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Progress in the research and pharmacoeconomic evaluation of drugs and devices for rare diseases in China

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SUMMARY: The development, importation, and reimbursement of drugs and medical devices for rare diseases have become critical issues within China's healthcare system. Since 2018, China has issued two national Rare Disease Lists, covering 207 diseases. As of December 2025, 223 drugs for rare diseases have been marketed domestically, with 136 (61.0%) included in the national list for reimbursement by basic medical insurance scheme. Advances have also been made in diagnostic technologies and treatment equipment. This article also examines the issues with and factors influencing the pharmacoeconomic evaluation of rare disease therapies. Additionally, over 100 registered patient organizations contribute substantially to care, education, research, and advocacy. China has piloted multi-level healthcare security system, including national and local healthcare security systems. The introduction of a list of innovative drugs covered by commercial insurance in 2025 further supplements this system. These measures have collectively expanded reimbursement coverage. Despite progress in drug development, insurance coverage, and evaluation of drugs in terms of health economics, continued efforts are needed to enhance treatment accessibility and equity. Key measures include putting forward rare disease legislation, promoting research on health technology assessment, improving health utility measurement, encouraging domestic orphan drug development, and strengthening international collaboration. China's experience offers valuable insights for global rare disease prevention and treatment initiatives.

Keywords: rare diseases, orphan drugs, rare disease medical devices, pharmacoeconomic evaluation, pharmaceutical policy

1. Introduction

Rare diseases in China are officially defined as conditions meeting any of the following criteria: an incidence of less than 1 in 10,000 among newborns, a prevalence below 1 in 10,000 in the general population, or a total patient population under 140,000 (*1*). Based on these definitions, the estimated number of rare disease patients in China is approximately 20 million. This definition is more stringent than that of the European Union (EU) and the United Kingdom (UK), which set the prevalence threshold at 5 in 10,000, and it suggests a lower absolute patient count than in the United States (US), where the benchmark is 200,000 individuals (*2*).

In 2018, China's National Health Commission, along with four other ministries, jointly issued the first national Rare Disease List, listing 121 conditions (*3*). A second installment was published in 2024, adding 86 more rare diseases, bringing the total to 207 (*4*). Additionally, regional initiatives such as the Shanghai Rare Disease List (2025 edition) have expanded the scope to 278 conditions, offering supplementary guidance for clinical practice and insurance coverage (*5*).

Most rare diseases are characterized by high rates of disability and mortality. The drafting of rare disease lists plays a critical role in guiding public health, regulatory, and insurance authorities in prioritizing prevention and treatment efforts. It also facilitates the regulatory review and approval of orphan drugs and stimulates pharmaceutical innovation. The Center for Drug Evaluation (CDE) under the National Medical Products Administration (NMPA) has established a priority review pathway, through which 15 rare disease drugs were approved for marketing in 2023 (*6*). Moreover, the CDE continues to publish lists of urgently needed imported drugs, allowing certain rare disease therapies to bypass Phase III clinical trials and proceed directly to market authorization (*7*).

The development, importation, and reimbursement of drugs and medical devices for rare diseases have emerged as key issues within China's evolving healthcare system. This paper aims to examine the progress made in

rare disease drug and device research, analyze the current landscape of pharmacoeconomic evaluation, and explore the role of patient organizations and policy innovation, with particular attention to the development of a multi-level healthcare security system, in improving access and equity for rare disease patients in China (Figure 1).

2. Progress in the development of rare disease drugs in China

China has made notable strides in the research and development (R&D) of rare disease drugs. According to publicly available information (*8,9*), as of December 2025, a total of 223 rare disease drugs had been approved for marketing in mainland China. While treatments exist, the lack of insurance coverage remains a barrier to access. Over two-thirds of these drugs are imported, with limited domestic innovation, resulting in unstable supply and high prices.

In 2025, China approved its first domestically developed gene therapy product — Dalnacogene Ponparvovec Injection (Chinese brand name: Xinjuning) — for moderate to severe hemophilia B. Developed by Belief Biomed Inc, this Class I innovative drug fills a critical gap in China's gene therapy landscape (*10*). Hemophilia B affects approximately 20,000 patients in China (*11*). The therapy uses a hepatotropic recombinant adeno-associated virus (rAAV) vector to enable long-term expression in liver cells. Initial clinical trials with 10 patients involving a median follow-up of 58 weeks indicated that average FIX activity reached 36.9 IU/dL and there were no Grade 3–4 adverse events (*12*). Long-term follow-up data from 26 patients, presented at the 66th American Society of Hematology (ASH) meeting, showed an annual bleeding rate (ABR) of 0.6 and average FIX activity of 55 IU/dL, with 80.8% of patients experiencing no bleeding episodes post-treatment (*13*). In 2023, Belief Biomed Inc. entered a strategic partnership with Takeda China, enabling more patients to receive this therapy (*14*).

As of 2025, Chinese companies have launched 52 gene therapy R&D projects targeting 28 rare

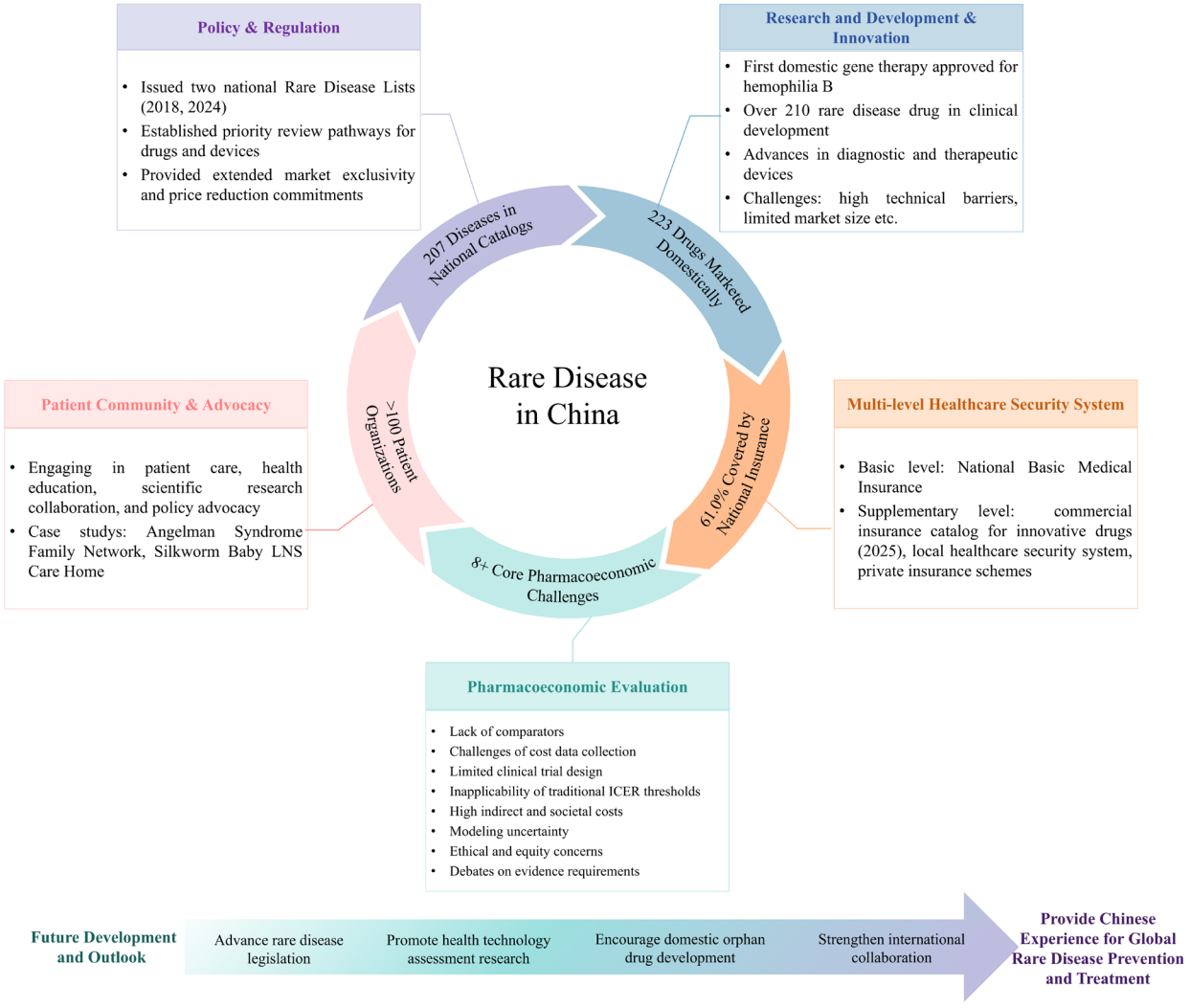

Figure 1. China's rare disease prevention and treatment system. ICER, incremental cost- effectiveness ratio; LNS, Lesch-Nyhan syndrome.

diseases, with five therapies in Phase III trials (*15*). Approximately 210 rare disease drugs are currently in clinical development (*9*). Overall, China's rare disease drug research is entering a phase of rapid expansion.

Generic drug policies have also been introduced, including priority review, extended market exclusivity, and price reduction commitments. For instance, the annual cost of velaglucerase beta for Gaucher disease was reduced to 50% of the imported drug price (*16*). Given the higher R&D costs of orphan drugs compared to common disease treatments, special policy support is essential — such as accelerated approval, tax incentives, and extended exclusivity periods (*e.g.*, 10 years in the EU, 7 years in the US).

3. Progress in the development of rare disease medical devices in China

China has provided substantial policy support for the R&D of medical devices targeting rare diseases. The release of the first national Rare Disease List in 2018 explicitly outlined directions for device innovation in this field (*17*). The National Medical Products Administration (NMPA) has encouraged the registration of innovative devices, with some rare disease-related products granted access to expedited approval pathways.

3.1. Diagnostic technologies

On the diagnostic front, China has launched a nationwide newborn genetic screening initiative using a combined approach of tandem mass spectrometry and next-generation sequencing (NGS), now implemented across 29 provinces (*18*). The National Health Commission issued the "Guidelines for Equipment Configuration in the Rare Disease Diagnosis and Treatment Network", recommending the deployment of high-throughput sequencers, mass spectrometers, and neuroimaging navigation systems. Provinces and municipality such as Shanghai, Zhejiang, and Jiangsu have begun including certain in vitro diagnostic reagents for rare diseases in their medical insurance reimbursement schemes.

3.2. Therapeutic devices

In terms of treatment technologies, deep brain stimulation systems have been used to treat primary dystonia. High-quality evidence from long-term follow-up studies has demonstrated that deep brain stimulation systems provides substantial and sustained improvements in motor function and quality of life (*19*). Exoskeleton robots (*e.g.*, the "Maibu Robot") have entered clinical trials for spinal muscular atrophy (SMA) patients at Peking Union Medical College Hospital. Brain-computer interface technologies, based on neuromorphic chips, have been deployed for precision interventions in pediatric brain tumors, refractory epilepsy, and neurodeveopmental disorders.

3.3. Challenges and barriers

Despite these advances, several challenges persist: *i*) high technical barriers: device development requires interdisciplinary integration and long R&D cycles; *ii*) limited market size: the small patient population leads to a low return on investment, dampening industry enthusiasm; *iii*) regulatory gaps: There is currently no dedicated approval pathway for rare disease devices, necessitating further regulatory refinement; and *iv*) health technology assessment (HTA) limitations: comparator selection is difficult, often relying on composite interventions as the "standard of care". Modeling studies involve a high level of uncertainty and risks of biased parameter assumptions.

4. Current status of the pharmacoeconomic evaluation of rare disease drugs in China

Orphan drugs are characterized by high pricing and increased R&D costs, with premiums largely driven by monopolistic pricing mechanisms. Due to the small patient population size, demand elasticity is limited. The pharmacoeconomic evaluation of rare disease drugs in China faces numerous challenges:

First is the lack of comparators, more than 95% of rare diseases lack effective treatments (*20*). The standard of care (SOC) often consists of palliative therapies or off-label use, resulting in either no comparator or multiple, inconsistent comparators.

Second is the challenge of collecting cost data, cost data are highly heterogeneous and difficult to standardize.

Third is limited clinical trial design. Most trials are single-arm with small sample sizes, leading to uncertainty in treatment effect estimations. Mixed treatment comparisons (MTC) and network meta-analyses are recommended to compensate for the lack of head-to-head trials, along with the use of global patient registries and real-world data (RWD) to construct synthetic control arms.

Fourth is the inapplicability of traditional incremental cost-effectiveness ratio (ICER) thresholds. The commonly used ICER threshold of three times per capita GDP (cost per QALY) is difficult to apply to rare diseases. Strict adherence to this threshold standard may result in inequitable access for rare disease patients.

Fifth are high indirect and societal costs. Rare disease patients often require long-term caregiving, and yet current evaluations lack any consideration of the caregiver burden and productivity loss.

Sixth is modeling uncertainty. Utility values and the probability of disease progression are unavailable for most rare disease. Survival curves often require long-term extrapolation. For gene or cell therapies with

high upfront costs, traditional pay-as-you-go insurance models are insufficient, necessitating innovative payment mechanisms.

Seventh are ethical and equity concerns. The high cost of orphan drugs raises ethical questions. Allocating limited resources to rare diseases may be perceived as unfair to patients with more common conditions.

Finally, there are debates on evidence requirements. There have been proposals to exempt orphan drugs from traditional economic evidence requirements, shifting the focus toward budget impact analysis (*21*).

To address these complexities, value assessment of orphan drugs should adopt a multi-criteria decision analysis (MCDA) framework, incorporating non-economic dimensions such as disease severity, unmet medical need, innovation level, and equity considerations. Manufacturers often seek to expand indications to maximize commercial value.

5. The role of patient organizations in orphan drug research

Over the past decade, China has established multiple rare disease advocacy organizations, including the China Organization for Rare Diseases (CORD), the China Alliance for Rare Diseases (CHARD), the Illness Challenge Foundation (ChinaICF), and the Shanghai Foundation for Rare Diseases. According to CORD statistic data, there are currently over 100 officially registered rare disease patient organizations nationwide (*22*). These groups play a vital role in patient care, health education, scientific research collaboration, and policy advocacy.

The Golden Snail Award is a grassroots honor in China's rare disease community, established by CORD to recognize individuals, teams, patient organizations, and research institutions that have made outstanding contributions to the field. The following two case studies are from the "2025 Golden Snail Award".

5.1. Case Study 1: Angelman Syndrome Family Network

Founded in 2011, this organization supports 1,522 families affected by Angelman syndrome, a condition listed in China's first national Rare Disease List. In collaboration with Roche Inc, the group participated in a National Natural Science Foundation project and conducted extensive outreach and education. It collected genotype data from 150 patients and conducted natural history and survival studies on over 500 cases. The organization helped establish a dedicated clinic at Fudan University Children's Hospital and proposed to establish "Children's Brain Health Centers" at a certain tier of care. The Network's 25-member management team includes physicians, rehabilitation specialists, and patient parents. In 2022, a market shortage of clonazepam was resolved swiftly following advocacy efforts by the organization and public support (*23*).

5.2. Case Study 2: Silkworm Baby Lesch-Nyhan Syndrome (LNS) Care Home

LNS is a rare X-linked recessive purine metabolism disorder characterized by motor dysfunction, intellectual disability, and self-injurious behavior. Cases have been identified across 19 provinces with a prevalence of 1 in 380,000. The organization was established in 2008, it has registered over 100 cases and launched the "China LNS Diagnosis and Research Alliance". It conducts natural history and genotype-phenotype studies, maintains a literature database of over 800 publications from 32 countries spanning 45 years, and developed China's first expert consensus on the diagnosis of LNS. The group pioneered HPRT enzyme activity testing, initiated a digital disease tracking tool, and built a national LNS patient registry system, fostering international collaboration (*24*).

6. Multi-level healthcare security system for rare diseases

In addition to the National Basic Medical Insurance (NBMI), China has explored multi-level local healthcare security system in terms of payment reform experience. In 2019, for example, Zhejiang Province established a provincial rare disease drug fund, financed by an annual contribution of 2 RMB per person from the critical illness insurance pool. The fund prioritized four ultra-rare diseases: Gaucher disease, phenylketonuria, Pompe disease (mucopolysaccharidosis type II), and Fabry disease. Over 90% of treatment costs were reimbursed, with an annual out-of-pocket capping out at 100,000 RMB per patient (*25*). In 2021, Jiangsu Province developed a mechanism linking rare disease drug coverage with national insurance negotiations, initially covering Gaucher disease, Pompe disease, Fabry disease, spinal muscular atrophy (SMA), and mucopolysaccharidosis type IVA (*26*).

Starting in 2025, a list of innovative drugs covered by commercial insurance has been developed to supplement coverage through urban inclusive supplementary commercial health insurance (Huiminbao) and other private insurance schemes. The latest medical insurance list, released in 2025, added a total of 114 new drugs. Ten of those drugs were for rare diseases, accounting for about 9% of the total. By the end of 2025, the total number of rare disease medications on the list had reached 136, covering 69 diseases on the First and Second Installments of the Rare Disease List. Medical coverage for rare disease drugs is expected to continue to expand (*27,28*).

7. Future development of and outlook for rare disease research in China

At the 78th World Health Assembly (WHA) in 2025, the World Health Organization (WHO) adopted a landmark resolution recognizing rare diseases as a global health priority. The resolution aims to enhance equity, inclusion, and access to care, thereby improving universal health coverage for over 300 million individuals living with rare diseases worldwide (*29,30*). This initiative is expected to significantly advance China's efforts in rare disease prevention, treatment, and drug development.

China is promoting legislation in the area of rare diseases, expanding the number of orphan drugs included in the NBMI reimbursement list and exploring commercial insurance pathways. For high-cost cell and gene therapies (CGTs), efforts are underway to include them in the national list of innovative drugs, along with the development of novel payment mechanisms to improve affordability and access.

China has also established the National Rare Disease Registry System (NRDRS), which currently includes data on 218 rare diseases and more than 100,000 registered cases (*31*). A nationwide network of 419 hospitals has been formed to provide collaborative diagnosis and treatment for rare diseases at the provincial level, and further improvements in clinical capacity are expected (*32*).

In the future, China should prioritize legislation for rare diseases and promote research on health technology assessment frameworks and methodologies for rare disease drugs and medical devices. Particular emphasis should be placed on promoting high-quality approaches to measuring health utilities, encouraging domestic orphan drug development, and fostering international collaboration. Breakthroughs in the field of rare diseases are not only a reflection of medical progress but also a testament to social equity and humanitarian care. China's exploration of and practical experience in rare disease prevention and treatment can make a meaningful contribution to the global advancement of rare disease initiatives.

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