ORPHAN DRUGS

5 WAYS TO PROVE PRODUCT VALUE

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Development and scrutiny are on the rise.

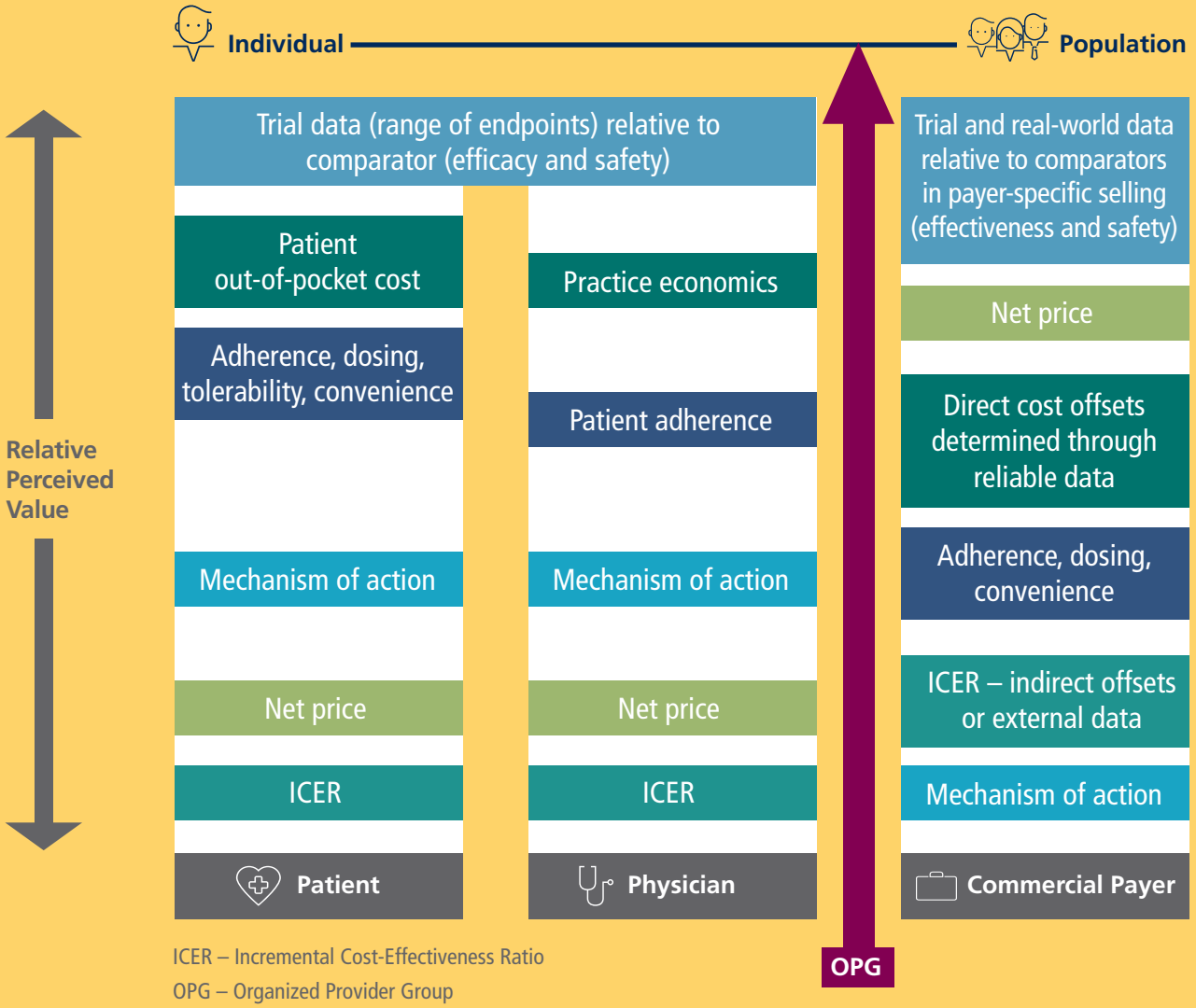
In 1983, the year the Orphan Drug Act (ODA) was passed, the FDA Office of Orphan Products Development (OOPD) saw fewer than 10 orphan drugs come to market.[1] Since then, the FDA has approved more than 500 orphan drugs for the treatment of rare diseases — a result that would have been unattainable without the ODA's incentives, including clinical research grants, tax credits and waivers, reductions and refunds associated with the Prescription Drug User Fee Act.[2] With the OOPD reporting a 30 percent year-over-year increase in the number of designation requests since 2013,[3] and a record 566 therapies currently in development,[4] the pharmaceutical industry has clearly placed a focus on innovating treatments that make a difference for even the smallest patient populations. In many cases, due to advancements in personalized medicine, innovations in rare disease are also advancing treatment within broader disease states like oncology. And while some new orphan products offer first-line treatment for patients with rare diseases, others offer additional treatment options for larger patient populations, such as those with multiple sclerosis or cystic fibrosis.

There are a record **566 rare disease therapies** currently in development.[5]

But rare disease is no longer a protected class. As market baskets become more competitive, payers are placing greater scrutiny on the budget impact of these treatments – even if they are only accessible to a very small percentage of their patient populations. As payers look more critically at the cost of therapies with indications for a rare disease, they are also evaluating the potential impact of expanded indications and how that could widen the appropriate patient population and increase the budget impact on their plans. The often cost-prohibitive price tag on orphan drugs contributes to restrictive behaviors for pharmacies, payers and patients alike.

As with other products, the burden of proving product value primarily falls on the manufacturer. But orphan drugs often have far more complex education and evidence hurdles to overcome. The manufacturer serves as a critical resource for every stakeholder in the patient journey and must clearly communicate the product's value to these stakeholders in a way that addresses how each one prioritizes and perceives value.

Stakeholder Perceptions of Product Value



ICER – Incremental Cost-Effectiveness Ratio
OPG – Organized Provider Group

Our unique position in the healthcare supply chain means we've provided commercialization services for more than 100 rare disease products. And because of that, we've seen a number of best practices emerge. Relative to demonstrating the value of rare disease therapies, there are five key ways to connect where patients, physicians and payers perceive the most value.

Five Ways to Prove Product Value

1

Create a community for patients.

2

Educate and support physicians early.

3

Overcome access barriers with evidence.

4

Invest in patient support programs.

5

Design a specialty pharmacy strategy that balances safety and access.

1 Create a community for patients.

Even before product access threats can be quelled, one must first overcome the challenge of diagnosis and of educating stakeholders on the rare disease itself. Often with orphan diseases, the journey to diagnosis is long and fraught with uncertainty. A Shire Rare Disease Impact Report[6] revealed that a patient suffering from an orphan disease typically visits up to eight physicians and receives two to three misdiagnoses before an accurate one is ultimately reached. This can lead to feelings of isolation, frustration and ambiguity in both patients and their caregivers, particularly for those where the hope of treatment is minimal. For this reason, it's critical these individuals connect with others suffering from the same condition, better understand their disease, know their treatment options and learn they are not alone.

A rare disease patient typically visits up to **eight physicians** and receives **two to three misdiagnoses** before an accurate one is ultimately reached.[7]

For most rare diseases, this calls for manufacturers to tap into existing charitable foundations and advocacy groups such as the National Organization for Rare Diseases (NORD), ensuring a link to a network of patients, physicians and/or caregivers. In addition to playing a crucial role in everything from sourcing patients for clinical trials to spreading awareness about the disease, these groups are well organized, vocal and active. They can help to smooth a treatment's path from research to approval, as well as make political waves, as appropriate, in matters of regulatory or payer restrictions. These networks also provide a way for rare drug developers to understand patient and family needs more completely, which can help manufacturers develop more effective support services. Connecting early with patients and their advocates can also help in the actual development of products, as manufacturers can find out which routes of administration and dosing schedules will be most effective and most adhered to.

For even rarer or ultra-orphan diseases, the manufacturer may need to build a community from the ground up. A non-branded website before launch of the orphan drug will not only help educate the public on the disease and provide a sense of community for sufferers, it may also serve as a patient registry, helping to facilitate direct communications post-launch. Through this means, manufacturers can manage the patient experience more closely, track adherence, progression and outcomes — all of which may bear out data to substantiate payer approval and reimbursement strategies down the road. To truly understand the diagnosis and treatment experience and obtain patient demographics and insights on the disease, treatments, preferences and more, many manufacturers invest in mapping the patient journey.

Find and Connect With Advocacy Groups

National Organization for Rare Diseases
rarediseases.org

Rare Diseases Clinical Research Network Coalition of Patient Advocacy Groups (RDCRN-CPAG)
rarediseasesnetwork.org/cpag

2 Educate and support physicians early.

Early engagement with physicians is paramount to ensure accurate diagnosis and ultimately patient access to the most appropriate treatment. As orphan drug manufacturers develop a deep understanding of the disease and its symptoms, it benefits them to compile and disseminate educational materials that can be used to help physicians recognize signs and symptoms. That might mean developing and publishing formal protocols or algorithms for diagnosis, or the creation of a diagnostic test. Treatment guidelines leveraging clinical trial data are equally important, ensuring clinicians are trained on the appropriate use of the drug. Whatever the methodology, the goal in these communications should be to use real-world evidence in combination with burden of illness information to create a sense of urgency and make the disease, its impact and the science of the drug tangible for physicians.

3 Overcome access barriers with evidence.

Inherent to rare diseases is a lack of expertise, an inability to predict the related healthcare costs and a series of interventions that may be required over a lifetime for a patient. Yet payers are in the unique position to have to make predictions about all of these factors, affecting both patient care and physician treatment, often with little to no data. The gap in guidance combined with pressures to manage budgets has many payers pushing more costs to patients and increasing prior authorization (PA) requirements. While this can limit access to treatment, manufacturers can overcome these barriers by communicating the product's clinical and economic value with a focus on the impact on the total cost of care. In addition, wraparound services like electronic prior authorization (ePA) solutions can reduce hurdles, especially in situations where the payer requires PA but ultimately approves the claim every time.

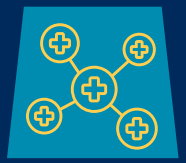
And while some orphan drugs are the only disease-modifying treatment available for those patients, the rise in competition has opened the door to more aggressive step therapy practices (especially where an approved biomarker-related test is available for even part of the labeled indication). In this practice, payers require patients to first undergo comparable, less-costly drug therapies, approving use of the prescribed orphan drug only after other therapies fail.

To combat these measures, manufacturers must build treatment models with low levels of uncertainty. This means providing strong clinical and economic evidence that illustrates a material impact on the patient's quality of life and longevity, demonstrating — with as much certainty as possible — the drug's ability to address key symptoms or to slow the progression of the underlying pathology relative to treatment alternatives.

Reduce access barriers with:

Communications that focus on the impact on total cost of care

ePA solutions that reduce hurdles where payers ultimately approve the claim every time



Treatment models with low levels of uncertainty

Strong clinical and economic evidence

4 Invest in patient support programs.

The lengthy journey to diagnosis and ongoing treatment takes a significant emotional and financial toll on patients and caregivers coping with rare diseases. These individuals must often serve as researcher, care coordinator and advocate, mining a multitude of websites, organizations and charities to better understand the disease and its treatment options. Then there is the challenge of identifying a specialty physician — often located a considerable distance from the patient. The high price of orphan drugs compounded by payers' more aggressive cost-sharing practices, along with associated expenses such as transportation, can leave rare disease patients and their loved ones financially depleted. This calls into question the risk of treatment adherence, accurate outcomes analysis and patient safety. For this reason, patient support programs have become a critical component in the commercialization success of orphan drugs.

Most urgently, support programs can improve product access and/or reduce time to therapy, supporting uninsured and underinsured patients by addressing affordability barriers to medications and providing financial assistance with insurance premiums and co-pays, diagnostic testing and travel. Equally important is the aspect of ongoing care in rare diseases, and the role of case manager within support programs. As the patient's single point of contact, the case manager provides continuity of care, confirming coverage and providing reimbursement support, overseeing the scheduling of medical appointments, working with specialty pharmacies to ensure access and the timely administering of drugs and coordinating with physicians to provide updates on the patient's progress. This latter aspect is especially important as it relates to the health outcomes data derived from support programs, helping manufacturers demonstrate real-world effectiveness and value of the orphan drug to all stakeholders.

As the patient's single point of contact, **the case manager provides continuity of care.**

5 Design a specialty pharmacy strategy that balances safety and access.

Support programs for orphan and ultra-orphan drugs exist due in large part to cooperative relationships with specialty pharmacies. Because specialty pharmacies have a vested interest in making sure patients receive treatment, they also serve as a patient advocate, leveraging their orphan drug expertise to advocate on behalf of the patient when payers attempt to limit access. Specialty pharmacies provide services like helping finding financial assistance to enable broad access and improve speed to therapy, and are well equipped to collect and report adverse events, patient-reported outcomes and other data elements that provide insights to help manufacturers and providers reduce risk and improve care. Comprehensive inventory management and pharmacist quality checks ensure that orphan medications are dispensed properly, maximizing valuable therapies that may be manufactured in small quantities, while technology solutions increase pharmacy transparency, providing manufacturer partners with real-time access to detailed program information and strategic insights throughout the product lifecycle.

The channel strategy for an orphan product is critical for commercialization success, and should be evaluated based on product attributes and patient needs. Network design decisions must balance two fundamental priorities that are centered on the patient – access and safety – to bring the most benefit to the patient.

Drivers of Network Design

Product Characteristics

- High cost
- Special storage or handling
- Severe side effect profile
- Complex or inconvenient regimen
- Narrow therapeutic range

Patient Population

- Small populations
- High level of training needs
- Frequent patient monitoring and dosage adjustments

Therapy Access & Coordination

- Reimbursement and financial assistance services needed
- FDA REMS requirements
- Nurse or physician administered

Manufacturer Requirements

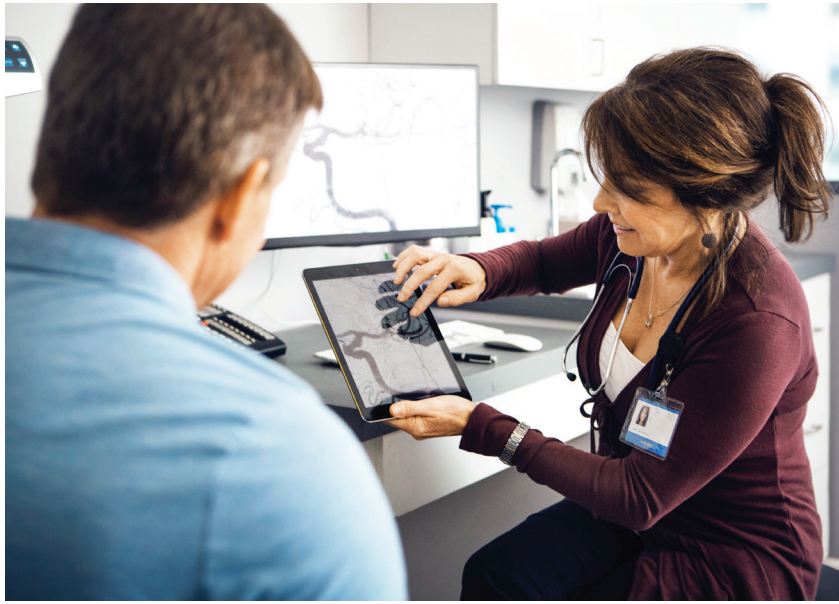
- Enhanced data reporting
- Pharmacovigilance and AE reporting
- Inventory management

Dispensing orphan products via specialty pharmacies and supporting their commercialization with hub programs that address patients' holistic needs are beneficial not only for patient access, but also to ensure an efficient supply chain. A limited distribution channel strategy can allow manufacturers to retain more control and, by leveraging third-party logistics (3PL) partners connected directly to the hub partner, can shorten the supply chain and help manage inventory levels among the network of pharmacies.

Engaging with a qualified strategic partner early in the launch process – as soon as two years pre-launch is ideal – can be key to designing the best strategy. Questions to ask such a hub partner might include:

- What are the pitfalls of this type of launch?
- What works well for this product's attributes/this patient population?
- What is going on across the market that might affect your product launch?
- How will the product's clinical roadmap/other indications affect the channel strategy?
- What is the best way to reach health systems and hospitals that specialize in rare disease?

The right partner will have a solid bench of experts with experience launching products across disease states – including rare diseases – and can help shape the strategy based on what they've seen work well (and poorly). A specialty distribution partner will know how answers to these questions and others could influence the decision to change the specialty pharmacy channel strategy post-launch as needs change and as the product advances through its life cycle. For example, a product could move from exclusive to limited distribution, narrow to broad, or limited to open. A specialty distribution partner has a shared interest in a product's success – their business is impacted by it, so the recommendations they make come with significant vetting and evaluation of what will create the best experience for the patient and the provider while supporting the manufacturer's commercial strategy and ultimately improving product performance.



Innovation Is Always a Best Practice

These five best practices may vary in depth and approach depending on the orphan drug, but they share one critical commonality outside of patient access and support. That is, they all feed the need for continual information. It is in this loop of knowledge, from outcomes and adherence data to patient insights and changes in reimbursement and payer perception, that manufacturers will find what they need to prove the value of orphan drugs, to evolve messaging and drive product success. And while the many challenges that come with marketing orphan drugs are time-limited, it's important to remember the knowledge that comes from their discovery is eternal. Research in rare diseases and orphan drugs has greatly advanced the industry's understanding of the molecular pathways that control even more diseases — an ancillary result that for many is priceless.

[1] Office of Orphan Products Development (OOPD) Budget Report. Wiley Encyclopedia of Clinical Trials. 2008. Accessed 26 September 2016. Available online at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM298358.pdf

[2] Financial Assistance and Incentives for Research and Development of New Drug/Biologic Products. U.S. Food & Drug Administration (FDA). 2008. Accessed 26 September 2016. Available online at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm091541.pdf

[3] FDA Voice. 18 July 2016. Accessed 22 September 2016. Available online at http://blogs.fda.gov/fdavoice/index.php/2016/07/the-rise-in-orphan-drug-designations-meeting-the-growing-demand/

[4] Medicines in Development for Rare Diseases: A 2016 Report. PhRMA. 2016. Accessed 26 September 2016. Available online at http://phrma.org/sites/default/files/pdf/medicines-in-development-report-rare-diseases.pdf.

[5] Ibid.

[6] Rare Disease Impact Report: Insights from patients and the medical community. Shire. April 2013. Accessed 26 September 2016. Available online at https://globalgenes.org/wp-content/uploads/2013/04/ShireReport-1.pdf

[7] Ibid.

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As Senior Vice President of Strategy and Commercialization for AmerisourceBergen Specialty Group, Dr. Amy Grogg advances the company's leadership and position in the pharmaceutical services industry as the preferred commercialization partner for specialty pharmaceutical manufacturers. Prior to her current role, Dr. Grogg was President of AmerisourceBergen Consulting Services where she led the growth of a portfolio of companies that included Xcenda, as well as Innomar Strategies and Lash Group.

About AmerisourceBergen

AmerisourceBergen (NYSE: ABC) is one of the world's largest pharmaceutical sourcing and distribution services companies, working alongside healthcare providers and pharmaceutical manufacturers to improve access to products and enhance patient care.

With services ranging from drug distribution and supply chain management to patient support solutions and pharmaceutical commercialization, AmerisourceBergen enables quality care and innovation in human and animal health. Tens of thousands of pharmacies, physician practices, health systems, veterinary practices, livestock producers and pharmaceutical manufacturers turn to AmerisourceBergen for the expertise they need to drive business performance.

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