Journal of Clinical Medicine and Research Vol 2 Issue 3 2025

Original Research Article

Open Access

Omniscient Pte.Ltd.

Barriers and Countermeasures to the Accessibility of Orphan Drugs from a Pharmacoeconomic Perspective

Jian-Ling Tan[1,2,*]

[1] Yichang Central People's Hospital, Yichang, Hubei, 444300, China
[2] Institute of Pharmaceutical Preparations, China Three Gorges University, Yichang, Hubei, 444300, China

***Correspondence to:** Jian-Ling Tan, Yichang Central People's Hospital, Yichang, Hubei, 444300, China, E-mail: 525743208@qq.com

Abstract: This paper focuses on the pharmacoeconomic barriers affecting the accessibility of orphan drugs and proposes corresponding countermeasures. It first outlines the fundamental framework and core concepts of pharmacoeconomic evaluation, as well as the unique characteristics involved in assessing orphan drugs. It then analyzes the key economic barriers arising during research and development, production, market access, reimbursement, distribution, and clinical use. Finally, it puts forward strategies such as improving multi-level systems ensuring drug accessibility, innovating payment models, optimizing policies for research, development, and regulatory approval, and strengthening pharmaceutical management and data sharing. The objective is to enhance the accessibility of orphan drugs and provide theoretical support for relevant policy-making.

Keywords: Orphan drugs; Pharmacoeconomics; Accessibility barriers; Countermeasure strategies

Introduction

Orphan drugs face significant challenges in accessibility due to small patient populations, high development costs, and limited market returns. Pharmacoeconomic evaluation, as a key tool for assessing drug value and guiding resource allocation, is essential for improving the accessibility of such therapies. This study analyzes the pharmacoeconomic barriers encountered during the development, approval, and distribution of orphan drugs and proposes targeted countermeasures to promote their rational development, market entry, and clinical use, ultimately meeting the treatment needs of patients with rare diseases.

1. Pharmacoeconomic Evaluation Framework for Accessibility of Orphan Drugs

1.1 Overview of the Pharmacoeconomic Evaluation of Orphan Drug Accessibility

The pharmacoeconomic evaluation framework for orphan drug accessibility serves as a core tool for assessing drug value and guiding resource allocation, balancing general pharmacoeconomic principles with the unique characteristics of orphan drugs. At its core, it is value-oriented, comprising four key components: evaluation objectives, dimensions, methods, and data sources. The evaluation objectives aim to unify clinical, economic, and societal value of the drug, ensuring

patient access while controlling costs. The evaluation dimensions include effectiveness, safety, economic performance, and humanistic value. Effectiveness is measured using disease-specific indicators tailored to the rare disease context; safety considerations include long-term data; economic performance is analyzed from multiple perspectives; and humanistic value emphasizes quality of life and social equity [1]. Evaluation methods are primarily cost-utility analyses, supplemented by other approaches. Modeling techniques are employed to address data scarcity issues. Data sources integrate multiple types of information to ensure comprehensive and reliable evidence, providing scientific support for orphan drug research and development, market access, and reimbursement decisions.

1.2 Core Concepts in Pharmacoeconomics

The core concepts of pharmacoeconomics form the theoretical foundation for constructing an evaluation system for orphan drugs. Key elements include costs, outcomes, utility, benefits, and value. Costs encompass direct medical costs, direct non-medical costs, indirect costs, and intangible costs. Outcomes measure objective improvements in clinical endpoints attributable to the drug. Utility quantifies patients' subjective perceptions of their health status using specific instruments. Benefits translate health outcomes into monetary terms. Value represents a comprehensive trade-off among costs, outcomes, and other considerations. In the context of orphan drug evaluation, these concepts require flexible adaptation. For instance, due to small patient sample sizes, outcome indicators must be precisely defined, and intangible costs must be thoroughly considered. Such adjustments ensure that evaluation results are both scientifically robust and practically relevant to real-world decision-making.

1.3 Specific Characteristics of Orphan Drug Evaluation

Orphan drug evaluation differs significantly from that of conventional drugs due to the unique epidemiology, disease features, and drug development patterns associated with rare diseases. From an epidemiological perspective, rare diseases have low incidence and small patient populations, making recruitment for clinical trials challenging and resulting in data that may be incomplete or insufficiently representative. Regarding disease characteristics, many rare diseases are genetic, with complex pathophysiological mechanisms, lack of standardized diagnostic criteria, and multi-system involvement. These factors complicate the establishment of uniform efficacy endpoints and limit the availability of long-term prognosis data. In terms of drug development, orphan drugs typically involve long development cycles, high investment, and limited market demand, leading to high unit costs and posing significant challenges for economic evaluation. Moreover, some drugs do not offer a cure but can improve quality of life or extend survival; the "life-saving" value of such treatments is difficult to quantify. Additionally, orphan drugs often attract high societal attention, so evaluations must balance medical and social value, taking into account both patient needs and the affordability constraints of healthcare systems. These complexities necessitate the establishment of a dedicated and specialized evaluation framework for orphan drugs.

2 Pharmacoeconomic Barriers to Orphan Drug Accessibility

2.1 Barriers in the Research, Development, and Production Phase

Economic barriers in the research, development, and production phases represent the primary bottleneck restricting the accessibility of orphan drugs, mainly manifested as a severe imbalance between high costs and low returns. In the research and development phase, the complex and often not fully understood pathogenesis of rare diseases requires substantial upfront investment in basic research, including extensive target screening and mechanism validation. The small patient population makes clinical trial recruitment extremely challenging, often necessitating cross-regional or international collaboration, which prolongs trial duration and significantly increases human and material costs. Furthermore, clinical trials for orphan drugs carry a higher risk of failure, with many projects terminated due to insufficient efficacy or safety concerns, further driving up development costs. In the production phase, the limited market size of orphan drugs prevents economies of scale, leading to high unit costs for production line construction, raw material procurement, and quality control. Some orphan drugs, particularly biologics, involve complex manufacturing processes that require stringent

environmental controls and advanced technical capabilities, further increasing production difficulty and cost[2]. Critically, the high costs of research, development, and production are often unsupported by sufficient market returns. The small patient population means that even with high pricing, overall sales rarely cover the initial investment. This creates a significant disincentive for enterprises to invest in orphan drug R&D and production, leaving many rare disease areas with "no available treatments" and forming a vicious cycle of "difficult R&D – limited production – low accessibility."

2.2 Barriers in the Market Access and Reimbursement Phase

Economic barriers in the market access and reimbursement phase directly determine whether orphan drugs can be clinically used, with the core issue being the conflict between high drug prices and the affordability of health insurance systems. In the market access phase, orphan drugs are generally priced high due to substantial R&D costs. Traditional health technology assessment frameworks often rely on benchmarks for conventional drugs, using fixed cost-effectiveness thresholds as access criteria. Orphan drugs frequently fail to meet these standards, making it difficult for them to be included in national reimbursement lists or essential medicines catalogs. Although some regions have established special access channels for rare disease treatments, unclear eligibility criteria and cumbersome approval procedures continue to hinder timely access. In the reimbursement phase, single-channel public insurance systems struggle to bear the high costs of orphan drugs. Basic medical insurance funds aim to cover the healthcare needs of the general population. Comprehensive coverage of high-cost orphan drugs could threaten the sustainability of these funds. Private health insurance coverage is limited; most policies either exclude rare diseases or impose high deductibles. Patients themselves typically lack the financial capacity to afford treatment, as annual costs for orphan drugs can reach tens or even hundreds of thousands of yuan, far beyond the means of ordinary households. Even when drugs gain access approval, out-of-pocket costs often remain prohibitive, resulting in a widespread phenomenon of "easy access, difficult payment."

2.3 Barriers in the Distribution and Utilization Phase

Economic barriers in the distribution and utilization phase result in orphan drugs being difficult to accurately deliver to patients and use appropriately, even after gaining market access. In the distribution phase, demand for orphan drugs is scattered and highly variable. In most regions, the patient population is small, and single procurement volumes are low, leading to disproportionately high warehousing and transportation costs for distribution companies. Some orphan drugs require specialized cold-chain logistics, further increasing distribution expenses. Due to the unstable market demand, distributors often fear inventory stagnation tying up capital, making them reluctant to stock orphan drugs at scale. This frequently results in supply interruptions and shortages. In the utilization phase, low diagnostic rates for rare diseases and the lack of diagnostic capacity in many primary healthcare institutions prevent timely identification of patients. Even when drugs are available, they cannot always be accurately administered. Some orphan drugs require specialized monitoring and care, but primary healthcare facilities often lack the necessary technical equipment and professional staff, restricting clinical application. Additionally, limited dissemination of pharmacoeconomic information results in insufficient awareness among clinicians regarding the cost-effectiveness of orphan drugs. Consequently, physicians tend to prescribe familiar conventional drugs or reduce prescriptions for high-cost orphan drugs to avoid imposing financial burdens on patients, further reducing actual drug accessibility.

3 Pharmacoeconomic Strategies to Improve Orphan Drug Accessibility

3.1 Improving a Multi-tiered Insurance and Support System

Establishing a comprehensive multi-tiered support system is a key strategy to address the affordability challenges of orphan drugs. This involves constructing a diversified framework combining basic medical insurance, critical illness insurance, medical assistance, commercial insurance, and charitable donations, thereby distributing the financial burden across different layers. For basic medical insurance, the coverage scope for orphan drugs should be clearly defined. Reimbursement

rates should be differentiated according to the cost-effectiveness of each drug, prioritizing those with high clinical value and favorable economic profiles. The coverage list should be dynamically updated to include newly developed effective drugs in a timely manner. Critical illness insurance should increase reimbursement limits for rare diseases and lower deductibles to reduce the high out-of-pocket burden on patients[3]. Medical assistance programs should focus on low-income patients with rare diseases, providing targeted subsidies for those who still cannot afford drugs after insurance reimbursement, ensuring that illness does not lead to financial hardship. Commercial insurance should develop specialized products for rare diseases, simplify enrollment processes, and expand coverage. Personalized protection plans can be designed for different rare disease types, using actuarial techniques to achieve risk pooling. Additionally, charitable organizations should be encouraged to establish dedicated funds for orphan drugs, sourcing finances through corporate donations and public fundraising to subsidize drug costs for patients. Together, this multi-layered system—leveraging government support, market mechanisms, and social resources—can comprehensively enhance the financial accessibility of orphan drugs.

3.2 Innovative Payment Models

Innovative payment models are a key approach to balancing the high cost of orphan drugs with patients' and insurers' payment capacity. By adopting flexible payment mechanisms, short-term financial pressure can be alleviated, thereby improving drug affordability. A value-based payment model can be implemented, in which reimbursement amounts are adjusted according to the actual clinical effectiveness of the drug. If the drug achieves predefined therapeutic outcomes, full payment is made by the insurance authority; if outcomes fall short, reimbursement is proportionally reduced. This approach incentivizes pharmaceutical companies to improve drug efficacy. A staggered or installment payment model spreads the annual treatment cost of high-priced drugs over multiple years, reducing short-term financial burden on both the insurance fund and patients. For example, drugs with annual treatment costs exceeding one million yuan could be paid over 3–5 years. Risk-sharing agreements between insurers and manufacturers can further mitigate financial risk. If actual clinical use results in lower-than-expected effectiveness or adverse events reduce drug utilization, manufacturers would refund a portion of the insurance payments, thus lowering the insurer's exposure. An indication-specific segmented payment model can also be explored. Reimbursement standards are differentiated based on the cost-effectiveness of various indications: higher reimbursement rates are allocated to core indications with significant therapeutic benefits, while lower rates apply to secondary or adjunctive indications. This ensures precise allocation of financial resources and enhances payment efficiency.

3.3 Optimizing R&D and Regulatory Policies

Optimizing R&D and regulatory policies is a critical measure to enhance the supply of orphan drugs from the source, by reducing development costs and accelerating market entry. In the R&D phase, special funds for orphan drug development can be established to provide financial subsidies for enterprises' investments, covering key stages such as basic research and clinical trials. Tax incentives, including exemptions or reductions in value-added tax and corporate income tax during the R&D process, can further reduce financial burdens. Additionally, the creation of an orphan drug R&D data-sharing platform—integrating research data from universities, research institutes, and companies—can prevent duplicated studies and shorten development cycles. In the regulatory phase, a priority review pathway for orphan drugs should be implemented, simplifying approval procedures and establishing dedicated review teams. Eligible drugs would benefit from early engagement, priority assessment, and expedited approval, thereby shortening regulatory timelines. The breakthrough therapy designation can be applied to orphan drugs with urgent clinical needs and significant efficacy, allowing guidance during the clinical trial phase and facilitating smooth transition to regulatory approval. Furthermore, the orphan drug designation system should be improved, granting market exclusivity for designated orphan products. During this exclusivity period, competition from similar drugs is restricted, ensuring returns on R&D investments, stimulating corporate motivation, and ultimately increasing the overall supply of orphan drugs.

3.4 Strengthening Pharmaceutical Management and Data Sharing

Strengthening pharmaceutical management and data

sharing is a key strategy to improve the efficiency of orphan drug distribution and utilization, optimizing accessibility across the entire process through standardized management and data empowerment. In terms of pharmaceutical management, a national unified orphan drug distribution management platform should be established, integrating information from production, distribution, and clinical use. This platform enables precise management of drug procurement, storage, and allocation. Distribution companies can access real-time demand information across regions, rationally allocate inventories, and ensure stable drug supply[4]. Medical institutions should strengthen pharmaceutical management by appointing dedicated orphan drug managers, responsible for procurement, storage, usage monitoring, and conducting regular training programs to enhance healthcare staff's competence in drug utilization and cost-effectiveness awareness. Regarding data sharing, a real-world research database for orphan drugs should be constructed, integrating clinical treatment data, drug usage data, and cost-effectiveness data to provide a robust evidence base for pharmacoeconomic evaluation. Real-world data can be used to verify long-term efficacy and economic value, supporting informed decisions in insurance reimbursement and clinical prescribing. Establishing a data-sharing mechanism that connects insurance systems, medical institutions, pharmaceutical companies, and research organizations can break data silos, enabling interconnectivity and promoting collaborative optimization across the full drug lifecycle—from R&D, market access, and payment to distribution and clinical use—ultimately enhancing overall accessibility.

Conclusion

Improving the accessibility of orphan drugs is a complex, systematic endeavor involving multiple stages, including research and development, market access, payment, and distribution. Implementing strategies such as establishing a multi-level insurance system, innovating payment models, optimizing R&D and regulatory policies, and strengthening pharmaceutical management and data sharing can effectively address the current pharmacoeconomic barriers. Looking ahead, sustained collaboration among governments, pharmaceutical companies, and healthcare institutions, combined with ongoing innovation, will be essential to further enhance orphan drug accessibility and safeguard the health rights of patients with rare diseases.

References

[1] Cui, N., Liu, K., Dong, Q., et al. Review and Implementation Effectiveness of Rare Disease Drug Policies in China. Chinese Journal of New Drugs, 2025, 34(19): 2027–2035.

[2] Cao, Y., Liu, X., Wang, S., et al. Current Status and Prospects of Digital Intelligence Technology in Rare Disease Drug Surveillance. Rare Disease Research, 2025, 4(1): 22–29.

[3] Chen, R., Zhang, S. Trends in Orphan Drug R&D. Rare Disease Research, 2024, 3(2): 221–223.

[4] Cui, H., Tang, L., Cui, C., et al. Considerations for Applying Decentralized Clinical Trials in Orphan Drug Clinical Development. Rare Disease Research, 2024, 3(2): 175–180.