June 9, 2016
Medicines Are Transforming the Treatment of Many Diseases

HEPATITIS C
The leading cause of liver transplants and the reason liver cancer is on the rise – is now curable in more than 90 percent of treated patients.

CANCER
New therapies have contributed to a 23% decline in the cancer death rate since its peak in 1991. Today, 2 out of 3 people diagnosed with cancer survive at least 5 years.

HIGH CHOLESTEROL
America’s biopharmaceutical companies are currently developing 190 medicines to treat heart disease, stroke and other cardiovascular diseases. New PCSK9 inhibitors have revolutionized high cholesterol therapy. Between 1991 and 2011, the death rate from heart disease dropped 46%.

Sources: National Multiple Sclerosis Society; Boston Healthcare; CDC; American Cancer Society
Cite: Medicines in Development Report, Pharmaceutical Research and Manufacturers of America (PhRMA) and the Association of Black Cardiologists (ABC), December 2015
HIV/AIDS:
As Treatment Improved Spending Became Sustainable

1989

The New York Times
September 15, 1989

AIDS Treatment Costs Put at $5 Billion a Year

“We have got to get our act together now because the medical system is going to be crushed in two years.”

–Daniel Hoth, director of the division of AIDS at the National Institute for Allergy and Infectious Diseases

“If we don’t act now, we will be soon rationing health by queuing,” ...

“People will wait longer and longer in the emergency rooms, more people will die, the whole level of care will decrease significantly.” He called it “a downward spiral of effects which we cannot afford.”

–Dr. Douglas Shenson, Montefiore Medical Center

Today

“WE USED TO THINK HIV COSTS WOULD OVERWHELM US....BUT WE FIGURED IT OUT AND LET DRUG DEVELOPMENT PROGRESS.”

– Ira Klein, M.D., M.B.A., FACP, Aetna

HIV/AIDS Death Rates

HAART COMBINATIONS INTRODUCED

10.2

16.2

5.2

4.2

2.7

Biopharmaceutical Industry Is on the Leading Edge of Science

- 42% of all medicines in development have the potential to be personalized medicines.
- 73% of cancer medicines have the potential to be personalized medicines.
Researchers Have Made Great Progress

Identifying Genes that—When Mutated—Drive Many Cancers, but Challenges Remain

We now know that cancer is not a single disease, but rather more than 200 unique diseases, many of which are caused by genetic mutations. Identifying these mutations has led to tremendous advances against many cancers, but the complexity of each disease presents great challenges for researchers, as they explore still yet unknown alterations.

Selected Genomic Alterations Known to Drive Disease Progression in Common Cancers

Cancer relapses and treatment resistance have always been among the most daunting challenges in cancer care...The good news is that genomic medicine is helping to overcome these challenges by revealing new ways to target a cancer cell’s inner workings.

- Gregory A. Masters, MD, Helen F. Graham Cancer Center

Growing Recognition
of Personalized Medicine in Changing the Face of Health Care

FAST COMPANY
Obama’s Precision Medicine Initiative Is The Ultimate Big-Data Project

ABC
President Obama’s Cancer ‘Moon Shot’: How Scientists Are Trying to Cure the Disease

CNN
How Obama’s cancer ‘moonshot’ can save many lives

Fierce Health Payer
21st Century Cures ‘next priority’ for Senate Health Committee
Rapid Change in the Market
for Medicines

- Value-based insurance design
- Value frameworks and clinical pathways
- Accountable care organizations
- Providers at risk for RX costs
- Bundled payments
Powerful Purchasers Negotiate Drug Prices

on Behalf of Payers

Negotiating power is increasingly concentrated among fewer pharmacy benefit managers (PBMs), with the TOP THREE PBMS ACCOUNTING FOR THREE QUARTERS OF THE MARKET.

PBM MARKET SHARE, BY TOTAL EQUIVALENT PRESCRIPTIONS, 2014

- Express Scripts: 25%
- CVS Health (Caremark): 22%
- OptumRx/Catamaran*: 24%
- All Other: 29%

Top 3 Market Share: 75%

*OptumRx and Catamaran merged in 2015. Their 2014 shares are shown combined.
Source: Drug Chandra Institute
Only 17% Of Oncologists Were In Independent Practice In 2015
Patients in Only 6 Countries Had Access to at Least Half of 49 New Oncology Medicines Launched 2010-2014

Notes: Includes innovative medicines, often referred to as New Active Substances or New Chemical Entities, first launched globally between 2010 and 2014. Availability is based on sales in audited markets, regardless of reimbursement rates. Supportive care medicines are not included.

Even When Commercially Available,
Not All Cancer Medicines Are Reimbursed Under Public Insurance Programs

<table>
<thead>
<tr>
<th>Country</th>
<th>Percent of Approved Cancer Medicines</th>
<th>Reimbursed</th>
<th>Not Reimbursed</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>France</td>
<td>43%</td>
<td>43%</td>
<td>57%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>62%</td>
<td>38%</td>
<td>62%</td>
</tr>
<tr>
<td>Australia</td>
<td>65%</td>
<td>35%</td>
<td>65%</td>
</tr>
<tr>
<td>Scotland</td>
<td>67%</td>
<td>33%</td>
<td>67%</td>
</tr>
<tr>
<td>Sweden</td>
<td>71%</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>Germany</td>
<td>71%</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>Italy</td>
<td>71%</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>Canada</td>
<td>76%</td>
<td>24%</td>
<td>76%</td>
</tr>
<tr>
<td>Spain</td>
<td>95%</td>
<td>5%</td>
<td>95%</td>
</tr>
</tbody>
</table>

Note: The categorization of not-reimbursed does not mean that there is no patient access to these medicines, and there may be non-standard means for obtaining access to new medicines through special funds and submission of applications for approval outside of standard guidelines.


11
Ongoing Research, Use of a Medicine Over Time Reveals Additional Benefits That May Not Have Been Recognized Initially

FDA approval and introduction of a new therapy is a significant milestone for patients but it is **only the beginning**.

Our knowledge of the full benefits of a therapy emerges **over time**, through continued research and real world clinical practice.

Additional value may be realized over time through:¹

- Earlier use
- Use in combination with other agents
- Use in specific sub-populations of patients using diagnostics
- Use in other disease indications

“**The relative value of a given cancer treatment is likely to change over its lifetime... the assessment of the value of any treatment must be dynamic and adapt to new medical information that may better inform its use, mitigate its toxicity, or modify its place in the treatment landscape.”**

— American Society of Clinical Oncology²

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Research Reveals Efficacy in Additional Targeted Patient Group: Crizotinib for Non-Small Cell Lung Cancer

Initially approved to treat patients with ALK+ mutated NSCLC, rapidly evolving science and ongoing research revealed that crizotinib is effective in treating another rare, difficult-to-treat form of the disease as well.

- **2011**
  - Accelerated approval in ALK+ patients, based on evidence of tumor shrinkage (surrogate endpoint)

- **2013**
  - Regular, confirmatory approval granted based on superior progression-free survival

- **2016**
  - NEW indication approved for patients with a different genetic subtype (ROS-1+)

“The expanded use of Xalkori will provide a valuable treatment option for patients with the rare and difficult to treat ROS-1 gene mutation by giving health care practitioners a more personalized way of targeting ROS-1 positive NSCLC.”

- Dr. Richard Pazdur, director of the Office of Hematology and Oncology Products, U.S. FDA Center for Drug Evaluation and Research

Sources:
**Promoting**

Value-Driven Health Care: Policy Agenda

- **Promote** innovative manufacturer partnering and contracting arrangements

- **Encourage** development of patient-centered value frameworks and assessments, and decision support tools

- **Align** value-based payment with personalized medicine
Regulations Should Be Updated to Support Value

- Payers seeking greater predictability and certainty regarding the biopharmaceutical pipeline
- Manufacturers conducting research on a range of endpoints not included in product labeling
- Biopharmaceutical companies exploring innovative partnerships with payers and providers
Patient-Centered Value Frameworks and Decision Support

- Describe open and transparent process
- Support patient-centered care
- Value continued scientific and medical progress
- Take a system-wide perspective on value
- Deliver reliable, relevant information
“The frameworks will require refinement, however, before they're ready to be broadly applied.”

Peter Neumann, Ph.D., et al.

“... health technology assessments are increasingly challenged by the rapid pace of change in science and medical practice, our growing understanding of heterogeneity in cancer, and growing sensitivity to the varying needs of patients.”

Amy Abernathy, M.D., et al.
ICER’s Value Framework Threatens Progress Against Cancer

ICER’s model chooses payer needs over patients’ needs. Its advisory panel and Governing Board are largely made up largely of payers.

<table>
<thead>
<tr>
<th>ISSUE</th>
<th>STAKEHOLDER COMMENTS</th>
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<tbody>
<tr>
<td>Does not account for the aspects of value that matter most to patients</td>
<td>“...the current ICER’s model represents only some components of the overall care and may overshadow other dimensions of care that are also available to patients...The patient perspective is not incorporated into ICER’s framework...absent is the guidance of real world experience and preferences of the patients.” – CANCER SUPPORT COMMUNITY</td>
</tr>
<tr>
<td>Does not accurately reflect how physicians treat patients and could be used to dictate physician prescribing and patient access</td>
<td>“Unfortunately, the scope of ICER’s analysis is far too narrow because it does not represent the realities of clinical practice. As such, [The American Society for Hematology] believes that the type of analysis has only limited value in determining the just price and utility of novel drugs and drug combinations in this rapidly advancing field...ASH is concerned that ICER’s analysis will be used to limit the options for patients in receiving the best possible treatment for a very difficult and complicated disease.” – AMERICAN SOCIETY FOR HEMATOLOGY</td>
</tr>
<tr>
<td>Relies on a QALY-based cost-effectiveness analysis that conflicts with movement toward personalized medicine</td>
<td>“The QALY is a rigid measure with many known limitations, especially the inability to assess the value of medicines for rare diseases, like refractory myeloma, where there are many DNA alterations in myeloma cells frequently differ from patient-to-patient.” – CUTANEOUS LYMPHOMA FOUNDATION</td>
</tr>
<tr>
<td></td>
<td>“ICER’s framework is not consistent with the current thinking in regard to the future of cancer treatment. The trend is towards more personal, customized approaches and not subjecting every patient to the same treatment regimen” – MULTIPLE MYELOMA RESEARCH FOUNDATION</td>
</tr>
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</table>
The majority of existing cancer quality measures are process measures, and other types of quality measures such as outcome, efficiency, and composite are lacking.
CMS’ Part B Demo Is Inconsistent with Value-Driven Health Care

<table>
<thead>
<tr>
<th>Value-Driven Health Care</th>
<th>Part B Demo</th>
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</thead>
<tbody>
<tr>
<td>Informed Decision Making</td>
<td>One-size-fits-all decision making</td>
</tr>
<tr>
<td>Holistic Approach</td>
<td>Narrow focus on drugs</td>
</tr>
<tr>
<td>Quality and Performance Measurement</td>
<td>Emphasizes cost alone, not quality</td>
</tr>
<tr>
<td>Adaptive to Changes in Science</td>
<td>Hinders access to innovation and personalized medicine</td>
</tr>
</tbody>
</table>
Expected Impact of Phase 1 on Access to Personalized Medicine

ASP + 0.86% + $16.53 disproportionately cuts payments for innovative and personalized medicines. Physicians expect to be under water on approximately 40% of the products they administer, including many personalized medicines.

- 67% Decrease Access
- 20% No Impact
- 13% Increase Access
Phase 2 proposals rely on flawed value metrics, like those developed by ICER, that systematically disadvantage newer treatments.

- 10% Decrease Autonomy
- 12% No Impact
- 79% Increase Autonomy

Base: Total Respondents (135)

41a1. What impact do you think that would have on your prescribing autonomy (ie, your ability to tailor prescriptions to the individual needs of each patient)?
One-Size-Fits-All CMS Standards vs. Individual Differences

“Rarely are two drugs interchangeable... While the drug costs may be lower, the likely costs to treat the resulting known side effects and predictable adverse events will more than surpass any savings.”

“Determining which treatments are ‘therapeutically similar’ is fraught with pitfalls, as treatments that work for the average at the population level may not work for the individual patient. This model homogenizes the patients, but in reality disease severity levels and stages demand treatment variations.”

“... what is likely to be clinically effective for a specific patient is a multifactorial determination based on a host of factors. The levels of effectiveness as determined by CMS could be based on population-based considerations that do not account for patient specific conditions or biomarkers.”

“Average assessments fail to consider differences in patient outcomes, needs and preferences and do not recognize the unique nature and value of targeted therapies that benefit specific groups of beneficiaries, including people with disabilities, complex conditions and multiple chronic conditions.” -
## One-Size-Fits-All Standards National Standards vs. Individual Differences

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Assumption of Clinical Equivalence</th>
<th>Clinical Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IV Metastatic Breast Cancer, HER2 Negative</td>
<td>National policy based on assumption of clinical equivalence of treatments for metastatic breast cancer</td>
<td>Stage IV MBC patients with comorbidities cannot tolerate older treatment option with higher rates of heart toxicity. Patients face higher risk of complications and hospitalization.</td>
</tr>
<tr>
<td>Metastatic Colorectal Cancer, Wild Type KRAS</td>
<td>National policy based on assumption of clinical equivalence for metastatic colorectal cancer.</td>
<td>Physician recommends Medicine A, taking into account the patient’s age and rapid tumor growth. However, without access to this treatment, patient treatment would be limited to a different medicine that presents a greater risk of neuropathy.</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Physician recommends Medicine A, a long-acting injectable, taking into account the patient’s past history of relapses as a result of non-adherence to oral medication. Patient remains adherent and is able to continue working.</td>
<td>Payer restricts patient’s options to only Medicine B. After beginning treatment, patient develops tardive dyskinesia, a side effect that causes the patient to lose control of some body movements. The patient is unable to continue working.</td>
</tr>
</tbody>
</table>
## Lack of Safeguards

<table>
<thead>
<tr>
<th>Patient Safeguards</th>
<th>Clinical Trials</th>
<th>Part B Drug Payment Model</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Review Committee</strong></td>
<td>Clinical trial protocols are reviewed and approved by an Institutional Review Board (IRB).</td>
<td>Analysis of potential benefits and unintended effects of the demonstration.</td>
</tr>
<tr>
<td><strong>Study size</strong></td>
<td>Limited to minimize risks to patients until initial data are examined</td>
<td>Small and voluntary to minimize unintended effects</td>
</tr>
<tr>
<td><strong>Patient is Aware of Potential Risks and Benefits</strong></td>
<td>Informed consent</td>
<td>Beneficiary notification and voluntary participation</td>
</tr>
<tr>
<td><strong>Ongoing Monitoring</strong></td>
<td>Data Safety Monitoring Board</td>
<td>Capacity for real-time monitoring of access and care quality</td>
</tr>
<tr>
<td><strong>Pre-specified Endpoints for Evaluation</strong></td>
<td>Study protocol description and approval by IRB</td>
<td>Pre-specified quality and cost measures and description of plan to evaluate them</td>
</tr>
</tbody>
</table>
Lack of Quality Measures

Measure Type

- Process: 10
- Efficiency: 2
- Cost/Resource Use: 1

NQF Endorsement

- Endorsed: 11
- Not Endorsed: 2

NQS Measure Domain

- Person and Caregiver-Centered Experience and Outcomes: 2
- Patient Safety: 0
- Efficiency and Cost Reduction: 3
- Effective Clinical Care: 7
- Community/Population Health: 1
- Communication and Care Coordination: 0

Pragmatic Solutions
to Address Cost Concerns

MODERNIZE THE DRUG DISCOVERY AND DEVELOPMENT PROCESS
- Increase competition by reducing the generic backlog at FDA, and providing financial and/or regulatory incentives to encourage generic entry for older, off-patent drugs for serious conditions
- Modernize the FDA to keep pace with scientific discovery and drive greater efficiencies in the discovery and development of new treatments and cures

PROMOTE VALUE-BASED HEALTH CARE
- Address barriers to paying for value by confronting regulatory barriers that impede companies from entering into innovative contracts

ENGAGE AND EMPOWER CONSUMERS
- Make quality and cost information public to aid in decisions, and enforce common-sense rules that prevent discrimination against vulnerable patients

ADDRESS MARKET DISTORTIONS
- Improve risk adjustment models, and reform the 340B program