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REGULATORY REQUIREMENTS FOR ORPHAN MEDICINE AS PER CDSCO IN INDIA COMPARISON WITH US AND EUROPE UNION

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ABSTRACT

The project aims to conduct an in-depth analysis and documentation of the regulatory framework governing orphan medicines in India as established by the Central Drugs Standard Control Organization (CDSCO). This comprehensive report is intended to serve as an invaluable resource for pharmaceutical companies, healthcare professionals, regulatory authorities, and other stakeholders involved in the development, approval, and accessibility of orphan medicines in India. The primary purpose of this project, "Regulatory Framework Analysis for Orphan Medicines in India: A CDSCO Perspective," is to conduct an exhaustive examination and documentation of the regulatory landscape governing orphan medicines in India. Specifically, the project focuses on the regulations and guidelines established by the Central Drugs Standard Control Organization (CDSCO). This section of the project report provides a detailed examination of the Central Drugs Standard Control Organization (CDSCO) guidelines related to orphan medicines in India. It covers the definition and criteria for orphan medicines, as well as the designation process for orphan drug status within the CDSCO framework. It's important to note that the criteria for orphan designation may evolve over time as scientific understanding of rare diseases advances and as regulatory authorities like the CDSCO refine their guidelines. These criteria ensure that orphan medicines meet high standards of safety and efficacy while addressing the unique healthcare challenges posed by rare diseases, ultimately aiming to improve the prospects and well-being of rare disease patients in India.

KEYWORDS: Rare diseases, Orphan medicine, CDSCO, Agendas, Union.

INTRODUCTION

The project aims to conduct an in-depth analysis and documentation of the regulatory framework governing orphan medicines in India as established by the Central Drugs Standard Control Organization (CDSCO). This comprehensive report is intended to serve as an invaluable resource for pharmaceutical companies, healthcare professionals, regulatory authorities, and other stakeholders involved in the development, approval, and accessibility of orphan medicines in India.

The regulatory framework for orphan medicines in India, as perceived from the perspective of the Central Drugs Standard Control Organization (CDSCO), plays a pivotal role in addressing the unique healthcare challenges posed by rare diseases. This project report aims to provide a comprehensive analysis of this regulatory framework, shedding light on the complexities, nuances, and opportunities that surround orphan drug development and accessibility within India.

1.1 Background on Rare Diseases and Orphan Medicines

Rare diseases, often referred to as orphan diseases, encompass a diverse group of medical conditions characterized by their low prevalence within a population. In India, a rare disease is defined as a life-threatening or chronically debilitating condition affecting fewer than 5 out of 10,000 individuals. Despite their rarity, collectively, rare diseases affect a significant portion of the global population.

These diseases can be genetic, congenital, or acquired and encompass a wide range of disorders, including metabolic diseases, genetic syndromes, autoimmune disorders, and various types of cancers. The rarity of each disease poses unique challenges, including delayed or misdiagnosis, limited treatment options, and a lack of research and development.

Purpose and Significance of the Project: The primary purpose of this project, "Regulatory Framework Analysis for Orphan Medicines in India: A CDSCO Perspective," is to conduct an exhaustive examination and documentation of the regulatory landscape governing

orphan medicines in India. Specifically, the project focuses on the regulations and guidelines established by the Central Drugs Standard Control Organization (CDSCO).

DISCUSSION

Case Studies

Analysis of Real-World Examples of Orphan Drug Approvals in India

This section of the project report provides an analysis of real-world case studies of orphan drug approvals in India. These case studies illustrate the challenges, successes, and lessons learned in the process of bringing orphan medicines to the Indian market within the regulatory framework of the Central Drugs Standard Control Organization (CDSCO).

Case Study 1: Imatinib (Gleevec) for Chronic Myeloid Leukaemia (CML)

Imatinib, marketed as Gleevec, is a groundbreaking orphan medicine developed by Novartis for the treatment of Chronic Myeloid Leukaemia (CML). This case study highlights the regulatory journey of Gleevec in India, illustrating both challenges and successes in the approval process.

Background

Disease: Chronic Myeloid Leukaemia (CML) is a rare form of blood cancer that affects a small but significant number of patients in India. Before the introduction of Gleevec, the treatment landscape for CML was limited, and outcomes were often poor.

Key Milestones

1. **Clinical Trials:** The journey of Gleevec in India began with clinical trials to assess its safety and efficacy in treating CML patients. These trials were conducted in compliance with CDSCO guidelines and international standards.
2. **Orphan Drug Designation:** Recognizing the potential of Gleevec to address an unmet medical need for CML patients, the drug was granted orphan drug status by CDSCO. This designation brought certain benefits, including expedited review and reduced fees.
3. **Approval:** After successful clinical trials and robust data demonstrating Gleevec's efficacy and safety, CDSCO granted approval for its use in treating CML in India. This approval marked a significant milestone in improving the prospects of CML patients.

Challenges

Access and Affordability: While Gleevec offered a life-saving treatment for CML patients, its high cost posed challenges for accessibility and affordability. Advocacy efforts were launched to address pricing concerns and expand patient access.

Supply Chain and Distribution: Ensuring a consistent supply chain and distribution of Gleevec to reach patients in remote areas of India posed logistical challenges. Collaborations with healthcare providers and patient groups were essential to overcoming these hurdles.

Successes: Life-Saving Impact: Gleevec's approval and availability in India had a life-saving impact on CML patients. Many individuals who previously had limited treatment options experienced significant improvements in their health and quality of life.

Pricing Negotiations: Successful negotiations between Novartis and Indian authorities led to price reductions for Gleevec, making it more accessible to a broader patient population.

Patient Advocacy: Patient advocacy groups played a pivotal role in raising awareness about CML and advocating for policy changes to improve patient access to Gleevec.

Lessons Learned

Collaboration is Key: The success of Gleevec in India underscores the importance of collaboration between pharmaceutical companies, regulatory authorities, patient advocacy groups, and healthcare providers. Working together, these stakeholders can overcome challenges and ensure that life-saving orphan medicines reach the patients who need them.

Policy Adaptations: The Gleevec case highlights the need for policy adaptations to address affordability concerns. Negotiations on pricing and access can lead to more equitable outcomes for patients.

Patient-Centric Approaches: Patient-centric approaches, including patient engagement and advocacy, are crucial in rare disease drug development. They ensure that the patient voice is heard and that policies prioritize patient welfare.

Case Study 2: Nusinersen (Spinraza) for Spinal Muscular Atrophy (SMA)

The case of Nusinersen, marketed as Spinraza, provides a compelling example of the regulatory framework for orphan medicines in India, specifically in the context of Spinal Muscular Atrophy (SMA) treatment.

Background

Disease: SMA is a rare genetic disorder characterized by progressive muscle weakness and atrophy. It affects a small but significant population of individuals in India, often with severe consequences for their quality of life and life expectancy.

Key Milestones

1. **Clinical Trials:** The development of Spinraza began with rigorous clinical trials conducted in India to

assess its safety and efficacy in treating SMA patients. These trials adhered to CDSCO guidelines and international standards.

2. **Orphan Drug Designation:** Recognizing the urgent medical need for SMA treatments, the CDSCO granted Spinraza orphan drug designation. This designation facilitated an expedited review process and reduced regulatory fees.
3. **Approval:** Following successful clinical trials and robust data demonstrating Spinraza's effectiveness in treating SMA, CDSCO granted approval for its use in India. This marked a significant advancement in addressing the unmet needs of SMA patients.

Challenges

High Treatment Cost: Spinraza, like many advanced orphan medicines, initially came with a high treatment cost, which posed challenges for affordability and access for SMA patients in India.

Awareness and Diagnosis: SMA is a genetically complex disease, and awareness among healthcare providers and the public about its diagnosis and treatment was limited. Many patients faced delays in diagnosis and treatment initiation.

Successes

Life-Changing Impact: The approval of Spinraza in India had a life-changing impact on SMA patients. The drug halted or even reversed the progression of the disease in many cases, leading to improved motor function and quality of life.

Pricing Negotiations: Collaborative efforts between the pharmaceutical company and Indian authorities led to price reductions for Spinraza, increasing accessibility for patients.

Disease Awareness: Spinraza's approval prompted increased awareness of SMA among healthcare providers, leading to earlier diagnosis and intervention for affected individuals.

Lessons Learned

Patient Advocacy: Patient advocacy groups played a pivotal role in raising awareness about SMA, advocating for timely diagnosis, and influencing pricing negotiations to improve patient access.

Access to Innovation: While high treatment costs can be a barrier, negotiations and policy adaptations can enhance access to innovative orphan medicines for rare disease patients.

Healthcare Provider Education: Education and training of healthcare providers are essential to ensure that they can recognize and diagnose rare diseases like SMA promptly.

Case Study 3: Miglustat (Zavesca) for Niemann-Pick Disease

The case of Miglustat, marketed as Zavesca, illustrates the regulatory framework for orphan medicines in India, specifically in the context of treating Niemann-Pick Disease, a rare genetic disorder.

Background

Disease: Niemann-Pick Disease is a rare and debilitating genetic disorder that affects lipid metabolism, leading to a range of symptoms, including neurological deterioration. It affects a small but significant population of individuals in India, posing substantial medical and emotional challenges.

Key Milestones

1. **Clinical Trials:** The development of Zavesca for Niemann-Pick Disease began with clinical trials conducted in India to assess its safety and efficacy. These trials followed CDSCO guidelines and international research standards.
2. **Orphan Drug Designation:** Recognizing the critical need for treatments for Niemann-Pick Disease, CDSCO granted Zavesca orphan drug designation. This designation facilitated an accelerated review process and reduced regulatory fees.
3. **Approval:** After successful clinical trials and robust data demonstrating Zavesca's effectiveness in treating Niemann-Pick Disease, CDSCO granted approval for its use in India. This marked a significant advancement in addressing the unmet medical needs of patients with this rare disease.

Challenges

Limited Disease Awareness: Niemann-Pick Disease is a complex and relatively unknown condition. Limited awareness among healthcare providers led to delays in diagnosis and treatment.

Access and Affordability: Zavesca initially came with a high treatment cost, posing challenges for affordability and access for Niemann-Pick Disease patients in India.

Successes

Improvement in Patient Outcomes: The approval of Zavesca in India led to improvements in the quality of life for Niemann-Pick Disease patients. Some patients experienced stabilization of their condition, slowing the progression of neurological symptoms.

Pricing Negotiations: Collaborative efforts between the pharmaceutical company and Indian authorities led to price negotiations, making Zavesca more accessible to patients.

Awareness and Education: The approval of Zavesca prompted increased awareness among healthcare providers about Niemann-Pick Disease, leading to earlier diagnosis and intervention.

Lessons Learned

Patient Advocacy: Patient advocacy groups played a crucial role in raising awareness about Niemann-Pick Disease, advocating for timely diagnosis, and influencing pricing negotiations to improve patient access.

Access to Innovation: Negotiations and policy adaptations can enhance access to innovative orphan medicines for rare disease patients, even in cases of initially high treatment costs.

Healthcare Provider Education: Ongoing education and training of healthcare providers are essential to ensure that they can recognize and diagnose rare diseases like Niemann-Pick Disease promptly.

The approval and accessibility of Zavesca in India for the treatment of Niemann-Pick Disease demonstrate the positive impact of orphan medicines on rare disease patients. Challenges related to awareness, diagnosis, and affordability were addressed through collaborative efforts, ultimately improving patient outcomes and access to life-changing treatments.

A COMPARATIVE STUDY OF ORPHAN DRUGS IN US, EU & INDIA

Today, more than 5,000 diseases are catalogued as "rare" by the scientific community, so long as they affect small sections of population. The drugs used for the treatment of rare diseases are known as orphan drugs. An orphan drug is a pharmaceutical agent that has been developed specifically to treat a rare medical condition, the condition itself being referred to as an orphan disease. Initially a guideline (Orphan Drug Act) for orphan drugs has been made in the USA In the United States (US) rare diseases are defined as a disease or a condition which affects fewer than 200,000 patients in the country (6.4 in 10,000). people in country).

Exemption from application filing fees, tax credits for clinical research, marketing exclusivity for definite period of time and grant for phase I/II clinical trials are among the benefits given to the manufacturer of orphan drugs. As a result of these benefits number of drugs for the treatment of rare disease has been increased significantly in the last few years. The definition of orphan and rare disease is different in different countries on the bases of the number of patients affected by them. Diseases that manifest in patient populations representing at the maximum 6-8 per cent of the world population are defined as "rare diseases" or "orphan diseases. A recent systematic review of cost-of-illness studies on 10 rare diseases (including cystic fibrosis and haemophilia) found overall limited information published. Nevertheless, it is generally accepted that a disease having fewer than 100 patients per 1,00,000 population is described as rare disease and fewer than two patients per 1,00,000 is described as ultra-rare disease

- Bacterial me
- ningitis
- Calciphylaxis
- Darier disease
- Ebola virus disease
- Geniospasm
- Hashimoto's encephalitis
- IgM deficiency
- Jensen syndrome
- Kabuki syndrome
- Laryngeal cancer
- Meigel disease
- Nelson syndrome
- Ochronosis
- Papular urticarial
- Quebec platelet disorder
- Sakoda complex
- Taurodontism

The objective of this review is to look into Indian orphan drug regulations and an emphasis has been laid on ODA (orphan drug act) of US and orphan drug policies of other developed countries such as Europe thus showing the requirement of adopting ODA like legislations in India. The orphan drug regulation varies in different countries. The US was the first country to introduce an orphan drug act in 1983. Exemption from application filing fees, tax credits for clinical research, marketing exclusivity for definite period of time and grant for phase1/2 clinical trials are among the benefits given to the manufacturer of orphan drugs.

DEFINATION

As defined in the United States, any drug developed under the Orphan Drug Act of January 1983 (ODA) is an orphan drug. The ODA is a federal law concerning rare diseases (orphan diseases) that affect fewer than 200,000 people in the United States or are of low prevalence (less than five per 10,000 in the community).

Europe

A disease or disorder that affects fewer than 5 in 10,000 citizens is the definition for rare in Europe (Orphan Drug Regulation 141/2000). At first glance, this may seem a small number, but by this definition, rare diseases can affect as many as 30 million European Union citizens. According to EURORDIS (European Organization for Rare Diseases), the number of rare diseases numbers from about 6,000 to 8,000, most of which have identified genetic conditions, with medical literature describing approximately five new rare conditions every week. Twenty-five to Thirty million people are reported to be affected by these diseases in Europe.

INDIA

The need for such an act is thus evident from the initiative by the Indian pharmacists and the Government to implement Laws, which would strengthen the health infrastructure and provide relief to the numerous rare disease sufferers throughout the country. A group of

pharmacologists at a conference held by the Indian Drugs Manufactures Association in 2001 requested the Indian Government to institute the Orphan Drug Act in India.

[US]
Orphan Drug Act (January 4, 1983).

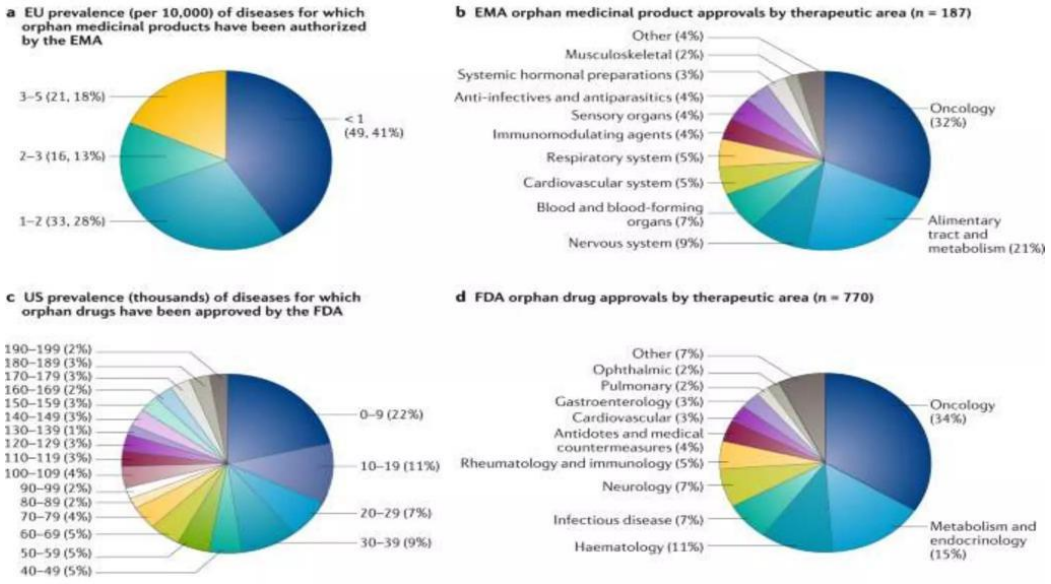
Designation granted based on prevalence of disease in the population of less than 200,000 people (approximately 0.1%) or no reasonable expectation of profitability

- Protocol assistance to design research protocols
- Tax credits for clinical research Market exclusivity
- Funding grants for clinical research to support development
- Penalty for intentionally false statement of orphan status
- Parallel track program and treatment INDs provide access to unapproved drugs
- Process patents granted for biotechnology products
- Accelerated approvals

The Food and Drug Administration (FDA) has charged The Office of Orphan Products Development (OOPD) to dedicate its mission to promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. It administers the major provisions of the Orphan Drug Act (ODA), which provide incentives for sponsors to develop products for rare diseases. The ODA has been very successful for more than 200 drugs and biological products for rare diseases have been brought to market since 1983. In contrast, the decade prior to 1983 saw fewer than ten such products come to market. In addition, the OOPD administers the Orphan Products Grants Program which provides funding for clinical research in rare diseases ODA. However, developing countries lack the resources to afford these drugs, with many devoting as little as $2 per capita per year to heath care. Also R&D costs have been rising and drug prices declining. Hence these figures too suggest a flow from less attractive to more attractive alternatives for investment.

A country should try to produce important drugs for the benefit of the whole world, depending on the R&D investment, the return on such investment, the tax and patent incentives, and its regulatory policies.

AIMS AND OBJECTIVES OF ORPHAN MEDICINE



CONCLUSION

Countries have proven as promoters in development of orphan drugs. The orphan drug regulation in the US and the EU has been successful in providing treatments to the patients with rare diseases. The orphan drug designations have increased drastically in the last few years. However, India in spite of having very large number of patients with rare diseases which can become a huge market for domestic pharmace.

REFFERENCE

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