatment of many malignancies. Cancer, in many cases, has become a chronic disease, with long-term remissions and even cures a commonplace event. However, these gains have come with a price. The cost of cancer care has increased significantly, and the potential for further cost increases is almost a certainty. Healthcare managers are experiencing unprecedented escalations in the cost of caring for patients with cancer and may reasonably expect these costs to rise at a rate of 20% or more annually. This dramatic rise in the cost of cancer-related care is testing the capacity of the healthcare system to provide access to treatment yet maintain affordability.

## Overview of the Epidemiology of Cancer

In 2008, an estimated 1,437,180 new cancer cases were diagnosed and 565,650 deaths were attributed to the disease. The most common fatal cancers are lung cancer (men and women), followed by prostate cancer (men), breast cancer (women), and colorectal cancer (men and women). These 4 malignancies account for half of the total cancer deaths in this country.<sup>1</sup>

Cancer may strike at any age; however, the majority of cancers are seen in individuals age 55 and older. The wave of baby boomers in the United States who have already reached that age (or who will soon reach it) is likely to drive the number of cancer cases to unprecedented levels. This rise in cancer cases, together with cost increases, will challenge health system managers as never before. New strategies will be necessary in order to continue to provide care for this growing population of cancer patients.

## Biologics as a New Driver of Cancer Care Cost

Demographics alone do not drive the cost of cancer care. Every year, physicians acquire more tools to treat cancer. Advances in technology include diagnostic imaging techniques, such as magnetic resonance imaging and positron emission tomography; nuclear medicine technologies; and newer methods of delivering radiation therapy with precise localization. These advances have made the diagnosis and treatment of cancer more precise and accurate than ever before.

Nowhere is the technology advancing faster than in the area of pharmaceuticals. In the last 2 decades, the US Food and Drug Administration (FDA) has approved a significant number of agents, including biotechnology products for therapeutic, diagnostic, and palliative purposes. In oncology, these agents include biologics, such as recombinant monoclonal antibodies

(eg, trastuzumab [Herceptin], cetuximab [Erbix], bevacizumab [Avastin]); small molecules aimed at selected molecular targets (eg, imatinib [Gleevec], sorafenib [Nexavar]), immunomodulators (lenalidomide [Revlimid]); and complex-molecule supportive agents, such as epoetin and filgrastim. While these agents have substantially changed the management of cancer care for patients, they have also increased the cost of care. For instance, 1 month of bevacizumab treatment for breast cancer costs approximately \$4400, whereas the same agent used at higher doses for non-small-cell lung cancer may cost \$8800 per month.

Meanwhile, the pipelines for cancer care agents are robust. In 2008, more than 200 biotechnology agents were on the market, and more than 600 agents were in development, a majority of which were for cancer.<sup>2</sup> This influx of new agents will continue, along with expanding indications for existing agents. Combination regimens of biologic therapies for selected cancers are also being tested. In short, these new agents continue to add significant cost to the care of the cancer patient. Health system managers must now find new ways to effectively provide access to appropriate and available treatments while ensuring that limited healthcare resources are spent on agents that are the most effective, both clinically and economically.

## Historical Issues in Cancer Care Management

Unfortunately, benefit designs and the process for developing coverage policies have evolved very little since the 1980s and 1990s. Medical benefit designs were developed to cover injectable drugs, most of which were used for the short-term treatment of chronic illness. Most forms of cancer were treated in facilities, often as part of an inpatient stay. Chemotherapy was generally used on a short-term basis, and biologic agents were not used at all. Moreover, there were relatively few guidelines for the treatment of cancer.

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Most large managed care organizations have medical policy departments that are overseen by a medical director and staffed by PhD-trained researchers, registered nurses, and other supportive staff who monitor the medical literature and community trends regarding treatment and respond with appropriate evidence-based policies. Unfortunately, the level of evidence needed to develop policy is only adequate to help determine the appropriateness of coverage within the benefit structure. Smaller plans often need to rely on analyses or evaluations done by third-party technology-evaluation groups, such as ECRI Institute, Hayes Management Consulting, or the Technology Evaluation Center of the Blue Cross and Blue Shield Association. True evaluation of the long-term outcomes of different treatment regimens and of their comparative cost-effectiveness is usually beyond the scope of these departments, as the data to conduct these types of analyses do not exist.

Clinical guidelines, such as those published by the National Comprehensive Cancer Network (NCCN), are useful in guiding policy makers, but even those guidelines are relatively broad and do not contain analyses of comparative clinical effectiveness and cost-effectiveness as a part of their development. The Centers for Medicare & Medicaid Services (CMS) relies on the use of FDA indications and multiple compendia to determine coverage for injectable agents. Recently, the CMS revised its policy and now permits 4 compendia to be used in determining coverage:

- Thomson Micromedex's DRUGDEX
- NCCN *Drugs & Biologics Compendium*
- American Society of Health-System Pharmacists' *AHFS DI*
- Elsevier's *Gold Standard's Clinical Pharmacology*.

Most health plans have followed the CMS's lead and will use these compendia to help determine coverage of individual agents. However, none of these resources allows the plan to determine the most effective regimens or to manage costs beyond the cost containment inherent in providing coverage only for treatments that have a use well supported by the medical literature, FDA indications, or compendia. Clearly, more information is needed in order to balance access and manage cost effectively.

### Current State of Benefits Design

Another major issue in benefits design in oncology is that current benefit plans were developed without considering biologic agents and biotechnology solutions for cancer care. Basic benefit designs, like their policy equivalents, have their roots in the 1980s and 1990s. Thus, medical benefit structures often do not contain specific language about coverage for injectable drugs and biologic agents beyond a limited description, such as "Injectable drugs are covered when administered in a physician's office for the treatment of short-term illness." Obviously, language such as this was adequate in an era of relatively few and low-cost agents. For similar reasons, medical benefits often do not consider out-

of-pocket costs associated with the drug itself and may provide only modest copayments for the physician services associated with drug administration.

On the other hand, pharmacy benefits have evolved significantly over the last decade. Depending on their structure, they have contributed, to varying degrees, to increased copayments to offset the rising price of drugs. It is not uncommon for copayments to range from \$50 to \$65 for non-preferred agents on many formularies. Additionally, the emergence of biologic and specialty agents has resulted in a significant number of pharmacy benefit plans introducing fourth and fifth tiers for biologic agents, including some cancer care agents, especially the oral ones. These formulary tiers may involve associated coinsurance rates in the 10% to 35% range. Medicare Part D plans often have fourth and fifth tier formulary levels for high-cost agents costing over \$600 per month. Out-of-pocket costs in those tiers may reach 35%.

While these benefit designs do provide coverage for patients in medically appropriate circumstances, the amount of coverage for a drug runs the gamut from no cost to the patient for many drugs administered under the medical benefit to 35% of the cost of an agent (such as an oral cancer agent or a self-injectable medication) when covered under the pharmacy benefit. It is evident that there may be many unintended consequences of such benefits. One scenario is that treatment choices, on the part of patients and physicians, may be made, at least in part, by considering which site of service or benefit results in the lowest out-of-pocket cost for the patient. Additionally, there is the incentive for physicians to use drugs for cancer that are administered in the office, as these agents are most frequently paid for under the plan's medical benefit as a buy-and-bill item. A significant portion of oncologists' revenue comes from the administration of chemotherapy. As Dr. Lee Newcomer has observed, "It is hardly surprising that their [oncologists'] behavior is influenced by that fact. This is not to say that they should not be paid at present levels, but they should be paid for providing an unbiased view of treatment options and for being an important source of information for patients."<sup>3</sup>

As one can readily see, the combination of benefit design, physician revenue incentives, and patient out-of-pocket costs often plays an interdependent role that can be as important a factor as clinical effectiveness in the selection of treatments for cancer. In order to provide better care in the future and to manage the medical resource effectively for the cancer patient, it will be essential for the system to make significant advances in measuring clinical outcomes and the cost-effectiveness of various treatment options.

### Health Plan Needs When Assessing Cancer Care

As noted previously, cancer has become a chronic disease for many patients. Treatments, including those involving biologic agents, often need to be maintained until disease progression and beyond. The cost associated with such

expensive and long-term treatments is part of the reason that cancer care expenditures have been increasing by up to 20% with each subsequent year.<sup>3</sup> Benefit designs permitting no out-of-pocket costs for members are rapidly disappearing and are being replaced by structures that position many anti-cancer agents in high-tier pharmacy benefit programs, with the potential for imposing significant patient liability. It is easy to envision scenarios in which even a modest coinsurance level of 20% applied to a \$25,000-per-year treatment could result in a financial barrier restricting access to that care for an average wage earner or retiree on a fixed income. On the other hand, the system can simply no longer afford to supplement the entire cost of all treatments available to patients regardless of the potential for outcome. Payment for treatments that result in little or minimal clinical gain will be difficult to justify in tight economic times. Raising insurance premiums and increasing the costs of healthcare for self-funded employers will only result in higher numbers of uninsured persons and in potentially even less access to needed care overall or more dependence on public support.

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What is needed by health plans is a system that allows coverage of care to be selectively provided in a scientific and evidence-based manner. There needs to be transparent measurement of performance and general agreement by providers that adherence to known standards of care is essential to providing clinically appropriate yet cost-effective cancer care. It seems likely that plans will need to apply some level of financial constraint on the provision of cancer care. Access to treatments with proven, clinically significant outcomes needs to be relatively unrestricted, while access to treatments not well founded in science may be relatively tightly managed or result in higher cost to the patient.

Oncology is a field in which therapeutic drug use rapidly diffuses beyond FDA-approved indications and even beyond compendium-supported indications. Plan managers will need to work with patients and providers to create better access to scientifically supported treatments. The emergence of national protocols and comparative effectiveness studies will be necessary to support this approach.

#### Achieving Value-Based Cancer Care Coverage

Developing value-based strategies for specialty agents involves several important steps:

1. It is important to define and understand the benefits of

biologic agents for a specific population by conducting basic research. At the same time, it is important to recognize that although new technologies are exciting, they are also expensive.

2. We have to define the appropriate levels of cost-sharing for biologics. This also requires research to help define the effect of cost-sharing on the appropriate use of biologic agents. We can build on the findings of previous research on the impact of lowering copayments on the uptake of medications for a specific disease. And once we have evidence as to which out-of-pocket amount is effective for a specific disease state, and a better understanding of the differences from one disease to another, we can tailor cost-sharing strategies according to these differences.
3. We must define the new value equation. This will involve identifying which patients should continue to use biologics, and how long they remain using those therapies. It also involves verifying turnover rates in candidates for biologics, with the health plan and with the employer group.
4. We have to develop new benefit designs that incorporate value for key stakeholders, including managed care organizations, employers, and patients, and ensure appropriate access to needed therapies. An interesting approach is the implementation of benefit-based copayments. In this model, the patient's copay amount is based on the clinical need and the expected therapeutic benefit. The new value equation can be reflected through premium pricing and copay structure.<sup>2</sup>

#### Summary

We are witnessing a rapid growth in the cost of cancer care, driven by both increasing numbers of patients with cancer and increasing costs of treating the disease. These cost increases are taxing the system's ability to pay. The health-care system is faced with the challenge of making treatments available to patients who need them while apportioning healthcare financial resources effectively. New approaches to the benefit management of cancer care must be considered. Member cost-sharing is important to help manage the cost of care appropriately, but the cost borne by the member cannot restrict access to necessary treatments. Therefore, plan policies and benefit changes must be considered in the context of the big picture, reflecting both pharmaceutical and medical expenditures for cancer care and their relative effectiveness in differing clinical situations. The challenge for all stakeholders will be to meet the needs of the patient, the health plan, and the plan sponsor. ■

#### References

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2. Owens GM. Value-based benefit: the concept, the reality, and the challenge. *Am Health Drug Benefits.* 2009;2(suppl):S16-S20.
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## Recent Updates to the NCCN Clinical Practice Guidelines in Oncology

### Breast Cancer

Breast cancer is the second leading cause of cancer death in women, after lung cancer. About 184,450 women in the US will be diagnosed with invasive breast cancer in 2008, and approximately 40,930 women will die of the disease.<sup>1</sup> An additional 67,770 women will be diagnosed with carcinoma in situ of the breast.

Recent updates to the NCCN Clinical Practice Guidelines in Oncology for Breast Cancer and Breast Cancer Risk Reduction<sup>2</sup> include a recommendation for genetic counseling if a patient is at high risk for hereditary breast cancer, as well as 6 new recommendations detailing when magnetic resonance imaging may be helpful in breast cancer evaluations.

In addition, the updated NCCN Guidelines for Breast Cancer state that positron emission tomography/computed tomography (PET/CT) scanning is not recommended for evaluation of newly diagnosed patients with early-stage disease except in those clinical situations where other staging studies are equivocal or suspicious, and even in these situations that biopsy is recommended. The panel noted that although there is limited evidence demonstrating the utility of PET/CT scan in the staging of patients, it considers biopsy to be more likely to provide useful staging information.

Bisphosphonates are still recognized as the preferred intervention to treat osteoporosis in women with breast cancer, while the use of estrogen, progesterone, or selective estrogen receptor modulators is discouraged.

Additions to the NCCN Guidelines for Breast Cancer Risk Reduction include updates to 2 risk-reduction agents, tamoxifen and raloxifene. Tamoxifen is recommended for premenopausal women with a history of atypical hyperplasia to reduce breast cancer risk. For postmenopausal women, raloxifene is listed as equivalent to tamoxifen in reducing the risk of developing invasive breast cancer; however, it did not provide the same level of risk reduction for developing non-invasive breast cancer.

### Multiple Myeloma

It is estimated that there will be 19,920 new cases of multiple myeloma (MM) diagnosed in the US in 2008, and 10,690 deaths attributed to the disease.<sup>1</sup>

The recently updated NCCN Clinical Practice Guidelines in Oncology for Multiple Myeloma<sup>2</sup> now include bortezomib in combination with pegylated liposomal doxorubicin as a category 1 recommendation for relapsed/refractory MM in patients with progressive disease following allogeneic or autologous stem cell transplant (SCT); in patients with primary progressive disease following initial autologous or allogeneic SCT; and in nontransplant candidates with progressive or relapsing disease after initial induction therapy.

These recommendations are based on the recent US Food and Drug Administration approval for combining bortezomib with pegylated liposomal doxorubicin for MM in patients who have not previously received bortezomib and those who have received at least 1 prior therapy. This approval was based on a review of interim data from an international phase 3 trial, showing that use of these drugs in combination significantly extended the median time to disease progression from 6.5 months for bortezomib to 9.3 months with the pegylated liposomal doxorubicin and bortezomib combination. An updated survival analysis of the study showed that median duration of response was increased from 7.0 to 10.2 months with the combination therapy. Updated overall survival (OS) analysis showed the combination significantly improved OS.

The NCCN panel states that although bortezomib monotherapy is also a category 1 recommendation, liposomal doxorubicin with bortezomib is preferred to bortezomib monotherapy for the treatment of patients with relapsed/refractory MM.

Other regimens added to the guidelines include dexamethasone/cyclophosphamide/etoposide/cisplatin for salvage therapy and bortezomib/thalidomide/dexamethasone for primary induction for transplant candidates.

### Prostate Cancer

Approximately 186,320 new cases of prostate cancer and 28,660 deaths from the disease are anticipated in the US in 2008.<sup>1</sup> Prostate cancer is the second leading cause of cancer death in men, exceeded only by lung cancer. However, increased public awareness and earlier detection and treatment have begun to affect death rates, and the age-adjusted mortality rates from prostate cancer have recently declined (-4.1% annually from 1994 to 2001).<sup>1</sup>

Incidence rates for prostate cancer increased 2.0% annually from 1995 to 2001, but they have since declined.<sup>1</sup> It is generally accepted that these trends reflect changes in utilization of prostate-specific antigen testing.

The NCCN recently announced updates to the Clinical Practice Guidelines in Oncology for Prostate Cancer,<sup>2</sup> including revised recommendations regarding pelvic lymph node dissection. Robotic techniques are now accepted for both pelvic lymph node dissection and radical prostatectomy. According to the panel, in experienced hands, the results of this approach appear comparable to open surgical techniques.

The NCCN panel also recommends that bisphosphonate therapy should be considered in patients with castration-recurrent prostate cancer and documented bone metastasis and creatinine clearance >30 mL/min, since this may prevent skeletal-related events and improve bone mineral density.

In addition, the guidelines now include a Principles of Life Expectancy Estimation section. Life expectancy is the basis of the initial clinical assessment and is critical to informed decision making in prostate cancer early detection and treatment. The combination of risk of recurrence and life expectancy estimation is a deciding factor for initial therapy.

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# The Role of NCCN Guidelines in Value-Based Benefit Design

An Interview with Al B. Benson III, MD, FACP



The escalating cost of managing patients with cancer requires that physicians, patients, and insurers have a means of identifying clinically effective therapies that are also cost-effective. As targeted therapy approaches and predictive markers have emerged from a better understanding of the complexity of tumor biology, an element of personalized medicine has been introduced into cancer management that is unprecedented in this therapeutic area. Improved survival rates seen among individuals with some forms of cancer have changed our expectations regarding the positive outcomes that are possible. The societal cost of such improvements, however, has sparked much of the debate about the high cost of healthcare in general and of oncology in particular. Collaborative efforts are urgently needed among the various stakeholders whose interests govern the design of oncology benefit solutions to ensure that these programs preserve value as well as balance cost and access. Clinical

practice guidelines are an integral part of the evidence base upon which critical decisions are made. This article is based on an interview with Al B. Benson III, MD, Chairman of the Board of National Comprehensive Cancer Network (NCCN), which has developed the NCCN Clinical Practice Guidelines in Oncology. In a discussion with *Value-Based Oncology Benefit Design (VBOBD)*, Dr. Benson shares his perspectives on some of the critical questions regarding the role of clinical practice guidelines in value-based benefit design for oncology.

**VBOBD:** *The record of improved outcomes achieved with new cancer agents over the past decade has reflected significant increases in both quality and cost. Cost increases, however, are beginning to retard access to care. What impact do the rising patient out-of-pocket costs have on current oncology practice?*

**Al Benson:** It is known that oncology care can be expensive. With specific targeted therapies costing up to \$30,000 to \$50,000<sup>1,2</sup> and some insurance programs imposing copayments of 20% or higher, many patients find the cost of their treatment to be unaffordable. Beyond the costs of the drugs themselves, treatment costs involve physician office visits, administration of intravenous drugs, imaging studies, and supportive care. Inadequate prescription coverage may leave some patients struggling to pay for not only chemotherapy drugs, especially the newer biologic agents, but also supportive medications such as antiemetic drugs. Out-of-pocket costs can add to the stress that patients are already experiencing due to their disease.

**VBOBD:** *As a cost-management tool, precertification is intended to ensure that finite resources are not distributed indiscriminately. However, if used to excess, this system devolves into a brute bureaucratic barrier to patients' access to care.*

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## One potential advantage of using the NCCN guidelines is to facilitate the precertification process.

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*What role do the NCCN guidelines play in directing practitioners to the most clinically effective and cost-effective treatments for their patients?*

**Benson:** Whether precertification truly results in a cost savings is debatable, when one considers the administrative costs involved. In the larger picture of healthcare delivery expense, precertification may well restrict costs in one area of the cancer-care equation but increase expenditures in another. Administrative support is a sizable component, but it is not one which insurers take into account. As regulations and requirements are added, the cost of this component increases.

Requirements for precertification from insurance carriers have increased. One potential advantage of using the NCCN guidelines is to facilitate the precertification process. In some instances, in which reimbursement for treatment has initially been denied, the NCCN guidelines have served as support for the desired course of therapy or imaging study.

The NCCN is developing chemotherapy templates that are linked to the *NCCN Drugs & Biologics Compendium*,

which in turn is linked to the treatment guidelines. The *Compendium* lists all of the indications for a given drug and cancer type. Thus, if a physician were to submit a chemotherapy template that corresponds to a patient's diagnosis, then approval of that regimen should be automatic. Even that submission, however, requires administrative time and effort from the practice staff. In the end, we want to adopt strategies that keep costs in line with quality practice.

**VBOBD:** *How can payers work with oncologists to identify those treatments that are both clinically effective and cost-effective? Can the guideline process support the identification and use of high-value services?*

**Benson:** For a given diagnosis, the NCCN guidelines provide a range of information, covering not only treatment but also diagnostic evaluation and supportive care (**Table**). Presumably, the cost of tests that are included in the guidelines would automatically be reimbursed. A technological system for linking guidelines with benefit plans needs to be implemented, however. To require precertification for a guideline-covered procedure would add an unnecessary step to the treatment-delivery process.

A more ideal situation would be to reserve precertification only for proposed actions that are not included in the relevant guidelines. This does not imply that such proposed therapies or evaluations are inappropriate. The existence of guidelines does not assume 100% concordance in their use, which would actually be indicative of less than optimal care, because of patient variability (eg, comorbid conditions, age), patient preference, etc. Deviation from the guidelines is necessary for an individualized approach. As part of the NCCN Oncology Outcomes Database Project, the evaluation of nonconcordance includes an explanation of why the guidelines were not followed in a particular case. In the majority of cases, deviation from the guidelines was justified. Guidelines remain just that: guidelines, rather than a prescriptive approach. Each patient must be evaluated individually when making treatment decisions.

**VBOBD:** *Clearly, we will need to come to a resolution of population-based research findings on the one hand with personalized medicine on the other. How will the role of biologic markers evolve to help select appropriate cancer treatment?*

**Benson:** Personalized medicine is becoming the new paradigm in oncology, along with evidence-based medicine. Oncology is also moving in the direction of becoming a laboratory-based science. The identification and validation of predictive markers, particularly as they relate to the use of biologic or targeted therapies, is the focus of much attention. Some progress has been made in developing biologic profiles that can predict which patients are most likely to benefit from a particular intervention. For breast cancer,

**Table** Features of NCCN Clinical Guidelines

- 110 guidelines cover 98% of all cancer patients
- Integrate clinical data and expert judgment to incorporate real-world clinical experience
- Evidence-based approach when evidence is available, and evidence-based expert consensus when high-level evidence is lacking
  - Panel members disclose potential conflicts of interest
- Level of evidence (Category 1 to Category 3) for each recommendation
  - Category 2A for most recommendations (uniform NCCN consensus, based on lower-level evidence)
- Address the entire continuum of cancer care, from initial diagnosis to end of life
- Comprehensive across all stages of cancer
- Describe all modalities of treatment
- Algorithm presentation is unique
- Include supporting references, background information, discussion of ongoing controversies
- Additional guidelines on screening, early detection, supportive care
- Yearly updates
  - Ad-hoc updates to respond to high-profile phase 3 trial results or FDA drug approvals
  - *Compendium* is revised simultaneously with the guidelines
- Special Task Force Reports on broad aspects of cancer care that cut across multiple different malignancies (eg, bone health, PET scans, oral mucositis)
- Patient versions and patient website, [www.nccn.com](http://www.nccn.com) (available April 1, 2009) for the most common malignancies

NCCN indicates National Comprehensive Cancer Network; FDA, Food and Drug Administration; PET, positron emission tomography.

Source: Benson AB III, Brown E. Role of NCCN in integrating cancer clinical practice guidelines into the healthcare debate. *Am Health Drug Benefits*. 2008;1;28-33.

this traces back to the recognition of estrogen-receptor-positive disease and the use of hormonal therapy<sup>3</sup> and extends to HER2/*neu* assessment and the benefits of trastuzumab (Herceptin).<sup>4</sup> In colorectal cancer, the most recent example is the assessment of *K-ras* as a marker for

selection of patients more likely to benefit from cetuximab (Erbix) or panitumumab (Vectibix).<sup>5,6</sup> The important point is that clinical research in oncology needs to continue to focus not only on developing new agents but also on defining the relationship between treatment efficacy and biologic profiles.

In discussions of cost-effectiveness analysis in oncology, the issue of personalized medicine will need to be factored into the equation. The most cost-effective strategy is to deliver interventions that have the greatest likelihood of benefit. To arrive at the evidence base in oncology, clinical trials data need to be interpreted judiciously. The design of clinical trials in oncology for the most part remains empiric. At present, we lack the biologic tools that would allow better stratification of study patient populations. Such tools would permit investigations to be conducted in an enriched population, that is, in a population that is most likely to benefit from the agent under study. For this reason, tumor collection is now a critical part of clinical trials in oncology.

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### The bioethical discussion is invoked when cost-effectiveness analysis attempts to define what amount of survival benefit is considered “worthwhile.”

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With an empirically designed trial, the study population includes patients who will receive no benefit from the investigational agent, an observation that can alter the overall results. The *K-ras* and cetuximab studies are a good example of this. Cetuximab trials were positive in that they met the statistical end point in the intent-to-treat population. The importance of *K-ras* mutations to therapeutic outcomes only emerged when the outcomes were assessed according to *K-ras* status, showing better (although not universal) response to cetuximab among patients with wild-type *K-ras*, with no benefit for those individuals with mutated *K-ras*.<sup>7</sup> Observations such as these provide the impetus for moving clinical trial design away from an empiric approach. It is becoming increasingly clear that for a given disease and stage, subsets of patients are being recognized that, in turn, will reflect choice of treatment. These subsets of patients also reflect the heterogeneity of most tumors, representing a collection of different tumor cells with variable molecular profiles. A “one-size-fits-all” approach, therefore, is predictably likely to fail for many patients.

**VBOBD:** *Will the treatment guidelines adapt to these marker-guided treatments?*

**Benson:** In the case of cetuximab and *K-ras*, this has already occurred. The NCCN guidelines for the management of colorectal cancer were updated to reflect the findings related to *K-ras*.

**VBOBD:** *How can we jointly gather the data needed to support the most cost-effective treatments in cancer?*

**Benson:** Cancer today is understood to represent a group of heterogeneous tumors arising from different biologic pathways. The key to effective treatment is to define the dominant pathway or pathways for the cancer and the resistance mechanisms and to find agents that can counteract the pathways and that are operative in an individual patient’s tumor profile. Clinical research that embraces this approach will be a very different strategy from large population-based studies and will add a different perspective to assessments of cost-effectiveness and comparative clinical effectiveness. The definitions of effectiveness will be much more precise than they are at present.

Debate about cost-effectiveness arises when, for example, a survival benefit seems to be relatively modest, such as a 2-month extension of life beyond that achieved with standard treatment. Is use of an expensive drug justified if all it buys is 2 months? In an empirically designed trial, the overall benefit may appear small, but actually the benefit for individual patients or certain subgroups may be quite substantial. Colorectal cancer is a case in point. Patients are living much longer and with good quality of life because of improved management strategies, which include newer treatment given sequentially over time, improved surgical techniques, and better patient selection criteria.

The bioethical discussion is invoked when cost-effectiveness analysis attempts to define what amount of survival benefit is considered “worthwhile.” Do the statistical analyses indicate that 2 months of additional survival is not worth the cost, but an additional 5 months is? The issue is extremely complex. If one asks patients what amount of survival benefit is worth the extra cost of treatment, the answer would be obvious. Society—through such mechanisms as benefits plans—could make a decision to limit treatment for patients who have metastatic disease, capping them at 1 or 2 treatments, after which, if they progress, they receive end-of-life care. That would be an extreme approach and one that would ultimately be detrimental in terms of research efforts, but it illustrates that such decisions need to be made extremely carefully, with full recognition of the types of messages they convey.

Cost-effectiveness involves many aspects. The medical system itself in the United States is a giant industry, employing thousands of people. It develops and exports products and thus is an important part of the country’s economy. Benefits that have implications for the medical

system and society as a whole are just as important to measure as the costs related to individual patient care. A treatment that keeps people living longer and functioning as productive members of society, gainfully employed and able to provide for their families, is a benefit that must be considered. The broader analysis of cost-effectiveness would factor in a societal benefit as well as the increased cost of an ongoing treatment that extends survival.

The integration of clinical research and evidence-based medicine into value propositions for benefits management will be more important than ever before. Clearly, advancements in technology and treatments have the potential to drive up the costs of care. In oncology, information from several large areas of inquiry needs to be gathered. The first area is prevention. It is well worth expending resources to prevent a serious, chronic illness such as cancer. Prevention is a societal, educational, and behavior-modification effort. The second important area that we need to better understand is tumor biology, for the applications already described. The better the process of carcinogenesis is understood, including the role of genetic and environmental factors, the greater the likelihood of successfully treating and preventing the disease.

The third important focus of research should be on specific categories of cancer patients. One category is the potentially curable cancer patient. Measures that are curative, whether they involve surgery, chemotherapy, or a combination of approaches, are obviously cost-effective for this type of patient. Another category is the patient who cannot be cured but who can be treated. This is the patient who, as mentioned before, can be treated over the long term with excellent quality of life. It is for this type of patient, in particular, that the most effective assessments and treatment approaches are needed, in order to maintain disease control for as long as possible.

Finally, more research is needed on end-of-life care. Cost analyses often emphasize the high cost of treatments delivered during the last 6 months of a patient's life, yet clinical trial research may provide useful information on effective symptom management as well as on therapies that extend survival. The decision to continue treatment even though it may be futile is often an emotional decision made between patient and physician. Nonetheless, physicians should strive to practice evidence-based medicine even in this setting, and that requires education. Such an effort is more likely to provide compassionate, appropriate, and most effective interventions, while saving costs associated with ineffective strategies.

**VBOBD:** *Who should lead this effort? Is there room for a collaborative effort between managed care organizations and oncologists?*

**Benson:** Several managed care organizations have already begun to collaborate with oncologists. UnitedHealthcare uses the NCCN *Compendium* as its primary evidence base for coverage decisions pertaining to drugs and biologic agents used in cancer care, and the Centers for Medicare & Medicaid Services also has adopted it. It is critical that all components of the healthcare system work together, including the pharmaceutical industry, the laboratory scientist, the imaging specialist, among others. The partnership should be transparent. The 2 profit-driven components of the healthcare system, the pharmaceutical industry and the third-party insurance carriers, are central to the partnership needed to intelligently design appropriate strategies for drug development and benefits programs. Under the guidance of evidence-based medicine and research providing a better understanding of tumor biology, collaborative efforts should get us much closer to where we want to be in terms of oncology benefits design. This will ensure that, when resources are spent, they are spent wisely in the most effective way. ■

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**The better the process of carcinogenesis is understood, including the role of genetic and environmental factors, the greater the likelihood of successfully treating and preventing the disease.**

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