

Value-Based Contracting for Oncology Drugs:

A NEHI White Paper

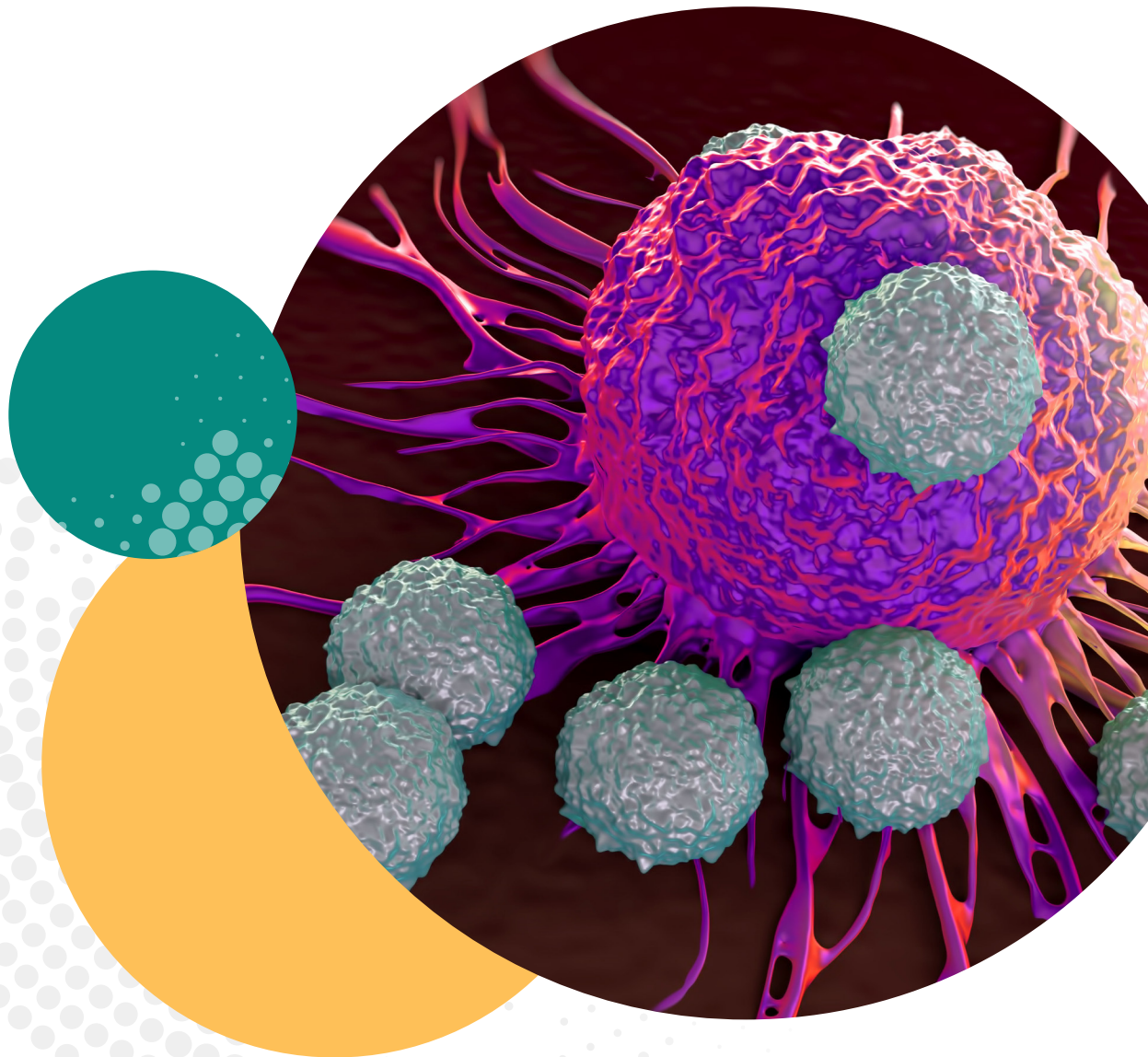




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Cover Art: A type of immune system cell known as a T-cell can be altered to attack cancer cells. Many new cancer therapies are based on these immunotherapy strategies.

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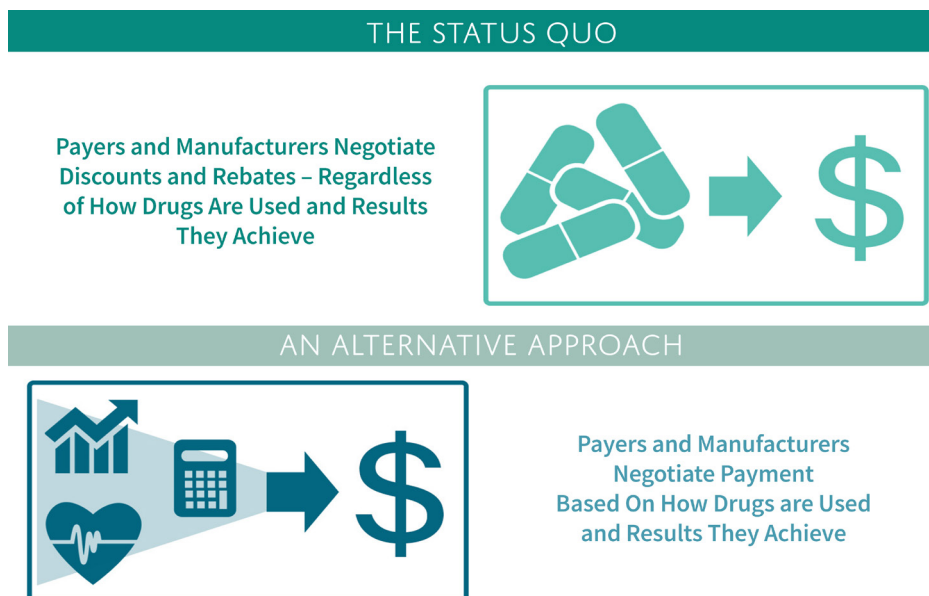
Executive Summary

A revolution is occurring in cancer treatment, based on new insights into the biology of cancer, and resulting in dozens of new drugs on the market or in the development pipeline. Many of these new drugs are “targeted” therapies that are tailored to the specific genetics and molecular pathways of different types of cancer. The drugs have demonstrated very successful outcomes for some patients and some cancer types; for example, they can produce added months of survival without any progression of disease, or total remission for some patients with previously untreatable or relapsed cancers. Yet stakeholders have expressed anxiety and concerns about these drugs’ high list prices.¹ For all payers, for patients, and for society, the potential benefit and costs heighten the need to understand the drugs’ value, and to know which patients will benefit from specific drugs.

Newer cancer drugs would thus seem to be prime candidates for value-based contracting – an emerging strategy under which payers and biopharmaceutical manufacturers agree to specific terms that tie payment to results, and that compensate manufacturers based on whether they obtain improved patient outcomes, or better financial outcomes, from the successful use of drugs in patients. In many instances, these contracts also involve shared financial risks between payers and biopharmaceutical

manufacturers; for example, drug manufacturers may have to pay more if drugs don’t work as well as demonstrated in clinical trials. There are multiple varieties of these contracts, but the overall objective is to hold manufacturers more accountable for value than more common arrangements that tie the net prices paid for drugs to the volume of drugs that are purchased. These emerging strategies are deemed by payers to be one part of a multi-pronged solution to the challenge of paying for high- cost medications.

A previous NEHI white paper described these value-based contracts in detail and set forth recommendations for policy, regulatory, and other changes that could facilitate their broader use. The U.S. Centers for Medicare and Medicaid Services (CMS) have now begun to examine these and other innovative payment models, and CMS recently agreed to enter one for Novartis’ new pediatric leukemia drug, Kymriah. Although other oncology drugs may also appear to be prime candidates for new pricing models, including



value-based contracting, multiple challenges still stand in the way. Some are unique to cancer drugs. Others, including legal and regulatory barriers, apply across all types of drugs and were discussed in NEHI's earlier paper, but also could have distinct impact on contracting for cancer drugs, as outlined further below.

Overall, value-based contracting for biopharmaceuticals is in its early stages, and the consensus among expert panels convened by NEHI is that thoughtful experimentation in these contracts should proceed. This NEHI white paper recommends a combination of strategies to foster innovation and experimentation, address operational challenges, and advance policy measures, including appropriate legislative or regulatory relief.

1 Recommendation #1: Payers, biopharmaceutical companies, data collection organizations, and other stakeholders should address challenges in collecting and analyzing data to execute value-based contracts.

The demand for data is rapidly increasing in cancer, from the research end of the spectrum all the way to tracking patients' responses to therapy. Greater standardization and sharing of routinely collected cancer data, albeit with appropriate privacy safeguards, could also make it easier and less costly to design, implement, and evaluate value-based contracts for cancer drugs. NEHI recommends that biopharmaceutical manufacturers, payers, and even health systems that are parties to value-based contracts consider adopting the Core Measure Set created for the Oncology Care Model, a multi-payer, performance-based payment model launched in 2016 by the Centers for Medicare and Medicaid Services to improve cancer care and lower costs. As these organizations develop their own cancer-related data sets for the purposes of value-based contracting, they also should commit to linking these to the larger cancer data ecosystem to benefit all stakeholders, including patients.

2 Recommendation #2: A cross-sector group of stakeholders, including patients, payers, and biopharmaceutical manufacturers, should develop a set of patient-centered and patient-reported measures for oncology care.

A related issue in the realm of data collection and analysis is the need for a core set of patient-centered and patient-reported outcomes measures. No such set of measures currently exists. In its absence, little is known about aspects of cancer treatment that anecdotal evidence suggests matter to patients nearly as much as common clinical metrics, such as survival or progression-free survival.

NEHI recommends that a cross-sector stakeholder group be established to take up this effort, and propose a set of core patient-centered and patient-reported cancer outcomes measures. Payers and biopharmaceutical manufacturers in particular should commit to helping to develop these measures and incorporating them into future value-based contracts. Importantly, a core measure set should gather information on financial toxicity, or the problems that cancer patients have that are related to their costs of treatment.

3

Recommendation #3: The Food and Drug Administration (FDA) should finalize draft guidance on communication among manufacturers, payers, and other entities deemed qualified under the agency's proposed guidance.

Several issues under the FDA's purview stand in the way of value-based contracts, and particularly for cancer drugs. These issues fall mainly into two categories: communications about drugs, including potential new indications, that are under review by the FDA but not yet approved, and communication about off-label uses.

The FDA should finalize its draft guidance issued in January 2017 to fully authorize exchange of health care economic information about new, not-yet-approved products, including potential new indications, from manufacturers to payers and entities deemed qualified under its proposed guidance, such as health system formulary committees. In the absence of FDA action, Congress should enact H.R. 2016, the Pharmaceutical Information Exchange Act of 2017, to make clear that such information can be communicated by biopharmaceutical manufacturers to payers and entities deemed qualified under the proposed FDA guidance without fear of sanction.

NEHI also recommends that FDA should consider issuing new guidance on communication between payers and manufacturers on off-label uses, at least as pertains to cancer therapies, and that as a reasonable first step, FDA should allow manufacturers to communicate off-label information to payers that is clinically relevant and also consistent with the approved clinical indications (for example, patient-reported outcomes).

4

Recommendation #4: The Centers for Medicare and Medicaid Services should provide a reasonable accommodation to Government Best Price and other price reporting requirements.

Such accommodation would prevent certain value-based contracts, such as "money-back guarantees," from triggering deeper rebates and other unintended adverse federal price reporting consequences across government programs. If CMS does not provide this accommodation in a reasonable time frame or address the substance of these issues, Congress should step in to make relevant changes in law to enable such contracts.

5

Recommendation #5: The Office of the Inspector General of the Department of Health and Human Services should develop new safe harbors to the Anti-Kickback Statute to enable certain activities that support value-based contracting.

New safe harbors should specifically allow biopharmaceutical manufacturers and payers to determine how to share the costs of analytical models, collection of data, services to support medication adherence, care coordination, and similar services, without triggering enforcement actions under the statute. New safe harbors should also provide clear authority for manufacturers to extend discounts and rebates to payers based on pre-

determined patient outcome and other value-based measures, in addition to discounts and rebates based on volume of sales, which are already permitted and regulated under an existing safe harbor.

6 Recommendation #6: The Office of Civil Rights of the Department of Health and Human Services should develop guidance on HIPAA compliance in the context of value-based contracts between manufacturers and payers.

Such guidance would pertain to sharing protected health information among providers, payers and manufacturers. Although not limited in importance to value-based contracting in oncology, as noted above, clarification of the applicability of the statute will be critical to building the cancer data ecosystem.

7 Recommendation #7: Stakeholders should continue discussion and investigation of new long-term financing approaches for high-cost therapies and cures in major disease states such as cancer.

For all the promise of value-based contracting, payers and purchasers on NEHI’s expert panels voiced doubts that the strategy will be a singular solution to the challenge of high-cost drugs. Particularly for breakthrough therapies that may come onto the market in future years – not just in cancer, but in other areas of unmet need, such as Alzheimer’s disease – the costs are likely to be so high, and the need so immense, as to impose a major burden on existing programs and payment mechanisms. Alternative approaches to financing high-cost therapies are needed. Congress should adopt into law a formal request of the National Academy of Medicine to study possible approaches, or should appoint an advisory panel focused on the same topic to advise to the Secretaries of Health and Human Services, the Treasury Department, and other relevant agencies.

Conclusion

The revolution occurring in cancer treatment is producing breakthrough medications that offer great benefit to many patients, at considerable cost. Many of these drugs could be strong candidates for value-based contracts that hold biopharmaceutical manufacturers more accountable for improved patient outcomes than conventional purchasing arrangements, while also offering the potential for more affordable pricing. A period of experimentation is needed to develop such contracts and learn from them. It is also important to establish the legal and regulatory framework to help facilitate these contracting opportunities. Some regulatory relief is needed to support these arrangements, as is a robust commitment from stakeholders to build the data systems and take other steps to shape a true “learning health system” in cancer care.

Although value-based contracts, and the lessons learned from their execution, will help all stakeholders better understand the value of many cancer drugs, they will not themselves solve the overarching challenge of affordability of high-cost medications for cancer or other conditions. A broader inquiry is also needed into possible long-term financing solutions that will support provision of high cost and potentially curative therapies. Cross-sector organizations such as NEHI, and the expert panels it assembled to create this white paper, can be instrumental in helping to forge solutions to benefit all.

Reference

- 1 See http://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/documents/2017-ASCO-Position-Statement-Affordability-Cancer-Drugs.pdf?et_cid=39454952&et_rid=1760459169&linkid=position+statement

Value-Based Contracting for Oncology Drugs: A NEHI White Paper

Introduction

A revolution is occurring in cancer treatment, based on new insights into the biology of cancer, and resulting in dozens of new drugs on the market or in the development pipeline. Many of these new drugs are “targeted” therapies that are tailored to the specific genetics and molecular pathways of different types of cancer. The drugs have demonstrated very successful outcomes for some patients and some cancer types – for example, added months of survival without any progression of disease, and total remission for some patients with previously untreatable or relapsed cancers. Yet stakeholders have expressed anxiety and concerns about these drugs’ high list prices.¹ For all payers, for patients, and for society, the potential benefit and costs heighten the need to understand the drugs’ value, and to know which patients will benefit from specific drugs.

Newer cancer drugs would thus seem to be prime candidates for value-based contracting – an emerging strategy under which payers and biopharmaceutical manufacturers agree to specific terms that tie payment to results, and in many instances, share in financial risks. There are multiple varieties of these contracts, as detailed below, but the overall objective is to hold manufacturers more accountable for value than more common

arrangements that tie the net prices paid for drugs to the volume of drugs that are purchased. Value-based contracting arrangements, in effect, compensate manufacturers based on obtaining improved outcomes for patients, and/or particular financial outcomes, from the successful use of drugs; they may also require manufacturers to share the risk with payers that the drugs may not work as demonstrated in clinical trials. This emerging strategy is deemed by payers to be one part of a multi-pronged solution to the challenge of paying for high-cost medications.

A previous NEHI white paper described these value-based contracts in detail and set forth recommendations for policy, regulatory, and other changes that could facilitate their broader use. The U.S.

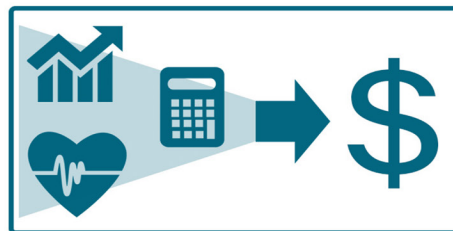
THE STATUS QUO

Payers and Manufacturers Negotiate Discounts and Rebates – Regardless of How Drugs Are Used and Results They Achieve



AN ALTERNATIVE APPROACH

Payers and Manufacturers Negotiate Payment Based On How Drugs are Used and Results They Achieve



Centers for Medicare and Medicaid Services (CMS) has now begun to examine these and other innovative payment models. It has also signaled that it is willing to consider alleviating certain regulatory barriers to test these approaches, beginning with an arrangement for paying for Kymriah (tisagenlecleucel), a recently approved leukemia therapy, as detailed below.² Although other oncology drugs may also appear to be prime candidates for new pricing models, including value-based contracting, multiple challenges still stand in the way. Some are unique to cancer drugs, and are detailed in the body of this paper. Others, including legal and regulatory barriers, apply across all types of drugs and were discussed in NEHI’s earlier paper, but also could have distinct impact on contracting for cancer drugs, as outlined further below.

Overall, value-based contracting for biopharmaceuticals is in its early stages, and the consensus among expert panels convened by NEHI is that thoughtful experimentation in these contracts should proceed. Much stands to be learned about which contracts achieve positive results; how they can be executed efficiently and at scale; and how they can create real benefits for patients, payers, taxpayers, and the health care system as a whole.

This NEHI white paper recommends a combination of strategies to foster innovation and experimentation in value-based contracting that is especially focused on cancer drugs. The strategies address operational challenges and advance policy measures, including appropriate legislative or regulatory relief. This paper also points to the possibility that still other, more far-reaching approaches may be needed to finance breakthrough, high-cost therapies in cancer and other conditions.

Oncology Drugs: The Background

As noted above, a revolution is occurring in cancer treatment, based on new insights into the biology of cancer and major advances in basic and translational scientific research. Since 2011, 68 new drugs have been approved for 22 different cancer indications, and a robust pipeline of drugs is under development.³ Many of these new drugs are “targeted” therapies tailored to specific molecular pathways of individual types of cancer. An important subset of these are “immunotherapy” drugs that stimulate patients’ own immune

systems to fight cancer. These drugs have often demonstrated very successful outcomes for some patients – in some instances, reversing tumor growth completely, and with far less toxicity for patients than older drugs. As such, they are contributing to an ongoing global decline in mortality from cancer. They are also contributing to cancer care costs, which are estimated to reach \$173 billion in 2020.⁴

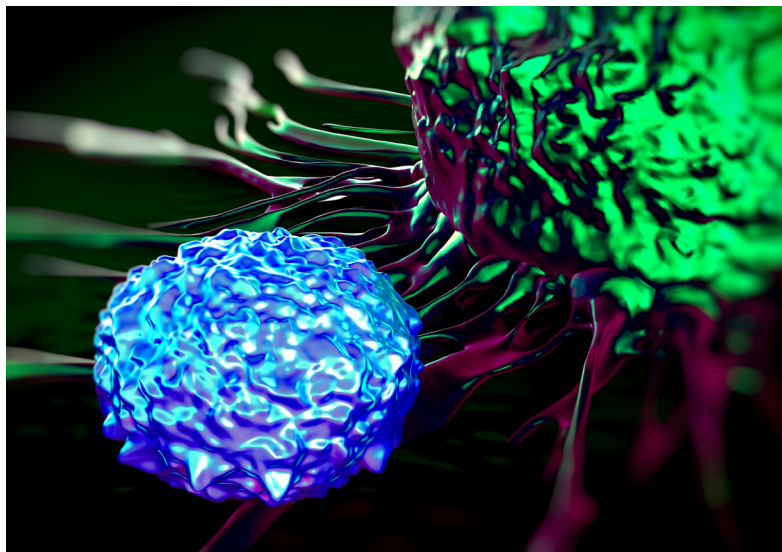


Image: T Cell (left) Attacking Cancer Cell (right)

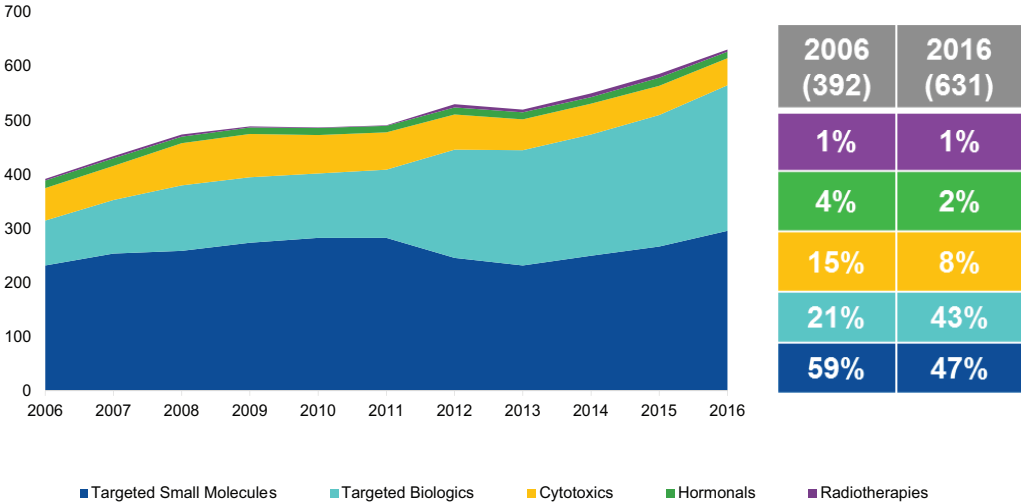
An example of one such new therapy is Keytruda (pembrolizumab), a monoclonal antibody initially approved for use in metastatic melanoma. This drug is now also approved for use in non-small cell lung cancer, bladder cancer, and several other types of cancer, for patients who have a specific genetic feature (a so-called biomarker), irrespective of where the tumor is located. In this context, it is the first cancer therapy to be approved by the Food and Drug Administration that does not focus on a specific tumor type. The drug, a so-called checkpoint inhibitor therapy, works to reactivate the immune system’s T cells – and enable them to attack cancers – by blocking the chemical mechanism through which cancer tumor cells normally disarm T cells. Many cancer patients taking the drug see lasting results; for example, in a follow-up study of patients with advanced melanoma taking Keytruda, 40 percent were alive after three years.⁵ The drug is also expensive, with a list price of about \$150,000 a year in the United States.

Keytruda is now being tested in almost 550 clinical trials across 30 tumor types, including more than 300 trials that combine Keytruda with other therapies. A second leading checkpoint inhibitor, Opdivo (nivolumab), is also being tested in nearly 250 combination therapy trials that have enrolled more than 25,000 patients.⁶

The evolving science behind these immune-oncology drugs, other targeted therapies, and the fundamental biology of cancer, is having a major impact not just on cancer therapy but also on cancer drug development. Clinical trials of some cancer drugs are now conducted in smaller populations of patients than was previously the case, as the drugs’ mechanisms must be matched carefully to the genotype of a particular patient’s forms of cancer. In one recent Keytruda trial in patients with advanced melanoma, for example, just 556 patients received the drug – a fraction of the number that were involved in trials for older, conventional chemotherapy drugs.⁷ Two oncology agents produced by Pfizer, Xalkori (crizotinib) and Bavencio (avelumab),

The Pipeline of Oncology Drugs in Clinical Development Has Expanded by 45% Over the Past 10 Years

Late Phase Oncology Pipeline Molecules, 2006–2016



Source: QuintilesIMS Institute, Global Oncology Trends 2017: Advances, Complexity and Cost, June 2017.

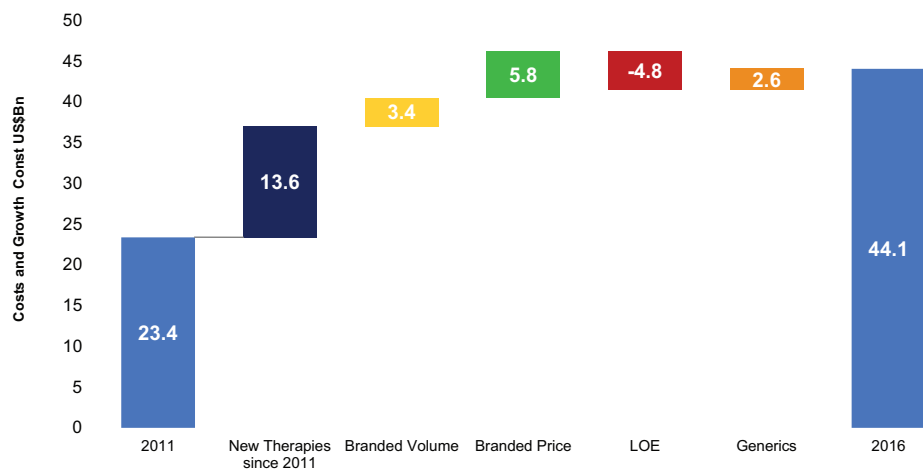
were each approved by the FDA based on so called “single-arm” trials of fewer than 100 patients, in which all trial participants received the experimental therapy.⁸

A given targeted drug is also typically tested in varying sequences in patients with different cancer types and subtypes. Even after a new drug has entered the market and has been approved for a particular cancer indication or indications, it may also be tried off-label in diverse patients with other cancer subtypes who may have no other options for treatment. Thus, a full understanding of how immunotherapy and other targeted therapies can benefit diverse groups of oncology patients is evolving over time – another reason why value-based contracts may prove attractive, despite the complexities outlined below.

As the science of cancer biology and drug development advances, an increasing number of more potentially effective and costly cancer therapies are in the pipeline. According to Quintiles IMS, 631 unique molecules are now in late-phase cancer drug development.⁹ So-called CAR-T (chimeric antigen receptor T-cell) therapy, which are Individualized treatments made from a patient’s own, genetically modified T-cells, are coming onto the market now. In August 2017, the U.S. Food and Drug Administration approved Kymriah (tisagenlecleucel), a CAR-T cell therapy to treat pediatric and young adult patients with a type of acute lymphoblastic leukemia (ALL) whose cancers have relapsed. In clinical trials, 83 percent of patients who received the therapy went into remission within three months. Novartis is expected to seek FDA’s likely approval for a second indication for Kymriah, for use in adults whose type of lymphoma, Diffuse B cell lymphoma, has not responded to treatment and whose disease has relapsed as a result.

Cost of US oncology medicines has increased in the past five years by 88%, primarily driven by new medicines

US Oncology Market Growth



Source: QuintilesIMS Institute, Global Oncology Trends 2017: Advances, Complexity and Cost, June 2017.

These “ultra”-personalized drugs may amount to one-time cures for many patients who previously had few, or no, treatment options, particularly in the case of advanced or relapsed cancers. Such drugs are also expected to be among the world’s most personalized, and most costly, drugs produced to date. Kymriah will cost \$475,000 for the one-time treatment for pediatric and young adult patients. However, the company is also offering assurance that if a patient treated with Kymriah for this indication does not respond in the first month, there will be no charge for the drug to patients, and to payers, including Medicaid, under an

arrangement with the Centers for Medicare and Medicaid Services (CMS). Novartis has also signaled that, under another anticipated agreement with CMS, the therapy will be priced differently for adult patients through an “indication-based” pricing arrangement (described further below).

With many more targeted cancer drugs in the pipeline, a new cancer drug calculus is taking hold for the nation’s biopharmaceutical manufacturers and payers alike. Key features of this calculus are as follows:

Narrower patient populations mean higher cost drugs. Therapies targeted at particular genetic and molecular pathways mean that many drugs under development will work for limited numbers of patients. For example, medications now on the market such as Alecensa, for treatment of lung cancer, have proven highly effective among patients with a genetic mutation found in 3-5 percent of all lung cancer patients, or approximately 75,000 patients worldwide. Larotrectinib, a drug still in clinical trials, has demonstrated highly effective results in as many as 17 types of cancer by targeting a genetic mutation found in 0.5 percent of all cancer patients.¹⁰ Larotrectinib will be reviewed by the FDA as a rare, so-called orphan drug.

With high development costs, greater therapeutic complexity, increased manufacturing costs, and a potentially limited group of patients to treat, the unit prices for treating a single patient will necessarily be high. For example, in contrast to the comparatively simple process of manufacturing a typical small molecule drug, the new CAR-T therapies require a patient’s white blood cells to be extracted through a special process in qualified hospitals, frozen, shipped to a special manufacturing facility where they are genetically re-programmed, shipped back to the hospital, and re-infused into the patient, but only after the patient has undergone a preparatory procedure. The entire “vein to vein” process may take upwards of three weeks in total. What’s more, some of the new therapies are intended for one-time use, or may represent cures, or both.

Thus, the new therapies may force the evolution of business models that will be starkly different from those of years past, in which manufacturers typically relied on ongoing sales of chronic disease drugs to large numbers of patients to stay in business.

Faster drug approvals. Faster drug approvals. An increasing number of new cancer therapies are reviewed and approved by the FDA on an expedited basis reserved for drugs that address unmet medical need in the treatment of a serious or life-threatening condition such as cancer.¹¹ An increasing number are also awarded status as orphan drugs, particularly drugs that act on single, cancer-causing genetic mutations, for which there are by definition small patient populations. Under FDA law, including the recent 21st Century Cures Act, the FDA may approve drugs with “substantial evidence” of effectiveness as early as the completion of Phase II trials if the apparent clinical benefits appear to outweigh clinical risks to patients. The FDA approved Idhifa (enasidenib), a targeted treatment for a type of acute myeloid leukemia, under precisely these terms in July 2017.¹²

As a result, new therapies for cancers in which there is a lack of alternative treatments are gaining FDA approval more quickly, and based on clinical trials of shorter duration and involving far fewer patients than was true in the past. Between 2009 and 2013, the FDA granted accelerated approval to 22 drugs for 24 indications, of which 19 were for cancer treatment.¹³ Payers say that this reality often gives them little notice to incorporate planned drug spending into their financial projections. They also point to findings that indicate that an insufficient number of drugs approved through accelerated pathways are subjected to robust and required “confirmatory” trials with three years of FDA approval; see Naci et al [supra].

Payers’ obligations to pay for cancer drugs. Once cancer drugs are approved, most payers generally cover them. Medicaid must cover all FDA-approved drugs, and Medicare covers the vast majority of them;¹⁴ what’s more, cancer drugs are one of the six “protected classes” in which all or “substantially all” drugs must be covered by Medicare Part D prescription drug plans. In 42 states, insurance regulations require commercial payers to pay for any new FDA-approved cancer therapies.¹⁵

Payers in NEHI’s expert panels thus reported that they are concerned about how they will be able to pay for high-cost cancer drugs while still making their overall premiums affordable for patients. They underscore, in effect, a tension between the value of these high-cost therapies to patients and society, and the affordability to them as payers, or to their policy holders who pay health insurance premiums.

The cumulative costs of many high-priced drugs may simply not fit within payers’ budgets. What’s more, although the benefits may be realized over a patient’s lifetime, that patient may only be enrolled with the health insurer who pays for his or her cancer therapy for several years at most. As a result, there may well be a time mismatch between paying for treatment and reaping the longer-term health benefits.

More need than ever to discern value. Physicians and payers alike say that these factors conspire to make it more urgent than ever that they understand the value of new cancer drugs for patients. One recent study for the American Society of Clinical Oncology (ASCO) showed that fewer than 1 in 5 recently approved cancer drugs met ASCO’s goals for producing “clinically meaningful survival outcomes” in patients. Smaller trials and accelerated approval pathways mean that drugs may be approved on the basis of so-called surrogate measures, such as biomarkers, rather than actual clinical endpoints, such as survival or progression-free survival (the length of time during treatment that a patient lives with cancer but does not get worse). Payers also point out that rarely are there any Phase III clinical trials that compare products that receive accelerated approval to other cancer therapies in head-to-head trials, so that they have a clearer understanding of relative efficacy of different types of drugs.

As a result, payers, many cancer physicians, and health systems alike are increasingly interested in value frameworks to assess cancer drugs' value prior to negotiating their purchase. Value frameworks, such as those developed by the Institute for Clinical and Economic Review,¹⁷ ASCO,¹⁸ and the National Comprehensive Cancer Network,¹⁹ incorporate assessments of clinical evidence and/or clinical and economic data to quantify the value of new cancer treatments.

The influence of framework-based value assessments on drug price negotiations and patient access to new therapies has sparked intense debate over the extent to which value frameworks assess interests beyond those of the payer. One example is the societal value of new therapies, or what economists term "option value," the value of prolonging a patient's life to the point where newer therapies may be available to treat the patient. What's more, patients have multiple interests that start with, but go beyond, clinical outcomes, which various value frameworks may or may not capture. For example, the "Patient-Perspective Value Framework" developed by Avalere and FasterCures identifies particular patient-related factors, including patients' preferences as well as costs to patients and their families, that may be undervalued by other value assessment methods.²⁰

Whereas value frameworks constitute a means of assessing value, value-based contracting constitutes an actual agreement to purchase drugs, and to tie payment to the achievement of certain specified outcomes. Thus, the contracts effectively hold the biopharmaceutical manufacturer accountable for those pre-identified outcomes.

To date, a small number of value-based contracts involving cancer drugs have been announced publicly, although most details are closely held. The biopharmaceutical company AstraZeneca has had a contract with ExpressScripts, the pharmacy benefit management firm, over Iressa (gefitinib), a drug used to treat certain breast, lung, or other cancers that bear a particular molecular signature. In this arrangement, AstraZeneca agreed to reimburse ExpressScript's clients the costs spent on the drug if a patient did not respond to treatment and discontinued the medication before filling the prescription a third time.²¹

In 2015, Genentech and Priority Health, a Michigan-based health plan, began to collaborate on an outcomes-based contract focused on Avastin (bevacizumab) in the treatment of patients with non-small cell lung cancer. In this arrangement, the two parties agreed on an initial price for Avastin, and Genentech agreed to pay rebates, or discounts, if it did not achieve targets for progression-free survival in individual patients.²²

Biopharmaceutical manufacturers, payers, and others on NEHI's expert panels expressed interest in building on these initial experiments to engage in additional innovative contracts. They believe that

value-based contracting arrangements could offer payers a way to approach the considerable uncertainties around these high-cost drugs, and adjust payments based on use of the drugs on actual patients in the “real world,” outside of the rarefied context of clinical trials. The next sections of this paper will explore both the opportunities and challenges they see in value-based contracting for cancer drugs, as well as provide recommendations for overcoming the challenges.

Opportunities for Value-Based Contracting in Oncology

Value-based contracts for biopharmaceuticals are evolving, but at present two main types of contracts are being adopted, as follows:

- **Outcomes-based contracts** tie prices and/or link discounts or rebates to achievement of particular outcomes for patients, such as overall survival or progression-free survival. The Genentech-Priority Health pilot described above is an example. Another example is Novartis’ description of its pricing model for Kymriah, the new CAR-T therapy, which as noted above offers no charge to pediatric and young adult patients whose cancer does not respond within the first month of treatment.
- **Indication-specific pricing contracts**, in which different levels of payment to a manufacturer are based on the efficacy of the drug when used for different indications. For example, the drug Tarceva (erlotinib), a so-called epidermal growth factor receptor (EGFR) inhibitor, is indicated to treat metastatic non-small cell lung cancer as well as advanced pancreatic cancer. In clinical studies, it provided a median survival gain of 12 months for the primary indication (lung cancer), but for pancreatic cancer patients the drug demonstrated a median survival advantage over standard therapy of just 2 weeks.²³ ExpressScripts has negotiated indication-based contracts that pay biopharmaceutical manufacturers different amounts for different indications in the cases of drugs that treat such cancers as multiple myeloma, non-small cell lung cancer, prostate cancer, and renal cell carcinoma.²⁴ As noted above, Novartis and CMS are pursuing an indication-based pricing approach for Kymriah that will yield a price of \$475,000 for use of the treatment in pediatric and young adult patients, but different prices tied to value for indications that FDA may approve in the future.
- A third type of value-based contract, a so-called **expenditure cap contract**, limits drug costs to a certain negotiated threshold, and according to the Pharmaceutical Research and Manufacturers of America, “has been implemented as a version of indication-specific pricing for infused cancer drugs.”²⁵ With no published reports on these types of contracts, however, it is unknown how widespread these contracts are, and none have been identified that apply specifically to oncology drugs.

Both payers and biopharmaceutical companies see multiple reasons to negotiate both outcomes-based and indication-based contracts over new cancer drugs. Among the key reasons they cite are the following:

Drive changes in the cancer care model. As with most aspects of U.S. health care, cancer care is marked by considerable variation, whether due to misdiagnosis or incorrect typing or staging of a cancer, failure to follow clinical guidelines, or inconsistent use of cancer drugs. To the degree that value-based contracts enhance incentives for biopharmaceutical manufacturers to tackle key problems in cancer care – for

example, to make sure that the “right” patients are on the “right” drugs, and that they stay adherent to them – the care model is likely to be improved. Outcomes-based contracts involving other drugs – for example, for hypercholesterolemia – have required biopharmaceutical companies to work with payers to identify only appropriate patients for treatment. An outcomes-based contract for a cancer drug that enlisted the biopharmaceutical company in a similar process of identifying the “right” patients for treatment could only stand to improve care quality while reducing costs.

Improve patient care in the “real world.” A related opportunity is to ascertain the true value of a drug by determining its results when used outside the clinical trial setting. Patients treated in the real world are often older and sicker, with more comorbidities, than those who participate in clinical trials,²⁷ and physician practices differ as well. Payers want to understand which patients will be most likely to respond to therapy, experience adverse reactions, or develop resistance to drugs. There is particular concern that new cancer immunotherapy drugs may create risks of serious immune system reactions for patients, as well as uncertainty as to how long patients may need to be on these costly therapies. Structuring value-based contracts to help capture data in all these categories could eventually lead to greater knowledge about how best to treat patients, and improvements in the quality of cancer care.

Collaborate in planning trials and incorporating payer-relevant endpoints. Many payers participating in NEHI’s expert panels expressed a desire to have input into biopharmaceutical manufacturers’ designs of Phase III and Phase IV trials (those that test safety; how well a treatment works compared to standard care; and that evaluate longer-term effects for larger groups of patients). Payers not only hope to gain greater visibility into manufacturers’ product pipelines, but they also want to see certain payer-relevant questions answered, if possible, through these trials. One example is how intensively patients will need to be managed by clinicians while under treatment from new oncology drugs, a factor that will clearly bear on the total costs of care. Some biopharmaceutical companies agree that greater collaboration is warranted, and see the payer engagement that could come about through value-based contracting as a key ingredient in fostering these deeper relationships.

Challenges in Value-Based Contracting

For all the perceived benefits of negotiating value-based contracts, there are also complicating factors, including operational, legal, and regulatory barriers. As noted in NEHI’s earlier white paper, some of these factors apply in general to value-based contracting for all types of drugs, while others are either unique to cancer drugs or more closely associated with them.

First and foremost, *not every drug, including a cancer drug, may be appropriate for value-based contracting.* The contracts are labor intensive, the relevant patient populations are often small, the data collection across differing sets of medical and pharmacy benefits can be challenging, and the contracts are costly to execute. As a result, there would be little point in executing a contract in cases where the treatment benefits are obvious, the drug is highly effective when used correctly, and/or the cost of the drug is low. It is possible that some future cancer drugs will fall into one of these categories, since they could constitute virtual cures for the right patients.

NEHI panel members also point out that as more biomarker-based cancer diagnostic tests are developed and validated, appropriate diagnostic screening of patients will guide oncologists to more precise and effective choices of therapies for patients, thus reducing uncertainty over the effectiveness of therapies. Payers may see less need for value-based contracting as a result.

By contrast, biopharmaceutical products that are deemed suitable for value-based contracts are those in which the patient outcomes are to some extent uncertain, costs are significant, and there is a need to determine whether the results seen in clinical trials also apply in the real world. But in such cases, metrics must be established and defined as the treatment outcomes that would constitute value – for example, progression-free survival that can be verified by radiographic imaging. What’s more, the duration of treatment must be short enough that it fits within a time period appropriate for the payer, who may experience frequent turnover in membership, with (as noted above) patients switching health plans every year or every few years.

The effort, time, and expense of data collection, integration, and analysis needed for value-based contracting is also considerable, especially in comparison to the more straightforward alternative of tracking sales volumes of a drug and using these figures to determine discounts or rebates to payers. For example, a provision common to many value-based contracts for oral medicines commits payers (often through their pharmacy benefit management company or through a specialty pharmacy network) to taking numerous steps within their power to assure that patients are adherent to medication. Ascertaining adherence may require extensive aggregation and analysis of health insurance claims data, pharmacy data, and electronic health record data. These processes may in turn require extensive collaboration, not only between payers and biopharmaceutical companies, but also with health care providers and systems.

In the case of indication-specific contracts, moreover, it is especially important to determine for which indication and in which setting an oncology medicine is prescribed and administered for the contract to be reliable and acceptable to both parties. Issues may also arise with respect to compliance with state and federal privacy law, lack of standardization of data sets, and other factors.

Legal and regulatory challenges may also stand in the way of value-based contracting, including federal government pricing regulations, the Anti-Kickback Statute, Food and Drug Administration regulations on manufacturer communications, and more. These issues, and potential remedies for them, were discussed in NEHI’s earlier white paper, but their specific applicability with respect to potential contracts for oncology drugs is examined further below.

In addition to these general concerns that pertain to all value-based contracting, there are challenges distinctly related to such contracting involving cancer drugs, as follows:

Unique disease processes of cancer: The complex genetic, molecular, and cellular changes that occur in the course of cancer contribute to another important phenomenon, which is the ability of cancers to develop treatment resistance. The increasing prevalence of treatment-resistant cancers has been noted in the literature.²⁸ As a result, drugs shown to be initially effective in clinical trials may prove ineffective over time in a given patient as resistance develops. It is not clear whether value-based contracts could be structured in a

way that would recognize the realities of treatment resistance in ways that did not penalize either payers or biopharmaceutical manufacturers.

Combination therapies: Most cancer is treated with multiple drugs used in combination with each other, even in the case of many of the newer, targeted therapies. Although clinical trial evidence may suggest that a targeted therapy produces a differential level of efficacy versus other drugs, even when it is used in combination with those drugs, it is not clear how value-based contracts could be structured around combination therapies if the drugs were produced by different manufacturers, or with different routes of administration.

On the other hand, such contracts could become attractive if combination therapies were produced by the same manufacturer. For example, based on a Phase II study, the FDA in 2015 approved the combination of two drugs produced by Bristol-Myers Squibb, Yervoy and Opdivo, for certain patients with a particular genetic variation of advanced melanoma.²⁹ The list prices for the two drugs used in combination is \$256,000 a year, suggesting that the combination might be a strong candidate for a value-based contract. Genentech has also piloted five value-based agreements for its oral and infused cancer medicines, to look at how pricing may change in part on whether a given medication is used in combination with another treatment.³⁰



A related issue in cancer care is the widespread prescribing and use of drugs “off label,” or outside the marketing authorization established by the FDA.

Off-label prescribing: A related issue in cancer care is the widespread prescribing and use of drugs “off label,” or outside the marketing authorization established for a given approved drug by the FDA. Studies have shown that as many as 30 percent of prescriptions for cancer drugs are for off-label uses.³¹ Off-label use of targeted cancer therapies is generally deemed to be in the same range.³² What’s more, off-label use of newly approved cancer therapies appear to grow over time: A recent study by the Friends of Cancer Research indicates that up to 79 percent of cancer therapies are eventually used off-label.³³

Off-label uses are routinely incorporated into oncology clinical practice guidelines and compendia, such the National Comprehensive Cancer Network (NCCN) compendium, when the oncology community deems that sufficient evidence from clinical research or from clinical practice supports the off-label use. Payers, including the federal Medicare program, will typically reimburse the off-label use of a cancer drug if the use is supported by an authoritative compendium such as the NCCN’s.

Despite these facts, NEHI’s expert panel generally concurred that manufacturers are unlikely in the near term to execute contracts with payers that cover off-label uses. As recently as January 2017, the FDA reiterated that it does not regulate the terms of manufacturer-payer contracts.³⁴ Nevertheless, many manufacturers believe that any contract that covers unapproved uses will expose the manufacturer to legal liability, since information exchanged in negotiation of the contract might be construed as an unpermitted promotion of the unapproved uses.

The FDA's traditional stance is that expanded indications for an already-approved drug should only be approved on the basis of positive results from new clinical trials or other, equally rigorous evaluations. Former FDA Commissioner Robert Califf recently suggested that such rigorous testing and approvals should lead to value-based arrangements. In an August 2017 interview, he said, "We should pay for drugs based on the value they bring...if you haven't demonstrated that in clinical trials [that lead to FDA approval], you have no way of knowing that" a drug is truly effective and does produce value.³⁵

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-- Former FDA Commissioner Robert Califf

By contrast, if value-based agreements involving off-label drug uses are to proceed, the FDA would have to reverse its position, and the FDA along with the Department of Justice would have to issue clear guidance allowing such contracts and the communications that would accompany their execution. Despite the FDA's re-statement in January that it does not regulate manufacturers' contracts with payers, manufacturers say that they need an explicit green light from these agencies to enter value-based agreements involving off-label drug uses without fear of sanction.

Small numbers of patients: Although in some respects negotiating value-based contracts for drugs administered to small groups of patients may seem relatively easy, there are concerns that the time, effort, and costs associated with negotiating these contracts may not be worthwhile. What's more, given a small patient population, outcomes experienced by just one or two patients could statistically sway overall patient outcomes considerably. A possible solution to these challenges may come in the cases where targeted cancer drugs are approved for multiple indications, in which case an indication-based contract that is spread over several different indications may be more viable. But indication-based contracts carry their own operational challenges, as discussed below.



There is broad concern among stakeholders that data collection, data aggregation, and data analytic capacities are not keeping pace with advances in cancer treatment.

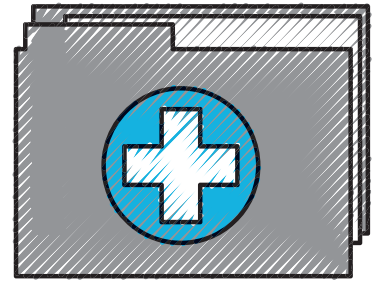
Lack of or inaccessibility of data: Interoperability and information exchange challenges remain pronounced in cancer care, as in much of the rest of U.S. health care. In addition, there is broad concern among stakeholders that data collection, data aggregation, and data analytic capacities are not keeping pace with advances in cancer treatment, and that these deficiencies will militate against use of value-based contracts for cancer drugs.

These deficiencies may reflect relatively simple problems, such as knowing whether or not a patient has discontinued use of a drug if that information is not reflected in any existing record (a problem that is becoming more acute as many cancer drugs are now oral, outpatient therapies). More complex challenges include assembling comprehensive clinical data from multiple sources, such as EHRs, radiographic imaging, genetic testing results, or claims data, to determine if a patient was actually benefiting from therapy, or even whether a given patient was properly diagnosed in the first place. Obviously, these are core concerns that would be of utmost importance in adjudicating the terms of a value-based contract.

Lack of data about outcomes: As discussed above, a major void in cancer data is lack of data outcomes related to the effects of specific therapies on broad groups of patients. Some biopharmaceutical manufacturers argue that value-based contracts should appropriately be based on surrogate outcomes, or endpoints, that can be measured in the short-term, such as tumor growth or shrinkage as seen through imaging, or progression-free survival. These measures could support the notion of “supportive” cancer therapies that might keep patients alive, even if not curing them.

Others in NEHI’s expert panel said it may be more feasible to think about “utilization based” as distinct from “outcomes based” contracting agreements. Features of “utilization” that could more readily be measured than actual outcomes include patients’ adherence to therapy, discontinuation of drugs, and number of cycles on therapy – although as discussed above, even compiling some of this information is challenging.

Yet there is an obvious tension inherent in using these surrogate measures, or utilization measures, as opposed to measuring other types of outcomes that may be more important to patients. In addition to survival, these can include duration of therapy, difficulty or complexity of a given treatment regimen, or quality of life (mobility, fatigue, depression, cognitive status, or pain) during or after therapy.³⁶ Very little data pertinent to these patient-centered outcomes is currently being collected, and there is no existing “core measure set” of patient-centered or patient-focused data that is being collected consistently across the health care system. Therefore, it is unlikely that



A major void in cancer data is lack of data outcomes.



NEHI’s expert panels raised concerns about whether value-based contracts should be made transparent to cancer patients.

information related to the issues that may matter most to patients will be incorporated into value-based contracts soon, even if it should.

Patient-centered outcomes are also unlikely to be explicitly referenced in FDA-approved labeling of therapies, creating uncertainties as to whether manufacturers will trigger FDA sanctions for off-label promotion in negotiating contracts that include such measures (see recommendation #3 below).

Transparency to Patients: Some members of NEHI's expert panels voiced concerns about the degree to which value-based contracts involving cancer drugs should be made transparent to patients. Some observed that the incentives inherent in contracts might influence patterns of care delivery, particularly if provider systems were a party to them. Others said that cancer patients had enough on their minds, and would be no more interested in the terms of a value-based contract than they would be over an oncology practice's participation in a bundled payment or an oncology medical home model.

Another concern, given that high costs of cancer care treatment costs are associated with considerable duress and worse outcomes in cancer patients,³⁷ is whether any rebates or discounts paid over the course of a value-based contract could flow back to patients. Given the high level of cost-sharing that even well-insured patients may be subject to, some on the expert panel said patients should be able to get their money back when drugs do not work for them, or that there should be appropriate adjustments in cost sharing under their insurance policies. Payers indicated that there are operational challenges in channeling discounts back to patients, particularly after the terms of a contract are adjudicated, which could be long after an individual patient's treatment.

A final, major set of operational challenges to value-based contracting in oncology is the raft of legislative and regulatory issues that might impede the practice or block it altogether. As noted above, NEHI identified several policy barriers in its earlier white paper on value-based contracting, published in March 2017. The application of these barriers to potential oncology drug contracts is discussed below.

Policy Barriers

In general, potential legal and regulatory barriers to value-based contracting fall into several categories: issues related to communications between biopharmaceutical manufacturers and payers as governed by FDA regulation; federal pricing regulations; the Anti-Kickback Statute; and federal and state privacy protections regarding personal or protected health information. How these issues may relate to value-based contracts in cancer drugs is detailed below.

A. Food and Drug Administration Regulation of Manufacturers' Communication with Payers

As noted in NEHI's earlier white paper, negotiation of value-based contracts implies ongoing communications between biopharmaceutical companies and payers that may be governed by aspects of FDA regulation. Issues that are especially relevant in the case of value-based contracts for oncology drugs are communication about health care economic information; communication about off-label uses of drugs; and communication about drugs before they are approved by the FDA.

1. Health Care Economic Information. Both the 21st Century Cures Act (enacted into law in 2016) and recently issued Food and Drug Administration guidance (2017) attempted to provide clarity on the subject of manufacturers' communications of health care economic information to payers, formulary committees, or similar entities. (Health care economic information was defined in the Cures law as "any analysis...that identifies, measures, or describes the economic consequences...of the use of the drug.")

The FDA's draft guidance would define the type of cost-related and comparative effectiveness data that manufacturers can share with payers, and allow manufacturers to share this information proactively (that is, on their own initiative) if it "relates to" the approved use of the drug. Given the issues described above, with respect to considerable uncertainty around the value of high-cost cancer medications, payers seeking to strike value-based contracts will need this information as soon as possible. As of this writing, however, the draft guidance has not been finalized, and therefore the effect on value-based contracting is uncertain.

2. Pre-Approval Communication. Federal law and FDA regulation does not yet allow manufacturers to communicate to payers about a drug that has not received final FDA approval, or about potential new indications of already approved drugs, (such indications by definition lie outside an FDA label specifying the drug's indications). As more novel drugs enter the market at higher costs, payers have begun to demand access to more information early regarding the likely impact of the drugs.³⁸ Payers note that under current insurance regulations set forth under the Affordable Care Act and by states, health insurers start the process of setting yearly insurance premium rates as much as 18 months in advance. Many insurers are especially sensitive to unanticipated cost increases caused by drugs or any other factor, particularly as they try to stabilize local insurance markets in the wake of Affordable Care Act coverage expansions and uncertainties over congressional action to repeal and replace the law.

As noted above, some novel cancer therapies, such as CAR-T cell therapy, that are beginning to enter the market will require extremely close collaboration among manufacturers and payers to understand both the costs and performance of these new therapies. The FDA issued draft guidance in January 2017 that it would not object to manufacturers providing payers with "unbiased, factual, accurate and non-misleading" information about investigational, or pre-approved, drugs, without any conclusions about the product's safety or effectiveness. The guidance does not apply to new, off-label indications of existing, already-approved drugs.

This statement would seem to clear the way for broader manufacturer-payer communication around new drugs for the purposes of drawing up value-based contracts. But here again, until the draft guidance is finalized by FDA, the effect on value-based contracting is uncertain – and even when the draft guidance is finalized, the industry may seek further clarity from the FDA before testing the limits of the guidance in practice.

In the interim, the Pharmaceutical Information Exchange Act of 2017³⁹ was introduced in April 2017 in the U.S. House of Representatives to clarify the scope of health care economic and scientific communications that will be permitted between biopharmaceutical manufacturers, payers and other "population health decision makers," as the bill describes them. As of the publication of this white paper, there is no information as to whether the House Energy and Commerce committee will take up the bill anytime soon.

3. Communication about off-label uses. As noted above, although off-label use of cancer drugs is widespread some manufacturers are concerned that contracts that explicitly set terms for off-label utilization of a drug could expose them to legal liability. Thus, an imperative for payers and manufacturers seeking to create such contracts would be identifying scenarios in which off-label uses of cancer drugs were essential to serving patients and meeting the goals of a value-based contract. A hypothetical example might be a contract on a combination therapy that includes drugs used on-label, and drugs prescribed off-label but in a “medically acceptable” use such as those referenced in authoritative oncology compendia. Such scenarios could provide a strong rationale for an explicit clarification by the FDA that medically acceptable uses of off-label drugs in furtherance of value-based contracts would not constitute impermissible promotion of off-label drug uses.

B. Federal Government Best Price and Price Reporting Requirements

Manufacturers are subject to stringent drug price and rebate reporting requirements as a condition of participating in federal health care programs such as Medicare and Medicaid. As discussed further below, regulatory flexibility may be needed from the Centers for Medicare and Medicaid Services, which oversees the Government Best Price and Price Reporting Requirements, to facilitate value-based contracting at greater scale. Many on NEHI’s expert panel believe that, if CMS reforms are not timely or are incomplete, legislation should be enacted to create sufficient predictability for stakeholders to make the necessary investments of time, money, and effort to advance value-based contracting.

Complex calculations carried out under these federal requirements are designed to ensure that federal health programs – Medicaid, the 340B Drug Discount Program, and Medicare Part B Drug Reimbursement – benefit from discounts provided in the broad commercial health care market. Nearly all manufacturers participate in these federal health programs, which provide varying levels of coverage of their drugs in the programs. At the same time, federal requirements for Medicaid stipulate a minimum discount of 23.1 percent off the Average Manufacturer Price (AMP), the average price paid by wholesalers to manufacturers for drugs distributed to retail pharmacy, minus discounts, and locks in a similar discount for hospitals, health centers, and various safety-net providers under the 340B program.

As noted in NEHI’s earlier white paper, Medicaid Best Price and related drug rebate obligations for the 340B Program and the Medicare Part B program create a roadblock to manufacturers’ ability to enter certain types of value-based contracts, such as those providing for warranties or “money-back guarantees.” Under such a contract, a manufacturer would refund the cost of a new drug when patients (either individual patients, or defined groups of patients) failed to respond to it or to achieve agreed-upon health outcomes. As far as payers are concerned, such money-back guarantees could be especially attractive features in value-based contracts involving oncology drugs, given the high cost and uncertainties around which patients will benefit from certain targeted therapies.

However, in instances in which a drug did not work, and manufacturers refunded the cost to a payer, the drug would in effect be free. Thus, the lowest “price” available in the market would be zero; a “best price” of \$0 would then have to be extended to Medicaid, the 340B program, and other relevant federal health programs. The value-based contract would thus result in losses for the manufacturer, even if the drug proved effective among many patients. Providers are potentially at financial risk as well. Providers serving

Medicare patients are entitled to directly purchase drugs and bill Medicare at the so-called Average Sales Price (calculated as the manufacturer's unit sales of a drug to all purchasers in the United States by calendar quarter, divided by the total number of units of the drug sold by that manufacturer in the same quarter), plus a mark-up of 6 percent. Cancer therapies administered directly by providers (such as infused therapies) are charged on this "book and bill" basis. A \$0 price for a therapy would reduce reimbursements to providers by reducing the Average Sales Price.

Another type of value-based contract, indication-based pricing, may also be impractical due to the federal health program price and rebate regulation. As noted above, however, CMS's comments on the approval of Kymriah signal that CMS may seek to facilitate this type of approach. Under an indication-based pricing scheme, prescribers and payers must, in effect, configure their information systems to treat a drug as if it were actually two or more drugs ("Drug A as used in Condition X, Drug B as used in Condition Y," etc.). NEHI stakeholder experts and others point out that few health systems are currently prepared to support this heightened level of reporting, and that the needed changes would require continued investment by providers, payers, and most likely manufacturers as well.

At the same time, there may be pragmatic, "workaround" strategies to facilitate early experimentation with indication-based pricing. For example, in an indication-based pricing arrangement that represents a "bundled sale" of the same product for multiple indications, the manufacturer could calculate the prices under the contract as a weighted-average price blending the sales for the different indications. This approach would require minimal alteration of current provider, payer, and manufacturer reporting.

Unfortunately, even this weighted average approach may provide little incentive for payers and manufacturers to engage in indication-based pricing. For example, the weighted average prices for a drug with a higher-priced, high-value indication and a lower priced, lower-value indication may be significantly lower than the price of the higher-priced indication. Such a result would clearly discourage manufacturers from participating in the arrangement. In the face of this reality, members of NEHI's expert panel cautioned that federal agencies such as CMS may simply lack the tools to make such arrangements work within the context of federal pricing and rebate reporting requirements. Statutory changes achieved through legislation may thus be required.

C. Anti-Kickback Statute Enforcement

The federal Anti-Kickback Statute (42 USC Sec 1320a-7b) is a criminal statute that prohibits the offering of anything of value in an effort to induce or reward the referral of federal health care program business. A key concern is whether the multiple existing exceptions and "safe harbors" to the statute provide sufficient protection for value-based contracts.

For example, negotiations between payers and manufacturers over a value-based contract may entail considerable exchange of data and analysis, and agreement to share the cost of data collection and analysis to adjudicate the contract once it has been finalized. What's more, as noted above, manufacturers may commit to taking such steps as assuring patients' adherence to medication. As discussed, these information exchanges and services could be critical in the case of contracts for oncology drugs. Yet, if provided by

manufacturers, and linked to discounts and rebates that flowed between manufacturers and payers, these services could be construed as impermissible inducements to use drugs under the Anti-Kickback law.

Certain activities that could otherwise be construed to be prohibited inducements are protected under statutory exceptions to the Anti-Kickback Statute or regulatory “safe harbors,” issued by the Office of the Inspector General of the U.S. Department of Health and Human Services. An additional safe harbor is likely to be essential in the case of value-based contracts for cancer drugs to cover the services necessary to administer them, including shared data collection and analysis and support for patients’ adherence.

D. Patient Privacy Protections Under Federal and State Law

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) required the Secretary of Health and Human Services to publish standards for the electronic exchange, privacy, and security of health information. The subsequent Privacy Rule set forth various privacy safeguards and set limits on the uses and disclosures of protected health information – generally, demographic information, medical history, test and laboratory results, insurance information, and other data that a health care professional collects to identify an individual and determine appropriate care.

Value-based contracts for pharmaceuticals do not violate the federal HIPAA statute and Privacy Rule, per se, as the statute allows most payers and providers to share protected health information in the interest of efficient and orderly payment of medical or pharmacy services. However, many health care systems and other providers take a cautious and conservative approach to disclosures of protected health information. Effective value-based contracting for cancer drugs may require disclosure of protected health information on a scale that goes beyond typical disclosures for settling medical claims, such as disclosure of genetic testing information. Patients may seek greater assurance of privacy, and to avoid sanctions, providers may seek greater assurance that information they submit to fulfill value-based contracting obligations complies with the HIPAA law.

Recommendations for Change

In June 2017, the administration of President Donald J. Trump was reported to be preparing an executive order aimed at lowering drug prices. According to drafts published in the news media, one policy aim of the order was to “facilitate, where appropriate, the ability of Federal health programs to enter into reimbursement arrangements for medical products that are based on the value of such products to patients rather than the volume of such products purchased.” The order was expected to direct the Department of Health and Human Services to take steps to facilitate value-based contracting for pharmaceuticals. As of the date of publication of this white paper, however, no such order has been issued.

Nonetheless, CMS has signaled a willingness to endorse value-based arrangements, as in its implicit approval of Novartis’s plans – both to impose no costs for use of Kymriah leukemia therapy on pediatric and young adult patients who fail to respond to the therapy in the first month, and to seek indication-based pricing for other uses that may be approved in the future. CMS also has signaled that it will issue future guidance “to explain how pharmaceutical manufacturers can engage in innovative payment

arrangements,”⁴⁰ and that it would “continue to work with states on other options,” suggesting that particular measures with respect to Medicaid contracting for biopharmaceuticals are also being considered.

Pending clarification of CMS’s future directions, NEHI’s expert panels believe that a series of steps should be taken to facilitate innovation in value-based contracting, particularly with respect to oncology drugs. The series of recommendations below reflects a graduated response to address the challenges described above, beginning with measures to facilitate value-based contracting and culminating with recommendations for a more far-reaching response to the advent of highly innovative, high cost drugs.

1 Recommendation #1: Payers, biopharmaceutical companies, data collection organizations, and other stakeholders should address challenges in collecting and analyzing data to execute value-based contracts.

NEHI’s earlier white paper contained several recommendations for addressing operational barriers to value-based contracting, all of which are applicable to contracts involving oncology drugs. However, recommendations previously made on data collection, integration, analysis, and data sharing warrant special attention in the case of cancer. In essence, building the health data ecosystem needed to support value-based contracting for cancer drugs is at one with an even broader agenda: building the data ecosystem needed to research, treat, and even cure cancers.

The demand for data is rapidly increasing in cancer, from the research end of the spectrum all the way to tracking patients’ responses to therapy. Accelerated progress toward creation of a “national cancer data ecosystem” is one of the national priorities identified in the Blue Ribbon Panel Report issued in 2016 by the Beau Biden Cancer Moonshot.⁴¹ The Blue Ribbon Panel specifically called for a national cancer data ecosystem that served both “upstream” research needs and “downstream” efforts to improve patients’ care.

Important building blocks for the cancer data ecosystem are already in place, including the FDA Sentinel System, through which the FDA monitors insurer claims data to monitor drug safety;⁴² PCORnet, the National Patient-Centered Clinical Research Network, a distributed network of clinical data centers designed to advance the use of electronic health record data in comparative effectiveness research;⁴³ and the American Society of Clinical Oncology’s CancerLinQ network, a health information technology platform that enables collection and analysis of real-world cancer data from oncology practices and other partners in cancer care.⁴⁴

Part and parcel of building this ecosystem is forging agreement among all parties to standardize the data collected and to commit to sharing it to advance knowledge. Many leading biopharmaceutical firms now recognize that standardizing data collection could accelerate research and development of new cancer therapies. As a result, the industry is supporting efforts to create common data collection formats and protocols, such as through the non-profit Transcelerate BioPharma collaborative formed by leading global biopharmaceutical companies.⁴⁵ And although data sharing is a complex issue in a competitive system dependent on intellectual property, some biopharmaceutical manufacturers are opening their clinical trial data to qualified researchers out of recognition that such a strategy can lead to acceleration of knowledge.

Greater standardization and sharing of routinely collected cancer data, albeit with appropriate privacy safeguards, could also make it easier and less costly to design, implement, and evaluate value-based contracts for cancer drugs. A “virtuous data cycle” could then ensue. As these contracts became more attractive for manufacturers and payers, outcomes data from them would contribute to the body of knowledge that researchers and clinicians could use to improve cancer drug discovery and cancer care.

NEHI thus recommends that biopharmaceutical manufacturers, payers, and even health systems that are parties to value-based contracts take two key steps in the realm of data standardization and data sharing. First, to measure aspects of cancer care in the context of value-based contracting, they should consider adopting the Core Measure Set created for the Oncology Care Model, a multi-payer, performance-based payment model launched in 2016 by the Center for Medicare and Medicaid Services to improve cancer care and lower the cost. Adopting this core measure set would ease the burden on providers to collect multiple different data sets for different payers and purposes.

Second, as biopharmaceutical manufacturers, payers, and others develop their own cancer-related data sets, potentially for the purposes of value-based contracting, they should commit to linking these to the larger cancer data ecosystem. Data on how patients respond to various drugs, for example, will be extraordinarily useful up and down the cancer research spectrum. Helping to evolve a true “learning health system” in cancer will thus benefit all stakeholders, including patients, and society – and not just the parties to value-based contracts.

2

Recommendation #2: A cross-sector group of stakeholders, patients, payers, and biopharmaceutical manufacturers, should develop a set of patient-centered and patient-reported measures for oncology care.

A related issue in the realm of data collection and analysis is the need for a core set of patient-centered and patient-reported outcomes measures. As noted above, no such set of measures currently exists, and in its absence, little is known about aspects of cancer treatment that anecdotal evidence suggests matter to patients as much, or nearly as much, as common clinical metrics as survival or progression-free survival. There is momentum to develop such measures: For example, the FDA Reauthorization Act of 2017, signed into law in August of this year, directs the FDA to expand the scope of patient experience data to be considered in FDA drug approval trials. On the other hand, although both the Medicare program and commercial health plans are moving to adopt a proposed set of medical oncology measures advanced by the Core Quality Measures Collaborative, a set of measures deemed extremely important to patients, such as measures of pain control, functional status, quality of life, and costs of treatment, has not yet been developed.⁴⁶

NEHI recommends that a cross-sector stakeholder group be established to take up this effort, and that it should propose a set of core patient-centered and patient-reported cancer care measures. Payers and biopharmaceutical manufacturers in particular should commit to helping to develop these measures and should incorporate them into future value-based contracts. The ultimate aim should be to collect data on these measures through electronic health records, and to disseminate the results widely through the larger

cancer data ecosystem. Importantly, a core measure set should gather information on financial toxicity, or the problems that cancer patients have that are related to their costs of treatment.

3 Recommendation #3: The Food and Drug Administration should finalize draft guidance on communication among manufacturers, payers, and other entities deemed qualified under the agency's proposed guidance.

As noted above, several issues under the FDA's purview, in the realm of communications between manufacturers and payers, stand in the way of value-based contracts, and particularly for cancer drugs. These issues fall mainly into two categories: communications about drugs, including potential new indications of already approved drugs, that are under review by the FDA but not yet approved, and communication about off-label uses. Two areas of recommendation follow.

Pre-approval communication: The FDA should finalize its draft guidance issued in January 2017 to fully authorize exchange of health care economic information about new, not-yet-approved products, and about potential new indications for already approved products, from manufacturers to payers and other entities deemed qualified under the FDA's proposed guidance, such as health system formulary committees. In the absence of FDA action, Congress should enact H.R. 2016, the Pharmaceutical Information Exchange Act of 2017, to make clear that such information can be communicated by biopharmaceutical manufacturers to payers and entities deemed qualified under its proposed guidance without fear of sanction.

Communication about off-label uses: As noted above, as recently as January 2017, the FDA reiterated its longstanding prohibition against manufacturers' communication of off-label information. But because the majority of cancer therapies are eventually prescribed off-label, the rising number of trials underway testing combinations of cancer drug therapies may portend even greater off-label use of drugs in the years ahead. For this reason, NEHI recommends that FDA should consider issuing new guidance on payer-manufacturer communication on off-label uses, at least as pertains to cancer therapies, in light of the rapid changes underway in cancer research and drug development. To encourage FDA to issue such guidance, manufacturers and payers should develop scenarios in which realistic combinations of drugs used on-label and off-label, and value-based contracting around them, will make such communication necessary. They could also enhance their case with the FDA by making good faith efforts to enroll every patient prescribed a cancer drug off-label into a clinical trial registered with the FDA, so that evidence can be gathered about the efficacy of off-label uses.

A somewhat separate but related area is the issue of communication that is consistent with the clinically indicated use of an FDA-approved drug, but is not contained in the FDA-approved label. An example could be a patient-reported outcome, such as ability to undertake activities of daily living, which may be clinically relevant even though the information was not included in the drug's label. Manufacturer-sponsored trials increasingly evaluate these outcomes, and since they may be valuable information for good clinical use of the drug, they could also be useful to incorporate into value-based contracts. As the FDA continues to consider scientifically robust approaches to including patient-reported and patient-centered outcomes in the drug approval process, NEHI recommends that it consider a reasonable first step by allowing communication of such off-label information to payers that is consistent with the approved clinical indications.

4

Recommendation #4: The Centers for Medicare and Medicaid Services should provide a reasonable accommodation to Government Best Price and other price reporting requirements so that certain value-based contracts, such as “money-back guarantees,” do not trigger deeper rebates and other unintended adverse federal price reporting consequences across government programs.

As noted above, such money-back guarantee contracts that may be especially worth attempting in the context of very expensive, arguably curative therapies such as CAR-T cell therapies. If CMS does not provide this accommodation in a reasonable time frame or address the substance of these issues, **Congress should step** in to make relevant changes in law to enable such contracts.

5

Recommendation #5: The Office of the Inspector General of the Department of Health and Human Services should develop new safe harbors to the Anti-Kickback Statute to enable certain activities that support value-based contracting.

New safe harbors should specifically allow biopharmaceutical manufacturers and payers to determine how to share the costs of analytical models, collection of data, services to support medication adherence, care coordination, and similar services, without triggering enforcement actions under the statute. As discussed above, such data collection and adherence efforts are especially critical in the case of value-based contracts for oncology drugs. New safe harbors should also provide clear authority for manufacturers to extend discounts and rebates to payers based on pre-determined patient outcome and other value-based measures, in addition to discounts and rebates based on volume of sales, which are already permitted and regulated under an existing safe harbor.

6

Recommendation #6: The Office of Civil Rights of the Department of Health and Human Services should develop guidance on HIPAA compliance in the context of value-based contracts between manufacturers and payers.

Such guidance would pertain to sharing protected health information among providers, payers and manufacturers. Although not limited in importance to value-based contracting in oncology, as noted above, clarification of the applicability of the statute will be critical to building the cancer data ecosystem.

7

Recommendation #7: Stakeholders should continue discussion and investigation of new long-term financing approaches for high-cost therapies and cures in major disease states such as cancer.

For all the promise of value-based contracting, payers and purchasers on NEHI’s expert panels voiced doubts that the strategy will be a singular solution to the challenge of high-cost drugs. Particularly

for breakthrough therapies that may come onto the market in future years – not just in cancer, but in other areas of unmet need, such as Alzheimer’s disease – the costs are likely to be so high, and the need so immense, as to impose a major burden on existing programs and payment mechanisms. Many payers and programs, such as the Medicaid program, find even existing curative therapies for conditions such as Hepatitis C unaffordable at current prices and within current fiscal constraints.

As noted above, the likely proliferation of curative therapies aimed at small pools of patients poses challenges to the biopharmaceutical sector as well. Unless these therapies command relatively high prices, it is unlikely manufacturers can recoup their investments in developing them. And society, in effect, could be left between the proverbial rock and a hard place: unable to afford high biopharmaceutical prices for breakthrough cures and treatments, and therefore unable to sustain the sector that seeks to bring these drugs to market.

To avoid such an impasse, alternative approaches to financing high-cost therapies are needed. Several efforts are under way, primarily at academic institutions and think tanks, to devise new public and private financing models for high-cost therapies, especially curative ones. It is time to organize these disparate efforts into a more coordinated and cogent examination of the options, perhaps under the aegis of the National Academy of Medicine. Congress should adopt into law a formal request of NAM to carry out such a study, or should appoint an advisory panel to the Secretaries of Health and Human Services, the Treasury Department and other relevant agencies to devise potential approaches.

Conclusion

As noted in this white paper, the revolution occurring in cancer treatment is producing breakthrough medications that offer great benefit to many patients, at considerable cost. Many of these drugs could be strong candidates for value-based contracts that hold biopharmaceutical manufacturers more accountable for improved patient outcomes than conventional purchasing arrangements, while also offering the potential for more affordable pricing. A period of experimentation is needed to develop such contracts and learn from them. It is also important to establish the legal and regulatory framework to help facilitate these contracting opportunities.

Payers, providers, biopharmaceutical companies, taxpayers, and government all have an interest in seeing these experiments and investments in value-based contracting proceed. Some regulatory relief is needed to support these arrangements, as is a robust commitment from stakeholders to build the data systems and take other steps to shape a true “learning health system” in cancer care.

Value-based contracts, and the lessons learned from their execution, will help all stakeholders better understand the value of many cancer drugs. They have the potential to make these drugs more affordable for the health care system, but they will not themselves solve the overarching challenge of affordability of high-cost medications for cancer or other conditions. A broader inquiry is also needed into possible long-term financing solutions that will support provision of high cost and potentially curative therapies. Cross-sector organizations such as NEHI, and the expert panels it assembled to create this white paper, can be instrumental in helping to forge solutions to benefit all.

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The views expressed herein are solely those of NEHI and are not intended to represent the individual viewpoints of sponsors, members, or advisors.

About NEHI

NEHI is a national nonprofit, nonpartisan organization composed of stakeholders from across all key sectors of health and health care. Its mission is to advance innovations that improve health, enhance the quality of health care, and achieve greater value for the money spent.

NEHI consults with its broad membership, and conducts independent, objective research and convenings, to accelerate these innovations and bring about changes within health care and in public policy.

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