Gene Therapy

Key Insights on Gene Therapy Coverage:

- **Financial Management & Coverage:** Payers are leaning towards innovative financial strategies, including per-member monthly charges and pooling systems, while coverage policies often align with FDA labels among payer groups, there are restrictions such as a one-time treatment limit.
- **Gene Therapy Management Approaches:** There are various strategies among payers for managing gene therapies, from specific product reviews to standardized processes. Self-funded employer plans are under pressure to distinguish between gene and cellular therapies, leading to potential additional costs when offered as extra benefit options.
- **Valuation Challenges:** Determining the value of gene therapies is challenging for payers, with a focus on outcomes, safety, and preference for long-lasting effects and durable disease survival data. Despite their high costs and low usage, these therapies are viewed as manageable within the broader healthcare system.

Perception of Elevidys for DMD

- **Efficacy Doubts & Data Limitations**: Payers express skepticism about Elevidys' clinical value, pointing to concerns about micro-dystrophin levels as an endpoint, its durability, and age-specific benefits, further exacerbated by perceived short trial durations and low patient numbers or sample size.
- **Coverage Considerations**: Coverage decisions for Elevidys are influenced by its perceived efficacy, safety, and cost, with age restrictions (4-6 years) on its label being a major determinant, and while large payers stress sustainability, statewide decisions, and Medicaid can override payer plan policies who may not expressly offer coverage albeit with certain restrictions.

Outcome-Based Agreements (OBAs)

- **Ethical and Practical Concerns:** Payers are grappling with ethical issues in OBAs, such as repayments for unsuccessful treatments, and are concerned about data security, the complexity of measuring meaningful outcomes, and handling administrative challenges and patient turnover.
- **Feasibility:** Payers favor simple and transparent OBA structures, like rebates for successful treatments or upfront payments with possible recourse, while acknowledging the need for clear, meaningful, and substantial outcome measures, despite the inherent challenges in long-term tracking and data management.

Key lessons and challenges

Payer Priorities on Gene Therapies: Payers stress the importance of durable clinical data and robust evidence of product effectiveness, showing a preference for curative treatments, occasionally limiting networks in favor of specific providers while demanding high impact/value from OBAs, and often addressing gene therapies on a case-by-case basis using policies similar to other treatments.

BMN 255

Perception of Unmet Need for Hyperoxaluria Patients:

- The current perception among payers is that there is a low unmet need for BMN 255, with payers primarily focused on managing and treating Non-Alcoholic Steatohepatitis (NASH). They are well-informed about NASH but are largely unaware of the specific requirements of the Nonalcoholic fatty liver disease (NAFLD) hyperoxaluria target patient population, resulting in a perception of low unmet need. NAFLD diagnosis is both underdiagnosed and underreported, making it difficult to ascertain the exact percentage of affected patients.

- Payers place more emphasis on addressing the underlying NAFLD disease over kidney stone recurrence. The presence of inexpensive treatments for kidney stone recurrence further reduces their sense of urgency to address this issue. Thus, payers do not see a pressing need to address this target group unless there's significant resource utilization.
- There are complexities arising from concurrent diseases such as obesity and potential overlaps between Glucagon-Like Peptide-1 (GLP-1) treatments and Recurrent Stone Formers (RSF) patients. The conflation of treatments for concomitant diseases and RSF patients raises potential concerns for payers that need to be addressed in the development of BMN 255.

- **Data Requirements & Patient Identification:** Payers emphasize that manufacturers must clearly define data parameters to effectively target patients for prophylactic treatment of recurrent kidney stones, despite varying definitions and doubts about NAFLD chart reviews.

- **Treatment Efficacy & Novel Therapies:** Payers recognize that while current treatments like diuretics are cost-effective, they may fall short for severe cases, underscoring the demand for new therapies. Yet, identifying the right patient population for these therapies, such as distinguishing oxalate stones, remains a significant challenge.

Clinical Development & Endpoints:

- **Concerns with Trial Design and Duration**: Payers highlight concerns regarding the head-to-head trial design of BMN255 versus placebo plus standard care, pointing out that the inclusion of weight loss and NASH therapies could confound results. They suggest that an 18-month duration may be insufficient, advocating for adjustments based on patient population and surgical interventions. They propose a three-arm study including BMN 255 alone for a more realistic representation of adherence scenarios.
- **Scenario 1 – Insufficient Endpoints**: Payers believe the endpoints in Scenario 1 might not fully capture the clinical value of BMN 255, recommending a primary focus on the reduction of kidney stones requiring surgical intervention. They express concerns over the ambiguity of using relative reduction in oxalate levels as a primary endpoint and highlight challenges in indirect treatment comparison versus surgery due to data limitations and multiple confounding factors.
- **Scenario 2 – Limited Enhancement by Quality of Life (QoL)**: Payers view the addition of QoL improvements in Scenario 2 as not significantly enhancing clinical value, emphasizing the availability of alternative pain management treatments and urging a focus on QoL factors that impact healthcare utilization. They note that while QoL improvements might be more relevant in the European Union, they do not substantially alter the clinical value in the United States.
- **Scenario 3 – Preferred Design with Modifications**: Payers prefer Scenario 3 for its focus on surgical utilization as a secondary endpoint but request modifications to the design. They express concerns about potential confounding factors and the importance of exploring the interaction between BMN 255 and NAFLD. Payers advocate for absolute reductions in surgical interventions, such as a 50-60% reduction, and emphasize the importance of measuring the time to the next intervention.
- **Emphasis on Absolute Improvements and Tangible QoL Metrics**: Payers favor absolute over relative improvements in clinical outcomes and suggest that while QoL endpoints may be globally required, they hold less importance for a U.S. product. They underline the need for an evaluation that considers meaningful impacts on daily life, balancing QoL improvements with cost-savings from other pain management treatments, and often prioritizing total cost of care over QoL.

Value Proposition

- To effectively determine cost comparators, endpoints like ER observation visits and lithotripsy procedures should be included. Scenarios 1 and 2 might fall short in terms of cost-effectiveness, while Scenario 3, which factors in surgical intervention costs, seems more promising.
- For determining the value and coverage of BMN 255, the emphasis should be on real events that translate to costs. Data on the disease's incidence and prevalence would be beneficial. Real-world analyses, time to the first event of kidney recurrence, and exploration of the interaction between BMN 255 and NAFLD could provide valuable insights.
- **Evaluating Treatment Efficacy and Designing Clinical Trials**: The pivotal trial design's focus on patients requiring surgical intervention might only offer marginal cost-savings, and the relative endpoints used, such as a 30-40% reduction in kidney stones, might not translate to clear clinical significance. Additional data, potentially considering medium time to reduction as an endpoint, and learning from analog disease areas could contribute to a more robust evaluation of BMN 255's value.

Payers will cover BMN 255 (using Prior Authorizations (PAs) or step therapies), but identifying the appropriate target population and impact on resource utilization is critical and challenging

- All Payers are willing to cover BMN 255, albeit through the use of PAs or step therapies with restrictions. However, they have emphasized the importance of accurately identifying the appropriate target population and understanding the impact of the drug on healthcare resource utilization.

- **Coverage Decision Factors:** The general consensus is towards providing coverage with PA, potentially influenced by the treatment cost and the need for addressing NAFLD first. The strictness of coverage will be heavily impacted by the treatment's price, with some payers considering not covering it at all if it's deemed too expensive. Concerns about not addressing the root cause and the necessity of step therapy might influence coverage decisions.

- **Target Population and Outcome Measures:** There is agreement on the need to narrow down the patient population to those who would benefit the most, as indicated by the study design, and utilizing absolute endpoints to increase confidence in the product’s effectiveness, leading to feasible coverage with certain restrictions.

Recommendations for BMN 255 Development

- Payers have provided clear guidance on their preferences and requirements for the development of BMN 255. They strongly advocate for the inclusion of healthcare resource utilization as a secondary endpoint, urging for a comprehensive approach that encompasses hospitalization, surgical intervention, Emergency Room (ER) visits, observations, and lithotripsy procedures.
- They suggest the use of a biomarker to identify patients for trial participation, though they acknowledge the challenges in identifying a suitable, codable biomarker. However, they do not believe that a biomarker could potentially identify moderate to severe patients who may not be responsive to treatments or are in danger of disease progression.
- Additionally, payers recommend incorporating time to intervention as an endpoint, capturing metrics such as time to hospitalization, surgery, and ER visits.
- For benchmarking and guidance on the development, payers suggest looking at analogs in kidney treatments that measure time to costly interventions, as well as cardiovascular treatments that incorporate endpoints like time to surgery and time to event. Analog treatments that emphasize time to costly interventions might provide relevant insights.