Maximising Value in the Rare Disease Sector: Begin with the End in Mind

Interest in the development of medicines to alleviate or cure rare diseases has increased due to (1) positive actions taken by global regulatory agencies; (2) advances in the understanding of disease pathophysiology; and (3) tools, such as exome and whole-genome sequencing, to produce more efficacious drugs. Accommodation by regulatory bodies in the form of reduced fees, expedited approval pathways, tax credits and patent exclusivity have been of particular benefit.

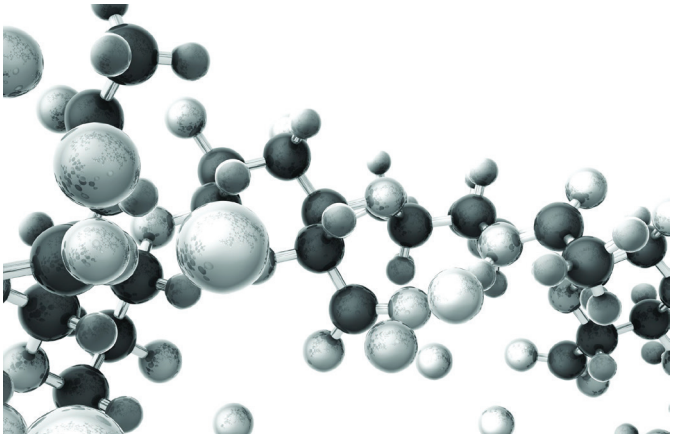
Nonetheless, the likelihood of a high-performing drug launch is approximately one in three, meaning that two-thirds of drug launches fall short of expectations, including in the rare disease sector. And once a drug launch stumbles, it is difficult to turn around. Capturing the full potential of a launch requires that we "begin with the end in mind." This means anticipating potential hurdles to reimbursement raised not only by regulators but also payers, physicians and even patients themselves.

In Europe, a Health Technology Assessment (HTA) process frequently determines whether an orphan drug should be made available or not, and with what restrictions. In the United States, there is gathering recognition of the power that payers have to deny coverage. However, with respect to rare diseases, the clinical data needed to support HTA or health insurer assessments are often weak because of the scarcity of study subjects. Therefore, the level of confidence on the part of regulatory authorities may be less than desired. This particularly affects treatments for rare diseases that typically demand a premium price. As a consequence, the appetite for additional data to support the reimbursement of new entities in this environment is strong.

It is often observed that the comparatively small budget impact of orphan drugs in terms of overall health spend has, in some cases, helped them gain market access. However, continued pressure on payers to curb health spending is resulting in new policy initiatives that will require the pharmaceutical sector to carefully think through its commercialisation strategy, even in the rare disease environment. For instance, in the UK there are plans to soon impose an additional affordability test post-approval, where NHS England will be able to delay making drugs available or restrict who is eligible if the total cost to the health service is more than £20 million annually. In the US, the new administration may compel Medicare to negotiate lower drug prices for its 41 million beneficiaries.

The Association of British Pharmaceutical Industry (ABPI) believes the UK plan could compromise care for patients with rare diseases. The US policy, on the other hand, could potentially cast a chill on R&D for drugs targeting rare conditions if sponsors were uncertain about the return on their investment; also, the inability of patients to access drugs because the price is in negotiation could spark widespread opposition. Finally, other countries may consider imposing similar policies in order to contain healthcare costs.

It is, therefore, essential to establish an integrated medical plan for drugs in development that clearly sets out not only the core development data required to prove safety and efficacy but also ensures that other evidence gaps are addressed. To best



achieve this, one should begin with the end in mind; that means having a clear understanding of why, where, when and how you intend your drug to be used subsequent to approval. With this mapped out, the evidence gaps can be established and addressed during pre-approval, thereby maximising value of the product through early adoption and reimbursement. This might include, for instance, creating the right evidence base and experience pool for a companion diagnostic. There is no point in having an approved cancer drug that targets a specific genetic mutation if the appropriate diagnostic is not in place to identify patients with that mutation. So, ensuring that the correct clinical environment is in place and understanding how to drive adoption of the relevant technologies will also be critical in the successful uptake of any new therapy.

As the NHS England and US Medicare cases demonstrate, despite having important value-based evidence, there may well still be hurdles to overcome. For this reason, it is important that any integrated medical plan delivers evidence for the regulator and for the payer but also now increasingly for the patient and the individual physician, as the clear differentiator now may need to come through patient and physician advocacy.

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