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Addressing Rare Disease Treatments with Biosimilars and Orphan Drugs

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Approximately 10,000 rare diseases (RDs) impact about 400 million people worldwide, with 30 million in the United States alone. In Europe, the European Medicines Agency estimates that up to 36 million people are diagnosed with an RD. However, approximately 5 per cent of RDs have US FDA-approved treatment options, while up to 15 per cent have at least one drug that exhibits potential for treatment, diagnosis, or prevention. The growing number of unaddressed RD needs is a major catalyst for R&D. There is a need for novel medicine to treat RDs that currently have limited therapeutic choices. Let's explore further.



Governments across the world have regulatory incentives to support orphan drug (OD) development. It is more appealing for pharmaceutical firms to engage in R&D for RDs because of these incentives, which include prolonged exclusivity, tax benefits, and simplified and expedited regulatory procedures and approvals.

Recent advancements in precision medicine and informatics, such as big data analytics, multi-omics, nanomedicine, gene-editing techniques, and next-generation diagnostics, have created opportunities to develop specific and individualised therapies for RDs. The convergence of cancer and RDs is becoming evident. Precision oncology and tailored medicine for rare tumours are emerging as prominent themes in the discipline, facilitating the OD industry's expansion.

There are multiple challenges restraining the development and adoption of orphan drugs. Owing to low awareness of RDs, many patients go undetected for extended periods. Apart from diagnosis, both prognostics and therapy are seeing significant gaps that must be filled. Challenges in prognosis assessment are due to the absence of reliable parameters to measure improvement and/or biomarkers as well as a lack of knowledge of underlying pathophysiological pathways. Furthermore, a limited patient sample size prevents the derivation of statistically significant parameters.

The development of orphan medication may be economically onerous due to RDs' intricacies, restricted patient groups, and the need for specialised R&D endeavours, resulting in higher expenditure that is sometimes not justified by industry potential. The high cost of developing and manufacturing next-generation biologics, such as Cell and Gene Therapy (CGT) and Ribonucleic acid (RNA) therapies, often presents considerable challenges in terms of pricing and reimbursement. Pharmaceutical firms may find it difficult to justify OD costs, and payers may hesitate to provide coverage, limiting patient access to these drugs.

Repurposing existing compounds offers significant advantages for small and emerging biotechnology companies. For instance, it helps them to better coordinate their economic and financial concerns with their medical and scientific goals. In addition, it enables them to enter an industry not currently occupied by large pharmaceutical companies and accelerates the validation of their drug development platforms. Examples of such companies include NovaBiotics, a Scottish biotechnology firm, and Healx, a computational drug repurposing firm that integrates omics and phenotyping.

Self-care advocacy organisations and patient support initiatives help propel the orphan drug market in developed countries. Compared to the US, India has fewer organisations to assist firms develop treatments or undertake clinical studies. Ad hoc patient access schemes are financed by philanthropic programmes like Sanofi's India Charitable Access Program ((INCAP), which gives free enzyme replacement medicine to lysosomal storage disease patients. Novartis is making significant investments in its rare diseases drug portfolio in response to the growing market demand in India and has 17 ongoing clinical programmes dedicated to rare diseases in India.

Some orphan drugs are at the tail-end of their market exclusivity as well as patent life, and therefore will become vulnerable to biosimilar and generic competition. Even though competition from generics for orphan drugs stands low because of lower addressable population size, off-label use of products for various indications often impacts the overall sales of existing products. Given the infrequency of these diseases and the difficulties in finding patients, it is crucial to extrapolate to other rare disease indications to get regulatory clearance for biosimilars. Biologics serve as a major therapeutic approach for many rare diseases.

Nevertheless, their growing use stands as a key catalyst for the rise of healthcare expenditures. But from an economic perspective, it is essential to consider the financial implications of paying for biologics treatments out of pocket or with a co-pay instead of adopting biosimilars.

A monoclonal IgG2/4k antibody called eculizumab RP (Soliris, Alexion) has been introduced in Russia as the first biosimilar for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). PNH is a rare haematological illness that is characterised by hemolytic anaemia, thrombosis, and peripheral blood cytopenias. Multiple firms such as Amgen, Samsung Bioepis and Biocad are now engaged in the development of biosimilars for eculizumab.

Biosimilar versions of biologics, such as eculizumab RP, that have been licensed for rare disorders may provide significant cost reductions and enhance accessibility. Non-clinical animal investigations may be omitted if there is limited variance in the analysis of the two molecules or if there is no accessible animal species that is pharmacologically relevant. Animal experiments were not performed during the preclinical evaluation of ABP 959, a potential biosimilar of eculizumab RP, due to its targeting of human complement protein 5. In addition, modelling and simulation may be used to enhance the design of more effective comparative clinical trials, a crucial aspect in the advancement of biosimilars for rare disease indications.

Biosimilar producers face resistance from originator companies, healthcare providers, and payers. Formulary restrictions, the bundling of reference products, and rebate strategies impede market expansion and increase entry barriers. It is imperative for pharmaceutical companies to dexterously navigate the balance between safeguarding their biologic products and nurturing an environment conducive to biosimilars, which inevitably contribute to a thriving competitive milieu. The implementation of robust regulatory frameworks to mitigate anticompetitive practices can expedite the entry of biosimilars into the market, encouraging enhanced accessibility. The evolving landscape of regulatory agencies has introduced certain waivers for animal testing and, in specific instances, clinical efficacy testing and interchangeability studies requirements.

Partnerships among pharmaceutical and biotechnology companies, research institutes, and patient advocacy organisations are gaining prominence. These collaborations use complementary knowledge and resources, promoting innovation. Often, government authorities and nonprofit institutions provide financial resources and subsidies to facilitate the advancement of R&D efforts focused on RDs. These monetary incentives compensate for the exorbitant expenses involved in the development of medicines for RDs. The acceptance and use of biosimilars are increasing as patients and healthcare stakeholders enhance their understanding and awareness driven by biosimilar manufacturers and regulators. As the availability of information and practical data supporting the safety and effectiveness of biosimilars rises, both patients and healthcare professionals are developing a greater level of confidence in these medications.

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