“Orphan” drugs: Good things for small populations

Preeti Karade[1], Popat Kumbhar[2], John Disouza[2]*, Vandana Patravale[3]*

[1]Department of Pharmaceutics, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, 416 416

[2] Department of Pharmaceutics, Tatyasaheb Kore College of Pharmacy, Warananagar, Tal.: Panhala, Dist.: Kolhapur, Maharashtra, 416 113

[3]Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Matunga, Mumbai, Maharashtra, 400 019

Email: jidisouza@tkcpwarana.ac.in; vb.patravale@ictmumbai.edu.in

1.Introduction

There is no satisfactory definition of a rare or orphan disease (OD). The World Health Organization has suggested that OD is any pathological condition that strikes fewer than 65 per 100,000 people. The USA defines a rare disorder as one that affects fewer than 2, 00,000 Americans. Australia has the limit at 5 in 10,000 individuals. A disease is deemed rare if it observe in less than 1 in 2,500 people in Japan (1). These numbers clearly relate to the population sizes of these countries. A disease may be prevalent in a particular region while being rare in another. Thalassemia is an inherited blood disorder that is rare in Northern Europe, but prevalent in Central Asia, India, and the Middle East and Mediterranean countries.

2. The Orphan Drug Act (ODA) of 1983

A rare disease is a health disorder with a low occurrence compared with common diseases, and an orphan drug is developed for the management of rare diseases. As a result, drugs for rare diseases have micromarkets that preclude researchers from recovering the money they spent on their studies.

The initial regulatory framework that fostered the creation of ODs for rare diseases was known as the Orphan Drug Act (ODA) (2). The Orphan Drug Act, was conceived and sanctioned in the United States on January 4th, 1983. At that time, treatments for such diseases were rarely developed. Before the passing of the ODA, only ten orphan drugs were accessible for patient use. The Orphan Drug Act, together with FDA policies, offers both “push” and “pull” incentives. Pull incentives include market exclusivity (3,4).

The function of the Orphan Drug Approval Law is to inspire pharmaceutical companies to enhance research for treatments of rare diseases. The FDA may award pharmaceutical manufacturers the orphan drug designation. It includes a waiver of prescription Drug User Fees, tax credits, and an extended market exclusivity period of 7 years (5). During the seven years’ marketing exclusivity period, the FDA may not award approval for the same drug for the same use but may approve a different drug for same disease (6). Since 1983, the ODA has approved a number of drugs and biologics that are useful in preventing or treating rare diseases, particularly in the fields of endocrinology, oncology, infectious disease, hematology, and neurology. A comparison of the various orphan drugs policies across the three regions is shown in Table 1.

Table 1. Comparison of the various policies on orphan drugs

Particulars	USA	Japan	Australia
Regulatory structure	Orphan Drug Act (1983)	Orphan Drug regulation (1993)	Orphan Drug Policy (1998)
Administrative authorities partnering	FDA/OOPD	MHLW/ OPSR Orphan drug division	TGA
Prevalence, for designating an Orphan status (per 10,000)	7.5	4	1.1
Marketing exclusivity period	7	10	5
Tax credit	50% of clinical studies	6 % of any sort of study + restricted to 10 % of company's corporation	No.

3. Indian perspective and initiatives by the Government

So far, only about 450 rare diseases have been recorded, and the estimated burden of rare genetic diseases is 72-96 million in India with an average time of 7 years for diagnosis. The most common among them are Thalassemia, Haemophilia, autoimmune diseases, sickle cell anaemia, Lysosomal storage disorders, primary immune-deficiency in children, Hirschsprung disease, Cystic Fibrosis, Gaucher's disease, Hemangioma, and some forms of muscular dystrophy (7).

Many of individuals afflicted with uncommon diseases increases regularly on a global scale, nations such as Canada and India ought to act decisively to address the escalating issue of orphan disease. In the meantime, the National Policy for Rare Diseases has finalized a policy and placed it on the website of the Ministry of Health and Family Welfare with a focus on the prevention of rare diseases identified by experts. The government has taken steps towards implementing legislation that will strengthen the country's healthcare system and offer assistance to many individuals who are afflicted with rare diseases.

As a response to this need, the government launched the National Policy for Rare Diseases (NPRD), 2021 in March, 2021. Under this policy, Eight Centres of Excellence (CoEs) have been identified. These are the best government tertiary health centres and their objectives are to mitigate the frequency of uncommon diseases by offering people with such diseases with access to reasonably priced treatment. The rare diseases have been recognized and classified into 3 categories as

Category 1: Disorders amenable to a single treatment

Category 2: Diseases requiring lifelong treatment with comparatively lower costs

Category 3: For which there is a convincing treatment available, however the difficulties include choosing the best patient for the best outcome, high costs, and lifetime therapy

For the diagnosis of an uncommon disease and the acquisition of funding for its treatment, patients may approach the nearest Centre of Excellence. The government is providing financial assistance of up to Rs. 50, 00,000 for the management of rare diseases in any of CoEs to the patients suffering from any category of the rare diseases mentioned in NPRD-2021. Furthermore, for genetic testing and counselling services five Nidan Kendras are now in place. Moreover, Central Technical Committee for Rare Diseases (CTCRD) under the Directorate General of Health Services has been formed under the Chairpersonship of Director General Health Services with technical experts.

4. The role of academic and research institutions in the development of drugs for rare diseases

According to the World Health Organization these conditions are strongly linked with poverty and flourish best in tropical areas. Even though many people suffer from these diseases, few medications are available on market. Historically, manufacturing companies have not shown interest in the development of drugs for rare diseases because of the poor return on investment. The government, not-for-profit organizations, pharmaceutical industry, and academic institutions, must address these issues and take initiative to provide relief from rare diseases.

Academia may face several hurdles in drug development. This appears to be attributable to various factors such as lack of resources and infrastructure, scientific guidance, deficiency of academic incentives, and the unavailability of expertise in regulatory affairs (8). Furthermore, many rare conditions are not yet linked to common diseases. Besides, challenges faced when caring for individuals with rare diseases are shown in Figure 1.

Figure 1. Challenges when caring for patient suffering from rare disease

Advanced technology in genetic science should be used for the identification of cellular and molecular pathways of orphan disease and the development of medicine. Market research, including patient population, availability, affordability, and efficacy of current treatments should be carried out to determine the potential for the development of orphan drugs. Academia can work with healthcare providers, patients, and caregivers to obtain insights into the unmet essentials in the rare disease community.

Training and experience on orphan diseases should be provided to healthcare professionals, including medical students. Furthermore, as pharmacists are credible sources of knowledge about orphan medications, they ought to be engaged with patient and parent education as well, since they are the primary caretakers (9-11). Additionally, it is crucial to offer financial, social, and psychological support systems for patients and their guardians or caretakers (12). It is important to provide the care required for patients living with orphan disease and to assist caregivers in improving the quality of life for these patients without having to compromise on their own lives (13). Academic and research institutions need to develop expertise in collaboration with multiple regulatory agencies so as to contribute to all stages of orphan drug development and disease management.

5. Conclusion

An orphan medicine is a pharmaceutical manufactured for the management of a rare disease. Since rare diseases are frequently inherited, infants, kids, and young adults are frequently impacted. A rare disease affects a small number of people, so these are often not 'adopted' by the pharmaceutical industry. Only 200 to 300 uncommon diseases have treatments available today. We believe that every individual deserves the greatest care available. The government needs to take the lead in ensuring that patients receive the best care possible and in motivating pharmaceutical companies to invest in rare disease treatment.

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