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AN INDUSTRY BRIEF FROM INSTITUTE@PRECISION

Securing Access & Reimbursement for Rare Disease Therapies

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> A rare disease is a condition that affets fewer than 200,000 people in the Untited States.

Approximately 95% of these conditions currently have no approved therapy. For those that do, the median cost of treatment at market entry exceeds $200,000 per year. Cumulatively, over 10,000 rare diseases have been identified to date, affecting more than 30 million Americans and making these conditions an area of focus for drug developers. As the number of rare disease therapies in the pipeline and on the market increases, there is concern among patients, providers, policymakers, and payers about their affordability, access, and value.

Historically, the high price tags of rare disease therapies may have been considered manageable by payers due to the small number of patients who would need them, particularly when compared to the levels of lifelong care required in the absence of available treatment. More than half of the novel therapeutics approved in 2024 were for rare diseases, continuing a consistently upward trajectory in the number of orphan drug approvals over the past 2 decades. From a payer perspective, the potential economic burden associated with rare diseases is growing rapidly. Consequently, payers are taking a closer look at disease prevalence in reimbursement determinations and a stricter stance on the clinical data limitations that are often associated with rare disease treatments.

Trends in rare disease management

To manage the high costs typically associated with rare diseases, payers are increasingly applying traditional utilization management (UM) programs to rare diseases. Precision AQ conducted a survey in 2024 of access decision makers to determine the current and future implementation of UM programs specific to rare/orphan diseases. The majority of respondents stated they apply confirmation of diagnosis, quantity limits, and prescriber requirements to all rare and orphan disease products.

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Understanding today's trends in rare disease management

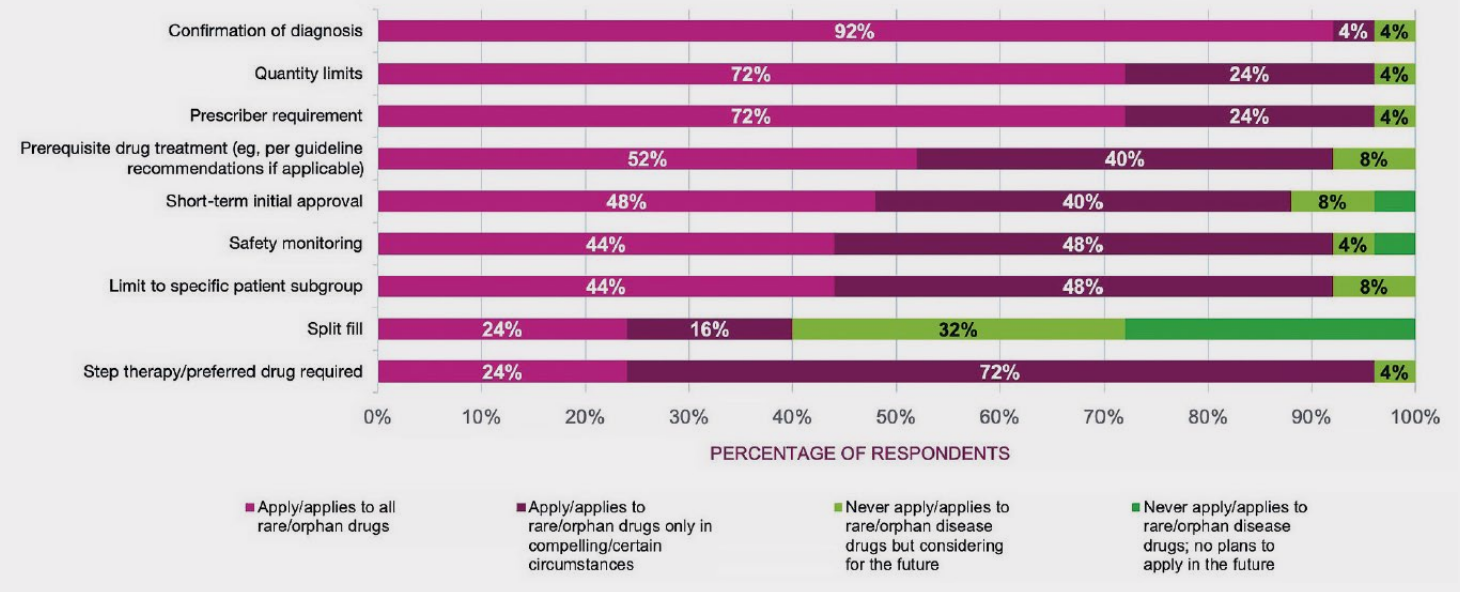

Figure 1. Utilization Management (UM) Applied to Rare Disease Drugs

Payers are evolving their approaches to formulary and reimbursement decisions for rare disease drugs. At Precision AQ, we understand the access landscape, including both government and commercial payers, and have identified 5 trends that developers of rare disease therapies need to be aware of:

1. Using case management programs

Increasingly, payers are playing an active role in rare disease management programs in which case managers work collaboratively with providers, patients, and caregivers to navigate the complexities of rare disease treatment and ensure the most appropriate plan of care. In addition to enabling proactive identification of gaps in care, case management programs allow for provision of meaningful interventions, within both the health care system and the community, that focus on holistic patient care, including education, comorbidity management, and support for non-medical needs.

2. Bringing in the experts

Payers have traditionally relied on key opinion leaders (KOLs) to provide expertise in directing the formulary decision and policy development process. Prior authorization reviews are performed by a pharmacist within a payer who is not necessarily a specialist in either the rare disease or the therapy being prescribed. Payers are increasingly utilizing KOLs to perform these reviews and assist in providing input on coverage determinations.

3. Adopting value-based contracts and alternative payment models

Across the biopharmaceutical industry, there has been increasing emphasis on enhancing the value of care while effectively managing cost. Value-based contracts (VBCs) are agreements in which payment is tied to predetermined, mutually agreed-upon terms that are based on clinical circumstances, patient outcomes, or other specified measures that reflect the appropriateness and efficacy of the treatment rendered. In some cases, this may include patient-reported outcomes (PROs). According to a recent survey, nearly one-third of payers are currently tracking PROs of activities of daily living, pain, and symptom burden for patients with rare diseases.

The success of VBCs relies on a deep understanding of the relevant endpoints and clinically meaningful outcomes of the rare disease, along with the appropriate evidence-generation activities to support value defined through a patient-centered lens. In rare diseases, understanding and quantifying the benefits of a drug can be challenging due to factors inherent to these conditions, including:

- Disease heterogeneity. Rare diseases often have varying pathologies, progression rates, and impacts on quality of life. Thus, it is difficult to establish a one-size-fits-all approach to evaluating the benefit or value of a treatment.
- Lack of historical and natural history data. This scarcity of baseline data hinders the ability to compare the efficacy of new treatments against the progression of the disease in the absence of intervention.
- Use of non-traditional endpoints. The benefits of rare disease drugs often extend beyond traditional clinical endpoints, such as morbidity and mortality, to include improvements in quality of life, reduction in caregiver burden, and other patient-reported outcomes. Quantifying these benefits may require complex, condition-specific measurement tools and methodologies, which may not be standardized, validated, or universally accepted.

Payers have also been exploring alternative payment models, such as pay for response or pay over time, to address the challenges associated with cost, especially for one-time, high-cost treatments such as gene therapies that may have a binary outcome.

4. Limiting the prescribing and administering of therapy to certain Centers of Excellence (COEs)

As part of their cost containment efforts, some payers are narrowing the provider network for certain rare disease therapies to COEs that have demonstrated expertise in caring for patients with specific rare diseases. Moreover, for complex or advanced therapies, such as gene therapy, COEs may be the only centers with the infrastructure, resources, and capabilities to support administration and safety monitoring.

> In a survey of access decision makers, over **90%** use prescriber specialty requirements in their prior authorization criteria for rare diseases

5. Complex management of multiple therapies for a rare disease

As the rare disease pipeline continues to grow and therapy options expand for a particular disease/condition, payers may attempt to manage utilization of multiple of these therapies. This can include various scenarios that payers are considering, such as preferencing among multiple options when there is overlap in the indication and target population. At least 70% of payers are likely to manage products more restrictively if there is more than one therapy in the class. Exploring value based contracts (VBCs) may be a differentiator between two therapies.

In the scenario of multiple therapies, there may also be consideration of how to manage sequencing of different therapies or even concomitant use of multiple therapies.

Payers often restrict or completely prevent use of one therapy after the other in the case where a gene therapy as they are viewed to be "curative."

In the case of non-gene therapies, payers typically do not allow concomitant use of multiple therapies at the same time.

Takeaways for rare disease therapy manufacturers

In order to secure optimal access for rare disease therapies, manufacturers should consider engaging with payers early in development to understand their priorities. Payers surveyed have expressed interest in many different areas within rare disease to partner with manufacturers. The results below show the top areas of interest.

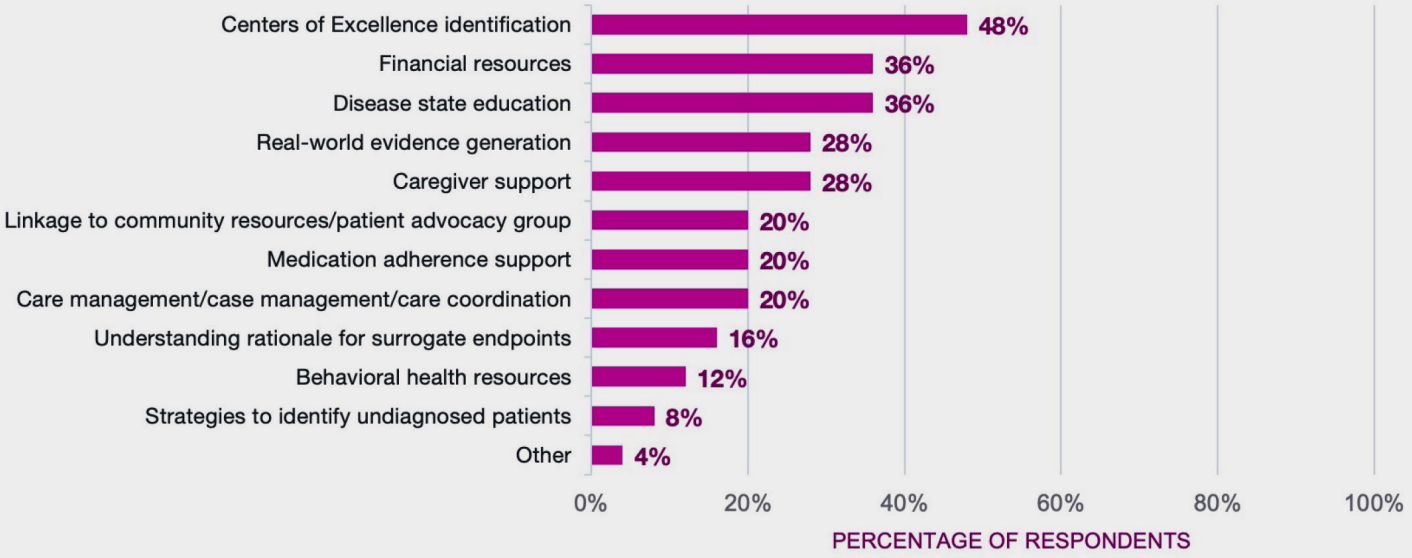

Figure 2: Areas of Payer Interest for Partnership With Manufacturers in Rare Disease

Based on this information and industry expertise, Precision AQ recommends the following 5 tips for engaging with payers regarding rare disease therapies:

1. **Educate payers on rare diseases and relevant outcomes.**

   Given limited knowledge on the natural history and progression of most rare diseases, there are also limited data to quantify disease impact, which is necessary for supporting holistic value assessments and developing case management programs. With thousands of rare diseases fragmented into small patient populations with heterogeneous clinical manifestations, it is critical for developers to educate payers on the clinical and economic burden of the disease of interest to provide important context.

2. **Understand the robustness of your data and prepare to demonstrate the strength of your clinical profile.**

   Evidence-generation activities should center on the burden of disease, the unmet needs, and the magnitude of clinical benefit, as measured by endpoints or outcomes that are appropriate for the disease of interest and for clear demonstration of value. It is also essential to consider evidence needs from the varying perspectives of influential stakeholders, including payers, employers, and the Institute for Clinical and Economic Review (ICER).

   When it comes to sequencing of therapies or use of multiple therapies, be prepared to showcase the value story through clinical and economic data of where and how different therapies could be utilized sequentially or concomitantly. While formal guidelines are not always available for each rare disease state, educate payers on any available and credible algorithms and/or consensus statements. Generation of real-world evidence may be key in these scenarios.

3. **Leverage or establish patient registries.**

   The ability to capture longitudinal data to assess real-world safety and efficacy is essential for maintaining access and reimbursement and engaging in value-based arrangements. Patient registries and patient-reported outcomes can be invaluable for demonstrating sustainable long-term value.

4. **Identify KOLs and potential COEs.**

   Knowing that payers may be relying on KOLs for reviews and contracted COEs for administration, developers may benefit from engaging with these individuals and institutions throughout the development process. Providing tools and resources to payers on COEs could also present a valuable resource and demonstrate strong partnership.

5. **Engage early and often.**

   Knowing that payers may be relying on KOLs for reviews and contracted COEs for administration, developers In this environment of more restrictive utilization management, manufacturers are advised to identify and implement strategies for engaging with key stakeholders, including payers, providers, and patients, early in the development process. Stakeholder engagement should not be a one-time activity. Instead, engaging early and often, such as through Preapproval Information Exchange (PIE) engagements facilitates a deeper understanding of each stakeholder's priorities and a more collaborative approach to access and reimbursement.

At Precision AQ, our team of experts covers the full spectrum of the healthcare journey, so we can understand and address each unique challenge. Our expertise and data-driven approach ensure rare disease treatments make a lasting impact on patient care and outcomes.

To learn more about how we can shift the trajectory, **contact us**.

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