Next Generation Therapies in Massachusetts:

New Solutions for Coverage and Payment

NEHI Network for Excellence in Health Innovation

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Executive Summary

In many ways, 2018 was a watershed year for medicine in Massachusetts.

The first American treated with an FDA-approved gene therapy was treated in Boston. The first therapy based on gene suppression (RNA interference) was approved – based in part on Nobel Prize-winning research from the University of Massachusetts Medical School. And Boston hospitals were among the first in the country to administer newly-approved chimeric antigen receptor-T cell (CAR-T) cancer therapies.

These are only three examples of what is expected to be a continuing wave of potentially transformative, and even curative, biopharmaceuticals that will be approved in coming years, many of them emerging from biopharma firms headquartered or with substantial presence in Massachusetts.

This oncoming surge of new therapies will create unprecedented opportunities for some patients as measured in lives saved, disabilities reduced or quality of life improved. But it creates an unprecedented challenge for insurance coverage and payment as well.

Health insurers and other health care payers have relied for years on volume-based discounts and rebates as their primary tools for managing or containing pharmaceutical costs. Essentially, the more they buy, the lower the net price. But this approach has real limitations when applied to the new wave of highly-innovative pharmaceuticals.

Many of the most transformative new pharmaceuticals are one-of-a-kind treatments, at least when they are first approved by the U.S. Food and Drug Administration. Many are approved as rare disease treatments or, more generally, as treatments targeting serious, unmet medical needs among highly-targeted and often small groups of patients. A new, highly-innovative therapy may become the standard of care for treatment when first introduced, with no alternative therapies competing on price. Meanwhile, the volume of drugs any one payer may purchase will be relatively small.

Competition may come along, even quickly. In fact, investment in some of the most promising areas of new drug development, such as cancer immunotherapies, is extremely high. Nevertheless, it can be difficult to predict when a clinically comparable new therapy may emerge to challenge a therapy which may have become the sole choice of treatment for patients who previously had few options. In some cases, such as with cancer therapies, insurance coverage in Massachusetts may even be legally mandated.

“Highly innovative” is not synonymous with “too expensive,” but some of the most innovative new therapies clearly are costly, at least at first. A case in point: health insurers throughout the country are now referencing price recommendations based on third-party cost effectiveness evaluations of new therapies such as those performed by the Boston-based Institute for Clinical and Economic Review (ICER). Some of the most innovative therapies are proving expensive compared to current standards of care, even if priced at levels consistent with cost-effectiveness review. Moreover, some of the most innovative therapies will only be administered to patients in concert with extensive diagnostic procedures, intensive or complex medical

services and sustained medical follow-up. This will generate additional costs. As it happens, the introduction of new and complex therapies such as the CAR-T cancer therapies is creating new issues for providers regarding billing procedures and adequate reimbursement for their costs.

The oncoming wave of new therapies creates a four-part challenge for health care: how to assure (1) timely access to therapies for those patients who need them; (2) overall costs of treatment that support initiation and adherence to therapy for all patients; (3)resulting impacts on spending that support sustainable health insurance coverage for all patients; and; (4) continued biopharma innovation.

NEHI found no easy answers in discussions among Massachusetts-based payers, providers, patients and biopharma firms. We did find support for engagement among all these stakeholders in the state that will identify more clearly where change is needed in public policy and in industry practices.

This white paper focuses on a wide array of new therapies we term "next generation therapies." They are most likely to be evaluated and managed by payers as "specialty pharmaceuticals" subject to such utilization management techniques as prior authorization and step therapy requirements. We focus on a very broad set of new and emerging therapies that share the following characteristics:

1. They employ an expanding number of scientific approaches to diagnose and treat disease, including gene therapy, cell therapy, immunotherapy and hybrids of these therapeutic modes;

2. They are approved by the FDA to meet significant unmet medical needs or as promising significant improvements in patients' health over current standards of care;

3. They are frequently approved through the FDA's Breakthrough Therapy, Rare Disease, and other priority review pathways, often after expedited reviews and clinical trials based on surrogate endpoints.

This last point is a major reason for encouraging engagement among payers and biopharma firms. The FDA is authorized to expedite review of new therapies based on clinical trials and endpoints it deems to be scientifically sound, and the agency recently reiterated that it stands behind the safety and efficacy of the drugs it approves. But it also acknowledges that the true effectiveness of therapies will only be revealed as they are utilized among "real world" patients, outside of the highly-controlled confines of clinical trials. Payers note that in real world use, "mileage may vary": highly-innovative drugs may prove more or less effective, depending on which patient receives them. Both patients and payers have an interest in determining "the right therapy for the right patient at the right time." Greater engagement may yield better approaches to the evaluation of new therapies, utilization management, coverage and payment.

Some Massachusetts-based payers, manufacturers and academic leaders are already at work devising new approaches, such as covering gene therapies administered on a one-time basis. This kind of collaboration needs to be both encouraged and expanded to encompass the much wider range of new treatments now emerging.

To this end our white paper makes two general recommendations based on discussions among NEHI member organizations.

First, biopharma organizations, providers, payers and patient communities in Massachusetts should join in a voluntary process of information sharing regarding next generation therapies now in development. Early information-sharing will reduce the chance that payers and providers are caught unaware of new therapies that could have a major impact on yearly health care budgets and insurance rates. It can also help payers and providers gauge the impact that next generation therapies will have on patient utilization and costs as the number of these therapies in use grows over time; the likelihood that competitive therapeutic options will arrive; and whether the availability of new diagnostics or advanced analytics will arrive to guide choices on "the right therapy for the right patient, at the right time." It may also encourage development of alternative policy on coverage and payment.

> Finding appropriate solutions begins with information sharing.

One form of information sharing is horizon scanning. Industry groups and government agencies around the world are familiar with horizon scanning methodologies that identify the potential impact of new therapies on patient care and health care spending. Our recommendation is to use a process that scans the drug development horizon for classes, new modes or categories of next generation therapies that treat diseases or conditions that are high priorities for payers, providers and pharmaceutical manufacturers alike. In NEHI stakeholder discussions, oncology and next generation cancer therapies emerged as a high priority. Understanding trends in next generation cancer treatment may not only lead to innovative solutions for coverage and payment for often-complex cancer treatment regimens but may also teach valuable lessons for new policy on coverage and payment of new therapies for non-cancer conditions.

Second, stakeholder groups should coalesce around a set of shared principles for assuring affordable patient access to next generation therapies at manageable cost to the health care system, all while sustaining the state's environment for continued innovation. These five principles stand out:

1. An agreement in principle to link payment for next generation therapies to a demonstration of durable health outcomes in real world medical practice.

2. An agreement in principle to expand the options available for reimbursement of physician-administered drugs, including:

    - Direct contracting between payers and biopharma manufacturers as an alternative to current buy-and-bill (cost-plus-mark-up) practices.

    - A commensurate commitment to models of fair reimbursement to providers for the administration of new and complex therapies.

3. Cross-sector collaboration to standardize and harmonize novel contract models in order to cut the complexity, time and expense of executing such contracts.

4. Greater engagement on measuring — and if possible, capturing in payment and finance models — the "all in" costs and benefits of new therapies. The highest and best use of next generation therapies may not be achieved within standard, one-year budgets supporting one-year insurance enrollments. These therapies may create medical spending offsets realized over a period of years; they may trigger new and ongoing medical costs as well. And they may create social benefits, such as reductions in social services otherwise needed by patients, raising the question as to whether health insurance programs should bear the total responsibility for covering treatment or whether government or other, non-insurance sources should support their use as well.

5. New engagement on innovations in reinsurance and risk adjustment so that insurers have a level competitive playing field that accommodates affordable coverage of next generation therapies.

The objective of information sharing among payers, providers, pharmaceutical manufacturers and patients in Massachusetts is not for the sake of sharing itself, but rather for providing a platform for collaborative decision-making. Our goals in this Next Generation Therapies project are to increase patient access to therapies at reasonable prices, ensure sustainable health care spending limits, provide affordable health insurance for all and foster a vibrant environment of medical and biopharmaceutical innovation in the Commonwealth.

> **The goal:** solutions that support patient access and affordability, sustainable overall health care spending, and an environment of medical and biopharma innovation in the Commonwealth.

Background

Next Generation Therapies

The year 2018 marked a watershed for medicine in Massachusetts. The Massachusetts Eye & Ear Infirmary became the first hospital to administer the newly approved gene therapy, Luxturna, for a form of inherited blindness. Boston hospitals were among the first in the country to administer the first CAR-T (chimeric antigen receptor-T cell) cancer therapies for leukemia patients. And pioneering research at the University of Massachusetts Medical School by Nobel prize winner Craig Mello came to fruition as Onpattro, the first drug based on gene suppression technology and approved to treat rare disease-causing peripheral nerve damage and other conditions.

Onpattro was among a record number of new pharmaceuticals approved by the FDA in 2018[1] and analysts predict that the FDA is likely to approve an increasing number of new pharmaceuticals over the decade. Many of these will be transformative treatments that herald significant improvements in patient health and, in some instances, outright cures. In this white paper, they are referred to as "next generation" therapies and they are defined by three major characteristics.

First, next generation therapies span an extremely wide range of approaches to treating disease, ranging from those that repair or replace faulty genes (gene therapy), suppress or alter the expression of genes (RNA interference therapies, for example), repair or replace cells (cell therapy), block the growth of disease-causing proteins , provoke the body's immune system to attack disease-bearing cells or viruses (immunotherapy), to therapies that combine more than one of these approaches (CAR-T therapy, for one). New and hybrid approaches will continue to emerge in the years ahead.

Since 2014, the FDA has approved an average of 43 new drugs per year, double the rate of a decade ago. Nearly 60% are approved as orphan drugs, and about 25% are cancer treatments.

Second, next generation therapies are apt to treat very small groups of patients. Many of the pioneering new therapies are approved by the FDA as treatments for rare or orphan diseases, and many rare disease treatments target only a small proportion of all patients diagnosed with the rare disease (about 10 percent of patients with orphan diseases for which therapies are available, according to IQVIA analysis.) [2] As science continues to pinpoint specific genetic or other molecular factors in disease, more and more newly-approved treatments will be for small subsets of patients. For example, an increasing number of new cancer medicines are approved by the FDA as rare disease treatments. However, there will be important exceptions to this rule, as some next generation therapies will be approved for diseases affecting larger numbers of patients, such as hemophilia, and even larger groups, such as patients with major depressive disorders.

Third, next generation therapies are more likely than not to be approved by the FDA after an expedited review. More than 40 percent of all drugs that are approved by the FDA are designated rare or orphan disease treatments, "breakthrough" therapies or both.[3] (See Exhibit A for the FDA's standards for award of

breakthrough therapy and other designations.) These designations generally allow new drugs to be tested in clinical trials that enroll fewer patients than conventional trials, in part reflecting the fact that these drugs will treat very small numbers of patients. These designations also allow for trials of shorter duration providing FDA deems the clinical trial to be scientifically sound.

In addition, breakthrough, rare and orphan drug designations allow the FDA to evaluate drugs based on their performance against so-called surrogate markers. Surrogate markers are typically results from images or laboratory tests (such as specific proteins identified in a blood sample) that have been linked to the presence or the progression of a disease. They do not represent more conventional or longstanding measures of disease treatment, such as measures of survival among patients treated with a cancer medicine. As a result, the results observed in a clinical trial for a next generation therapy may not be entirely replicated among patients treated in "real world" practice. The overall impact of the new drug on all patients can only be determined as "real world evidence" is collected over time.

Health Care Payers' Perspective

As therapies approved as therapeutic breakthroughs or as promising significant improvements in patient care, next generation therapies may represent a superior or sole treatment choice for patients when first introduced. As such payers may be obliged or even legally mandated to cover them.

When payers have therapies that are clinically comparable, they enjoy leverage in negotiations with pharmaceutical manufacturers, enabling them to bargain to give preferential treatment to a lower-priced pharmaceutical over a higher-priced alternative as long as it is a comparable treatment for patients. But payers have limited leverage when there is no alternative.

Although there may be little or no market competition to help constrain the initial prices of next generation therapies, payers may still subject use of the therapies to various management controls. They may require clinicians to seek and receive prior authorization before a given therapy can be used and reimbursed or may require patients and clinicians to attempt less costly alternatives first, as in "step" therapy. Even then, payers' options are limited as many next generation therapies will be recommended for cases in which "speed to therapy" is crucial, such as for patients with cancer or for children diagnosed with a genetically-related disease.

Payers face two other potential effects from the introduction of next generation therapies. First, there may be a budget impact as patients become newly eligible for a treatment that never existed before and the payer must accommodate a new source of demand. Budget impact is a special concern for Medicaid (MassHealth), the state's largest health insurance program, since Medicaid is paid for by single-year appropriations from the Legislature and Governor that then also draw on federal matching funds.

As use of a new therapy becomes routine, the cost becomes built into the payer's year-to-year cost projections, and thus contributes to the base level of insurance premiums that insurers expect to charge year to year. Next generation therapies may actually result in a decrease in a patient's health care needs and costs over time, leading to medical cost offsets, and may also decrease demand for other, non-medical services, yielding social

benefits. Yet insurance outlays are booked annually, premiums are regulated and set on a one-year basis, and patients frequently move from one source of health insurance coverage to another. Thus, there may be limited practical incentive for individual payers to invest upfront in a new therapy in expectation of recouping costs in later years.

Secondly, payers are concerned whether a highly novel, next generation therapy represents "the right therapy for the right patient at the right time." Once next generation therapies are in routine use, results among patients may not replicate results seen in highly controlled clinical trials. Next generation therapies are apt to be approved by the FDA based on expedited trials that may be smaller and of shorter duration than conventional trials and evaluated against surrogate endpoints.

More than 40 percent of new cancer therapies are now approved directly out of Phase II clinical trials (typically smaller trials used to establish a drug's fundamental efficacy) and not out of larger and longer Phase III trials.[4] Recently, the FDA reiterated that drugs approved from expedited trials are not to be considered experimental drugs, but fully approved for safe and effective use. However, MassHealth officials, in a Section 1115 Medicaid waiver request that was eventually denied by CMS, questioned the strength of evidence around drugs approved on an expedited basis.[5]

Since MassHealth was denied this waiver in August 2018, officials of the Baker Administration have called once again for "better tools" to control prices when drugs face little or no competition, which is likely when many next generation therapies are launched as first-in-class or superior treatments for significant unmet medical needs. [6]

While these efforts are still in an early stage, it is worth noting that there are at least three types of arbitration or compromise that could lead to "better tools."

- One is early dialogue and information-sharing among manufacturers and payers well before a new therapy is approved and launched. Recently, ICER considered formally offering consultation to pharmaceutical companies on the design of clinical trials to better demonstrate a new therapy's cost effectiveness. This is part of a larger effort to encourage early communication with manufacturers before ICER conducts a formal cost-effectiveness analysis (often called a "value assessment") on a newly launched pharmaceutical. [7] One recent example of a breakthrough therapy launched after early consultation with payers and ICER is the psoriasis treatment, Dupixent.[8]

- The second possibility is a move among some manufacturers of next generation therapies to reduce or eliminate charges to payers and patients in the event that a patient fails to respond to therapy, a contingency sometimes called a "no charge" or "money-back" guarantee. [9]

- And the third is the area of value-based contracts more generally; that is, payer-manufacturer contracts that link payments to specified patient outcomes or other goals as demonstrated in the real world use of the pharmaceutical.[10]

These early trends suggest areas for possible further engagement among patients, providers, the biopharma industry and payers in Massachusetts.

> **Trends to watch include:** early dialogue and information-sharing among pharmaceutical manufacturers and payers; "no charge" or "money back" contingencies in payment contracts; and value-based arrangements between payers and manufacturers.

At the same time, it must be noted that the state's commercial health plans must respond to multiple, different insurance markets, providing fully-insured insurance plans to individuals and to employer-sponsors of insurance, to Medicare beneficiaries (through Medicare Advantage plans), to Medicaid recipients (through Medicaid managed care), and to self-insured employers for whom they administer health insurance benefits. About 60 percent of all privately insured individuals in Massachusetts are insured under self-insured, employer-sponsored plans. Faced with this diverse set of insurance markets, the state's commercial health plans can and do take different approaches to the evaluation and coverage of new pharmaceuticals.[11]

The resulting variation in benefit design naturally results in variation in policies on access to therapies, such as "tiering" of drugs, and on patient-cost sharing, such as co-insurance, co-pay and deductible limits. Coverage and patient-cost sharing is also influenced by payers' negotiations with pharmaceutical manufacturers and their ability to get favorable pricing.[12]

In addition, as Attorney General Maura Healey's office demonstrated in its 2016 report on pharmaceutical spending trends, there is significant variation in the processes that the state's payers utilize to evaluate new drugs and make decisions on contracting. For example, there is variation in the use of outside vendors and services such as the services of prescription benefit managers (PBMs).

The single largest health insurer in the Commonwealth, MassHealth (Massachusetts Medicaid), is required by the federal government to cover all FDA-approved drugs but it too has the discretion to impose utilization controls on the use of some drugs. MassHealth has specifically identified new drugs that enter the market with little or no competition as a priority for new action to control costs.[13] MassHealth will have a major stake in new policies to cover and pay for next generation therapies, and not only because of cost control. As this paper describes, many next generation therapies are directed at curing or modifying genetically-related disease and as such they are most likely to be directed to the treatment of children. Medicaid is by far the largest insurer of children in Massachusetts and in other states throughout the U.S.

Creating common approaches to coverage of next generation therapies in Massachusetts will thus require stakeholders to work with, or work around, this extensive degree of variation in coverage, benefit design and the finances of public and private payers. Writing in the journal Health Affairs, a team associated with Harvard Pilgrim Health Care and the Harvard Pilgrim Health Care Institute observed that " … the substantial contribution of medications, particularly specialty medications, to total health care spending requires systemwide, coordinated strategies by all stakeholders." [14]

Health Care Providers' Perspective

Next generation therapies create new treatment options for patients and clinicians and will expand the services offered by hospital systems and physician practices in Massachusetts. The impact will likely be inconsistent: in some cases, next generation therapies will only be administered in facilities that are qualified to administer the therapy under FDA standards. For example, the few gene therapies and CAR-T therapies approved by the FDA so far are administered in only a few Massachusetts hospitals, all of them major academic medical centers.

Next generation therapies such as CAR-T and gene therapies are already creating new financial challenges for hospitals and physicians. Providers have found that existing codes for billing the Medicare program and other insurers are not adequate to cover the new procedures required by these new treatments.[15, 16] Moreover, Medicare and other health insurance programs typically reimburse the purchase of physician-administered pharmaceuticals (including drugs administered in a hospital) after the physician or hospital has bought the drugs directly from manufacturers. Providers are reimbursed for the cost of the pharmaceutical (typically set at a pre-negotiated or benchmark price), plus a mark-up. (Medicare currently allows for a 4.3 percent mark-up to providers). Under this "buy-and-bill" approach, providers carry the cost of pharmaceuticals until they are used in a patient's treatment, at which point insurers are billed. With the emergence of new and often complex new therapies, providers must now weigh the costs of carrying high-cost next generation therapies as inventory, in addition to the costs of investing in new equipment and new staff training that may be necessary to administer the new treatments. This new burden has made some providers receptive to alternatives to the buy-and-bill reimbursement system. Harvard Pilgrim Health Care and Spark Therapeutics are utilizing this approach for the reimbursement of Luxturna, the first FDA-approved gene therapy.[17]

Next generation therapies such as CAR-T and gene therapies are already creating new financial challenges for hospitals and physicians.

This kind of alternative payment model - using direct contracts between health care payers and pharmaceutical manufacturers - may represent an efficient and pragmatic alternative for the reimbursement of other next generation therapies. Indeed, there is a movement among payers throughout the country to either eliminate or cut back on the use of the traditional buy-and-bill contracts. The Trump Administration recently proposed just such a cutback for the Medicare Part B program, which reimburses for physician-administered drugs.[18] Payers charge that reimbursements based on a mark-up to the provider create an incentive for providers to over-utilize high cost drugs. But many providers reject that assertion and point out that revenue from mark-ups often serves to subsidize under-compensated services to patients, such as patient care coordination.

Patients' Perspectives

Patients are the ultimate beneficiaries of next generation therapies but they are also caught in the middle of the discussion over how to evaluate, cover and reimburse for these new treatments, and are personally affected by the issues of access to new therapies and their costs. Although patients share an interest with drug

manufacturers in gaining rapid access to new therapies, they also share with payers an interest in affordability of therapy and in real world evidence of effectiveness.

Patient demand for access to next generation therapies is likely to be very high, since these new therapies hold out the potential for dramatic improvements in health outcomes, and in some cases cures, for diseases in which few if any treatment options have been available in the past. Patients in Massachusetts may be more likely than most to be aware of these new treatment options because of the size and sophistication of the state's academic health centers and the state's growing biopharmaceutical industry. A 2015 Battelle Institute study ranked Massachusetts, the 15th largest state in terms of population, as tenth in the nation for the number of active, industry-sponsored clinical trials underway in the state, with more than 33,000 people enrolled in clinical trials. [19] Although many next generation therapies may be effective for very small patient populations, when they are first approved they may trigger a one-time surge in demand as previously untreated or under-treated patients seek care. The result may create the large budget impact on payers described above.

> Patients are the ultimate beneficiaries of next generation therapies, but they are caught in the middle of the discussion over evaluation, coverage and reimbursement of therapies.

In many cases, rapid access ("speed to therapy") will be critical for patients. As noted previously, many next generation therapies will target genetic conditions that may best be treated in children soon after diagnosis. This reality could create a tension with existing practices and policies, in that new therapies for cancer among children and adults are often approved initially as third or fourth-line treatment, at a point when prior treatments have failed.

At the same time, the high prices of some next generation therapies may prompt payers to increase out-of-pocket costs specifically for patients who use them. Cost-sharing obligations, including co-payments, co-insurance and deductibles, have risen steadily over the last decade, particularly among patients who buy individual or small group insurance through the state's insurance marketplace, the Commonwealth Health Connector. Higher cost-sharing raises concerns that patients will choose to decline or discontinue treatment, or will incur unsustainable personal debt, a result that can also cause uncollectable debt for health care providers. [20]

As a standard practice, biopharmaceutical manufacturers offer assistance to patients in financial need, although these programs are subject to of continuing controversy. Patient assistance is available in three forms. Assistance may be provided directly by the manufacturer in accordance with the manufacturer's own rules; for example, free drugs for patients in serious financial need. Financial aid may also be available from patient assistance charities that are subject to regulation by the Inspector General of the U.S. Department of Health and Human Services under the federal Anti-Kickback Statute; the charity must provide funds (including manufacturer-provided funds) without steering patients towards use of specific drugs.

A third form of co-pay assistance is provided through discount coupons offered by manufacturers. Massachusetts currently allows use of coupons only for drugs for which there is no generic alternative; next generation therapies will typically have no generic alternatives until years after approval. The current Massachusetts law on use of coupons is set to expire on December 31, 2019 and will be subject to re-authorization by the Legislature.[21]

With Growing Diversity of Next Generation Therapies — No Single Solution for Payment, Coverage and Finance

As noted above, next generation therapies encompass an extraordinarily diverse set of new biological approaches to treating disease and they are likely to become even more diverse over time. Some therapies may be one-time, so-called "one-and-done" treatments but others will be administered on a chronic basis indefinitely or for a lifetime. The growing diversity of next generation therapies suggests that there will be no one-size-fits-all payment model, provider care modelor health insurance coverage policy that applies to all the different circumstances of next generation therapies.

> New policy is needed to address next generation therapies in all their widely differing characteristics.

New policies in all these areas must be tailored to meet differing demands. To accomplish this, the state's health care stakeholders should have a shared understanding of the factors that differentiate one next generation therapy from another. There are at least ten differentiating factors that shape how patients, providers, payers and manufacturers devise coverage and payment solutions for next generation therapies.

1. **Dosage:** How often will a patient receive a therapy? Is it administered just once ("one-and-done") or is it administered on a recurring (chronic) basis?

2. **Route of Administration and Site of Service:** How and where is the therapy administered to the patient? Will it be administered via a pill, injected or infused? Will the site-of-service for the therapy be a hospital, an outpatient clinic or the patient's home?

3. **Size of Patient Population Eligible for Treatment:** How large is the patient demand for the therapy and how many patients are likely to need it? Does the treatment address a rare or a highly prevalent condition, or something in between?

4. **Off-label Use:** How likely is it that the therapy will be used off-label (legally prescribed by a licensed physician but for uses or for patients not explicitly approved by the FDA)?

5. **Diagnostics:** Are there diagnostic tests available that will indicate which patients should receive the therapy and which should not, or which patients are most likely to respond well to treatment?

6. **Strength of Evidence:** How strong is the available evidence on whether the therapy will be as effective among "real world" patients as it was among patients in clinical trials? How strong is the evidence that the benefits of the therapy, as experienced by patients, will last?

7. **Competitive Options for Treatment:** Are there alternative therapies available? Are they comparably effective and how likely is it that new, competitive choices will become available, and how soon?

8. **Outcomes Data:** Can good outcomes data provide definitive answers to whether the therapy is as effective as promised? Is it feasible to collect outcomes data on patients from the best sources, such as health insurance claims data, clinical data or pharmacy data?

9. **Attribution of Health Effects:** If good data is available, is it possible to attribute a patient's health outcomes to the effectiveness of the therapy, particularly in cases where the therapy is used in combination or in a sequence with other therapies (as is often the case in cancer treatment)?

10. **Cost Offsets and Impact on Other Spending:** Can medical cost savings be attributed to use of the therapy? If so, over what period of time? Does the therapy offset other costs (such as costs of social services)? Conversely, will use of the therapy be paid for by reducing spending for other priorities?

Building Blocks for Solutions: Public Policy and Industry Practices

Discussions convened by NEHI suggest that if payers, providers, and manufacturers agree on one thing regarding next generation therapies, it is wariness about the cost and the administrative burden of customizing new models of coverage and payment for next generation therapies. All stakeholders are grappling with the challenge of finding the most efficient way to develop cost-effective solutions that will assure patient access, affordability, sustainable cost for health insurance, while sustaining innovation as well.

Moreover, effective solutions cannot be achieved solely by cooperation among stakeholders at the state level, within Massachusetts alone. Designing and implementing new solutions will require changes in federal and state policy. For example, payer-manufacturer contracts for the purchase of pharmaceuticals that link payment to a demonstration of real world patient outcomes are constrained directly by provisions of the federal Anti-Kickback Statute and indirectly by provisions of the Medicaid Drug Rebate program. (NEHI examined these constraints in detail in two white papers released in 2017, "Rewarding Results: Moving Forward with Value-Based Contracting," and "Value-Based Contracting for Oncology Drugs.")[22]

Nevertheless, there are still at least five areas for further development of public policy and industry practice that could lead to better solutions that accommodate adoption of next generation therapies.

Value assessment: Health plans and prescription benefit managers throughout the country are beginning to reference, if not commission, cost effectiveness analyses of new therapies. Findings from these analyses are used to support payers' negotiating positions with pharmaceutical manufacturers. At least one state Medicaid program is also using cost effectiveness analyses, also known as value assessments that utilize studies performed by ICER.[23, 24] While value assessment remains a controversial topic among manufacturers and some patient groups, it seems likely to play a continuing role in payers' negotiation strategies.

Stakeholders in NEHI's discussions generally agreed that voluntary initiatives to promote greater information sharing regarding next generation therapies in the drug development pipeline would help payers, providers and patient communities assess the potential implications of the new therapies for patient access and affordability, and help shape good use of value assessment as well as appropriate coverage and payment policy.

Value-based contracts: While standard payer-manufacturer contracts for purchase of pharmaceuticals are based on negotiated discounts and rebates tied to the volume of drugs purchased, value-based contracts tie some or all of payment to measures of successful treatment, such as proof that a patient has responded successfully to treatment. This alternative form of contracting can include a "money back guarantee" or "no charge" contingency that reduces or eliminates payments for unsuccessful therapies. This is an attractive option for payers when there is uncertainty over how "real world" patients will respond to a newly approved therapy, as may be the case with some next generation therapies.

It appears that payers and manufacturers are executing an increasing number of value-based contracts despite the regulatory and operational barriers cited above (see Endnote 14). Many of these contracts remain confidential, with few details available to the public. In Massachusetts, Harvard Pilgrim Health Care acknowledges executing over 15 value-based contracts since 2015.

Payment-over-time: An entirely new concept in payment for pharmaceuticals is payments made over time. Payment-over-time models would be most pertinent for curative therapies, or therapies creating significant, long-lasting benefits for patients, and when payers agree that the therapy, while valuable, will cost too much to be absorbed in one payment. A payment-over-time approach has been suggested by developers of potentially curative gene therapies and it is a major target of payers and biopharma firms engaged in MIT's FOCUS (Financing and Reimbursement of Cures in the U.S.) initiative, a project of the MIT NewDigs program. [25, 26]

In theory, payment-over-time models would allow a payer to cushion the budget impact resulting from covering a therapy with a high, one-time cost. Payments-over-time could also be financed by pooling payments from multiple payers, so that patients who switch their health insurance coverage would be covered continuously and multiple payers could share the expense and administrative burden of providing coverage to patients who "churn" among them over time. Payment-over-time models can be seen as a version of value-based contracting, in that the period payments made under these models would likely be contingent upon continued demonstration that a patient is responding successfully to treatment or achieving specific, pre-negotiated treatment goals.

Reinsurance: Commercial reinsurance companies typically provide reinsurance policies that enable health insurers and other health care payers to absorb unexpected costs, including an influx of insurance subscribers with high-cost medical conditions or unexpected costs created when new medical services or therapies become available and trigger an unexpected demand. Reinsurance covers these costs on a one-time basis; claims that are predictable from one year to the next are not reinsured and the costs are absorbed within the payers' year-to-year budget and within insurance premiums.

The oncoming stream of next generation therapies is already compelling some biopharma manufacturers to consider innovative uses of reinsurance and may compel similar thinking among payers and providers in Massachusetts in coming years.[27] Reinsurance, or a reinsurance-like financial backstop for health insurers, would cushion the budget impact that might be caused by a surge of new costs as a next generation therapy enters the market. Recently, several states have created publicly-subsidized reinsurance pools specifically to stabilize insurance premiums charged by health plans marketed through the state health insurance exchanges authorized by the Affordable Care Act.[28] The reinsurance pools cushion the financial impact caused by patients with serious medical needs when they first sign up or re-enroll in Affordable Care Act coverage. Patients eligible for treatment with next generation therapies may or may not be patients typically considered as high-cost, chronically-ill patients but they are patients with serious and previously untreated, pre-existing medical conditions such as genetic disorders. A reinsurance-type approach to cushioning costs, or a model similar in concept to the Commonwealth's special education circuit breaker payments to local school districts, may prove to be useful in assuring access and affordability for next generation therapies.

Risk adjustment: Where reinsurance cushions payers from the impact of unpredicted risks, risk adjustment protects payers from adverse selection, or an influx of costs due to coverage of patients with predictable risk, such as pre-existing medical conditions. Risk adjustment is applied throughout public sector health care programs, including Medicare Advantage, Medicaid managed care plans and health plans offered through the Affordable Care Act exchanges, including the Massachusetts Health Connector. Risk adjustments direct higher subsidies to plans that cover patients with higher medical needs. Many next generation therapies are targeted at medical conditions that are pre-existing. As genetic testing and molecular diagnostics expand in future years, a greater number of patients are likely to be diagnosed with pre-existing health risks and pre-existing medical conditions.

Recommendations

Next generation therapies will arrive in increasing numbers over the next few years as scientific advances create more avenues to diagnose and treat unmet medical needs and as drug developers perfect methods to manufacture and deliver complex new therapies. Next generation therapies will differ greatly in key attributes such as dosage, the site of administration and the durability of their health benefits. Thus it is unlikely that a one-size-fits-all approach to coverage and payment will assure patient access to and affordability of these therapies, while at the same time yielding costs that maintain sustainable health care insurance for all and maintain continued biopharma innovation.

Health care stakeholders in Massachusetts should work systematically to address the multiple challenges to coverage and payment that are now emerging with the launch of next generation therapies. Two steps can help start this process:

INFORMATION SHARING

While payers and providers have existing methods and procedures to assess potential drug approvals and drug launches, adding voluntary information sharing regarding emerging groups of therapies would serve three purposes:

1. Reduce the chance that payers, providers, and patients will be caught unaware when a new class or mode of therapy results in new drug launches that may be challenging for any reason: price, total costs of care, questions of real world effectiveness, and so on.

2. Help all stakeholders gauge the impact on patient health and on health care spending if, as expected, an increasing number of highly-personalized and highly-advanced new therapies come into use over the next several years.

3. Help stakeholders identify specifically where changes in public policy and in coverage and payment practices will be needed to accommodate the adoption of next generation therapies.

One form of information sharing is horizon scanning. Industry groups and government agencies around the world are familiar with horizon scanning methodologies that identify the potential impact of new therapies on patient care and health care spending. Our recommendation is to use a process that scans the drug development horizon for classes, new modes or categories of next generation therapies that treat diseases or conditions that are high priorities for payers, providers and pharmaceutical manufacturers alike. In NEHI stakeholder discussions, oncology and next generation cancer therapies emerged as a high priority. Understanding trends in next generation cancer treatment may not only lead to innovative solutions for coverage and payment for often-complex cancer treatment regimens but may also teach valuable lessons for new policy on coverage and payment of new therapies for non-cancer conditions.

COLLABORATION

Horizon scans should be guided by a shared set of principles for collaboration among payers, providers, and the biopharma sector in Massachusetts. Ideally, stakeholders could adopt these principles for a wider set of collaborations to ensure appropriate evaluation, coverage and payment for next generation therapies. Stakeholders in NEHI's discussions suggested the following as key principles:

1 **Payment for durability of health outcomes**

In principle, stakeholders should strive to link payments for next generation therapies to the durability of the health outcomes realized by patients, if the long-term durability of the treatment is in question.

2 **Evaluation, coverage and payment that recognize the "all in" costs and benefits of next generation therapies**

Payers, providers, patient groups and the biopharma sector should engage seriously in finding models of evaluation, coverage and payment that recognize cost offsets generated by use of a next generation therapy, as well as costs that may be increased or spending that may be reduced or crowded-out elsewhere to accommodate coverage of a next generation therapy. They should address the mismatch that may occur when use of new therapies creates upfront costs but benefits accrue over a much longer time period.[29] New models are needed to encourage the highest-value use of next generation therapies and all health care services.

3 **More options for reimbursement of physician-administered drugs**

Payers should have the option to purchase next generation therapies directly from pharmaceutical manufacturers and to execute payment contracts directly with manufacturers, especially when direct contracting will reduce complexity and lower costs for patients, payers and providers alike. However, since direct contracting between payers and manufacturers could remove a source of revenue from providers that may support needed patient services, payers should make a commensurate commitment to models of fair reimbursement to providers, particularly for next generation therapies that require providers to make new investments in facilities and personnel.

4 **Standardization of novel contract models**

Lack of consensus on measures of treatment durability has proven a barrier to implementing outcomes-based payments for new therapies. This barrier is one of a larger set of obstacles cited by payers and manufacturers, who assert that existing value-based payment contracts are one-offs and not based on standard templates that might cut the time and expense of negotiating and executing contracts. Thus, standardizing formats and approaches for novel contracts should be a goal of collaboration among payers, providers and manufacturers.

5 **New thinking on insurance underwriting and regulation**

Increasing adoption of next generation therapies may impose unpredicted, one-time cost surges on payers but also increase the number of patients with previously untreatable conditions who will now qualify for a next generation therapy. The horizon scanning process called for above should encourage payers, providers and the biopharma sector to consider new forms of reinsurance and, for risk-adjusted health insurance plans, new and appropriate forms of risk adjustment that will ensure a level competitive playing field for all health insurers and other payers.

Conclusion

Next generation therapies represent potential life-saving cures for some and life-changing improvements in quality of life for others. For some patients, next generation therapies will fail or fall short, while for others they will become an interim step towards newer therapies yet to come.

Health care policy in Massachusetts should be prepared to address these differences through innovative coverage and payment policies that provide access to patients who need therapy but compensate therapy based on its real world value. The challenge is not unlike the challenge the proponents of the Triple Aim have made to U.S. health policy over the last decade: the challenge of improving health outcomes for patients and improving their experience with health care while harnessing innovation to control costs and achieving a sustainable level of overall health care spending.

In the case of next generation therapies in Massachusetts, we need to work together systematically to assure patient access to, and affordability of, next generation therapies while supporting sustainable health care costs and affordable health insurance coverage for all the state's residents and maintaining the state's world-class environment for biopharmaceutical innovation.

Exhibit A

FDA Approval Pathways and Standards of Evidence

FDA Approval Pathway	Standard	Incentive
Accelerated Approval	Product fills an unmet medical need for a serious condition based on performance against surrogate endpoints.	Approval based on surrogate endpoints.
Priority Review	Significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.	FDA review in 6 months.
Fast Track	Product demonstrates advantage over available therapy (superior effectiveness, reduced side effects, improved diagnosis, decreased toxicity); or product addresses emerging or anticipated public health need.	Reduced duration of clinical trials.
Breakthrough Therapy	Substantial improvement over available therapy based on performance against clinically significant endpoints, including surrogate endpoints.	Reduced duration of clinical trials.
Regenerative Medicine / Advanced Therapy (RMAT)	Cell and tissue therapies that: (a) treat, modify, reverse, or cure a serious condition, and (b) show preliminary clinical evidence that the therapy has potential to address unmet medical needs for such condition, are made eligible for other FDA expedited approvals.	Increased meetings with FDA staff, possible designation for other expedited pathways.
Orphan Drug	Products intended for safe, effective treatment of conditions affecting fewer than 200,000 persons in the U.S.	7-year market exclusivity, tax credits, FDA fees waived; FDA assistance during development.

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This report would not have been possible without the support of the NEHI team including:
Valerie Fleishman, *Executive Director*
Amanda Mehlman, *Manager of External Relations*
NEHI is also grateful to **Nick King** for his contributions.

Support

Funding for this work was provided by **MassBio** with additional support from:
Blue Cross Blue Shield of Massachusetts, Harvard Pilgrim Health Care, and Tufts Health Plan.

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

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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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