Pathways, Affordability, and Utilization for Precision Therapies

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> A good intention, with a bad approach, often leads to a poor result.
>
> *Thomas Edison*

In patient-centered care, there remains stakeholder disconnect, middleman distractions, and misalignment with siloed disengagement; this is illustrated by continued patient or provider access problems and manufacturer production and distribution reengineering, including value-based contracting approaches. This leaves employers and other commercial plans or administrators seeking solutions as they face emerging risks from precision therapies.

In this context, the "good intentions" of supporting plan members and delivering clinically appropriate, cost-effective therapies with ever-improving outcomes are increasingly falling short. Meanwhile, numerous public lawsuits and research have exposed the "bad approach" and "poor results" in pharmacy benefit offerings, pricing, or claims.[1-5]

Existing and proposed conventional solutions and structural offerings promote—rather than mitigate—barriers to patient access for novel, and potentially curative, precision cell and gene therapies (CAGTs). Despite manufacturer attempts, financial or insurance solutions have not been comprehensive enough to thoroughly cover these emerging therapies. The impact on the market was confirmed at the January 2023 and January 2024 annual JPMorgan Healthcare Conferences. For example, coverage from the 2023 conference described small deal announcements in the pharmaceutical industry, among other insights like patent cliffs and lost revenue, which highlighted that commercialization for these precision therapies is not going well.[6]

CLINICAL PATHWAYS AND PRECISION THERAPIES

Tufts Medicine has estimated the US pipeline of new precision therapies to be in the range of 54-74 products with indication approvals by 2032.[7] By 2027, an estimated 41 conditions will be treated with CAGTs based on the existing product indication approvals and the average new annual approval rate for the next 4 years (**Table**). The population treated by CAGT would peak around that time and then decline as the overall number of untreated patients decreases; by 2032, around 105,000 patients or more per year are expected to be treated with CAGT.[7]

Given the rapid pace of research and development before, during, and after the pandemic, the clinical marketplace is facing an inflection point of new therapies for which limited efficacy information is available. Orphan drug and rapid approval protocols used before and during the pandemic by the US Food and Drug Administration (FDA) have created an unusual therapy marketplace where nominal human testing has been done at the time of therapy approval, bolstered by requirements for risk evaluation and mitigation strategies or post-marketing surveillance that can run from a few years up to 15 years.

A shortfall in data required to promulgate a pathway that remains up to date will likely impact future health policy decision tools around value-based care and will make incentivizing higher value care difficult. This lack of therapy development data limits the ability to document potential care cost saving opportunities. All of this has led to calls for reexamining the extent of clinical pathway effectiveness to achieve lower care costs.[8]

On top of this, the many terms used to describe precision therapies only add to the dilemma. These interchangeable terms have created confusion or misinterpretation within and outside the clinical care arena. Starting around 2010, the term "theranostics" was popular to identify laboratory testing techniques related to improved therapy decision-making.[9] Since 2020, that definition has evolved to include diagnostics, nanomedicine, molecular imaging, and molecular therapy.[10]

In a summary from the US National Library of Medicine, they write that "according to the [US] National Research Council, personalized medicine is an older term with a meaning similar to precision medicine. However, there was concern that the word 'personalized' could be misinterpreted to imply that treatments and preventions are being developed uniquely for each individual. The Council therefore preferred the term precision medicine to personalized medicine."[11,12]

Similarly, the US National Human Genome Research Institute states, "Precision medicine (generally considered analogous to personalized medicine or individualized medicine) is an innovative approach that uses information about an individual's

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Table. Examples of Precision Therapies, 2017-2023

Name	Manufacturer	Indication(s)
Kymriah (tisagenlecleucel)	Novartis	R/R FL, R/R DLBCL, R/R ALL
Zolgensma (onasemnogene abeparvovec-xioi)	Novartis	SMA T1
Tecartus (brexucabtagene autoleucel)	Kite Pharma	R/R MCL, ALL
Abecma (idecabtagene vicleucel)	Bristol-Myers Squibb	R/R MM
Carvykti (ciltacabtagene autoleucel)	Janssen Biotech, Inc.	R/R MM
Hemgenix (etranacogene dezaparvovec-drlb)	CSL Behring	Hemophilia B
Elevidys (delandistrogene moxeparvovec-rokl)	Sarepta Therapeutics	DMS
Roctavian (valoctocogene roxaparvovec-rvox)	BioMarin	Hemophilia A
Casgevy (exagamglogene autotemcel)	Vertex	SCD, TDT
Lyfgenia (lovotibeglogene autotemcel)	bluebird bio	SCD

Abbreviations: ALL, acute lymphoblastic leukemia; DMS, Duchenne muscular dystrophy; R/R ALL, relapsed/refractory ALL; R/R DLBCL, relapsed/refractory diffuse large B-cell lymphoma; R/R FL, relapsed/refractory follicular lymphoma; R/R MCL, relapsed/refractory mantel cell lymphoma; R/R MM, relapsed/refractory multiple myeloma; SCD, sickle cell disease; SMA T1, spinal muscular atrophy type 1; TDT, transfusion-dependent β-thalassemia.

genomic, environmental and lifestyle information to guide decisions related to their medical management. The goal of precision medicine is to provide a more precise approach for the prevention, diagnosis and treatment of disease."[13] This definition is similar to the one used by the US National Cancer Institute.

These areas illuminate the challenges facing clinical care management in the next decade. Some of the key action items for stakeholders are creating consistent terminology; testing clinical parameter limitations that direct action to take or not; improving data collection, analyses, and interpretation; integrating tools for translational medicine; developing up-to-date care pathways, branching, and indication specificity; and estimating an accurate number of treatable patients.

FINANCIAL RISK AND ENHANCED CARE MANAGEMENT BARRIERS

A 2024 *Reuters* analysis found that the median annual price of new drugs introduced in the US climbed 35% from $222,000 in 2022 to $300,000 in 2023, driven in part by the high cost of treatments for rare disorders[14]; however, the price of top precision therapies ranged from $2.2 million to $3.2 million annually. Such catastrophic claims for reimbursement represent a significant sustainability issue for commercial insurance. For example, the 8 non-oncology gene therapies approved through mid-2023 had prices ranging from $630,000 to $3.5 million.[15]

Since 2020, CAGT approvals represent a larger portion of overall FDA approvals. While they are an exciting advancement in patient care, their development is also greatly outpacing reimbursement systems and government pricing contracts. For manufacturers of these therapies, insurers and their uncertainty in this space is one of the largest challenges when navigating pricing or reimbursement. Compared with conventional biopharmaceuticals, CAGTs are still unique and relatively untested because each therapy is based on an individual's genome.[16]

According to IQVIA, "Breakthrough therapies launched over the past decade for multiple diseases are re-shaping patient care in many areas and the outlook for medicines use—and the related spending—through 2028 is higher than prior forecasts as more novel drugs become available."[17] Later in the same report, they state, "The updated outlook for the US market, using estimated net prices, is being raised by 3 percentage points to 2%-5% CAGR [compound annual growth rate] through 2028, reflecting higher recent growth and expected further increased patient use of higher value therapies." They credit this mostly to "patients getting treated with better medicines, especially in immunology, endocrinology, and oncology," and mention that "global spending on medicine using list prices grew by 35% over the past 5 years and is forecast to increase by 38% through 2028."

Adding to issues of uncertainty, the Institute for Clinical and Economic Review, among others in the health economics field, struggle with analysis methods around value and pricing for novel therapies. They note that standard-of-care price distortions also warp value-based pricing of potentially curative treatments.[18]

NEW APPROACHES REQUIRED TO SOLVE UNCERTAINTIES

Previous efforts to amortize, spread risk, or apply performance-based payment have not been sustainable in solving precision therapy claims. Continued use of outcome-based contracts, warranties, or patient insurance coverage laser (exclusion)

modifications from stop-loss carriers are tail-end responses that do not address the complex patient in any insured population. Such complexity requires sophisticated resources and clinical knowledge to identify medical needs and match those patients to available approved precision therapy. Optimizing the use of all provider resources, including care pathways, can help identify such patients and better predict risk exposure. Conventional solutions do not address how manufacturers commercialize these therapies or the ignominious impact of high out-of-pocket costs on patients today due to unknown risk exposure.

A comprehensive approach is required that engages the patient appropriately, applies the financial solution required, and solidifies the patient–provider relationship based on manufacturer innovations over a longer time horizon. The goal should be to bring together all these pieces under a single independent conductor, who, from a greater vantage point, could evaluate and then oversee how best to connect the pieces and players to ensure predictable, longer-term operational outcomes and sustainable success—both for clinical utilization and financial affordability.

SUMMARY

Patients, providers, employer plans or insurers, and manufacturers deserve a better approach to precision therapies. Facilitating effective clinical and financial risk management via a new managed approach would align key stakeholder interests with patient needs. A customizable care pathway may be the solution to manage this for the entire patient journey. Furthermore, leveraging pathways makes patient care, education, engagement, and adherence transportable beyond the current payer focused on the annual risk of care.

The anticipated and actual emergence of precision therapies has reached the point where change in managing the financial risk of these small populations needs to happen. An exponential increase in marketed products combined with the pipeline of precision products moving toward FDA approval represent a serious challenge to the health care status quo. In both clinical care and financial risk management, the application of alternate methods can be applied to address both the rapid market growth and the economic impacts for all concerned.

What the marketplace needs first are movers and risk experts to change the status quo for small patient populations where precision therapies are an obvious fit. Traditional and contemporary health care management strategies have not solved for the inequities that are rapidly emerging around CAGTs for patients, providers, and plan sponsors. Despite the general desire to make precision therapies widely available, similar to nonspecialty prescription products, rushing the process poses great risk to both patients and plan sponsors. First, the underlying issues outlined here must be effectively addressed for these novel therapies. Continuing on the traditional path of siloed vendors, management, and cost is no longer a sustainable option. In particular, commercial insurance plans have the greatest potential to innovate and deliver the means and methods to make CAGTs more widely available.

Reader questions, feedback, and suggestions are always welcome and can be directed to JCPEditors@hmpglobal.com. ◆

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