Optimising the Value of Treatment in Rare Diseases

Accurately scoping out the human burden of a rare medical condition is important for a company seeking orphan drug designation for its pharmaceutical agent. Understanding the full burden of a disease on the patient and their family, is also vital in order to ultimately comprehend the true value of a treatment to patients, the HC system, society and to Pharma.

The full burden is much greater than the sum of the clinical symptoms. It also includes the emotional impact, which can be crippling to family units, and because patients are 'different', the social and psychological repercussions of isolation and alienation need to be considered as well.

There is almost always a heavy financial impact to bear. Many a parent, for example, faced with raising a child with a genetic rare disease, will sacrifice his or her career to become a carer. This burden is often compounded by the need for expensive equipment to maintain the child's quality of life.

Such broader health outcomes can easily be left out of the value equation, but value is much more than simply cost versus clinical benefit, especially when a disease is severe, stigmatised and rare.

Act early

A rare medical condition is often unknown territory to all but the patients, carers and key opinion leaders (KOLs). For this reason it is important for the pharmaceutical company to gain as much information as possible about life with the disease from its earliest stages and across the whole journey

The pathway to diagnosis is rarely well-trodden; often patients are 'lost' for many years without access to expert care. Many parents report a rollercoaster process, trekking with their sick child from one healthcare professional to the next - each addressing a single symptom but no one putting the full puzzle together to reach the proper diagnosis. Inefficiency in getting a diagnosis is obviously a barrier to getting timely treatment, which may even allow a disease to progress irreversibly. Clearly this is to the detriment of the patient and his or her family, but it also means lost revenue for the pharmaceutical company. The delay reduces the potential benefits of treatment and that in turn can weaken perceived and actual value.

As a rare disease progresses and a patient's health deteriorates, the condition's impact multiplies. The associated burden can grow exponentially along with the impact on the household.

Carers and family members are not typically accounted for in the value demonstration equation. But because most rare diseases are genetic, the carer or other family members may be fellow sufferers. One parent is likely to be a carrier, which means he or she can be inextricably part of the disease burden in several ways. They will feel guilt for passing on the disease and the difficulties of managing in the household may be multiplied if they themselves are ill as well as one or more child. The weighty burden on the family unit is surely a strong argument for its inclusion in the value demonstration equation.

Now patients and their families are so interconnected online via social media, it becomes ever more important for Pharmas to ensure that early patient experiences online around a disease and treatments are positive. We know that in the rare disease world news travels very quickly around the world – good and bad news, correct information and misinformation. If a company is slow to enter into the early dialogue online, it is possible to lose control of communication about a new brand or the organisation. The potential value of the new asset can be badly undermined by unfavourable hearsay.

What matters to patients?

If orphan status is to be granted for a product, there is a need to ground the trial design and proof of value in terms that are meaningful priorities to patients.

This approach to defining and measuring all the parameters of a disease that impact the patient and carer leads to refreshing insights and points to the most differentiating clinical measures to be taken on into clinical trial design. It also gives a basis for understanding the economic burden of the disease and hence the route to understanding the true cost of the illness and the value of the orphan drug to patients and to society.

Of course, it is crucial to align and connect the patient and carer burden outputs with the needs and thinking of the experts in the field - the payers, medics and the patient support organisations. In this way the beneficial health outcomes of a treatment resonate with all stakeholders. The value of the product may be defined and perceived somewhat differently by each stakeholder. For some, the value is purely objective and is a trade-off of the

clinical benefit versus cost. For others, it has wider meaning such as the economic cost on society in recognition of the fact that a life-long disease brings long-term financial hardship and loss of work. For patients and their families, terms like 'value' and 'cost of a successful treatment' are at once objective and subjective. For them, the meaning of 'value' of the drug is understandably deeply personal and may be considered 'priceless'.

So often, there is a clear need for better communication between patients and HCPs around the disease and the treatments. Even the recognised experts may not be privy to the reality of the disease on a day to day basis and can benefit from additional insight into what patients truly value (both clinically and beyond the clinical)

For a pharmaceutical company bringing an orphan product into a new area it is crucial to recognise the global network and to work with all the players. The universe is small, if not tiny and each patient is of significance. Patients matter as human beings of course, but to the pharmaceutical company they are valuable financially both as recipients of the treatment for their lifetime but also as potential patient opinion leaders. Patients thus come to be seen less as the object of the disease and more as partners in the research process; a further argument for their early inclusion.

In preparing to market an orphan drug it is essential to build a foundation in the real life impact of the disease on the patient and carer at a much earlier stage of asset development than usual. The 'unknown unknowns' of the disease burden that only the sufferer and his or her family can truly identify can then be taken forward and aligned with the perspectives of the players in the rare disease 'universe', namely the KOLs, other healthcare professionals, payers, patient support organisations and pharmaceutical company stakeholders (eg health economics and outcomes research, and market access). In this way, the strongest case can be made for the orphan product value and its subsequent clinical development can be steered in an optimal way. By engaging all parties from the outset, everyone is aligned and the challenges and delays to market access can be minimised.

Researching value for launch

Once the orphan designation is achieved, payers require further proof of the value of the product. As market researchers, we have seen how capabilities of patients fall away with disease progression. At times the percentages have fallen like a stone as the patient moves from an early, through mid, to late stage. Mobility decreases with severity and patients' need for support mounts.

Carers spend sometimes thirty or more extra hours a week on their care and reduce their work hours by this amount or more. The household finances take a significant hit. These are concrete numbers in hard cash that can be weighed against the treatment costs. How can these figures gained through market research achieve scientific credibility and necessary recognition?

In our experience, this credibility can come from a Steering Committee of experts including global KOLs, heads of patient support organisations, specialist nurses, internal scientific advisers. All of which set up hypotheses for evaluation and exploration in the market research. Gathering together the perspectives of a broad spread of stakeholders has the added benefit of accelerating the thinking process as it allows them to explore, challenge, create hypotheses and refine these ahead of the research process so that objectives are focused on the key issues from the start.

Initially qualitative patient and carer research can help to get us as close as possible to day-to-day life with the disease and tease out the full burden physically, practically, emotionally, socially and financially for the patient and their family. We ask questions about their quality of life, the effect of their symptoms and feelings on their ability to work, socialise, care for their dependents, their intimate relationships as well as their knowledge and pathway to and through diagnosis.

Next, we take these fresh insights to the Steering Committee to determine the parameters that are most relevant to them, before performing quantitative research to measure the impact across all meaningful parameters and the fall in these metrics across disease progression.

These patient and carer survey results can then be put to KOLs and payers to overlap with their needs and practices in order to optimally design phase II trials so that the most meaningful endpoints are selected. Market research alone cannot prove the monetary value of a new asset however we believe that it can steer those in the quest to demonstrate value in the right directions.

Omitting the most meaningful endpoints risks a drug failing to demonstrate its true benefits and deprives a population with a desperate need for improvements of a potential treatment. We have seen this is a rare disorder where the trial measures failed to recognise improved stamina in the patients struggling with their mobility. Caregivers with patients in the trial were adamant that the six minute walk had not been the best measure to capture the positive response to the trial drug. Those who were in the trial were online

sharing video and testimonials about the trial results, posting their own real world evidence of their drug's perceived successes.

Understanding the nature of the burden of the disease can also reap benefits in trial recruitment and retention for Pharma. If a company can pre-empt the barriers and hurdles of possible candidates then trials can be run more smoothly and provide results with more substance. In a rare disease, every patient counts and each one lost from a trial endangers the results and increases the costs.

In orphan drug development for rare diseases, the rules of engagement and the treatment pathways are different. Patient centricity is no longer simply a nebulous mission statement, it is at its core. Hopefully, we have laid out here some of the reasons why rare disease patients need to be engaged and understood at the very earliest stages of asset development and throughout their journey.

The patient and his or her family are the best placed to shine a light on where the quality of life has been improved by drug intervention. Their accounts will not necessarily conform neatly to the language used in standard quality of life questionnaires, but they will tell us the truth of their experiences and it is important for the future of the industry that we listen to what they say and measure value in terms that matter to them.

Jane Barrett

Rare Diseases Expert Hub

Cello Health