Evolving Access Considerations for Commercializing BioPharma Assets for Rare Diseases

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Rare Disease Drugs are the Future

The current BioPharma pipeline includes over 1,300 molecules in Phase II or Phase III trials for rare diseases. The coming change to the branded drug landscape is evident in the FDA's 2018 drug approvals, nearly 60% of which were for rare disease drugs[1]. The shift in the industry's R&D focus from large population diseases treated with small molecules to small population diseases treated with large molecules has changed the market access landscape significantly.

As the rare disease drug category expands to include gene therapies, cellular therapies, and other new technologies, rare disease drugs will become increasingly complicated to produce and administer. BioPharma companies need to anticipate the economic and clinical repercussions of these new therapies for healthcare provider systems.

Health Systems and Payers are Equally Important Access Stakeholders in the Rare Disease Space

While reimbursement for rare disease treatments isn't assured, payers are generally reluctant to interfere with care of complex patients. Consequently, coverage is generally in place for novel rare disease treatments such as CAR-Ts and other gene therapies for patients who meet the criteria of those studied in clinical trials. However, evolving payment models in healthcare are increasing health systems' accountability for the costs of care. Examples of these changes include adoption of inpatient prospective payment among commercial payers and CMS's implementation of the Quality Payment Program (QPP) and Oncology Care Model, both of which include provider incentives for higher-quality and lower-cost outpatient care. This trend toward provider accountability for healthcare cost is motivating health systems to change their delivery of care in ways that will affect patient access to new treatments for rare diseases.

Shift of Patient Care to Outpatient Settings Whenever Possible

Prospective payment models for inpatient care, such as CMS's Medicare Severity Diagnosis Related Groups (MS-DRGs), cap hospital payments for each patient case. Adoption of this system by commercial payers and many Medicaid programs has extended the limit on diagnosis-specific hospital charges to patients with other types of healthcare benefits. MS-DRG payments tend to align with hospitals' costs for treatment of common diagnoses, such as myocardial infarctions, but not for uncommon admissions, such as those related to the administration of CAR-T cells for rare cancers, such as refractory diffuse large B-cell lymphoma (DLBCL). The misalignment of payments and costs for inpatient care is motivating hospitals to move as many treatments as possible from the fixed-reimbursement inpatient environment to the outpatient setting where reimbursement isn't capped. However, for patients with rare diseases, the incentives for health systems to administer complex treatments in the outpatient setting have patient safety and treatment access implications.

Advice for Manufacturers Seeking to Facilitate Outpatient Drug Administration

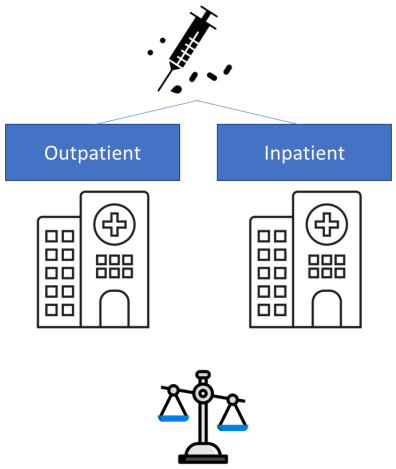
For manufacturers, the barriers to outpatient administration have significant implications for development and access strategy planning for rare disease assets:

1. **Identify patient subgroups** that can be safely treated in the outpatient setting
2. **Collaborate with relevant physician organizations** to facilitate the development of care pathways that can guide provider organizations in safely administering new treatments in the outpatient setting
3. **Develop training curricula** for care teams to ensure the feasibility and safety of outpatient administration of new treatments

Standardization of Care

Another implication of provider accountability for healthcare costs that will affect rare disease drug developers is standardizing care delivery for given diagnoses around evidence-based, cost-effective pathways. This is particularly challenging for rare disease patient populations because robust clinical data on optimal care pathways seldom exists. In the absence of evidence-based clinical consensus, inconsistencies in hospital treatment protocols and policies lead to wide variation in treatment setting and cost for similar patients across different institutions.

For example, in a recent study, we found that providers at one hospital administered BioMarin's Brineura in the outpatient setting ,while a hospital in a different city had internal policies that required inpatient administration by highly specialized physicians. These differences mean that the economics of Brineura differ substantially for each institution and may create an access barrier for patients whose providers require inpatient administration.



Manufacturers of drugs for rare diseases need to anticipate variations in protocols across institutions likely to treat target patients and work before launch to help providers align on treatment paradigms that adequately address safety concerns, ensure patient drug access, and minimize hospital costs.

Health System Specialization in Patient Populations

The expansion of prospective payment models and other incentive programs have led health systems to specialize in the treatment of specific patient groups or diseases types. However, the cost of assembling and maintaining the provider teams and resources needed to treat patients with rare diseases often limits access to care to just a few institutions among otherwise qualified centers. While patients with rare diseases frequently travel to, or even relocate to be near highly specialized providers, super-specialization of care is clearly a barrier to treatment access with considerable implications for manufacturers.

Advice for Manufacturers Seeking to Overcome Health System Specialization Barriers

1. **Ensure distribution of clinical trial sites among a broad network of centers of excellence** with qualified practitioners, not only those centers with the highest volumes of target patients.
2. **Develop secondary networks of specialists in target disease areas** who can support ongoing complex drug administration and clinical follow up for patients whose primary specialists are in distant regional centers of excellence. This is a common practice in oncology, where a specialist at a comprehensive center directs a patient's treatment which is subsequently administered by a local oncology office. To accomplish this, rare disease drug developers need to ensure that providers in these secondary sites have clear protocols for administering their drugs and that staff are trained in using them. Protocols should also specify when patients need to be referred to their primary comprehensive cancer center.

Healthcare System Practicalities Affecting Access for Rare Disease Drugs

Aligning with Non-Clinical Stakeholders

Health system finances are highly complex and require management of myriad daily transactions and multiple reimbursement contracts , each with unique payment terms. Manufacturers of drugs for rare diseases should anticipate the implications to health systems' financial management processes for high cost drugs. Biogen's Spinraza for spinal muscular atrophy provides an example of how hospital finances can impact access. At the time of its launch, Spinraza was one of the most expensive drugs ever produced. While it had excellent access among payers, uptake at some health systems was low due to concerns among finance departments about lags in the timing of purchase expenses and payer reimbursement. These concerns are multiplied when health systems have many patients with a target disease who are eligible for a new treatment or when system specialists treat a variety of different rare diseases, all of which require high cost treatments.

Some of health systems' financial concerns about purchasing high-cost drugs can be mitigated by distribution strategies, such as using specialty pharmacies which bill payers directly. However, unique preparation requirements for some drugs may make distribution by specialty pharmacies unworkable. Moreover, some health system customers prefer to purchase these drugs through specialty distributors. Consequently, manufacturers need strategies for supporting hospital administrators in managing the financial impact of purchasing and stocking high-cost drugs. For example, using third-party logistics firms (3PLs) to provide "just-in-time" delivery can minimize inventory costs for health systems.

Outpatient Care Team Operations

Patients within rare disease populations present with a variety of functional and wellness states. This diversity of health status increases health systems' perception of the risk of outpatient administration of new drugs for target rare disease conditions. It also affects health systems' decisions about the level of HCPs who can safely administer these drugs in outpatient settings. Leveraging ancillary HCPs such as registered nurses, nurse practitioners and physician assistants makes outpatient administration more cost effective for health systems. Supporting health systems in administering new rare disease drugs in the outpatient setting will reduce access barriers for manufacturers. A key part of manufacturers' health system strategy will need to be training for clinical teams in safe outpatient drug administration. This training will also help health systems determine the type of provider who should administer a new rare disease drug. Equipping least costly resources to safely administer the product will reduce access barriers for patients and costs for health systems.

Types of Training that Manufacturers Can Provide to Facilitate Outpatient Drug Administration

1. Instruction for nursing on patient preparation
2. Skills needed for safe administration
3. Management of administration-related adverse events

Purchasing Flexibility

The timing between expenses incurred by health systems and their corresponding reimbursement by insurers can vary widely, and lengthy delays can have financial implications for the health systems. As the number of patients that health systems treat with high cost drugs grows, health systems will become more sensitive to their "incurred but not reimbursed" expenses and may manage them by controlling patient access. Offering flexible payment terms is a simple strategy for addressing health systems needs in this area.

Alternatives to Inpatient & Outpatient Care

Some patients with rare diseases are too sick to receive treatments as outpatients, but don't require inpatient care. For example, prior to a label change, clinicians at some institutions administered daratumumab in inpatient settings due to its lengthy infusion time (8-12 hours) and high incidence of adverse reactions. To avoid the cost of this practice, physicians began dividing the dose of daratumumab across two infusions. Janssen ultimately obtained a label change that authorizes promotion of this practice. Other institutions have established "day medicine" units located near emergency departments that can accommodate patients at risk of severe reactions to medications. These units are sub-acute and not subject to fixed prospective payments. Another option for some complex drugs is home infusion. When patient safety can be assured, home infusion can deliver medications that require lengthy administration. Manufacturers should anticipate that some patients could benefit from these types of care and support healthcare systems in developing appropriate protocols for administering rare disease treatments in these settings.

Conclusions

The number of new drugs for rare diseases in development has grown substantially in recent years. According to ClinTrials.gov, 1,535 drugs were in development for rare diseases as of 2018. While not all of these assets will reach the market, the sheer number of drugs in development points to a dramatic challenge to healthcare economics in the coming years. Rare disease drug developers will, no doubt, need to engage in larger societal debates related to affordability. More practically, though, they need to anticipate that health systems will be important access stakeholders. Supporting these customers in addressing the operational and economic pressures they face in caring for patients with rare diseases will ensure that drug developers' life-enhancing treatments ultimately reach the patients who need them.

Herspiegel Consulting's Market Access Practice specializes in helping clients succeed in commercializing new products, particularly those for rare diseases. Clients value our deep experience in, and understanding of, the health system market which helps them anticipate and overcome access challenges for rare disease drugs among providers. Contact David Rees, Market Access Practice Leader, to learn more about how we can help your organization commercialize a rare disease asset.

Reference

1. Sakate et al ; Journal of Clinical Pharmacology, 2018, Vol. 13, No.3

Contact Us to Learn How We Can Help Your Organization Commercialize a Rare Disease Asset

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David's market access expertise is built on 25+ years of experience assisting biopharmaceutical companies in developing brand and channel strategies to optimize access in the competitive biopharmaceutical market. Prior to joining Herspiegel Consulting, David co-founded Health Strategies Group and was instrumental in building its industry-leading reputation for strategic insight into the evolving US access landscape. Over his 30+ year career in pharmaceutical marketing, David has led marketing teams in the US and EU and provided strategic access guidance to hundreds of clients in large and small molecule drug categories.

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Herspiegel Consulting has provided integrated pharmaceutical commercialization consulting services, tailored and scaled to meet business needs across a wide variety of therapeutic areas for the last 12 years. Service areas include pharmaceutical new product planning, product launch preparation, marketing excellence, market access strategy, and medical affairs. Industry focus and depth of functional expertise, combined with strong scientific and market knowledge, uniquely positions the company to develop achievable strategies and solutions for clients. **Learn more about us at www.herspiegelconsulting.com**