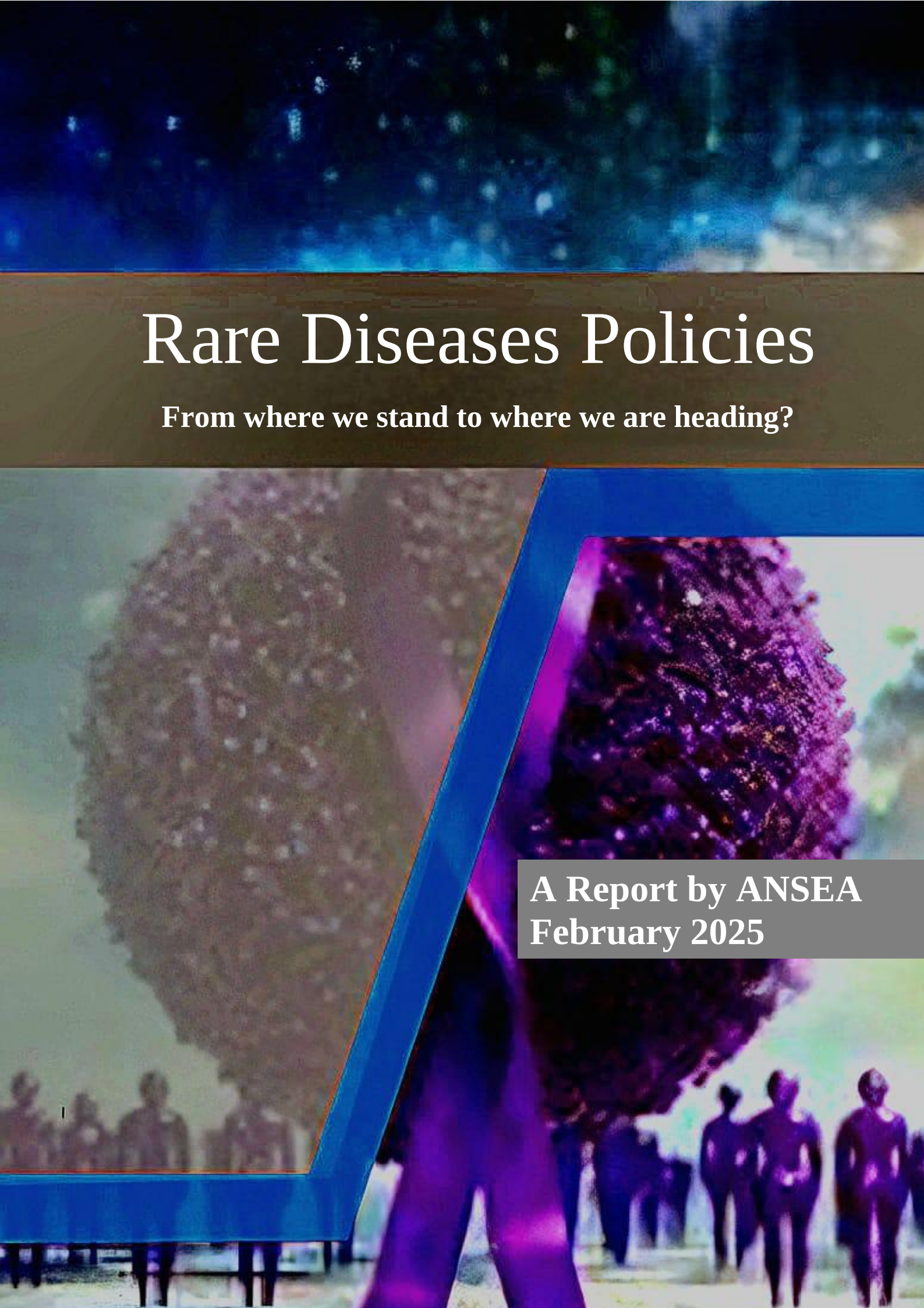

Rare Diseases Policies

From where we stand to where we are heading?

A Report by ANSEA
February 2025

About ANSEA

ANSEA is a global healthcare consulting firm committed to supporting public and private sector institutions in improving patient health outcomes. Our expertise ranges from Commercial Planning, Market Access, Health Systems Research and Stakeholder Engagement. With our network of over 30 country experts, we bring forward unparalleled, innovative solutions and local insights to support our clients across the world.

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1 Rare Diseases Overview

1.1 Overview and Global Burden

Rare diseases, also known as orphan diseases, are often characterized by their low prevalence affecting fewer than 1 to 5 individuals per 10,000 in the general population (fewer than 1 in 2000 people in any WHO region). These diseases are heterogeneous, with variable prognoses, often leading to higher mortality rates and reduced life expectancy compared to the general population. As of 2024, the current world population stands at ~ 8.2 billion of which [3.5% - 5.9% of the global population], approximately 260 to 440 million individuals worldwide are affected by rare diseases. Currently, the medical community recognizes over 7,000 rare diseases; however, it is important to note that this figure is steadily increasing, with approximately 250 new conditions being identified each year. At present more than 7000 rare diseases are known to medical community but stay wary that this number is continuously rising at the rate of about 250 new conditions being added every year [1]. Around 80% of rare diseases have a genetic cause, almost 70% of which present in childhood; about 95% lack approved treatments; the average time for an accurate diagnosis is 4·8 years; and about 30% of children with a rare disease die before age 5 years[2].

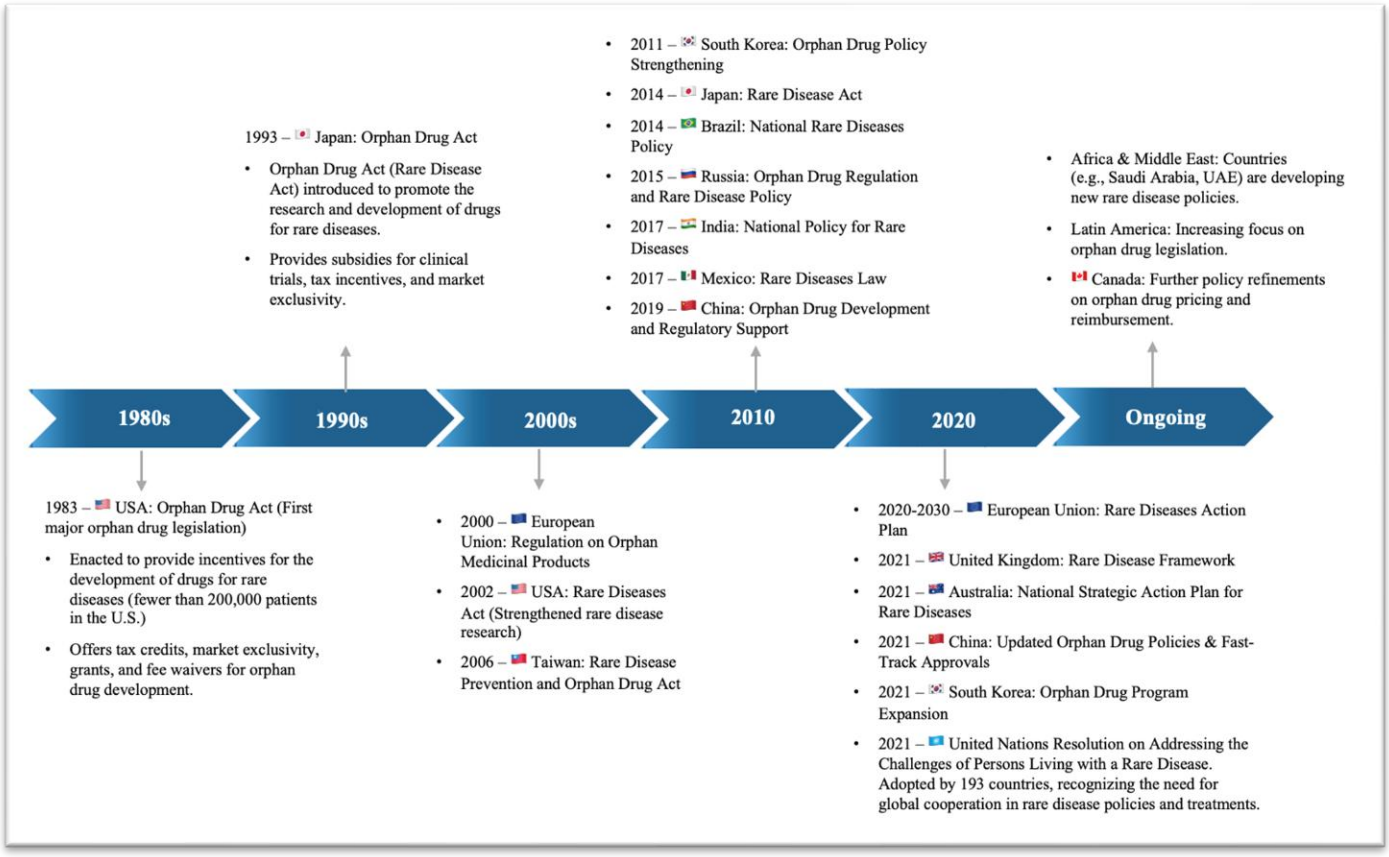
The fundamental cause of rare diseases continues to pose a significant challenge. These diseases are considered uncommon and affect a reasonably low proportion of the population, which is a major responsible factor for the negligence towards their diagnosis, available treatment options, awareness and support. Due to the lack of big enough market, heavy cost involved in drug development, clinical trials and low revenue generation potential, pharmaceutical industries have been averse to develop and market drugs for rare diseases. This has led to the classification of drugs for rare diseases as “orphan drugs”. When in

fact, the total number of rare disease suffering population is astronomical, and the effects of these diseases are agonizingly devastating to warrant particular and timely attention. It was for the first time in 1983 that the development of orphan drugs was given attention when the “Orphan Drug Act” by the United States (US) Food and Drug Administration (FDA) was implemented[3], [4].

Additionally, given the challenges faced by people living with rare diseases and their families UN General Assembly adopted its first-ever landmark resolution on 16th December 2021, recognizing approximately 300 million people worldwide suffer from rare diseases and emphasizes the need to promote and protect their human rights [298] **marking the historic commitment by all 193 UN Member States, including the 27 European Union Member States.**

The United Nations (UN) resolution on Rare Diseases adopted in 2021 render a foundation for the health systems combating the challenges and inequities faced by RD patients, as well as their caregivers and families. Furthermore, it presents an opportunity for policymakers to expand the provision of universal healthcare within their countries and health services. With 11 European Union (EU) countries as co-sponsors, the resolution acknowledges the barriers faced by 30 million people with rare diseases in Europe and reinforces a commitment to strengthening health systems, ensuring universal access to healthcare, and improving access to essential medicines and health technologies. It also promotes empowerment, inclusion, and equity, the creation of expert networks, and the development of national policies and strategies. Additionally, it calls for increased international collaboration in research and data sharing to advance rare disease understanding and treatment. This resolution represents a significant step toward recognizing and addressing the multifaceted challenges faced by persons living with rare diseases and their families. It underscores the global commitment to ensuring that no one is left behind, aligning with the broader objectives of the 2030 Agenda for Sustainable Development.

Figure 1. Timeline depicting orphan drug acts, rare disease acts & national policies as adopted & implemented in various countries across globe



(US– United States, SG– Singapore, JP– Japan, SK– South Korea, AU– Australia, EU – European Union, TW– Taiwan, FR– France, KZ– Kazakhstan, CO– Columbia, AR– Argentina, PE– Peru, MX– Mexico, GE– Germany, BR– Brazil, UK– United Kingdom, CA– Canada, PH– Philippines, IN– India)

Moreover, the 156th WHO Executive Board (EB) advocated for significant milestones in February 2025 for the adoption of the Resolution on Rare Diseases at the upcoming 78th World Health Assembly (WHA) in May 2025. This effort led under the leadership of Arab Republic of Egypt and Spain in initiating the process towards this landmark achievement along with the 26 Member States co-sponsoring the resolution including Brazil, Chile, China, Ecuador, France, Greece, India, Iraq, Jordan, Kuwait, Luxemburg, Malaysia, Pakistan, Palestine, Panama, Philippines, Qatar, Romania, Russia, Slovakia, Slovenia, Somalia, Thailand, and Vanuatu and 224 organizations worldwide forming a robust coalition. This momentum powerfully underscores the growing global consensus that rare diseases must be prioritized in the global health agenda. Moreover, the resolution officially submitted by Rare Diseases International (RDI) marks a significant milestone in the global effort in addressing social and financial burden such as global disparities in care, research, and treatment to improve the lives of over 300 million persons living with a rare disease (PLWRD) worldwide. The draft resolution emphasizes the importance of integrating rare diseases into national health planning, promoting early diagnosis through universal screening programs, and ensuring equitable access to affordable treatments. It also highlights the need for global collaboration to foster innovation in research and to develop new therapies.

This report explores the global and regional burden of rare diseases, examining their types, classifications, and the challenges associated with them. It presents a comprehensive analysis of rare diseases policies across 13 Asia-Pacific countries, highlighting country-specific approaches to rare diseases management. Additionally, the report assesses best practices from leading regions, offering insights into effective strategies for improving rare disease policies and healthcare systems. This report concludes with key recommendations aimed at strengthening rare disease policies and management, efforts, with the goal of enhancing patient care, fostering innovation, and ensuring equitable access to treatment.

1.2 Definition of rare diseases in different countries

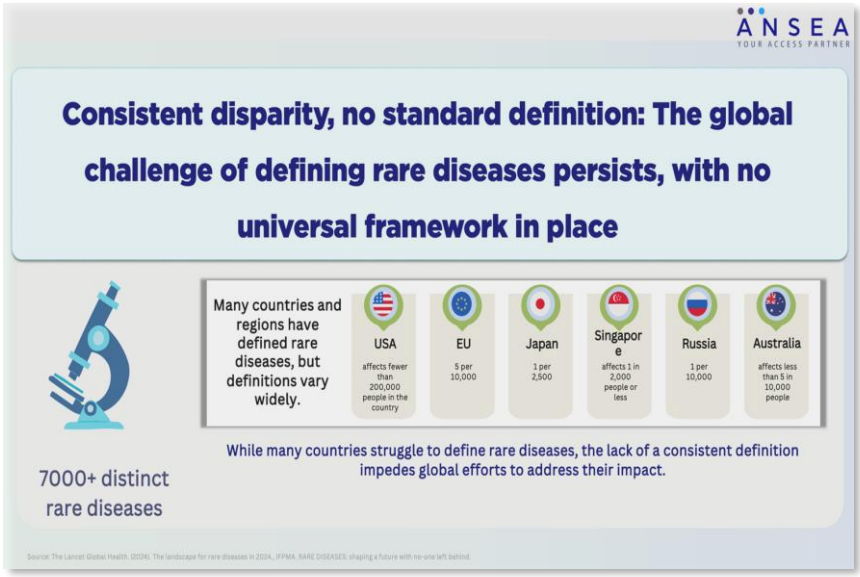
A rare disease is known to impact a lesser number of individuals when compared with the other known diseases which affects the mass population. Rare diseases are often chronic, and progressive leading to significant morbidity and mortality. Their heterogeneous and complex nature makes them individually rare, difficult to diagnose, and challenging to assess on a broader scale. Patients with rare disease face prolonged diagnostic journeys, lifelong disabilities, limited compensatory support, and few effective but costly treatments. These challenges impact the health, psychosocial well-being, and economic stability of rare disease patients and their families. As of today, there is no single universally recognized definition for rare disease and their classification differs across the globe. However, World Health Organization (WHO), defines rare disease as often debilitating, lifelong disorder with a prevalence of fewer than 1 in 2000 people [423]. Table 1 shows the definition of rare disease as defined or adopted by different countries across the world.

Country	Definition	Total RD population	Remarks (Reference)
US	<200,000 individuals	25-30 million	[5]
Europe	<5:10,000 individuals	27-36 million	[6]
Canada	<5:10,000 individuals	~ 3 million	[6]
Japan	<4:10,000 individuals	N/A	[6]
South Korea	< 20,000 individuals	500,000	[7]
Philippines	1:20,000 individuals	6500	[8], [9]
Australia	1:10,000 individuals	1.2 million	[6]
Taiwan	1:10,000 individuals	> 2000	[6]
China	1:10,000 individuals	780,000 in 2023	[10]
Thailand	<10,000 individuals	3 million in 2023	[11]
India	1:5000 individuals	70 million	[12]
Malaysia	1:4000 individuals	0.3 million	[13]
Singapore	1:2000 individuals	2000-3000	[14], [15]
New Zealand	1:2000 individuals	300,000	[15]
Indonesia	N/A	12.5 million in 2018	[16]
Vietnam	N/A	6 million in 2024	[16]
Hong Kong	N/A	110,000 (1.5%)	Not defined as per HKA [17]

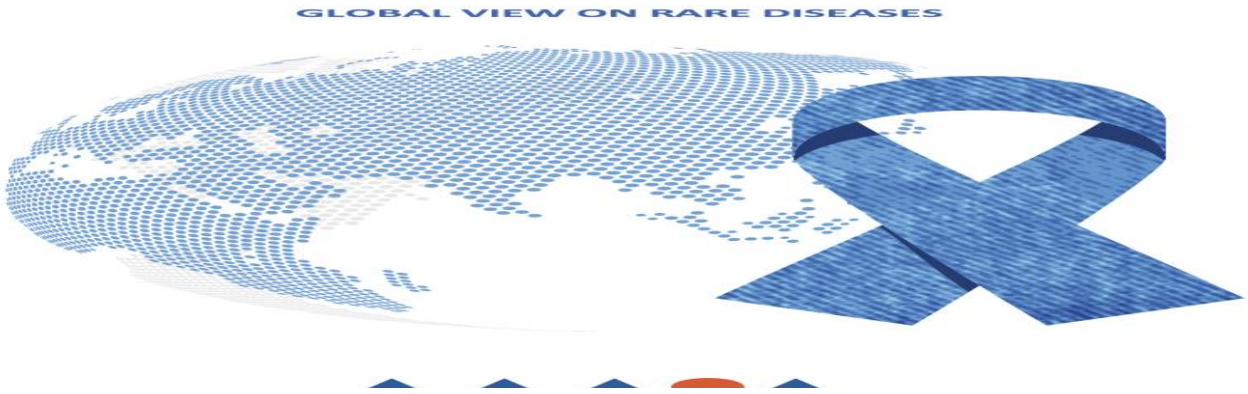
Table 1.Definition of RD defined in different countries as per government agency or other accepted bodies

(N/A: Not available; HKARD: Hong Kong Alliance for Rare Diseases)

Rare diseases lack a universal definition, and their prevalence varies across different regions worldwide. For instance, the European Union's Orphan Drug Regulation classifies rare diseases as those affecting fewer than 50 people per 100,000 in the population, whereas the United States' Orphan Drug Act defines them as conditions affecting fewer than 200,000 individuals nationwide [18]. Other jurisdictions propose prevalence thresholds ranging from 5 to 76 cases per 100,000, with a global average of approximately 40 cases per 100,000 [19]. In China, 121 rare diseases have been identified, 66 of which have a prevalence exceeding 1 in 10,000 [19], [20]. Meanwhile, India faces considerable challenges in addressing rare diseases due to limited epidemiological data and the high costs of treatment.



In 2019, Rare Diseases International highlighted the need for universal health coverage (UHC) policies to address the needs of rare disease populations [19]. The United Nations also recognized rare diseases as a critical issue, emphasizing that UHC cannot be fully realized without considering the needs of rare disease patients, who are often marginalized in healthcare planning. Despite this recognition, resource allocation and healthcare planning for rare diseases remain inadequate.



2 Types of Rare Diseases

2.1 Classification of rare disease

The following section describes the diseases included under the rare disease umbrella. The list of rare diseases is exhaustingly long with the inclusion of approximately 6000-8000 diseases, as reported in the literature till date. We are enlisting some of the rare diseases which are commonly known.

Rare Diseases in Hematology	
Anemia-type red blood cell conditions	Sickle cell disease, Beta thalassemia, Diamond-Blackfan anemia
White blood cell dysfunctions associated with various malignancies	Follicular lymphoma, Mantle cell lymphoma, Chronic myeloid leukemia, Hairy cell leukemia, Multiple myeloma
Immuno-disorders	Antiphospholipid syndrome, Evans syndrome, Idiopathic neutropenia
Platelet-based abnormalities that affect coagulation	Thrombotic thrombocytopenic purpura, Bernard-Soulier syndrome, Glanzmann's thrombasthenia, Gray platelet syndrome
Plasma-based issues	Hemophilia A and B, von Willebrand disease
Rare Diseases in Cardiology	
Arrhythmias	Wolff-Parkinson White syndrome, Supraventricular tachycardia
Lipidemias	Familial combined hyperlipidemia, Homozygous familial hypercholesterolemia, Lysosomal acid lipase deficiency
Gene-based congenital heart defects	Arrhythmogenic right ventricular dysplasia, Brugada syndrome, familial hypertrophic cardiomyopathy, Long QT syndrome, Hypertrophic obstructive cardiomyopathy, Holt-Orams syndrome, Marfan syndrome, Tetralogy of Fallot
Benign & cancerous tumors	Atrial myxoma
Others	Hutchinson-Gilford progeria syndrome, Duchenne muscular dystrophy, Fabry disease
Rare Diseases in Endocrine	
Gland-based hormonal imbalances	Acromegaly, Gigantism, Prader-Willi syndrome
Weight regulation issues and physical abnormalities	Addison's disease, Cushing's disease
Autoimmune conditions	Graves' disease
Neurological diseases	Fragile X syndrome
Blood diseases	Sickle-cell disease, Beta thalassemia
Numerous carcinogenic and noncarcinogenic endocrine-related tumor disorders	Neuroendocrine cancer, Multiple endocrine neoplasia, Adrenocortical carcinoma, Papillary thyroid carcinoma, Primary thyroid lymphoma
Rare **Diseases** of Lysosomal storage	

Lysosomal storage disorder	Tay-Sachs disease
Rare Diseases involving Musculoskeletal conditions	
Genetic	Duchenne muscular dystrophy
Neurological	Charcot-Marie-Tooth disease
Motor neuron	Amyotrophic lateral sclerosis (ALS)
Bones	Osteogenesis imperfecta
Rare Diseases s in Nephrology	
Effect urinary system	Membranous nephropathy, Alport syndrome
Inflammatory & autoimmune diseases	Goodpasture syndrome
Others	Henonch-Schönlein purpura nephritis
Rare Diseases in Neurology	
Autoimmune conditions	Transverse myelitis, Optic neuritis, Vascular myelopathy, Acute disseminated encephalomyelitis
Musculoskeletal disorders	Amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy, spinal muscle atrophy
Developmental conditions	Batten disease, Charcot-Marie-Tooth disease
Other	Fabry disease
Rare Diseases in Oncology	
Breast	Angiosarcoma of the breast
Gastrinomas	Gastrin-producing small intestine cells
Others	Childhood acute myeloid leukemia (from myeloid blood cells), schwannomas (from the sheath cells covering nerves) retinoblastomas (from retinal cells), or thymomas (from thymus gland cells)
Respiratory Rare Diseases	
Lungs	Idiopathic alveolar proteinosis, Wegener's disease
Autoimmune	Anti-glomerular basement membrane disease
Vasculitis	Takayasu's arteritis
Others	Cystic fibrosis (CF), Pulmonary arterial hypertension (PAH), Idiopathic pulmonary fibrosis (IPF) and hereditary angioedema (HAE)
Other Rare Diseases	
Myeloproliferative disorders	Polycythemia vera, Myelofibrosis, Essential thrombocythemia, Mastocytosis, Eosinophilia
Gene mutations	Noonan syndrome, Imerslund-Grasbeck syndrome, Prolidase deficiency, Von Hippel-Lindau disease

Table 2. List of rare diseases based on the part of the body affected

(Note: This is not an exhaustive list of rare diseases. For more updated and extensive list refer *https://globalgenes.org/rarelist/* [21].

2.2 Well-Known rare diseases

2.2.1 Phenylketonuria (PKU)

Phenylketonuria (PKU) is a genetic disorder which is caused due to a defect in the phenylalanine hydroxylase (PAH) gene. PAH gene produces the enzyme responsible for the breakdown of phenylalanine and its mutation causes buildup of phenylalanine within the body [3]. Increased level of phenylalanine is toxic to brain tissues and if left untreated leads to permanent intellectual disability. It is estimated that globally 0.45 million individuals have PKU, with global prevalence 1:23,930 live births (range 1:4,500 [Italy]–1:125,000 [Japan])[22], [23] as per the study in 2020. Children with PKU tend to have unusually light skin and hair, seizures, development delays, behavioral problems and psychiatric disorders[24], [25]. Newborns are screened for PKU within 1-2 days of their birth and diagnosed newborn should receive special infant formula. Currently, Kuvan® (sapropterin dihydrochloride) has been approved by US FDA for PKU but is advised to be used in junction with the PKU diet [25].

2.2.2 Duchenne Muscular Dystrophy (DMD)

Duchenne Muscular Dystrophy (DMD) is a progressive rare neuromuscular X-linked disorder that belongs to a group of disorders known as dystrophinopathies, a genetic disorder and is characterized by progressive muscle degeneration and weakness. DMD is caused by mutation of DMD gene that codes for protein dystrophin, responsible for keeping the muscle cells intact. According to published study in 2020, globally, fewer than 10 out of every 100,000 individuals assigned male at birth are diagnosed with Duchenne muscular dystrophy (DMD). Overall, muscular dystrophy disorders affect approximately 1 in 5,000 to 1 in 6,000 people assigned male at birth. It is estimated that around 250,000 individuals in the United States have some form of muscular dystrophy, with fewer than 50,000 of those cases being DMD[26]. The disease begins as early as 3-4 years of age and affects the hips, pelvic area, upper legs and shoulders. Most children by the age of 13 years need wheelchair for mobility. No known cure for DMD exists however, the symptoms can be controlled. Given the medical advancement, the life expectancy of patients is increasing. Current treatment option includes glucocorticoids such as prednisone and deflazacort, gene therapy, exon skipping, aminoglycosides, ataluren (PTC124), myostatin, utrophin, vitamin D supplement [3], [27], [28].

2.2.3 Gaucher Disease (GD)

Gaucher disease (GD) is among the most prevalent of the lysosomal storage disorders (LSDs) with the mutation in GBA gene that regulates the synthesis of beta-glucocerebrosidase (G-case), an enzyme responsible for the breakdown of glucocerebroside. Accumulation of fatty chemicals leads to GD which affects different parts of the body [29]. The disease is known to affect 1 in 40,000–60,000 individuals[30] .A standard blood test called a beta-glucosidase leukocyte (BGL) test exists to test for GD. Current treatments help to minimize symptoms and permanent damage to patient body. Two different treatments

are used: enzyme replacement therapy (ERT) namely Cerezyme (Imiglucerase), Vpriv (Velaglucerase alfa) and Elelyso (Tagliglucerase alfa) and substrate reduction therapy (SRT) namely Zavesca (Miglustat) and Cerdelga (Eliglustat)[3], [31].

2.2.4 Thalassemia

Thalassemia is an inherited blood disorder that reduces the production of functional hemoglobin in the body. This results in a deficiency of red blood cells (RBCs) and lower oxygen levels in the bloodstream, leading to various health complications. Globally, thalassemia affects approximately 4.4 per 10,000 live births. The condition primarily includes two main types: alpha thalassemia and beta thalassemia. Around 5% of the global population carries a variation in either the alpha or beta components of the hemoglobin molecule, though many of these individuals are asymptomatic and classified as silent carriers. Only about 1.7% of the global population exhibits signs of the gene mutations, referred to as thalassemia traits. Certain ethnic groups are disproportionately affected, with 5% to 30% of individuals in these populations experiencing symptoms of thalassemia [32]. Treatment for moderate to severe cases typically involves frequent blood transfusions, stem cell transplantation, and/or folic acid supplementation [33].

2.2.5 Pompe Disease (PD)

Pompe disease (PD) or glycogen storage disease type II is an inherited lysosomal disease. Mutation of GAA gene causes PD. GAA is responsible for the production of enzyme acid alpha-glucosidase (aka acid maltase) which breaks down glycogen. Accumulation of glycogen causes impairment of muscles, tissues and organs [34].The prevalence of infantile-onset of Pompe estimated to be 1 in 138,000 and that of late-onset Pompe disease (LOPD) to be 1 in 57,000 [445]. PD is classified into two types: 1) classic form of infantile-onset PD which presents within a few months of birth, and 2) non-classic form of infantile-onset PD usually appears by age of 1 year. Enzyme replacement therapy (ERT) has shown positive effect in disease treatment. FDA approved drugs: Myozyme© (Alglucosidase alfa) and Lumizyme© (Alglucosidase alfa) for the treatment of PD [35].

2.2.6 Hunter Disease/ Mucopolysaccharidosis II (MPS II)

Hunter Disease/ Mucopolysaccharidosis II (MPS II) is a rare, X-linked, life-limiting lysosomal disease whereby the body is unable to breakdown complex mucopolysaccharides (glycosaminoglycans, GAGs) due to the absence of an enzyme iduronate-2-sulfatase (I2S). Mutation of I2S gene leads to accumulation of GAGs. The incidence of MPS II is estimated to be 1: 100,000 to 1: 170,000 male births [446]. No signs of disease are evident in babies however, with age most of the organs are affected. Currently, no cure for

MPS II exists, enzyme replacement therapy (ERT) and haematopoietic stem cell transplant (HSCT) are available for the treatment of hunter's disease. Elaprase (Idursulfase) is US FDA approved ERT [39,40].

2.2.7 Osteogenesis Imperfecta (OI)

Osteogenesis imperfecta (OI) is a group of rare genetic disease which mainly affect the bones. Patients suffering from OI have fragile bones that break easily with little or no trauma. The disease is caused by a mutation in gene COL1A1 or COL1A2, which is responsible for the production of collagen, material which strengthens the bones. OI prevalence is estimated to be 1 in 15,000 to 20,000 births [36]. The disease is currently treated using a combination of physical therapy, surgery and medication. Bisphosphonates such as Aredia® (Pamidronate) and Reclast®/Zometa® (Zoledronate) are used to increase bone mass along with vitamin D and calcium supplement [37].

2.2.8 Hemophilia

Hemophilia is a rare blood disorder which is characterized by the reduction of the blood clotting process. People with this disorder experience prolonged bleeding following an injury, surgery, or sometimes with no trauma[38]. The major types of this disorder are hemophilia A and hemophilia B. Hemophilia A is caused by mutation in the F8 gene (xq28) which encodes for coagulation factor VIII, and hemophilia B by the F9 gene (Xq27) which encodes for coagulation factor IX. Globally, over 200,000 people are affected by some form of hemophilia [39]. However, recent data suggest that the actual number of cases may be higher due to underdiagnosis. This can result from mild cases going unnoticed, limited healthcare access, misdiagnosis, and unrecognized symptoms in female carriers. Current treatment of the disease is replacement of missing clotting factor. The FDA has approved recombinant factor VIII for hemophilia A treatment e.g., Helixate®FS, Recombinate®, Kogenate®FS, ReFacto®, Eloctate®, Xyntha®. Human plasma-derived preparations include Monarc-M, Monoclate-P®, Hemofil M and Koate-DVI[40], [41]. Treatment of hemophilia B includes coagulation factor IX: AlphaNine, Alprolix, BeneFix®, Mononine, NovoSeven®RT (recombinant). rIX-FP, Rixubis[39].

2.2.9 Epidermolysis Bullosa (EB)

Epidermolysis bullosa (EB) defines a group of rare genetic disorder identified by extremely fragile skin and recurrent blister formation, which can occur even minor mechanical friction or trauma. Normally, human skin has two layers: epidermis and dermis namely. The two layers are maintained by anchors which holds them in place. In EB patients, the two skin layers lack the anchors and as such any action leads to friction between the layers resulting in blisters and painful sores. The estimated EB prevalence is 10 per million people and an incidence of 20 per million live births [42]. Over the past two decades, 13 genes have been associated with EB which causes defects in the proteins that adhere the epidermis to the dermis.

Mutation in the COL7A1 gene causes EB. This mutation leads to disruption of protein Type VII collagen, which gives structure and strength to connective tissues [43]. Children suffering with this condition are also known as “Butterfly children or Cotton wool babies” due to fragile skin. The current treatment for EB is primarily preventive and supportive. Potential future treatments include gene therapy, bone marrow transplantation, protein replacement therapies, cell-based therapies [44].

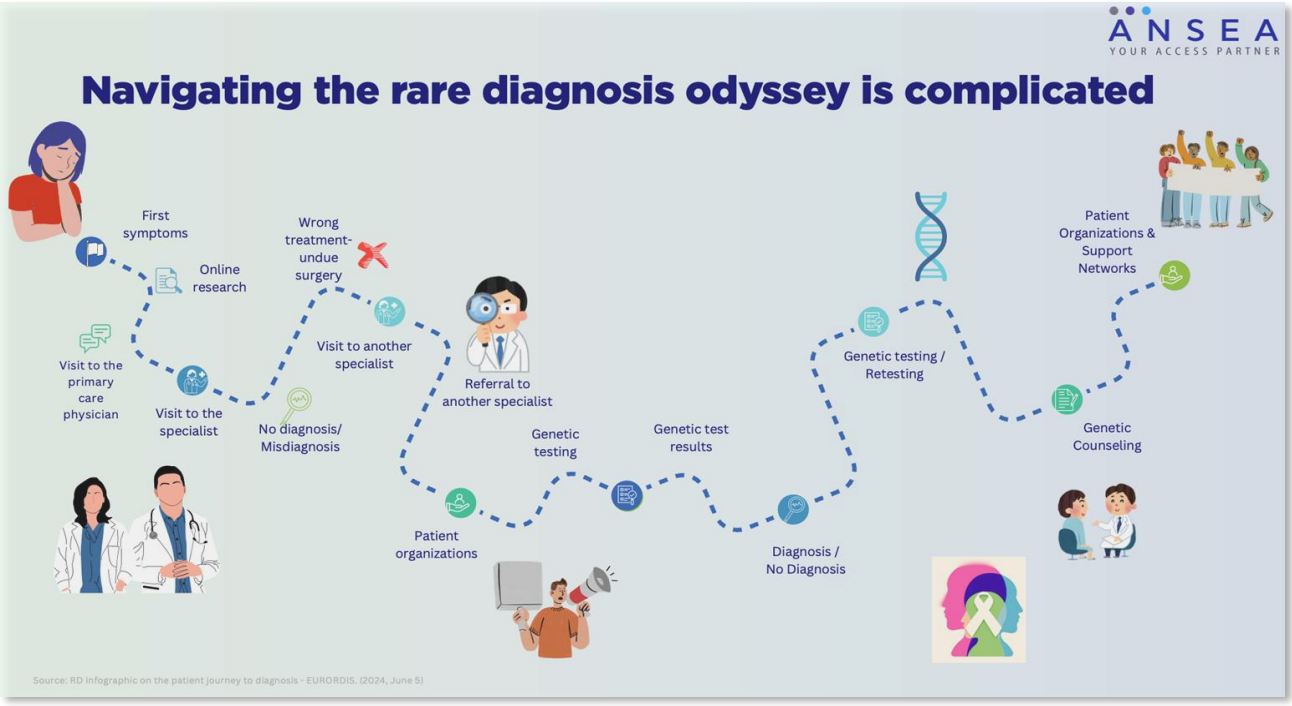
2.2.10 Hereditary Angioedema (HAE)

Hereditary angioedema (HAE) is a rare genetic disorder autosomal dominant disease, characterized by recurrent episodes of severe swelling attacks. The estimated prevalence is 1 in 50,000[45]. Three main areas are affected due to accumulation of fluids outside the blood vessels which leads to swelling: skin, gastrointestinal tract and upper respiratory airways. There are several types of HAE: Type I and II, are caused due to mutation in the C1NH (SERPING1) gene which regulates the level of a complex protein, C1 esterase inhibitor responsible for flow of fluids in and out of cells. Type III is characterized by normal C1 levels. HAE affects both genders equally and its symptoms usually arise during childhood. Prevalence of HAE is 1-9 per 100,000 individuals. Several FDA approved treatments for HAE are currently available: Cinryze, Berinert, Kalbitor, Ruconest, Haegards, Firazyr and Takhzyro[24].

3 Challenges Associated with Rare Disease

Rare disease impacts not only the health and well-being of a patient but affects several aspects of their life including social facet. The condition many a times impact even the basic daily-routine tasks. Many of these conditions are life-long and debilitating and in severe cases can lead to death at a very young age. Patients often report that the effect of their rare condition stretch well beyond health and trespasses into their emotional and mental wellbeing. While genetic testing has offered hope to many, the average time from the onset of symptoms to an accurate diagnosis is about 5 years

Depression, stress and anxiety are common conditions associated with rare disease patients owing to various reasons ranging from being unwell to years of misdiagnosis and difficulty in accessing correct treatment[46]. On social front, patients are at disadvantage when accessing basic privileges as education and employment. This is not only due to their inability in attaining a job but in part due to insufficient facilities to support such patients (Figure 23). Integration of rare disease patients in society is considerable. In addition, the financial wellbeing of rare disease patients and their family can be adversely and brutally impacted due to the long-lasting effect of these conditions.



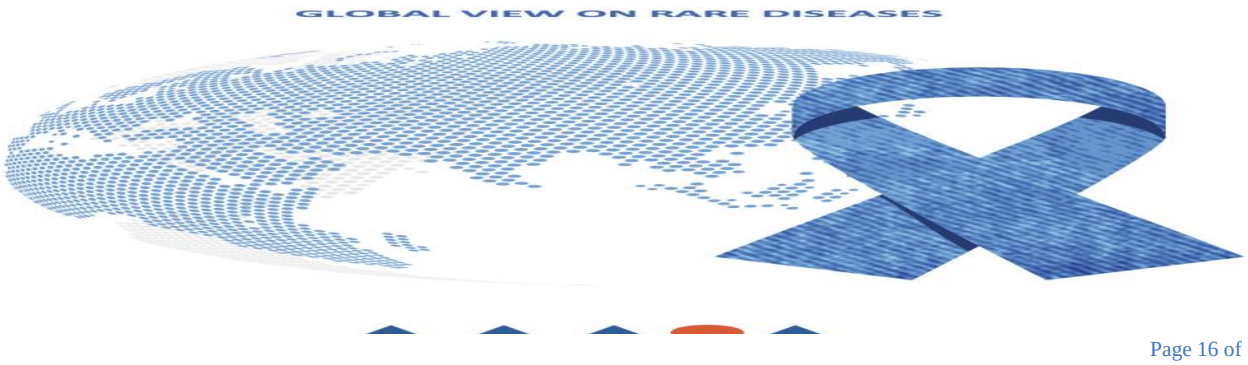


Figure 2. Complex health and social challenges affecting rare disease patients

The rare diseases are gradually receiving attention worldwide to stimulate the research, development and marketing of medicinal products of rare diseases. Even with all the advancements, there are myriad challenges associated with rare diseases such as lack of knowledge/training, delayed diagnosis, limited understanding about the pathophysiology of diseases, lack of treatment, and lack/limited access to therapy or medical care [47].

3.1 Lack of Universal Rare Diseases Definition

Many countries have defined rare diseases (RDs) in their jurisdictions, such as the EU, the UK, the US, and Japan, have implemented regulations to create a more favorable environment for the development and access of orphan drugs. However, inconsistencies persist as there is no universally accepted definition of RD. Even advanced economies like Australia and Canada lack clear definitions, complicating research, treatment access, and global collaboration [46], [299]. The varied terminology and inconsistent definitions of RD pose significant challenges to treatment accessibility, rare disease research, and policy making. This disparity further complicates data collection, limits global collaboration, and affects equitable access to treatments and insurance coverage [300]. Recently, in a major setback after introducing national policy for the treatment of rare diseases in India in 2017, the Central government withdrew the policy. One of the reasons cited for this withdrawal is inaccurate definition of rare diseases.

3.2 Lack of Knowledge and Training

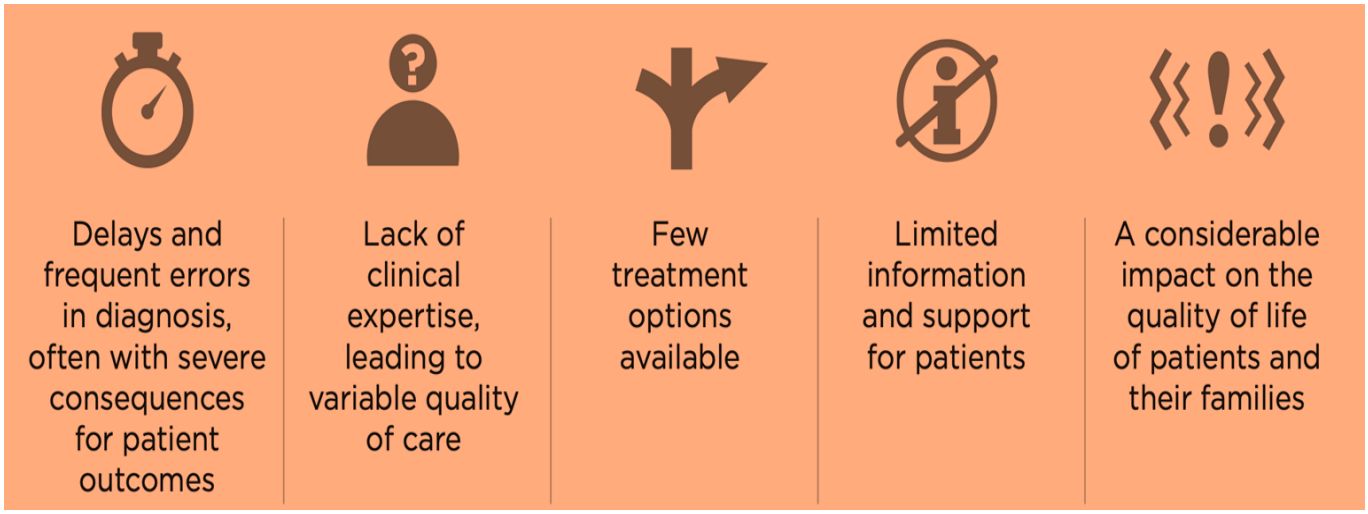
The lack of knowledge and training about rare diseases presents significant challenges in diagnosis and treatment. Many physicians are not knowledgeable about many of these conditions and cannot identify the symptoms correctly and are either not trained in rare diseases. A recent report by the UK think-tank "2020 health" confirms lack of experience in the medical specialists, the scarcity of specialists and the need for continuous professional development further complicate efforts to improve awareness and expertise in rare diseases [301]. This results in misdiagnosis, delayed treatment, or incorrect management. Furthermore, medical education often lacks comprehensive coverage of rare diseases, leaving healthcare professionals ill-prepared to recognize or properly treat these conditions. As a result, patients may experience long waits for correct diagnoses, and treatments may be delayed or ineffective, contributing to poorer outcomes. , the scarcity of specialists and the need for continuous professional development further complicate efforts to improve awareness and expertise in rare diseases [474].

3.3 Inadequate Rare Disease Data and Infrastructure

Insufficient rare disease data and infrastructure pose significant barriers to effective diagnosis, treatment, and research. The limited patient population for each rare disease complicates the gathering of comprehensive data, resulting in significant knowledge gaps regarding disease progression, potential therapeutic options, and long-term outcomes [191]. The lack of centralized databases and standardized data collection systems further hinders the ability to track rare disease prevalence and trends across populations. Furthermore, the absence of robust healthcare infrastructure dedicated to rare diseases means that diagnostic tools, specialized care centers, and treatment options are often not readily available. This lack of infrastructure slows research efforts, limits patient access to expert care, and prevents the development of targeted therapies. In other words, dearth of information leads to less interest from research community, pharmaceutical industries, medical doctors, government and policymakers. Without improved data collection systems and investment in infrastructure, progress in rare disease management remains limited. According to several reports, patients often complain that there is lack of information either in early stages of diseases or after initial diagnosis[47].

3.4 Delay in Diagnosis and Prevention

Rare diseases are challenging to diagnose due to their heterogeneous and variable clinical presentations as well as a lack of local population data on the conditions of the diseases. Approximately 50% of the individuals with rare disease are undiagnosed, while patients who have received a diagnosis encounter several challenges due to delays or misdiagnosis, treatment, care, and social acceptance. For instance, in Europe, 25% of rare disease patients had to wait between 5 and 30 years from the onset of symptoms to receive a genetic diagnosis, while 40% were misdiagnosed multiple times, resulting in ineffective and unnecessary medical treatments [19]. Scarcity of medical experts, research gaps and information insufficiency, further leads to delayed diagnosis. Moreover, these delays can impact patients by causing prolonged suffering, missed treatment opportunities, increased medical costs, psychological distress, and disruptions to daily life due to the "diagnostic odyssey" of visiting multiple doctors and undergoing extensive testing before receiving a definitive diagnosis; this further worsen situation due to disease progression and a negative impact on the patient's quality of life and well-being.



3.5 Inadequate Specialized Care and Treatment

The population affected by rare diseases is often small, heterogeneous and the diseases are complex in nature. This warrants specialized care and treatment for these patients. Often time the symptoms of one patient varies significantly from other patient affected with same rare condition. Hence, patients may need personalized treatment. Normal clinics and hospitals are often lacking in the proper facilities needed to provide primary and palliative care to these patients. Establishing special clinics and rare disease expert centers will go miles to help these patients and their caregivers with timely and required attention.

3.6 Limited Treatment and Health Disparities

According to the current available information, only 5% of known rare diseases have some treatment options, which essentially means 95% of the patients are still desperately waiting to get treatment for their condition. The fundamental issue with development of rare disease treatment is their complex pathophysiology or the natural history of the rare conditions, which remains a mystery in most cases. Amongst the available treatments, most therapies are aimed at managing the diseases as against to curing them. However, the accessible treatments have helped patients with improvement of their quality of life and extended their life span. In a study by Heemstra et al., prevalent rare diseases receive more attention for research and drug discovery programme compared to less prevalent diseases [302]. This was further reinforced by a report by Yin, according to which "the US Orphan Drug Act" led to a substantial and steady growth in number of clinical trials for prevalent rare diseases, but not for less prevalent rare disorders [303]. Additionally, health disparities amplify the problem, as individuals from lower-income regions or disadvantaged communities often face barriers to accessing the few available treatments [55], [191]. These barriers include limited access to specialized care, high treatment costs, and healthcare infrastructure gaps. Disparities are further compounded by geographic differences in healthcare quality, meaning that patients in resource-poor areas may not have access to the same standard of care or innovative treatments as those in wealthier regions. Such challenges contribute to a pronounced inequality in health outcomes for those suffering from rare diseases.

3.7 Challenges in Regulatory and Market Access

Another hurdle associated with delivery of orphan drugs to rare disease patients is unreliable access and reimbursement of orphan drugs after-market authorization. The accessibility is often hindered due to plethora of reasons ranging from: high cost of orphan drugs, pressure on national healthcare budgets, public policies, and reimbursement of orphan drugs[304]. Another reason for the accessibility of orphan drugs is the delay in market authorization. In advanced countries such as US and EU, drugs are generally approved in few years but in several others, it may take up to 8 years.

3.8 Public Health Priorities

According to health systems and policymakers, the number of patients suffering with rare diseases are scarce when compared to any common disease. As a result, rare diseases receive limited attention in public health policy, research funding, and healthcare planning. Governments and organizations tend to prioritize more common health issues that affect larger segments of the population, leaving rare diseases marginalized. This lack of focus hampers efforts to raise awareness, develop preventive measures, and create accessible treatment options. Additionally, public health campaigns and resources are typically not tailored to the unique needs of rare disease patients, resulting in insufficient support and education. To improve the lives of those affected, rare diseases need to be integrated into broader public health strategies, with increased funding, targeted research, and improved access to care.

3.9 Pricing and reimbursement

The cost of research and development of orphan drugs is substantially high, especially owing to the low prevalence of rare diseases. Pharmaceutical companies are dispassionate about focusing on this area of disease since the market is relatively small, highly specialized needs, development costs of orphan drugs are high, navigation of procedure for market authorization are intricate and the incentives from governments are not favorable or non-existent in different economies. Some of the advanced economies such as the US and Europe have national plans and insurance coverage to cover the costs of these exorbitant drugs for the rare disease population. Orphan drugs that are not covered by insurance are realistically inaccessible to patients owing to their high cost[33]. Even with the costs-sharing the extent of coverage varies country to country and patients still have to share costs either as co-payment or coinsurance, which hinders orphan drug accessibility [305]. In many countries, for example, India and China, which currently do not have orphan drug legislations, these drugs are often

3.10 Lack of funding in research and clinical trials

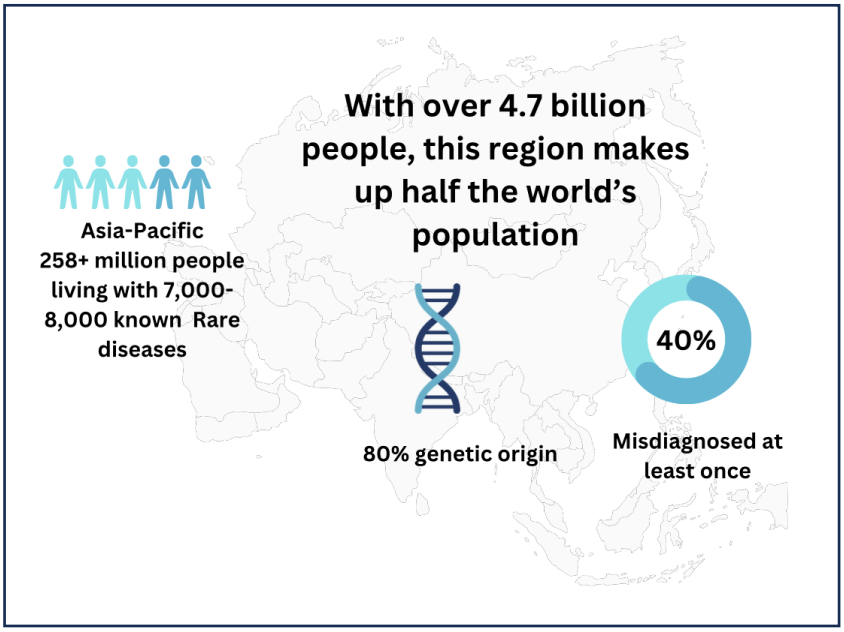
A fundamental challenge in drug development for rare diseases is the lack of in-depth knowledge about the pathophysiology of the diseases. Even for the rare conditions which have some kind of treatment available or under research, face a major issue while navigating drug development and clinical development path. These issues are further complicated by lack of funding. The high cost associated with the research especially in terms of requirement of sophisticated method and machinery of drug development deters interests of venture capitalist and other investors from investing into R&D for orphan drugs. Further down the line, during the clinical phase orphan drugs face numerous challenges such as: small patient population, clinical trial logistics, lack of acceptable preclinical model, insufficient know-how about the potential biomarkers of rare diseases, meaningful clinical endpoints, limited number of experts and ethical issues such as use of placebo.

3.11 Lack of Awareness and Collaborative Approach

Over the last several decades, with the institution of orphan drug legislation in the US and other countries, various advancements have been witnessed by the rare disease community. Based on our independent secondary research, we observed that countries across Asia and other continents, have many patient organizations pushing a particular rare disease cause forward within their jurisdiction. However, most of them have not been able to make any significant progress. It is imperative that different stakeholders which includes patients, families, caregivers, patient organizations, pharmaceutical companies and policymakers should come together, may be as an umbrella organization to make a unified voice. In this way, a more coordinated approach can be adopted by the concerned bodies to come up with solutions to solve the challenges associated with rare diseases. Interest from different stakeholders has been seen in the field of rare diseases and efforts have been made to advance the causes of rare disease patients and families, in terms of access to treatment or social benefits. However, one thing that has been pointed by many patients and caregivers is that although stakeholders are advancing the cause, but they do so from their individual perspectives which often leads to futile efforts or means less benefit for the suffering community.

4 Overview of Rare Disease in Asia-Pacific

Approximately 4.7 billion people, or 60% of the world's population, currently reside in Asia and the Pacific, with China and India being the world's most populous countries. This number is expected to reach 5.2 billion by 2050 [48]. The Asia-Pacific region has the largest number of people living with rare diseases (PLWRD). Within this large population, it is estimated that more than 258 million people live with rare diseases [49]. The region's diverse population and complex health environment present challenges in addressing rare disease. At the same time, the scale of the region, the size of the rare disease population, and the willingness of diverse stakeholders suggest the potential for new solutions and approaches to health equity. Many countries in the region are increasingly recognizing the importance of developing comprehensive policies and strategies to support people living with rare diseases (PLWRD) and their families through concerted efforts in research, diagnosis, treatment, patient support, and public awareness initiatives. APAC's diverse population and complex healthcare environment present challenges in the fight against rare diseases.



The Asia-Pacific Economy

Asia is the largest and most populated continent and had the most rapid economic growth in the world for several decades (see Table 3 below). The Asia-Pacific region continues to demonstrate robust economic growth, contributing significantly to the global economy. In 2024, the International Monetary Fund (IMF) projects the region's growth at 4.6%, a slight increase from earlier forecasts, with an expected moderation to 4.4% in 2025[50]. Asia's economic expansion has helped reduce poverty throughout the region and increase living standards [49], [51], [52].

Country	Population (millions) 2023	Population growth (2023) %	GDP (PPP) in billion USD (2023)	GDP real growth (2023) %	Per capita GDP (PPP) (2023)
China	1,412.17	0.35%	$27,861	5.3	$22135
India	1,417.72	1.19	$15,689	6.7	$9172

Indonesia	275.5	0.76	$3,246	4.3	$14073
Japan	125.12	-0.41	$5,126	2.4	$46268
Philippines	115.55	1.58	$921.8	3.9	$9695
Vietnam	98.19	0.63	$1,036	4.3	$13696
Thailand	71.7	0.20	$1,223	1.7	$21113
Korea	51.63	0.23	$2,289	1.3	$50572
Malaysia	33.94	1.01	$884.1	2.6	$33574
Australia	25.98	2.4	$1,279	2.7	$52,960
Hong Kong	5.64	2.6	$484	0.6	$64431
Singapore	6	0.90	$578.3	-3.7	$127544
New Zealand	5.12	2.07	$279	0.6	$48,527.8

Table 3. Representation of economies in Asia-Pacific.[49], [51], [52]

PPP = purchasing power parity

While orphan drugs in Asia-Pacific region face significant challenges due to small patient populations, complex clinical trials, and high development costs, there is growing interest from pharmaceutical companies. The orphan drug market is projected to worth $38.13 billion in 2023 and estimated to reach $58.45 billion by 2028, driven by the expiration of patents for many blockbuster drugs [53], [54]. There is a high unmet need in this area, which is pushing governments and regulatory authorities in Asian countries to address the issue with urgency. However, the lack of a robust legal framework and government incentives in many countries has limited orphan drug development, and high costs make imported treatments inaccessible to many patients [54].

Moreover, the 7th APEC High-Level Meeting on Health & the Economy (HLM7) held in 2017 acknowledged the necessity of overcoming obstacles related to the diagnosis and treatment of rare diseases, highlighting the importance of economic and social inclusion contributing to a more inclusive Healthy Asia Pacific 2020[55]. This recognition resulted in the establishment of the APEC Life Sciences Innovation Forum (LSIF) Rare Disease Network (RDN), which brings together government entities, academic institutions, and industry stakeholders with a focus to identify and document challenges faced by economies in managing rare diseases. Over the years, its mission has evolved from solely focusing on policy development to actively facilitating the implementation of rare disease strategies throughout the APEC region. In 2018, the RDN organized Stakeholder Consultations in Australia, China, Korea, Chinese Taipei, Thailand, and Vietnam, collecting insights from healthcare professionals, policymakers, industry experts, and patient communities. These consultations yielded valuable firsthand perspectives that informed the inaugural APEC Policy Dialogue on Rare Diseases in June 2018[55]. advocated to discuss policies, exchange best practices, and explore opportunities for collaboration. This represented a crucial advancement toward a unified regional approach, assisting APEC economies in the development and implementation of rare disease strategies including raising awareness, utilizing technology for improved diagnostics, and enhancing healthcare systems to ensure timely diagnosis and treatment. In parallel, the Asia Pacific Alliance of Rare Disease Organizations (APARDO) has introduced a 3-Year Action Plan that focuses on diagnosis, access to orphan drugs, treatment, patient care, and financial and social support. Their strategy includes identifying gaps in healthcare policies, promoting collaborations among stakeholders, and empowering rare disease patient leaders to invigorate regional support and advocacy.

*A significant regional initiative is the **APEC Rare Disease Asia-Pacific Action Plan**, endorsed in 2018, which seeks to improve economic and social inclusion for people with **rare diseases across 21 member economies by 2025**.*

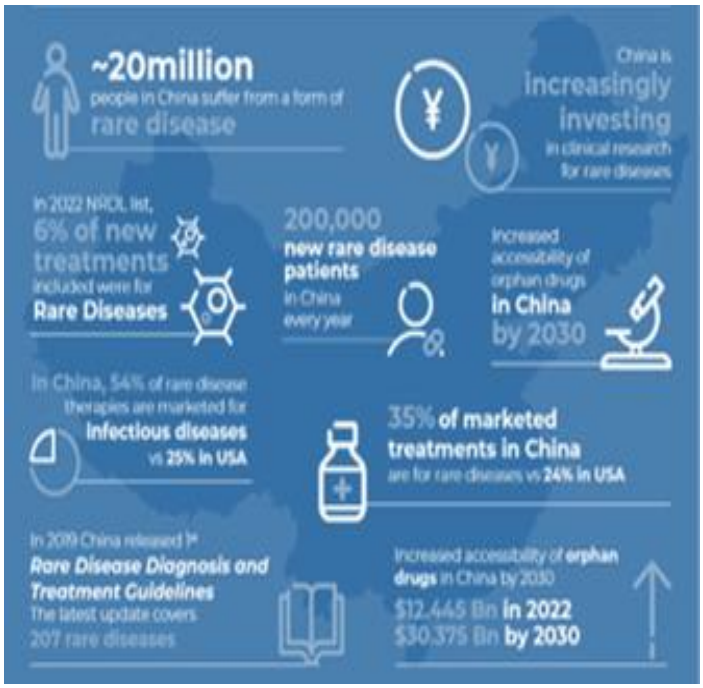
Over the past three decades, numerous countries in the APAC region have introduced dedicated policies or legislation to address the needs of Persons Living with Rare Diseases (PLWRD) and their families. Japan was among the first to establish a dedicated policy in 1993 through the Japanese Pharmaceutical Affairs Law (now the Pharmaceuticals and Medical Devices Act), which defined rare and intractable diseases (referred to as NANBYO). This legislation also introduced measures to promote orphan drug research and development while streamlining review procedures. Similarly, Australia has shown leadership with its progressive policies. The Australia Therapeutic Goods Regulations of 1997 provided guidance for orphan drug programs and offered incentives to bring these medicines to market[49]. In 2020, the country launched the "National Strategic Action Plan for Rare Disease," emphasizing collaboration between healthcare providers, researchers, patient organizations, and the government to enhance coordination, research, and access to treatment.

Between 2000 and 2010, several other APAC countries, including Singapore, South Korea, and Taiwan, enacted dedicated legislation for rare diseases and orphan medicines. This trend continued between 2010 and 2021, with the introduction of policies in Hong Kong, mainland China, India, Indonesia, Malaysia, the Philippines, and Thailand. Although New Zealand has made a commitment to developing a strategy, it has yet to establish formal policies. Despite the progress made, many countries in the APAC region lack a specific policy framework. The scope and focus of existing policies vary widely, addressing areas such as public awareness, patient support, research, diagnosis, and treatment access. As a result, the level of implementation and the effectiveness of these policies differ significantly across the region. The section below gives insight into the country specific rare disease initiatives, rare disease strategy and policy shaping.

5 Status of rare disease in different countries in Asia

5.1 China

5.1.1 Rare Disease Landscape in China



With the largest population in the world, China also has the largest number of rare disease patients, estimated to reach 20 million rare disease patients by 2024, and more than 200,000 new patients are added each year [56]. According to the latest definition in 2021, a rare disease in China is defined as a condition that meets at least one of the following three criteria: an incidence in newborns less than 1/10,000, a prevalence less than 1/10,000, and an affected population of less than 140,000. The number of 140,000 was calculated based on China's total population of 1.4 billion multiplied by a prevalence of 1/10,000[10] . By the end of September 2023, approximately 780,000 cases of rare diseases had been recorded in China since the establishment of an information system for the diagnosis and treatment of rare diseases in 2019[57]. There are about 121 rare diseases, 80% of which have a genetic link and about 50% of which occur in childhood. In addition, many

patients with rare diseases usually lack therapeutic drugs and treatments in time, which often results in irreversible physical and mental damage.

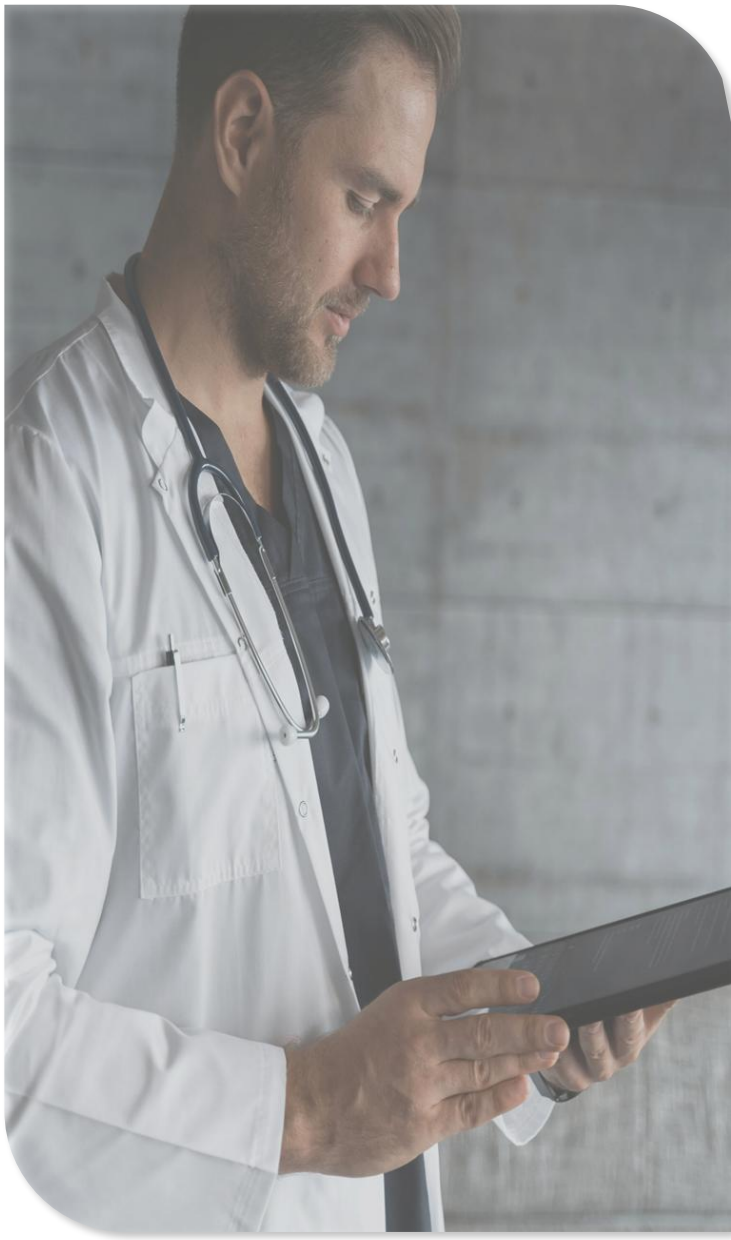
It is estimated that China has a GDP per capita of USD $12,617.5, while health expenditure per capita of USD $670.51 indicates moderate investment in healthcare relative to high-income nations [58]. However, the high out-of-pocket (OOP) expenditure at 35% of total health spending poses significant challenges, including financial strain on households, limited access to care for low-income populations, and potential delays in seeking treatment. In recent years, the Chinese Government has announced a series of policies to support diagnosis and treatment of rare diseases, including the acceleration of orphan drugs, coverage by medical insurance, and disease registration. In 2018, five bodies including the National Health Commission of the People's Republic of China and the National Medical Products Administration issued China's First List of Rare Diseases in May 2018 [10].

5.1.2 National Strategy Framework and Policy Shaping

The Chinese government has made considerable efforts to gradually improve the situation of patients with rare diseases in terms of diagnosis and treatment, access to medicines, and affordability of care. The National Health Commission has implemented a series of measures, including the first catalogue of rare diseases, the establishment of an alliance for rare diseases, the establishment of a collaboration network for the diagnosis and treatment of rare diseases, and the formulation of Guidelines for the diagnosis Treatment of Rare Diseases, sharing of diagnostic and treatment information, and creation of expert committees, to ensure the standardization of rare disease diagnosis and treatment and to promote the improvement of rare disease diagnosis and treatment capabilities nationwide[59].

National Plan and Legislation

- Efforts to improve rare disease care in China include legislative motions in the National People's Congress, such as Liu Gexin's proposal to support patients with rare diseases by encouraging the development of orphan drugs in the country through special funding, incentives for manufacturers, accelerated approvals and a dedicated medical insurance system. To increase cooperation, the National Research Foundation of Singapore and the National Natural Science Foundation of China signed a five-year memorandum of understanding in 2015, providing SGD 500,000 (USD $373,649) per project for joint research. In addition, the Shanghai Children's Medical Center (SCMC) Rare Disease Treatment Center was established on February 28, 2015, focusing on congenital blood disorders, immune deficiencies, metabolic disorders and cardiovascular diseases. SCMC also donated 120,000 yuan (approximately USD $17,500) to the Shanghai Rare Disease Prevention Foundation to support these initiatives.



- Shanghai Health and Family Planning Commission released its first local list of rare diseases in China titled “The list of major rare diseases in Shanghai (edition 2016)”. This list included 56 rare diseases and 50 of them are a part of the Chinese Rare Disease List (CRDL).
- On May 22, 2018, the Chinese Government officially released its first list of rare diseases entitled Chinese Rare Diseases List (CRDL; see list below in Appendix Table 2). This list aims to facilitate the medical practitioners to treat RDs, to introduce incentives for R&D of orphan drugs and to increase the availability and accessibility of medicinal products for RD patients[60].
- The Chinese central government has included rare diseases in major health planning and strategy, including five-year plan on public healthcare (2016-2020)[61] and “Healthy China 2030” planning outline [62].
- China has made tremendous progresses in addressing the needs of rare disease population over the past decade. The Chinese government's systematic approach included a series of coordinated initiatives including, establishing the Rare Disease Expert Committee (2016), funding the Rare Disease Study Group (2016–2020), and publishing the first rare disease catalogue (2018) [20].
- In 2017, China established a committee to formulate medical strategies for rare diseases to improve its national efforts towards the cause [63].
- In 2018, China published the first National Catalogue of Rare Diseases, which contains a list of rare diseases that receive special attention from the government. This initiative provides a foundational step toward ensuring that these conditions are recognized for specific medical research, treatment options, and policy planning.
- The new list of drugs covered by national health insurance came into effect on 1 January 2020 in China. It includes 70 new drugs whose prices have been reduced by an average of 60.7%. The list will include

about 22 anti-cancer drugs, 7 drugs for the treatment of diseases, 14 drugs for the treatment of chronic diseases and 4 drugs for the treatment of pediatric diseases. After price reductions and health insurance reimbursements, the financial burden on patients is expected to be reduced by more than 80% [59].

- China published its first official list of rare diseases, identifying 121 conditions in 2018. The list aims to prioritize research, diagnosis, and treatment efforts. The list is updated periodically, with the most recent version from 2023 bringing the total number to 207 rare diseases [59].
- In 2024, the National Health Security Administration (NHSA) added 13 rare disease drugs to its health insurance catalogue, bringing the total number of covered drugs to over 90. These additions include treatments for conditions such as hypertrophic cardiomyopathy, intractable epilepsy, and paroxysmal nocturnal hemoglobinuria [59], [64].

Programs and Initiatives

- The China-Dolls Centre for Rare Disorders started a voluntary rare disease patient registry in May 2010 and to date it has registered approximately 3,000 patients representing 30 rare diseases. One-third of patients in the registry were reported to have osteogenesis imperfecta (OI)[65].
- In 2013, China launched the China Rare Disease Prevention and Treatment Alliance (CRDPTA) and the China Rare Disease Pilot Project, which target 20 rare diseases and involve 17 medical institutions in 13 provinces. The initiative aims to develop specialized medical centers with guidelines and management pathways for these diseases, establish a national patient registry and data repository through retrospective and prospective case reviews, and create an online system for additional registrations. It also aims to improve molecular genetic testing capabilities using single-gene and next-generation sequencing (NGS) analysis for 15 rare diseases. These efforts aim to improve prevention, treatment, and data integration for rare diseases at the national level.
- On September 14, 2013, the China Rare Diseases Research Consortium (CRDRC) was launched at the First China Rare Diseases Symposium, marking a major milestone in the development of rare disease policy. Composed of more than 20 institutions and 50 experts, the consortium aims to establish a national rare disease registry with a pledged fund of 30 million yuan (about USD $4 million), provide access to harmonized data and samples, identify 5 to 30 rare disease genes each year, and make genetic testing accessible to patients. It also seeks to develop therapies based on the identified genes, secure research funding through alliances with major national organizations, and establish a centralized rare disease research institute in China.
- Another special research program on rare diseases called the "Rare Diseases Clinical Cohort Study" was launched in December 2016 by the Chinese government. According to their research plan, the unified National Rare Diseases Registry System of China (NRDRS) will be established by 2020, and a

large-scale cohort study will be conducted from 2016 to 2020. The project plans to develop 109 technical standards, to establish and improve 2 national databases of rare diseases - a multi-centre clinical database and a biological sample library, and to conduct studies on more than 50,000 registered cases of 50 different rare diseases. More so, this study will be combined with the concept of precision medicine. Chinese population-specific basic information on rare diseases, clinical information, and genomic information will be integrated to create a comprehensive predictive model with a follow-up database system and a model to evaluate prognosis. The collected information will be evidence for accurate classification, diagnosis, treatment, and estimation of prognosis for rare diseases in China [66]. The allocated budget for this project is 40 million yuan (USD $5.52 million).

- As per a report published in March 2018, China launched a program which aims to help patients with rare diseases in diagnosis and treatment and offers financial support to those in need. This program will be sponsored by the Illness Challenge and China Social Assistance foundations and will help with the diagnosis and treatment of up to 100 diseases. The program's purpose is to bridge the gaps between individual patients, medical resources and insurance[67] . In March 2018, China launched its first major project which aims at diagnosing rare children's diseases. The country's pediatric experts will use a technique known as whole genome sequencing (WGS) which will help to create a database of rare and undiagnosed conditions, including mental disorders and physical deformities. WGS, or mapping the entire human genome, has garnered attention of Chinese investors in recent years. In 2017, China's gene-sequencing industry raised over 6.8 billion yuan (USD $1.08 billion)[68].
- The National Rare Disease Registration System (NRDRS), introduced in 2019, systematically collects data on rare diseases, provides a platform for the diagnosis and treatment of rare diseases, and improves the understanding of rare diseases in China. It also facilitates the development of rare disease management policies, encourages research, and contributes to awareness [69].

5.1.3 Funding and Financial Support

- In 2011, the Shanghai government initiated coverage for 12 specific rare diseases, providing financial assistance of 100,000 yuan (USD $13,793) per child for conditions such as Gaucher's disease, Pompe disease, Fabry disease, and mucopolysaccharidosis (MPS). This support was increased to 200,000 yuan (USD $27,580) in 2012. However, the average annual treatment cost for rare disease patients was estimated at 2 million yuan (USD $275,860), indicating a significant shortfall in coverage [70].
- Additionally, in early 2011, the Shanghai Rare Disease Society was established to promote legislation, research, and insurance coverage for rare diseases [71][64].
- In July 2012, Qingdao city of Shandong province, issued opinions on establishing an urban medical system and dynamically explored policies on social security on major and rare disease drug use. In the

same year, Qingdao government approved a proposal that covered the treatment cost of all disease including rare diseases for up to 400,000 yuan (USD $55,172) in the national medical insurance[72]. In 2020, Shandong province further bolster its assistance for patients with rare diseases by incorporating treatments for ailments such as Gaucher disease, Fabry disease, and glycogen storage disease type II into its major illness insurance framework. This initiative provides reimbursement rates of 80% for expenses ranging from 20,000 to 400,000 yuan USD $2,758.60-$55,172), and 85% for costs that surpass 400,000 yuan (USD $55,172), with an annual reimbursement cap set at 900,000 yuan (USD $124,137)[73].

- On December 26, 2014, China's Social Assistance Foundation (CSAF) launched the 'China Child Rare Disease Aid Fund'. This was a special fund for children and young people with rare diseases and was designed to help them cope with their illness and at the same time establish a support system around them. DeExpo donated 5,000,000 yuan (USD $804,531) for the cause [74].
- China's basic-research spending has historically been extremely low- about 4.8% in 2012 and 2013, compared with 10–25% in developed nations. But in 2014, the allotment for basic research was increased by 12.5% to USD $6.6 billion - of which the National Natural Science Foundation of China (NSFC) was announced to receive USD $3.1 billion. The major areas that the foundation funds included studies of biodiversity, air pollution, supercomputers, neurodegenerative diseases and scientific equipment [75].
- In 2016, Zhejiang province medical insurance started to cover Gaucher's disease, amyotrophic lateral sclerosis (ALS), and phenylketonuria (PKU) [76].
- The China Social Welfare Foundation (CSWF) and the China-Dolls Center for Rare Disorders jointly announced the establishment of the Working Commission on Rare Diseases on February 29th, 2016. This initiative was supported by a funding of 1 million yuan (USD $144,015) from CSWF, aiming to enhance research, provide policy advice, and promote international collaboration in the field of rare diseases in China [77].
- In 2017, in Shanghai, a fund with an initial capital of 3 million yuan (USD $435,000) was jointly established by rare disease prevention and treatment institutions and pharmaceutical industries such as Sanofi. The fund will be used primarily to improve medical treatment of lysosomal storage diseases (LSDs)[78].
- National Natural Science Fund guide to programs 2018 by National Natural Science Foundation of China (NSFC) details funding for R&D to research institutes in China. NSFC's funding portfolio consists of 4 categories of programs, namely, Exploration, Talent, Instrument and Convergence, with respective preferential focuses, constituting an integrated funding instrument of the National Natural Science Fund[79].

- The Ministry of Finance has also helped to implement tax incentives for drugs to treat rare diseases, to encourage the marketing and importation of drugs to treat rare diseases, and to reduce the cost of drugs for patients with rare diseases [59]. Through adjustment of the List of Drugs Covered by National Medical Insurance, the National Healthcare Security Administration (NHSA) has covered an increasing number of drugs to treat rare diseases under basic medical insurance. It has also negotiated to reduce the price of some drugs to treat rare diseases, further reducing the economic burden on patients with rare diseases.
- In 2024, China has implemented several measures to improve access to rare disease treatments, with 95 orphan drugs now included in the national medical insurance catalogue. To reduce costs, the government has lowered the import value-added tax on rare disease medications to 3% and introduced various provincial-level assistance programs, including special funds and serious disease insurance schemes. The National Healthcare Security Administration (NHSA) has also negotiated with pharmaceutical companies to lower drug prices, significantly reducing the cost of treatments for conditions such as spinal muscular atrophy, Gaucher disease, and myasthenia gravis.[59], [64].

5.1.4 Regulatory and Market Access

- The Drug Registration Management Measures published in 1999 was the first medical regulation that mentioned about rare diseases in China. However, there was no clear definition of rare diseases. The updated Drug Registration Management Measures in 2007 established two favorable measures for rare disease clinical test and approval, but it still failed to give a clear definition of rare diseases, which presents the first barrier in rare disease research, diagnosis and treatment. Since 2006, several institutes and individuals have made proposals to the government every year for the release of a policy on rare diseases.
- On April 14, 2009, the World Federation of Hemophilia (WFH) officially launched the Global Alliance for Progress (GAP) project in China. This international collaboration with Hemophilia House of China was an intense 4-year effort (2009-12) to identify and diagnose more people with bleeding disorders in China, in order to improve access to safe and affordable treatment and help develop sustained programs for comprehensive care [80].
- In 2012, Baxter International Inc. received an approval in China for ADVATE, a recombinant human coagulation factor VIII for the treatment of hemophilia, which offers advanced treatment options, said Professor Yang Renchi of the hospital's Institute of Hematology and Blood Diseases. Previously, in 2010, Baxter partnered with the Chinese Ministry of Health to create the country's first hemophilia management system for comprehensive patient registration and treatment integration. Baxter has also donated more than 5 million IU of hemophilia products and raised awareness of the disease. Hemophilia, one of China's rare diseases, has benefited from more supportive medical policies, with

several eastern and central provinces developing treatment support initiatives and establishing diagnostic, processing and registration centers.

- In contrast to other positive initiatives for rare diseases, in 2014 China's Food and Drug Administration (CDFA) imposed regulatory constraints on the provision of clinical genetic testing including non-invasive prenatal DNA testing, due to concerns over quality control and regulatory oversight. This ban had significant implications, with the Beijing Genome Institute (BGI) estimating that it could result in the birth of around 11,000 babies with congenital disorders annually in Beijing alone, contributing to the growing burden of rare diseases. However, by July 2014, the China Food and Drug Administration (CFDA) lifted the ban, permitting BGI to register sequencing devices for prenatal genetic testing, ensuring better regulation and safety. Nevertheless, issues such as limited access to testing in low-income regions and concerns over data privacy persisted, particularly with reports of genetic data collection by Chinese companies for research purposes. The situation underscored the need for balanced policies that regulate genetic testing while ensuring accessibility, affordability, and data security [81].
- On May 11, 2017, the CFDA published the Innovative Orphan Drug Policy Proposes (Circular No. 52) for public consultation. The CFDA proposes that drugs and devices that treat designated rare diseases may be eligible for an exemption from clinical trials. Orphan drugs and devices that have already been approved abroad can be granted conditional approval without domestic clinical studies. Follow-up studies, according to the CFDA guidelines, must be carried out in China after approval. The Chinese government will work to make new drugs available to patients by encouraging hospitals to purchase new drugs. The government is committed to including more innovative drugs in the national health insurance system and updating the list of reimbursable drugs more frequently to make products more accessible to the public [82].
- The Chinese government is expanding access to rare disease medicines by prioritizing their marketing review and approval, listing them as clinically urgent, and introducing them through pilot zones. Between 2018 and 2022, 56 rare disease medicines were approved. From 2018 to 2020, 39 rare disease medicines were included in urgent clinical-need lists, with 23 applying for marketing by March 2022 and 22 completing the process [83]. Despite these efforts, the approval time in China remains 9.5 years longer than in the EU.
- In 2021, to encourage the research, development, and production of drugs to treat rare diseases, the National Medical Products Administration has drafted a series of policies to accelerate the review and approval of drug registration and to support the research and development of drugs to treat rare diseases [59].
- Managed Access Programs (MAPs) in China allow early access to unapproved therapies under compassionate use, following IRB/IEC approval. In June 2021, Iptacopan for paroxysmal nocturnal

hemoglobinuria (PNH) became the first drug approved through Novartis' MAP supporting access to treatments for rare diseases [84].

- The Medicine Connect program, launched to improve access to rare disease treatments in the Greater Bay area, allows for early access to drugs approved in Hong Kong but not yet available in mainland China. In 2021, RhoGAM became the first therapy approved through the program, facilitating access to specialized medicines in the region[84].
- In August 2024, introduced the Patient-Centered Rare Disease Drug Research and Development Pilot Work Plan (CARE Plan) to enhance the development of treatments for rare diseases by incorporating patient perspectives, improving the integration of patient experience data in clinical research, and fostering collaboration among regulators, sponsors, and patients [85]. Additionally, this will offer opportunity for increased interaction between companies and the Center for Drug Evaluation (CDE) during the development process.
- In addition to increasing the number of reimbursed drugs, China has developed a National Network to Collaborate on Diagnosis and Treatment of Rare Diseases (NCDTRD) in 2019, which initially included 324 hospitals nationwide. As of October 2024, over 400 medical institutions have joined this network, which features medical referral and telemedicine mechanisms and covers all provincial-level regions across the country[69].
- China has recently intensified its efforts to improve access to treatments for rare diseases by expanding its medical insurance coverage. In December 2024, the National Healthcare Security Administration (NHSA) added 13 rare-disease drugs to the national medical insurance drug catalogue. This initiative is part of China's broader strategy to enhance the accessibility and affordability of rare disease medications[59].

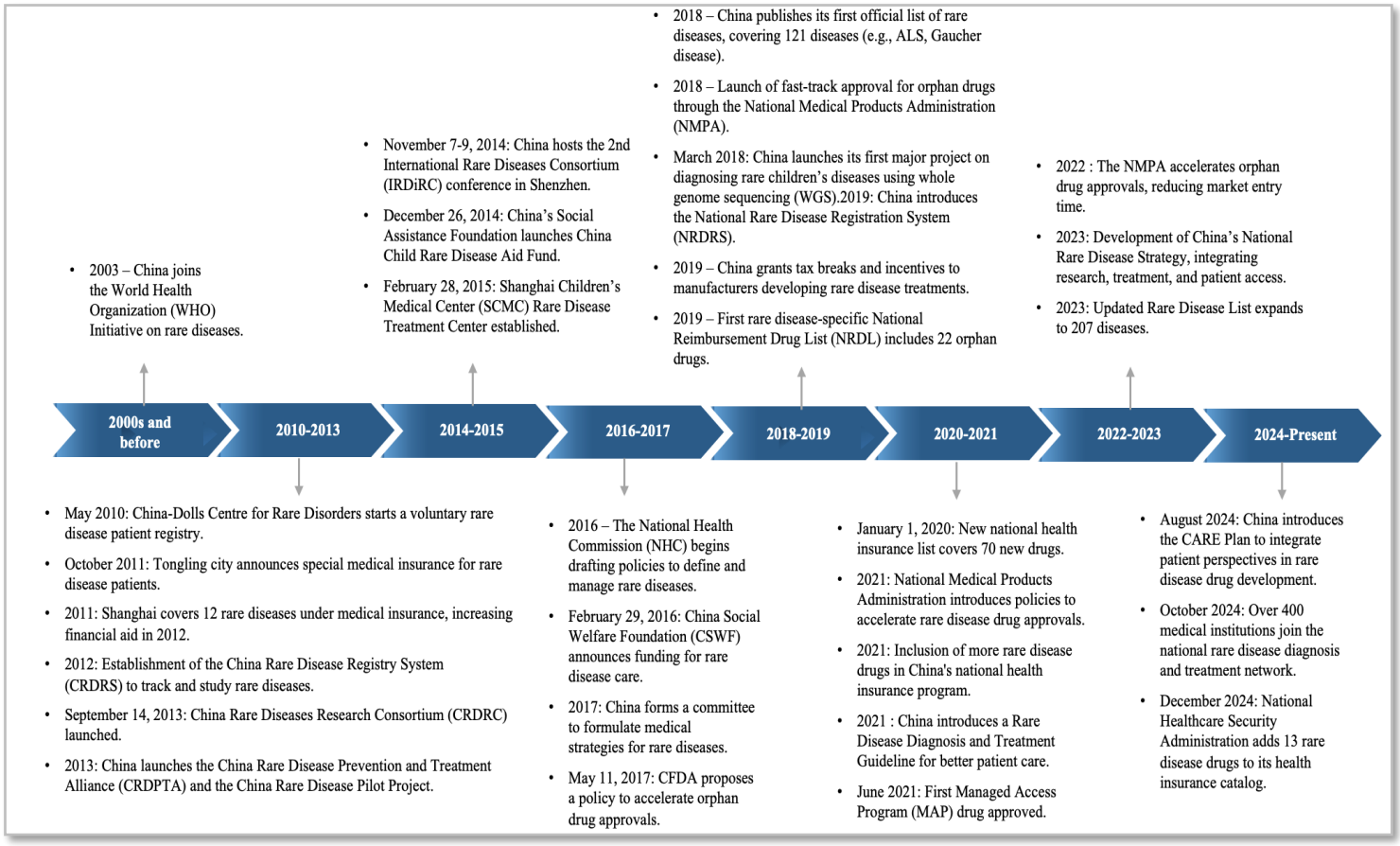
5.1.5 Care Pathways and Infrastructure

- In the early 1980s, the Shandong Academy of Medical Sciences (SAMS) founded the Key Laboratory for Rare Disease Research in Shandong Province, concentrating on the epidemiology, case registration, and fundamental research related to rare diseases. This initiative was designed to tackle the significant gap in documented epidemiological data concerning rare diseases in China, as there was no established system for registering cases of the majority of rare diseases [65], [71].
- Chinese health-care system underwent overhauling for the first time since 2009 with the expansion of National Reimbursable Drug List (NRDL), though the system is still governed by cheaper and essential medicines. In addition, groundwork to speed up "orphan drug approval" was flagged by government given the huge regulatory backlog and even clinical trial wavers[86].
- Many academic institutions and major hospitals in China have been playing an important role in translational medicine for the treatment of rare diseases, and particularly in cutting-edge technologies.

One such example is, the Shanghai Institute of Materia Medica (SIMM) of the Chinese Academy of Sciences which announced the CFDA approval of one of their orphan drug programs targeting pulmonary arterial hypertension (PAH) to conduct human clinical trials [87].With respect to cutting-edge technologies, Sichuan University's West China Hospital in Chengdu announced their preparation to conduct the world's first human trial using *CRISPR* gene editing technology in 2016[88].

- In addition, a team of scientists from Tongji Medical College, in collaboration with FivePlus Molecular Medicine Institute in Beijing, successfully conducted a long-term trial of gene therapy in human patients with a rare genetic disorder known as Leber's hereditary optic neuropathy (LHON), more than 10 years after the world's first gene therapy was approved in China[89], [90].
- In October 2018, a Chinese medical research alliance was established to accelerate the study of rare diseases [59]. The China Alliance for Rare Diseases is comprised of more than 50 entities, including medical institutions, universities, academic institutions, and enterprises. The alliance plays a key role in pooling resources and promoting the treatment of rare diseases in China. At its launch on October 24, the Alliance released an explanation of China's first rare disease catalogue.
- In 2019, China established the National Network to Collaborate on Diagnosis and Treatment of Rare Diseases (NCDTRD) consisting of 324 hospitals nationwide, including a leading national institution (Peking Union Medical College Hospital), and 32 provincial key institutions, achieving rare disease resource sharing [69].

Figure 3. Shows the timeline of the rare diseases progress in China



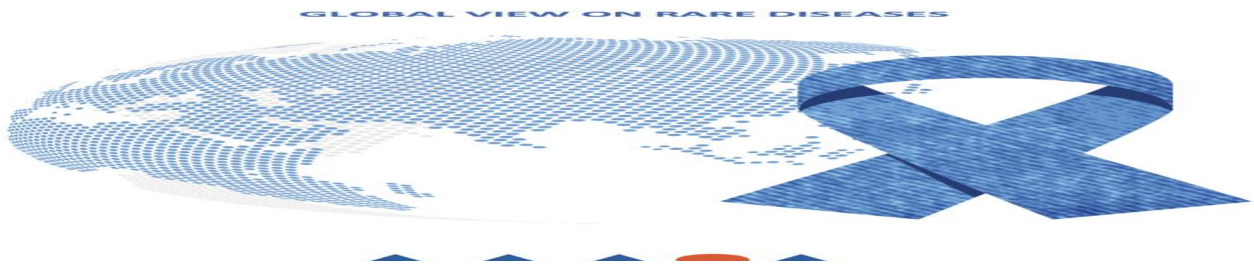
5.1.6 Key Organizations Advancing Rare Disease Initiatives in China

Organization Name	Established Year	Description
Chinese Organization for Rare Disorders (CORD)	2013	- NGO to establish an official platform of RDs, treatment and a database for patient information - Supports RD patient organizations - Raise awareness about RD via public education - Policy advocacy and research - Funded by several pharma companies
China Organization of Albinism (COA)	2008 (Founded) 2011 (Govt. recognized)	- National, Non-profit organization to support Albino patients and families - Part of Albinism World Alliance (AWA) in 2012
Chinese Rare Disease Research Consortium (CRDRC)	September 14, 2013	- Establishing national registry for RDs - Provide access to harmonized data and samples - Identifying 5-30 RD genes per year - Facilitate development of therapeutic strategies - Joint efforts under alliance to support funding for RD research - Seek to launch a Rare disease research institute in China
International Rare Disease Research Consortium (IRDiRC)	2009	- The main objective was to accelerate medical breakthroughs for people affected by RDs by establishing a network of research funders
China Rare Diseases Prevention and Treatment Alliance	February 28, 2013	- Launched in Jinan, China - Includes 17 medical institutions from 13 provinces in China - Committed to the establishment of RD treatment centers across the country - Assist in data collection of RDs, carry out epidemiological studies and improved treatment - Implementing Chinese Pilot Project (2013BAI07B02)
China-Doll Center for Rare Diseases	May 2008	- NGO to provide care and help to patients with Osteogenesis Imperfecta and protect their rights - August 2009: established China-Dolls Rare Disorders Care Foundation - March 2010, established Shandong Jinan China-Dolls Home of Care to provide service for Shandong patients
Beijing Rare Disease Care Center of the Hemophilia Home of China	September 2009	- NGO that provides treatment and financial aid for hemophilia patients
China Food and Drug Administration (CFDA)	March 2013	- Drafts laws, regulations and policies on the administration of food and different drugs
National Science Foundation of China (NSFC)	February 14, 1986	- Institution directly under the jurisdiction of the State Council - Tasked with the administration of the National Natural Science Fund from the Central government - Support basic research and stimulate free exploration, identify and foster scientific talents, as well as promotes progress in science and technology and the harmonious socioeconomic development of the nation
China Social Assistance Foundation (CSAF)	July 25, 2013	- Established in Beijing; national public-fundraising foundation and governed by the Ministry of Civil Affairs of China - Support research, public education and social assistance to people in need - *China Child Rare Disease Aid Fund* (USD $804,531)
Shanghai Rare Disease Foundation	April 9, 2017	- First foundation to look for new models on diagnosis, treatment and help to patients with LSDs

		- Establishment of Shanghai Rare Disease Prevention and Treatment Fund
China Social Welfare Foundation (CSWF)	September 2013	- Funding of 1 million yuan to set up a working commission on RDs
China Charity Federation (CCF)	1994	- Nationwide non-governmental charity organization - Provides high cost orphan drugs to RD patients free of cost. Eg. Cerezyme
Illness Challenge Foundation		- Establishing platform and multilateral cooperation, solve urgent problems faced by people with RD together
Beijing Genomics Institute (BGI)	September 9, 1999	- Non-governmental independent research institute - Gene sequencing to identify and support treatment of RDs
Sichuan Kelun Pharmaceutical Co Ltd	1996	- Development of orphan drugs - Supports policy making in China
Baxter International Inc.		- Set up of "Hemophilia disease management system" - Donated 5 million IUs of hemophilia products - Introduction of ADVATE (recombinant FVIII therapies
Huazhong University of Science and Technology (HUST)	1907	- Involved in research and publication on RDs - Lead formation of CRDRC
Sichuan University's West China Hospital	1914	- Preparing to conduct the world's first human trial using CRISPR gene editing technology
Hope for Rare Foundation	2022	- Non-profit aim to enhance investments in basic and translational clinical research to advance the care and cure for patients with rare diseases
China Alliance for Rare Disease (CHARD)	2023	- Non-profit focused on creating patient-centered solutions, through bringing together multiple stakeholders, to build a robust and efficient rare disease infrastructure in China that can improve the quality of life for patients and their families.
Illness Challenge Foundation (ICF)	2016	- Charitable foundation founded by rare disease patients. It provides resources and opportunities for patient services, organizational support, community development, and policy research.
Chinese Organization for Scleroderma	2018	- Non-profit providing resources and assistance to individuals diagnosed with scleroderma. - Raising awareness about scleroderma and advocating for patient rights and access to treatment.
National Network to Collaborate on Diagnosis and Treatment of Rare Diseases (NCDTRD)	2019	- Enhance the collaboration among hospitals, researchers, and policymakers to create a standardized approach to diagnosing and treating rare diseases. - Provide access to specialized medical resources for rare disease patients

Table 4. Key organizations in the area of rare diseases in China

(RD = Rare disease)



5.2 India

5.2.1 Rare Disease Landscape in India

Of the approximately 10,000 rare diseases identified worldwide, about 450 have been reported in the Indian population [401].

India, with a population of 1.3 billion, faces a significant burden of rare diseases, driven by factors such as high birth rates, high conception rates and socio-economic challenges. India doesn't have a standard definition for rare diseases, but the Organization for Rare Disorders India (ORDI) suggests that a disease is rare if it affects 1 in 5,000 people or fewer [91]. The Rare Diseases and Disorders Research Foundation estimates that approximately 70 million people in India are affected by rare genetic diseases. To address this, the Indian Council of Medical Research (ICMR) has established a National Registry of Rare Diseases, which compiles epidemiological data and identifies 4001 rare diseases [12]. However, treatment options for many of these diseases are either rare or extremely expensive. The availability of information on the prevalence of rare genetic diseases in India is limited, due to the lack of a centralized patient registry, diagnostic centers, affordable therapeutic interventions and widespread awareness. On average, it takes seven years for a rare disease to be diagnosed in India from the onset of symptoms, and many cases likely remain undiagnosed due to lack of awareness among patients and healthcare providers.

Despite the implementation of numerous government-sponsored insurance programs and schemes, India's health expenditure has recently increased from 1.2% to 1.6% of gross domestic product (GDP) in 2021,

this is extremely low when compared to other countries in the world, such as Sri Lanka, China, Thailand, the United Kingdom and the United States [92], [93]. A significant part of this growth is attributed to private sources. Private health expenditure accounted for 62.14% of total health expenditure in 2018-19. Although public sector spending on health has increased in recent years, it remains insufficient to meet the basic health needs of the country's growing population. In addition, out-of-pocket (OOP) expenditures, which accounted for 69.4% of total health expenditures in 2004-2005, have decreased over time, but remain at a high level of 48.2% in 2018- 2019

5.2.2 National Strategy Framework and Policy Shaping

National Plan and Legislation

- Hemophilia incidence in India is estimated to be 1 in 5,000 and clotting factors needed for its treatment is expensive. In year 2010, the Uttar Pradesh government took an initiative to cover the cost of clotting factors for the patients in need[94].
- In 2014, the Ministry of Health and Family Welfare in India constituted an expert committee to develop policies and guidelines for the approval of new drugs, clinical trials, and prohibition of certain drugs (Circular No. 12-01/14-DC Pt.47). A significant resolution by the committee was to waive the requirement for clinical trials in the Indian population for the approval of orphan drugs for rare diseases and drugs intended for conditions or diseases where no therapy was available. This initiative was intended to expedite access to potentially life-saving treatments for individuals afflicted by rare and neglected conditions [95].
- Strand Life Sciences, a Bengaluru based precision diagnostic company spearheaded a consortium of doctors, researchers and biotech companies that drafted a rare disease and orphan drug policy for the state of Karnataka in 2015. This document is under consideration of state health secretary. The framework is based on the US Orphan Drug Act and aims to provide for federal grants for research, tax credits for clinical trials and 7 years of exclusive marketing of orphan drugs[96].
- In 2016, the Karnataka Vision Group on Biotechnology (VGBT) presented a draft framework for the Rare Diseases and Orphan Drugs Policy in the state. This policy was designed to create a comprehensive and multidisciplinary strategy for the diagnosis, treatment, and management of rare diseases, ensuring that all affected individuals have equitable access to care. The framework prioritized early detection, prevention, and prompt intervention, while also advocating for research and the development of orphan drugs. Furthermore, it underscored the necessity of incorporating rare disease education into medical training to raise awareness among healthcare professionals. The policy aimed to establish a strong infrastructure for rare disease care, which would include specialized centers and support systems for patients and their families. Additionally, it recommended the creation of a disease registry to track the

incidence and prevalence of rare diseases within the state, thereby enhancing resource allocation and policy formulation [97].

- In 2019, India introduced a rare disease component to the Rashtriya Arogya Nidhi (RAN) Umbrella Scheme. It has three components namely (i) Rashtriya Arogya Nidhi (RAN), (ii) Health Minister's Cancer Patients Fund (HMCPF) and (iii) Scheme for financial assistance for patients suffering from specified rare diseases [98].Providing one-time financial assistance upto Rs.15 lakh (USD $ $17,205.85) not limited to patients belonging to families living below threshold poverty line for treatment of identified Rare Diseases amenable to one-time treatment in Government hospitals but extended to 40% of the population who are eligible as per norms of Pradhan Mantri Jan Arogya Yojana, for their treatment in Government tertiary hospitals only [99]. An amount of Rs.100 crore (USD $11.47 million) has been allocated for Rare Disease component of Umbrella Scheme of Rashtriya Arogya Nidhi during 2019-20.
- Currently, 63 rare diseases are included under National Policy for Rare Diseases on recommendation of Central Technical Committee for Rare Diseases (CTCRD). The list of rare diseases is at Annexure II. Financial support of up to Rs. 50 lakhs (USD $57,350) per patient is provided for the treatment at the notified Centres of Excellence (CoEs) for Rare Diseases in 2024. Since the launch of the policy, total 1,118 patients benefited under NPRD. Patients can approach any CoE across the country as per their convenience [100].

Programs and Initiatives

- In 2009, the government of Uttar Pradesh launched a program aimed at providing free anti-hemophilic factors (AHF) to individuals suffering from hemophilia, improving the care available to approximately 4,200 patients throughout the state. Initially, 8 hemophilia treatment centers (HTCs) were established, and in 2015, the program has expanded to 26 centers providing free AHF to approximately 4,200 persons with hemophilia (PwH) [94].
- The Dystrophy Annihilation Research Trust (DART), established in 2012 in Bengaluru, is a non-governmental organization funded by parents that is dedicated to the development of a tailored genetic therapy for Duchenne Muscular Dystrophy (DMD). The DART functions as a research laboratory focused on personalized treatment strategies aimed at restoring the dystrophin protein, essential for maintaining muscle cell integrity. The organization employs methods such as antisense oligonucleotide therapy for exon skipping, which may help to decelerate the progression of the disease and enhance the quality of life for patients [**Error! Reference source not found.**].
- First large-scale initiative to understand rare genetic disorder mechanisms and diagnosis was launched as “Genomics for Understanding Rare Diseases India Alliance Network (GUaRDIAN)” in the year 2014. This network performs next-generation sequencing (NGS), genotyping microarrays and extensive

computational analysis. The collaborator network has developed an online portal where the disease information and clinical details along with the contact details can be submitted directly. Following this the investigation team contacts the patient along with sample collection procedure. Samples are then processed and analyzed. Cost of this testing can be between INR 10,000-80,000 (USD $ 150-$1,100); however, this service is done at no cost to the public[101], [102].

- The first attempt to bring together all experts of rare disease under a common platform was initiated by Indian National Science Academy (INSA), conducted first of its kind rare disease workshop titled “To develop a scientific program or research on rare diseases” in 2016. The program deliberated on issues of rare disease definition, research avenues, policy framework to boost and incentivize R&D efforts and state government involvement. Drug Controller General of India (DCGI) head stated that genetic differences in Indian population necessitates Indian-centered studies, rather than using data from studies in other countries. Expert suggestions were also invited on the needs of changes in the drugs and cosmetic act to meet the requirements of research in rare diseases[94].
- In April 2017, the Indian Council of Medical Research (ICMR) launched the ‘Indian Registry of Rare Diseases’, which aims to address the unmet needs of patients with rare diseases and contribute to the development of data and information to support R&D to improve innovation. This effort will enable better visibility of patients suffering from rare diseases and will initially be carried out in hospitals or with doctors. Initially, the information will be collected only on diseases that can be treated locally or globally, and over time, other diseases will be included. The registry will benefit various stakeholders of rare diseases in several ways, including: 1) For patients: identification will increase access to treatment 2) For government: accurate number of patients with rare diseases to help meet their needs and provide necessary resources 3) For research organizations: ensure that a wealth of information is available on R&D activities in India 4) For Publications: To serve as a basis for many publications and thus strengthen India’s position as a global leader in healthcare and clinical trials 5) Other benefits: help monitor disease prevalence, incidence and mortality, which in turn will help shape policy decisions and facilitate innovation and patient care [103], [104].
- In India, the National Initiative for Rare Diseases (NIRD) was launched by Indian Council of Medical Research (ICMR), All India Institute of Medical Sciences (AIIMS), Jawaharlal Nehru University (JNU), and Program for Research in Smart and Intelligent Devices (PRESIDE) inviting projects for rare disease research. In May 2017, the government rolled out a National Policy for the Treatment of Rare Diseases, allocating an initial fund of INR 100 crore (USD $15 million). Short-term measures include encouraging states to implement similar structures, creating a web-based application for fund access, establishing a patient registry, and developing public awareness and healthcare provider training. Long-term measures focus on improving R&D for rare disease treatments, supporting orphan drug production, reducing import duties on enzyme replacement therapies, and ensuring affordability

and insurance coverage for rare diseases. The policy also promotes genetic counseling, prenatal screening, and the establishment of Centers of Excellence (CoE) for rare disease diagnosis and treatment.

- The ICMR National Registry for Rare and Other Inherited Disorders was launched in 2019 to document cases, though uptake remains limited. Data, collected digitally from various healthcare facilities, including primary centers and hospitals, early-stage diagnosis, and morbidity and mortality data from MCTS, RCH, and MDSR databases can help create demographic maps and compile epidemiological information. The NRROID currently has 13,972 records covering 12 disease areas. However, the current information is insufficient to provide a proper epidemiological landscape and perform statistical analysis of clinical data [105].

5.2.3 Funding and Financial Support

- Aten Biopharmaceutical (Bengaluru) is one of the few local companies working to develop drugs for rare diseases in India. Established in 2013, the company has received some funding from the central Department of Biotechnology. These companies are seeking government support to innovate drugs for a small market in a feasible and profitable way.
- Since the 1970s, the government has given greater priority to healthcare by allocating significant financial resources. The government budget allocation to the Ministry of Health has increased significantly from 2.8% in 1970 to 7.82% in 2021 (MoH, 2021). The government provides free health services to its citizens, including expatriates working in the public sector, while private sector employees are covered by health insurance schemes (Al-Dussary, 2009) [106].
- The Ministry of Finance has issued notifications providing full waivers of Basic Customs Duty (BCD) and Integrated Goods and Services Tax (IGST) on drugs imported for personal use in treating specific rare diseases, such as Spinal Muscular Atrophy (SMA) in 2021. Additionally, exemptions from BCD are available for drugs or medicines used in the treatment of rare diseases when imported by CoEs or on their recommendation.
- The Department of Pharmaceuticals is implementing the Production Linked Incentive (PLI) Scheme for Pharmaceuticals with a total financial outlay of Rs. 15,000 crore (USD $1,720.5 million) and scheme tenure up to FY 2027-28[107]. The scheme provides for financial incentive to 55 selected applicants for manufacturing of identified products under three categories for a period of 6 years. The product Category 1 covers drugs such as biopharmaceuticals, complex generics, gene therapy drugs, complex excipients, orphan drugs etc. Orphan drugs are those drugs which are used for treatment of rare diseases. Under the scheme, total 8 orphan drugs have been approved for manufacturing. The orphan drugs approved under the PLI scheme for Pharmaceuticals.

5.2.4 Regulatory and Market Access

- Since 2008, Bayer Zydus Pharma has been operating a Patient Assistance Program in India for Nexavar™ (sorafenib), an orphan drug used to treat hepatocellular carcinoma, advanced renal cell carcinoma, and differentiated thyroid carcinoma. This program aims to reduce the monthly treatment cost, enhancing accessibility for patients with limited financial resources. Additionally, in 2012, the Indian government granted a compulsory license to Natco Pharma, allowing them to produce a generic version of sorafenib at a significantly lower price, further improving affordability for patients [108].
- In 2008, Sutent was launched to treat rare and difficult-to-treat forms of cancer. Pfizer developed a Sutent patient assistance programme which made the drug available to patients irrespective of their incomes. The programme offered eligible patients with a partial or fully subsidized treatment. V-Care Foundation is an NGO partner in India which manages this programme
- In a meeting held between pharma stakeholders and Drug Controller General of India (DCGI) on May 4, 2016, to explore possibilities to provide cheaper medicines for patients with rare diseases, Indian Drug Manufacturers Association (IDMA) and the Organization of Pharmaceutical Producers of India (OPPI) were give the responsibility to formulate the definition for rare diseases, JDC (ER) was given the responsibility to revise timelines for orphan drug approvals, and a separate cell was suggested to address the issues of rare diseases, possibility of separate pricing mechanism for orphan drugs, and possibility of custom duty exemption[109].
- On 5th February 2018, an announcement by the Oraxion Therapeutics, a spin-off from Bengaluru based Aten Porus Lifesciences announced that the company has entered into an option agreement with a US-based biopharmaceutical company. The agreement provides the biopharma partner with the exclusive option to license its lead asset ORX-301 for the treatment of Niemann-Pick Type C disorder (NPC) and Focal Segmental Glomerulosclerosis (FSGS)[109].
- India provides expedited approval processes and regulatory exemptions for orphan drugs, which may include waivers from local clinical trials if the drugs have already received approval in regulated markets such as the United States or the European Union. The Drugs and Clinical Trials Rules (2019) support these accelerated approvals and offer incentives, including fee waivers. In cases where adequate global data is available, clinical trials may be partially or entirely waived, thereby ensuring faster access to essential treatments [105], [110].
- National Policy on Research and Development and Innovation in Pharma-MedTech Sector in India Scheme for promotion of the development of innovative drugs and medical technologies, particularly for rare diseases, which are often underfunded in traditional healthcare research initiatives.India's regulatory framework for rare diseases is governed by the National Policy for Rare Diseases (NPRD) 2021 and the Central Drugs Standard Control Organization (CDSCO) under the Drugs and Cosmetics

Act, 1940[105], [110]. Rare diseases are classified into three categories: those that can be addressed with a one-time curative intervention, those that necessitate long-term treatment options that are currently available, and those that require additional research. The objective of the policy is to enhance financial assistance and facilitate access to treatment via established Centers of Excellence (CoEs) and patient registries.

- To support affordability, NPRD 2021 provides financial support of up to ₹50 lakh (USD $57,350) per patient for certain diseases[105], [110]. It promotes the utilization of Corporate Social Responsibility (CSR) funding and may implement compulsory licensing to facilitate affordable pricing. Nonetheless, challenges remain, such as elevated drug prices, reliance on imports, and delayed diagnoses stemming from insufficient awareness. Ongoing initiatives aim to strengthen local manufacturing, research, and financial assistance systems to improve access to treatments for rare diseases in India.
- In 2023, the National Policy on Research and Development and Innovation in Pharma-MedTech Sector in India Scheme was drafted aiming to promote a regulatory framework that supports innovation, encourages both public and private sector investments in research, and develops an ecosystem aimed at promoting sustainable growth is essential, particularly for rare diseases, which are often underfunded in traditional healthcare research initiatives [111]. Additionally, the establishment of the Indian Council of Pharmaceuticals and Med-tech Research and Development is proposed to facilitate collaboration among various sectors. This policy seeks to increase India's share in the global pharmaceutical market, strengthen drug security, enhance healthcare services, generate high-quality employment opportunities, and draw skilled professionals back to India, thereby contributing to the nation's GDP and fostering long-term economic development.
- The Department of Pharmaceutical has proposed PRIP (Promotion of Research and Innovation in Pharma MedTech Sector) scheme with a budget outlay of Rs. 5000 crores (USD $570.5 million) on 17th August 2023[111]. The objective of the scheme is to transform Indian pharmaceuticals sector from cost based to innovation-based growth by strengthening the research infrastructure in the country. It aims to incentivize the creation of new drugs, therapies, and diagnostic tools for rare diseases by offering grants, subsidies, and a regulatory framework that accelerates the approval and availability of these innovations. This will further lead to sustained global competitive advantage and contribute to quality employment generation in the country.

5.2.5 Care Pathways and Infrastructure

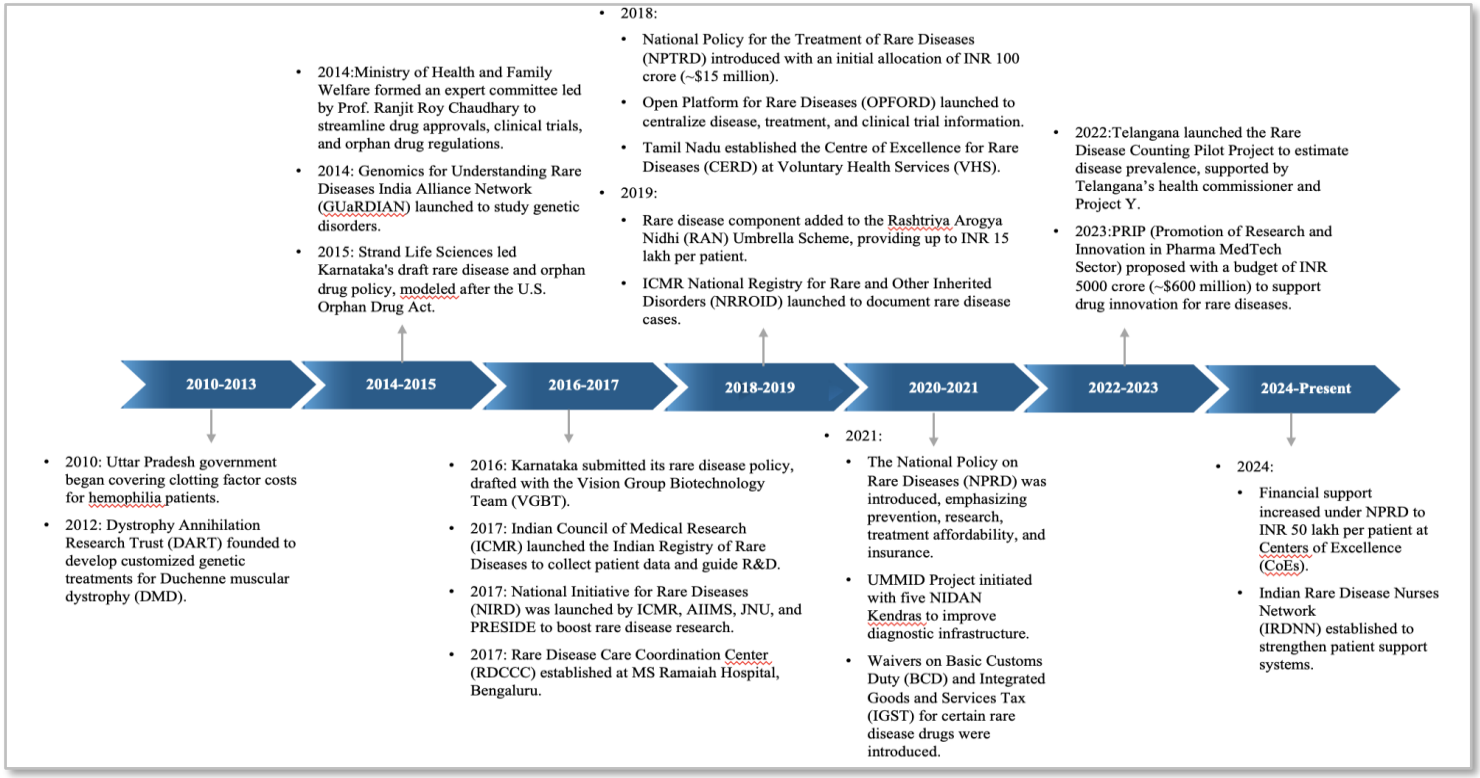
- Bengaluru became the first city in India to have a center of excellence for rare diseases at the Indira Gandhi Institute of Child Health. India’s first exclusive rare disease ward and free treatment facility are jointly staffed by the Organization for Rare Diseases India (ORDI). The center is supported by the Center of Human Genetics, Bengaluru. Since its inception the center has diagnosed nearly 100 patients

with rare diseases and provided treatments in case of treatable conditions or else given palliative care to patients in need. The center provides free clinical diagnosis, genetic counselling, prenatal care, treatment as well as daycare facilities to 15,000 families [112].

- Diagnosis of rare diseases on an average takes 7 years and a single test can cost between INR 25,000-30,000 (USD $350-$400) which is a huge burden for most patient families. To address this challenge, ORDI designed an innovative program called Rare Disease Care Coordination Center (RDCCC) at MS Ramaiah hospital, Bengaluru in 2017 which serves as a nation-wide hub. The center gathers patient information, needs and their pain points and consequently arranges for consultation with rare disease expert to help the patients[112].
- In early 2018, Open Platform for Rare Diseases (OPFORD), an idea conceived at the Center for Health Ecologies (CHET), Bengaluru and executed by Strand Life Foundation (SLF), Bengaluru was launched. This portal will allow access to information on specific diseases, diagnostics, therapeutics, clinical trial information, list of doctors, clinical geneticists, treatment centers and patient support groups[113] .
- Centre of Excellence for Rare Diseases (CERD) was launched in Tamil Nadu in 2018 at Voluntary Health Services (VHS) as a one-stop center to offer multidisciplinary facilities with doctors/clinical experts coming to treat children with rare diseases. The center will provide comprehensive care which will include medical and surgical management, rehabilitation, day care facilities and in-patient services [114].
- The National Policy on Rare Diseases (NPRD), introduced by the Government of India in 2021, focuses on prevention, awareness, research, diagnosis, treatment, affordable orphan drugs, insurance coverage and progressive implementation work. Under the UMMID project, five NIDAN Kendras have been established to improve the diagnostic infrastructure for rare diseases through advanced genetic screening. In addition, 11 government health institutions have been designated as Centres of Excellence (CoEs) for diagnosis and treatment, with a budgetary allocation of Rs 928 million (approximately USD $11.3 million)[105], [110]. The policy emphasizes inter-ministerial cooperation, centralized funding, a national disease registry and coordination between the central and state governments. It also includes a categorized list of rare diseases prevalent in India, which will guide interventions.
- The Rare Disease Counting Pilot Project in Telangana is a pioneering initiative led by the Indian Organization for Rare Diseases (IORD) in 2022 to accurately estimate the prevalence of rare diseases in the state[115]. Supported by Telangana's state health commissioner, Dr. Sweta Mohanty, the project collaborates with Project Y and the Rare Care Centre at Perth Children's Hospital in Australia. Local healthcare workers, including Accredited Social Health Activists (ASHAs) and Auxiliary Nurse Midwives (ANMs), play a crucial role in data collection and community engagement. The project's success in could serve as a model for similar initiatives across India, addressing the significant challenge of underreported rare disease cases in the country.

- The Indian Rare Disease Nurses Network (IRDNN) established in 2024 as a pioneering initiative to strengthen support systems for people with rare and undiagnosed diseases. It also promotes collaboration and sharing of expertise among healthcare professionals [115].

Figure 4. Shows the timeline of the rare diseases progress in India



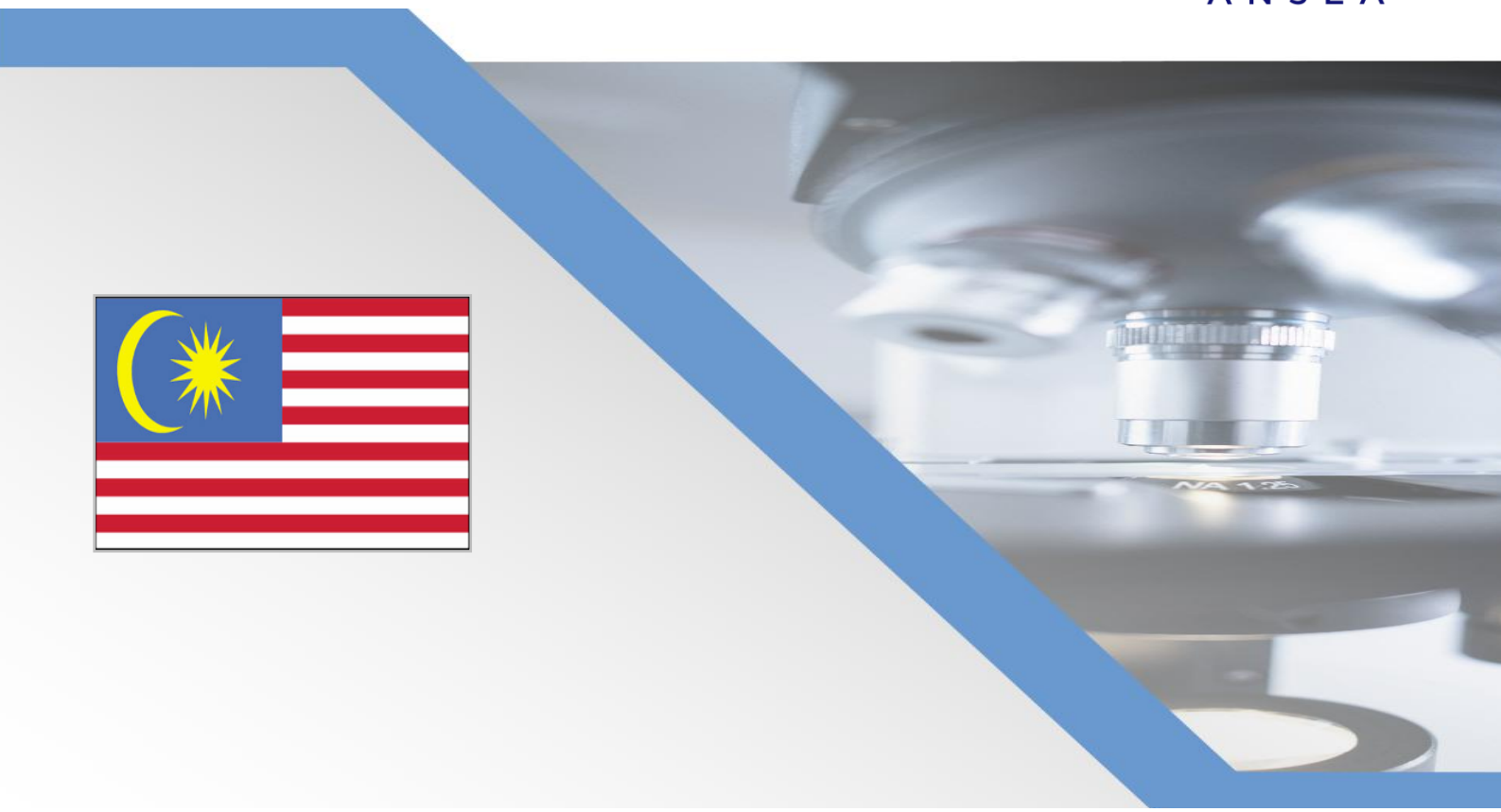
5.2.6 Key Organizations Advancing Rare Disease Initiatives in India

Organization Name	Established Year	Description
Indian Organization for Rare Diseases (I-ORD)	2005	- NGO in India and US - Umbrella organization and represents interests of all RDs, individual patients, patient support groups, health policy advocates and health care provider for RDs
Organization for Rare Diseases India (ORDI)	2013	- National umbrella organization representing the collective voice of all patients with RDs in India
Lysosomal Storage Disorders Support Society (LSDSS)	December 2009	- NGO with aim to raise awareness about various rare genetic life-threatening LSDs - Advocate the needs for early diagnosis, screening and treatment of LSDs with various stakeholders
Ataxia Awareness Society (AAS)	March 2018	- NGO with aim to raise awareness about ataxia among patients as well as medical professionals - Help patients receive financial, medical, educational grants and other benefits from govt. or other sources - Registry of ataxia patients
Seek a Miracle Ataxia Group (SAMAG)	2006	- Non-profit support group working for ataxia and muscular dystrophies
Amrithavarashini (Society for Osteogenesis Imperfecta)	April 2011	- NGO to raise awareness and helps OI suffering patients - Provides support of INR 500 per month to patients
Dystrophy Annihilation Research Trust (DART)	2012	- DART is the first research lab in India focusing on DMD - Supports patients and families, raises awareness and medical advisory and rehabilitation
India Spina Bifda Association (ISBA)	1999	- NGO aims to raise awareness about Spina Bifda

Metabolic Error and Rare Diseases Organization of India (MERD India)	2011	- The mission of MERD India is to promote awareness for Inborn Errors of Metabolism & Rare Genetic Disorders - Provide moral and informative support to the parents of such children and to campaign newborn screening in India
Pompe Foundation	____	- To support parents for treatment and create awareness among medical fraternity - Advocacy with Govt for a proper Health care model for Pompe Disease in India. - To promote early diagnosis and new born screening
Primary Immunodeficiency Patients Welfare Society (PID)	2012	- To raise awareness of the disease in public and medical fraternity - Advocates creating database registry, local manufacturing of "human immunoglobulin", tax exemption of orphan drugs, set up of immunology research department at major hospitals
Hemophilia Federation India (HFI)	1983	- National umbrella organization in India working for the welfare of PWH through a network of 76 chapters spread over 4 regions - To provide quality care, education, making treatment affordable and support economic rehabilitation of patients
Indian Rett Syndrome Foundation (IRSF)	2010	- To raise public and professional awareness - To counsel and educate families and doctors
V Care Foundation (V CARE)	1994	- NGO which works to help cancer patients and their families cope with the crisis in their live
Center of excellence for rare disorders (CERD), Tamil Nadu	2018	- The center will provide the treatment for various RDs, give supportive treatment, monitor the patients, conditions regularly and also provide rehabilitation services
Sjögren's India (SI)	2006	- Informal patient support group for providing education and counselling support to patients suffering from the Sjögren's syndrome
Shire	2017	- Raising awareness on the importance of timely and appropriate diagnosis that can help make difference in the lives of patients suffering from rare diseases
Strand Genomics	2000	- Biotechnology focuses on providing solutions related to genomic data analysis, including services for rare diseases, oncology, and genetic disorders.
Genomics for understanding rare disease India alliance network (GUaRDIAN)	2014	- Research collaboration involving basic scientists and clinicians to explore potential translational applications of genomic technologies
Aten Biotherapeutics	-	- Developing new therapeutics to treat Pompe with gene therapy and nanotechnology
Indo-US Organization for Rare Diseases (IndoUSRare)	2019	- Non-profit organization dedicated to advancing research, advocacy, and collaboration in the field of rare diseases through Indo-US partnerships
Ministry of Health and Family Welfare (MoHFW)	2021	- Facilitate voluntary donations from individuals, corporates, and other donors to support the treatment of patients with rare diseases. - Bridge the gap between the financial assistance required and available government funding.
The Sickle Cell Anemia Welfare Society (SCAWS)	1993	- Focused on sickle cell anemia, a genetic blood disorder, this organization provides advocacy, treatment support, and education to families and individuals affected by the disease.
Rare Diseases India (RDI)/ Foundation for Research on Rare Diseases and Disorders (FRRDD)	2009	- Non-profit brings together various stakeholders, including patients, healthcare professionals, and policymakers, to advocate for rare diseases in India. - Offers information about rare diseases, treatment options, and connects patients to healthcare services and other resources.

Table 5. Key organizations in the area of rare diseases in India

RDs = Rare diseases; DMD = Duchenne muscular dystrophy; PWH = patients with hemophilia



5.3.1 Rare Disease Landscape in Malaysia

Rare diseases are not officially defined in Malaysia. However, upon request, the Ministry of Health provides an internally approved definition, namely “any disease that is prevalent in 0.65% to 1% of the population and for which diagnosis and treatment are complicated” [116]. In 2020, Malaysia recorded 491 rare diseases, but limited epidemiological data makes it difficult to fully understand the extent of their prevalence [1]. These diseases are estimated to affect approximately 0.3 million people out of Malaysia’s total population of 34.31 million by 2023 [13]. Although rare diseases may be less common, they often present significant challenges due to limited awareness, late diagnosis and high cost of treatment. Malaysia's GDP per capita is USD $11,649 in 2023 and however, healthcare expenditure per capita at USD $487 in 2021 is relatively low compared to global averages for similar-income nations, which could constrain resources needed for comprehensive healthcare, including rare disease management[117].

Malaysian Rare Disorders Society (MRDS), defines them as diseases that affect fewer than 1 in 4,000 people

5.3.2 National Strategy Framework and Policy Shaping

Malaysia’s Ministry of Health is actively working to improve the management and treatment of rare diseases in the country. Diagnostic tests, including enzyme assays and genetic screening, are expensive and often inaccessible in rural areas, leading to delays in diagnosis. Treatments such as enzyme replacement

therapy can cost up to RM 1 million (USD $0.22 million) per year per patient, which is far beyond the financial capacity of most families. Government allocations, such as RM 25 million (USD $5.5 million) for rare disease patients in 2024, are insufficient and only benefit a small portion of those in need. On average, a rare disease patient in Langkawi pays RM 333.20 (~USD $70) per hospital admission, which is only 5.2% of the annual cost of disease-related hospitalization per patient supported by the hospital (RM 6,436.81 or ~USD $1,350) [376]. In previous years, Malaysia did not have the capacity to conduct in-house testing. Most lysosomal storage disease testing would be conducted in Australia and Taiwan. However, since 2014, these tests can be performed at the Institute of Medical Research, reducing the cost from AUD 2,5000 (USD $15,938) to just AUD 240–750 (RM 800–2,000 / USD $178.89-$448.83)[13].

National Plan and Legislation

- In 2016, as per a report from University Sains Malaysia, Penang, Malaysian health ministry is working to develop a rare disease policy. A team at this university is formulating an access policy for orphan drugs. According to Assoc. Prof Asrul Akmal Safie, Azuwana Supian and Prof Mohamed Azmi Hassali it is important that different stakeholders such as policymakers, ministries, healthcare providers, families and NGO's need to support the formulation of these policies [118].
- Rare disease management in Malaysia evolved in recent years, with increasing attention given to addressing the unique challenges faced by individuals with rare diseases. Malaysia has streamlined a comprehensive approach to addressing rare diseases through its Rare Disease Strategic Plan in 2022, which features a three-phased implementation strategy designed to systematically enhance the identification, management, and treatment of rare diseases in the country [119].In 2025, the Ministry of Health (MOH) identified 502 rare diseases (of which 88 linked to neurological conditions) requiring prioritization to improve access to diagnosis, treatment, and care [120] [121] additionally, the National Rare Disease Committee actively supports these efforts by providing technical assistance to the MOH, ensuring a coordinated and strategic response to the challenges posed by rare diseases in the country.

Programs and Initiatives

- Since the establishment of diagnostic facilities in 1999, Malaysia has expanded newborn screening to include inborn errors of metabolism. Although it is not mandatory and the expanded tests are only available in four centres, which are the Institute for Medical Research (IMR), Hospital Kuala Lumpur (HKL), UMMC and the Centre for Advanced Analytical Toxicology Services (research and service laboratory in University Sains Malaysia) on request by the public and some private hospitals [13].
- Recent study at the Institute for Medical Research (IMR) published in 2016 showed that the detection rate of inborn errors of metabolism (IEM) was 1 in 2,916 newborns comparable to those in other Asian countries, such as Singapore (1 in 3,165) and South Korea (1 in 2,800) [13].

- However, rare diseases registry is currently lacking to accurately determine the number of patients affected. A national policy on rare diseases would allow clearer designation of duties and responsibilities of various governmental ministries and agencies to coordinate efforts into better care and services for the community [122].

5.3.3 Funding and Financial Support

- Treatment and diagnostics can be selectively covered by private insurance, but very limited in scope. In 2018, Malaysia introduced the Patient Access Scheme (PAS), an alternative market access approach involving managed entry agreements implemented. This scheme allows for provisional or conditional coverage of high-cost and innovative drugs, helping to bridge the gap in accessibility to advanced treatments [123].
- In 2021, RM 10 million (around USD $2.45 million) was allocated by the Malaysian Ministry of Health (MOH) to assist patients requiring orphan drugs at the genetic clinic of Hospital Kuala Lumpur [124]. The budget represented an increase from the prior annual allocation of RM 8.5 million (USD $2.09 million), which had been established since the 2009 budget.
- Malaysia established a Rare Disease Trust Fund in 2022, aimed at supporting individuals affected by rare diseases. This initiative relies on public donations and contributions from corporations[120] .The fund has accumulated RM 105,000 (USD $23,100). However, concerns remain about the sustainability of the fund, given the growing needs and limited financial resources [331]. An additional RM 1 million (USD $0.22 million) was allocated to the Genetics Lab at Tunku Azizah Hospital in Kuala Lumpur to strengthen laboratory testing for patients with rare diseases. Treatment and diagnostics for rare diseases can be selectively covered by private insurance, but the scope of coverage is highly limited. This leaves many patients facing significant financial barriers to accessing necessary care [125].

5.3.4 Regulatory and Market Access

- In 2013, the Malaysian government highlighted its efforts to promote local pharmaceutical companies to venture into orphan drugs. And for this under federal government's Economic Transformation Programme, Early Point Project (EPP) status were awarded to pharmaceutical companies to develop an orphan drug ASEAN manufacturing and an export hub in Malaysia. Within the project margin, the government seeks to address multiple barriers to access quality orphan drugs in the country, such as low sales opportunity, complex regulatory environment and lack of knowledge for effective treatment of rare diseases. This project is spearheaded by a local pharmaceutical, Hovid Berhad in collaboration with AFT pharma (a New Zealand pharmaceutical company)[126].
- The National Pharmaceutical Regulatory Agency (NPRA) in Malaysia is responsible for regulating pharmaceutical products, including orphan drugs. It evaluates the safety, efficacy, and quality of

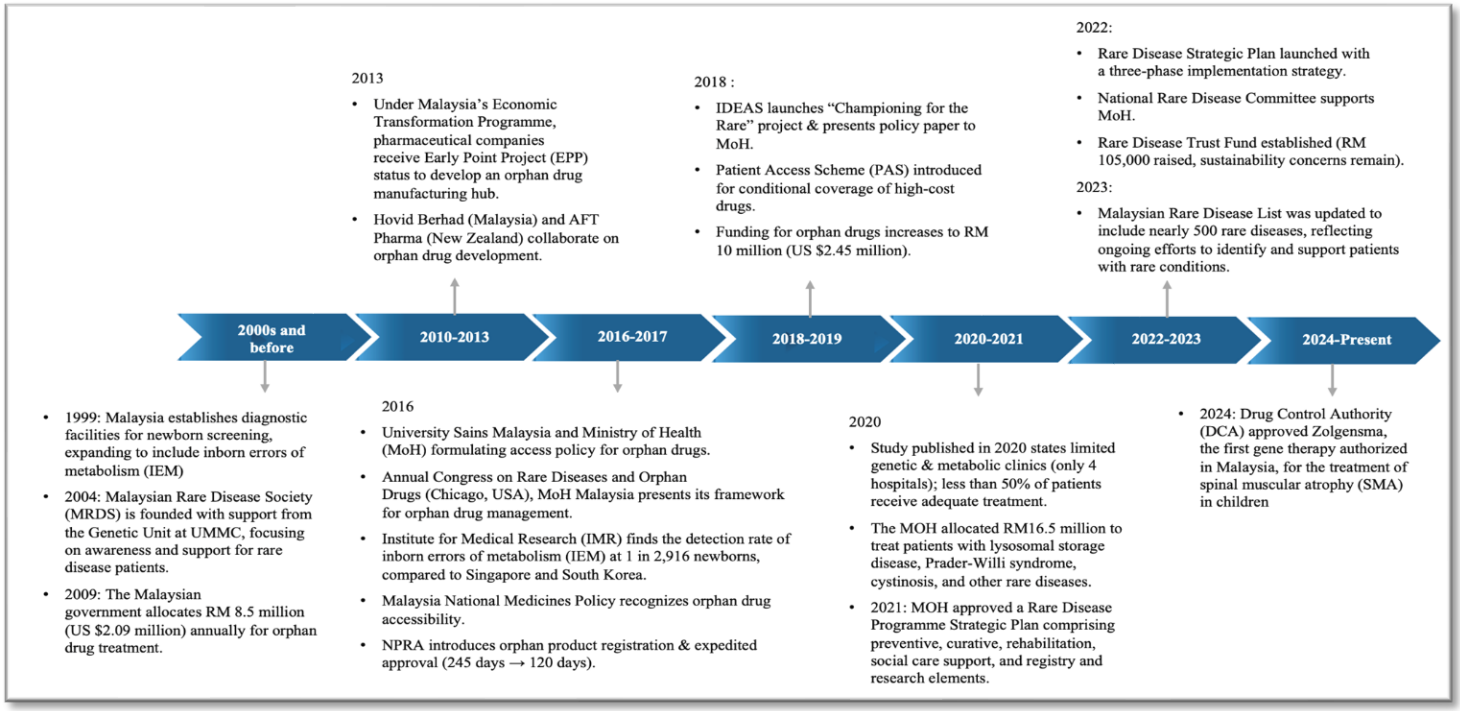
medicines before they can be marketed. The NPRA plays a critical role in ensuring that rare disease treatments meet the necessary standards for patient use while facilitating faster approval for orphan drugs under special regulatory pathways like orphan drug status.

- In September 2016, Malaysia's NPRA updated its Drug Registration Guidance Document (DRGD) to include a section for orphan drugs (ODs), assigning them special registration numbers for monitoring [1]. However, there are no specific economic incentives for developing or supplying ODs. Additionally, ODs are subject to the same processes and considerations for inclusion in the national formulary as other drugs, with no special considerations provided. For more information, you can refer to the official source.
- Additionally, orphan drugs benefit from an expedited approval pathway, reducing the approval time from 245 days to 120 days, accelerating patient access to life-saving treatments. However, while the Malaysian Health Technology Assessment Section (MaHTAS) and the Formulary Management Branch conduct Health Technology Assessments (HTAs), there is no dedicated HTA process for orphan drugs [127].
- In Malaysia, Managed Entry Agreements (MEAs) are being explored to manage the financial and clinical risks of introducing high-cost orphan drugs (ODs). These agreements, which can be financial-based (price-volume) or performance-based (linked to health outcomes), help improve access to medicines that may otherwise be restricted. In 2018, Malaysia introduced the Patient Access Scheme (PASc), which allows for innovative pricing agreements to improve cost-effectiveness, though it requires substantial administrative effort [122].
- In 2024, Malaysia’s Drug Control Authority (DCA) has approved Zolgensma, the country’s first gene therapy since regulations on cell and gene therapy products began in 2021. Zolgensma, developed by Novartis Gene Therapies Inc., is an adeno-associated virus vector-based therapy for treating spinal muscular atrophy (SMA) in children<2years SMA, a rare neuromuscular disease that causes weakness and paralysis, is listed in the Malaysian Rare Disease List. Given Orphan Medicine status, Zolgensma received priority review from the National Pharmaceutical Regulatory Agency (NPRA) to ensure quicker access for patients in need [128].

5.3.5 Care Pathways and Infrastructure

- In 2004, Malaysian Rare Disease Society (MRDS) was established with the support of the Genetic Unit, Department of Pediatrics at University Malaya Medical Centre (UMMC). Its aim is to raise awareness about rare diseases in Malaysia, provide[116].
- In Malaysia, the provision of genetic and metabolic clinic services is limited as per the study in 2020, with only 4 hospitals offering such specialized care. Hospital Kuala Lumpur stands out as the primary center, housing many specialists in this field [14].

Figure 5. Shows the timeline of the rare diseases progress in Malaysia



Abbreviation: MRDS = Malaysian rare disorder society, MoH = Ministry of health, KL = Kuala Lumpur, IDEAS = Institute for democracy and economic affairs

5.3.6 Key Organizations Advancing Rare Disease Initiatives in Malaysia

Organization Name	Established Year	Description
Malaysian Rare Disorders Society (MRDS)	2007	- Voluntary organization which works for the welfare of RD patients and their families.
Malaysia Lysosomal Diseases Association (MLDA)	2011	- Non-profit organization which advocates for RD patient's rights. - Raises awareness about LSD.
Spinal Muscular Atrophy Malaysia (SMAM)	-	- Spinal Muscular Atrophy Malaysia is an organization built to promote awareness and support for children and parents suffering from SMA.
We Care Journey	2015	- The group aims at the treatment of SMA and support the RD patients and their families affected by SMA.
Malaysia Metabolic Society (MMS)	2005	- Non-profit organization established by a group of parents and medical profession to help patients who suffered from rare diseases / disorders, publicly known as inborn error of metabolism.
Hovid Berhad	1980	- Pharmaceutical company that works on orphan drugs. - Part of EPP.
Institute for Democracy & Economic Affairs (IDEAS)	2010	- Non-profit research institute dedicated to promoting solutions to public policy challenges. - Raise awareness about rare diseases and advocates national policy on RDs.
Rare Diseases International (RDI)	2013	- Advocate for rare diseases as an international policy priority - Empowerment of RDI members through knowledge exchange, networking, mutual support and joint actions
Hospital Kuala Lumpur (HKL)	1870	- Healthcare institution collaborates with advocacy groups to provide resources, training and support to affected families. - Provide genetic counseling and diagnosis; research and clinical trial support
University Malaya Medical Center (UMMC)	1962	- Healthcare institution strive to provide the best services and treatment. Efforts that are ongoing are to provide medical services, learning and research with the best efficiency to our customer.

Penang General Hospital (Hospital Pulau Pinang)	1854	- Healthcare institution offering specialized care, research, and education - Raise awareness, improve access to treatment, and advocate for rare disease patients.
Beacon for rare diseases	2012	- Non-profit upskills rare disease patient groups through trainings, guided programmes, community projects and research initiatives
National Rare Disease Committee (NRDC)	2016	- Established to address the needs of individuals living with rare diseases. - To improve the healthcare landscape for rare disease patients, raising awareness, advocating for better policies, and improving access to treatment and support services
Ministry of Health Malaysia	1955	- Government organization focusing on public health, healthcare service delivery, regulation, disease prevention, and health policy. - To improve healthcare access, enhance the quality of care, and address emerging health challenges, including the management of rare diseases.

Table 6. Key organizations in the area of rare diseases in Malaysia

Abbreviation: RD = Rare disease, LSD = Lysosomal storage disorder, SMA = Spinal muscular atrophy, EPP = Early point project

5.4 Singapore

5.4.1 Rare Disease Landscape in Singapore

In Singapore, a rare disease is defined as one affecting fewer than 1 in 2,000 individuals [14]. Around 2000-3000 individuals are estimated to be suffering from rare diseases in 2023 of the total 5.92 million population [129]. A significant number of rare diseases lead to fatal outcomes, and the majority have their roots in genetics, stemming from mutations in genes or chromosomes. Treatments for rare diseases, such as enzyme replacement therapies can be expensive for example, therapies for conditions like Fabry disease or Gaucher disease can exceed SGD 500,000 (USD $370,000) per year. Additionally, conventional health insurance schemes may not fully cover rare disease treatments, leading to out-of-pocket expenses for families. According to estimates Singapore has a GDP per capita of USD $84,734 in 2023, health care expenditure per capita of USD $3,970, and out-of-pocket expenditure accounted for 36.7% of the total health care expenditure in 2021 respectively [130]. The rarity and high cost of these treatments pose unique challenges for healthcare policy and funding. Different

countries have adopted various strategies to manage these challenges. For example, Australia utilizes the Life Saving Drugs Program (LSDP) and risk-sharing agreements, while Singapore relies on a rare disease fund that matches public donations [131].

5.4.2 National Strategy Framework and Policy Shaping

Singapore has implemented various initiatives aimed at addressing the challenges posed by rare diseases, with a focus on raising awareness, enhancing research, improving treatment accessibility, and providing patient support. A significant component of this effort is the establishment of the Rare Disease Fund (RDF), which provides financial support to individuals diagnosed with rare diseases. Additionally, the Singapore Rare Disease Models and Mechanisms (RDMM) Network brings together researchers and clinicians to advance the understanding of the genetic causes of rare conditions. The country has also established the Orphan Drug Act, a legal framework designed to encourage the availability of orphan drugs by providing guidelines for their importation, ensuring access to essential treatments that may not be commercially viable. Furthermore, advocacy efforts by organizations like the Rare Disorders Society (Singapore) push for a National Rare Disease Plan to improve healthcare for individuals affected by rare diseases in Singapore.

National Plan and Legislation

- Singapore currently lacks a national policy regarding rare diseases and does not have an Orphan Drugs Act similar to the United States' "Medicines Orphan Drug Act" of 1991. Nevertheless, there are provisions for rare disease medications established under the Medicines (Orphan Drugs) Exemption Order under Medicines Act (chapter 176, sec 9) (G.N. No. S 470/1991) introduced on November 4, 1991. This framework permits the supply of certain orphan drugs for the treatment of rare conditions, subject to specific exemptions [132] [133] [134].

Programs and Initiatives

- The National expanded newborn screening (NENS) programme launched in October 2006, offers more than 25-30 metabolic screening tests for inborn errors of metabolism (IEM) to all newborns in Singapore [140]. This test is available to all newborns but is not compulsory. The testing cost falls between SGD $35-$45 (USD $26.20-$33.68) for subsidized patients in public hospitals, whereas in private hospitals it is priced at SGD $140 (USD $104.80) [135].
- The Rare Disorders Society (Singapore) (RDSS) is a non-profit entity established in 2011 with the mission of assisting individuals and families impacted by rare diseases. The organization focuses on

increasing awareness, advocating for improved diagnostic and treatment options, and offering a range of support services. Additionally, RDSS hosts events such as the "Carry Hope" Walk & Run to generate funds and enhance awareness. At present, the society supports over 180 beneficiaries, impacting more than 700 lives. Through its initiatives, RDSS strives to empower those with rare diseases and foster inclusivity within the community[136].

- Asia Pacific Alliance for Rare Diseases Organizations (APARDO) meeting took place in 2015 in Singapore. This alliance aims to bring together various rare disease organizations across countries to raise voice for rare diseases and influence national policies for rare diseases and orphan drugs[137].
- The ASEAN+ Rare Disease Network was established by RAB in 2017, with the aim to bring together patient support groups from across Southeast Asia (SEA) (Singapore, Malaysia, Indonesia, Philippines and Vietnam) and Hong Kong. As one of its initial initiatives, the network planned to launch the Rare Disease Impact study across the region to better understand the needs of rare disease patients and their caregivers that will ultimately catalyze strategic solutions for the management and care of rare disease suffering families.
- The Rare Disease Models and Mechanisms (RDMM) Network, launched in 2022, is a collaborative initiative designed to bridge the gap between clinicians and basic researchers in Singapore. Its primary objective is to expedite the molecular understanding of genes responsible for rare diseases by fostering partnerships that facilitate gene discovery and the development of model systems. These efforts aim to elucidate molecular pathways and, ultimately, identify therapeutic interventions beneficial to patients with rare diseases[138]. RDMM Network is part of a broader international consortium, connecting with similar networks in Canada, Australia, Europe, and Japan. This global collaboration enhances data sharing and facilitates clinician-scientist matchmaking across borders, thereby accelerating research and therapeutic development in the field of rare diseases.

5.4.3 Funding and Financial Support

- By the end 2015, MediShield Life (Singapore’s basic health-care insurance) started to cover congenital illness for those diagnosed after March 1, 2013. The insurance premium costs about SGD $100 (USD $74.86) per year which is 30% higher than what it costs to normal population. This insurance gives support to the suffering families when they are turned away by private insurers [139].
- As per Senior Minister of State Chee Hong Tat, the Ministry of Health (MoH) will release a proposal letter towards the end of 2018 with the aim to provide better support for children with rare diseases. In response to an adjournment motion by Junior member of Parliament, Dr Tan Wu Meng, Mr. Chee mentioned that the government is looking into various options which includes insurance, discretionary funds such as Medifund, Medication Assistance Fund (MAF) and a separate fund composed of

contributions from the government, companies, charities, community groups and individual donors to help rare disease patients[140].

- The Ministry of Health (MOH) and the SingHealth Fund have jointly established the Rare Disease Fund (RDF) in 2019, a charity fund that combines community donations and government matching contribution to support Singapore Citizens with specific rare diseases who require treatment with high-cost medicines [130].
- The RDF operates through government matching public donations. For every SGD $1donated by the public, the government contributes SGD $3. In 2022, RDF raised a total of SGD $19.2 million (USD $ 14.36 million) and has supported 9 patients (about 0.4% of the rare disease population) since its inception in 2019 [141].The fund is used to cover treatments that are otherwise financially burdensome for patients. Although useful, the fund supports only a small percentage of patients with rare diseases, and many patients still face financial difficulties in managing expensive long-term treatments. Other schemes Medisave, MediShield Life, and MediFund provide limited coverage for treatment and medical bills [130].
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5.4.4 Regulatory and Market Access

- Medicines Act (Chapter 176, Section 9) (1991): Focuses on managing and encouraging the use of orphan drugs for rare disease patients[14][142].
- A drug can be designated as orphan drug in Singapore, are primarily regulated by the Health Sciences Authority (HSA). The HSA evaluates these drugs based on their safety, efficacy, and quality, similar to other pharmaceuticals. While Singapore does not have a specific legislative framework for orphan drugs, the Medicines Order ('Orphan Drugs Exemption') enacted in 1991 provides certain exemptions for these medications [143].
- Regulation No. 15 of 2019: Requires justification and supporting documents for drugs intended for serious and rare diseases, life-threatening conditions, or with limited treatment options [339]. Frequently used for rare and life-saving conditions, but pharmaceutical companies often lack economic incentives to register these drugs due to small patient numbers [144].

- Regarding pricing and reimbursement, Singapore's approach is influenced by the RDF, which offers subsidies for high-cost medications used to treat rare diseases that are chronically debilitating or life-threatening. However, the scope of the RDF is limited, and not all orphan drugs may be covered. The decision to include a drug in the RDF depends on factors such as the severity of the disease, the availability of alternative treatments, and the cost-effectiveness of the medication. This selective coverage can result in high out-of-pocket expenses for patients requiring treatments not subsidized by the RDF [138]. For instance, the average annual cost of Risdiplam in public healthcare institutions is approximately SGD $375,000 (USD $280,725). There are no further subsidies by the Singaporean government and SMA treatment is not currently covered by RDF.
- Since April 2023, Zolgensma® has been approved by local Health Sciences Authority (HSA) under the Register of Class 2 Cell, Tissue or Gene Therapy Products for use in Singapore. Zolgensma®, however, costs around USD $2.1 million per dose, and the staggering cost poses an immense financial barrier for the vast majority of patients and their families [131].

5.4.5 Care Pathways and Infrastructure

- The BRIDGES (Bringing Research Innovations to Genetic Disease Diagnosis in Singapore) program, launched in 2014, aims to shorten the diagnostic journey for patients using genomic sequencing technology[145]. Over 380 families with undiagnosed rare genetic diseases have been recruited for BRIDGES [146].
- In 2017, The National Precision Medicine (NPM) programme in Singapore established the SG10K_Health Portal, a comprehensive genomic database containing data over 10,000 including participants from three main ethnic groups—Chinese, Indians, and Malays. Enabling research in precision medicine and improving healthcare outcomes tailored to Singapore's multi-ethnic society [146].
- The Singapore Undiagnosed Diseases Research Endeavour for Kids (SUREKids) program, conducted between 2014-2019, enrolled 196 children and achieved a diagnosis rate of 37.8% [144]. This initiative utilized next-generation sequencing technologies, such as whole exome sequencing (WES) and whole genome sequencing (WGS) to diagnose rare genetic disorders in pediatric patients. The findings were published in the Archives of Disease in Childhood in January 2021.

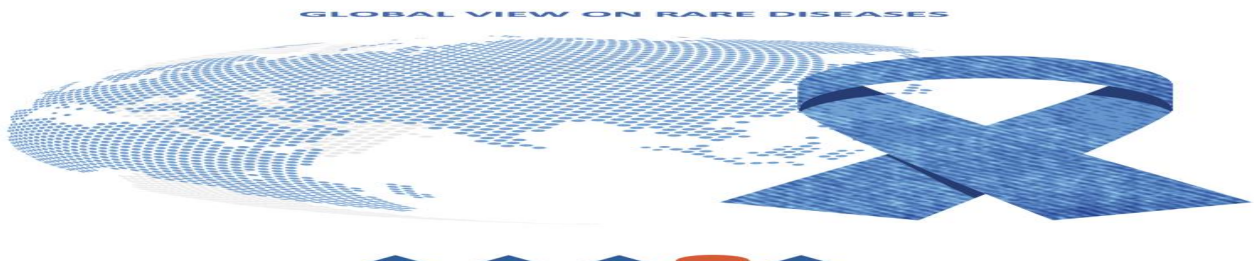
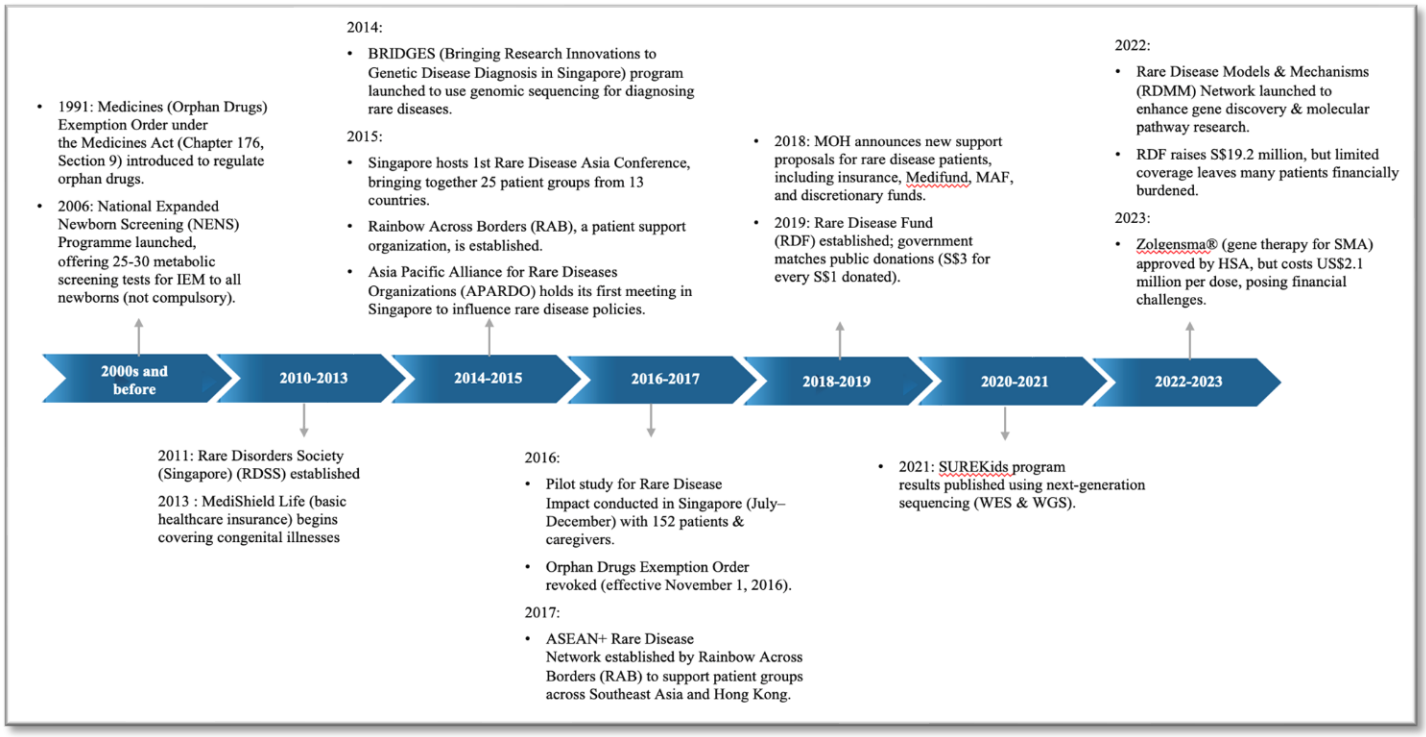


Figure 6. Shows the timeline of the rare diseases progress in Singapore



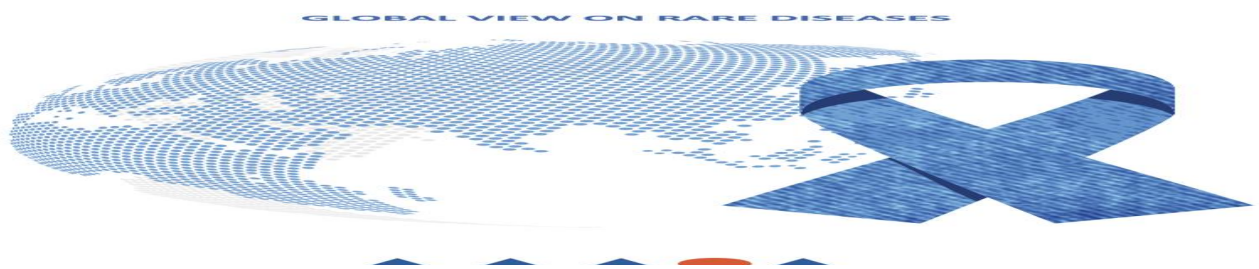
Abbreviation: NENS = National expanded newborn screening, RDSS = Rare disease society Singapore; APARDO = Asia-Pacific alliance rare disease organization; HWG = Hemophila working group; MoH = Ministry of health; RAB = Rainbow across borders

5.4.6 Key Organizations Advancing Rare Disease Initiatives in Singapore

Organization Name	Established Year	Description
Rare Disorders Society Singapore (RDSS)	2011	- It aims to create awareness on various life threatening RDs. - Offers emotional, counselling and financial support to children, family or friends with RDs. - Directs patients to medical resources and raise funds.
Rainbows Across Borders (RAB)	2015	- Promotes regional collaboration and networking among patient support organizations within Asia-Pacific region.
ASEAN+ Rare Disease Network	2017	- The network aims to better understand the needs and pain points of the RD patients and caregivers to help manage and utilize the resources better.
Carcinoid-Neuroendocrine Tumor Society (Singapore) (CNETS)	2009	- The CNETS is a support group for carcinoid and neuroendocrine tumor patients, family caregivers, researchers and physicians
Asia-Pacific Alliance of Rare Disease Organizations (APARDO)	2015	- Regional organization established to amplify the voices of rare disease advocacy groups across the Asia-Pacific region. - Aims to improve the lives of individuals and families affected by rare diseases by fostering collaboration, increasing awareness, and advocating for better healthcare policies and access to treatments.
Ministry of Health	1955	- Government agency for managing the public healthcare system, formulating health policies, and ensuring access to quality and affordable healthcare - Subsidizing treatments, including those for rare diseases, through programs like the Rare Disease Fund (RDF) and other medical financial assistance schemes.
National University Hospital	1972	- Heads the pediatric genetics and metabolism division
KK Women's and Children's Hospital	1858	- Senior consultant with the genetic service
National Cancer Centre Singapore, Agency for Care Effectiveness	2015	- National organization under the Ministry of Health (MOH), established to drive the adoption of evidence-based healthcare practices in Singapore. Focuses on improving healthcare value by promoting the appropriate use of medical interventions based on cost-effectiveness and clinical effectiveness.

Rare Disease Fund Committee	2019	- Government-supported initiative by the Ministry of Health (MOH) and SingHealth to provide financial assistance for rare disease treatments. Promote access to high-cost therapies
Singapore General Hospital (SGH) Rare Disease Clinic / SingHealth	1821	- Operates specialized clinics for rare diseases, offering multidisciplinary care and genetic testing for accurate diagnoses. Leads several initiatives including the Rare Disease Fund (RDF) and research collaborations
Society for the Physically Disabled (SPD)	1964	- Supports individuals with physical disabilities, including those arising from rare diseases, by providing therapy, financial assistance, and vocational training.
Children's Cancer Foundation (CCF)		- Supports children with rare cancers and provide assistance to the families.
Muscular Dystrophy Association Singapore (MDAS)	2000	- Focuses on improving the quality of life for individuals with muscular dystrophy, a rare genetic condition that causes progressive muscle weakness.
Rainbow Across Borders (RAB)	2011	- Regional patient advocacy group headquartered in Singapore that works with rare disease patients across Asia. - Aims to support patients, advocate for better healthcare policies, and foster collaboration among rare disease stakeholders.

Table 7. Key stakeholders in the area of rare diseases in Singapore



5.5 Philippines

5.5.1 Rare Disease Landscape in Philippines

Affects less than 1 in 20,000 individuals

Rare disease is defined as a genetic disorder which affects less than 1in 20,000 individuals and there are 156 conditions that are considered rare in Philippines affecting 6500 people in 2023 [8] [9]. In 2021, GDP per capita of Philippines was USD $3,548.8, healthcare expenditure per capita reported approximately USD $159 and the out-of-pocket expenditure was around 55.5% of total health expenditure [147]. Currently, rare disease affected Filipinos receive limited support in terms of finance and medical expertise. There is a lack of information and experienced doctors to provide accurate diagnosis and treatment for the patients. As rare disease is known to affect a small population within the country, there is a little interest among research institutions in the country to study these disorders in detail.

However, to address these challenges, the Philippines introduced the Rare Disease Act in 2016, with the goal of enhancing the diagnosis, treatment, and care for individuals with rare diseases. The law highlights the importance of incorporating genetic services into the public health system, utilizing established networks like the national newborn screening (NBS) program to improve access to genetic counseling and

testing. The NBS program now extends to over 7,100 hospitals and birthing centers across the country. Thanks to national and local policies, the program has successfully reached 94.6% of the 1.2 million annual births in the Philippines. Additionally, the Act mandated the creation of the Rare Disease Registry, which is being utilized to formulate policies, identify program interventions, and design research to address the needs of patients with rare diseases. In line with the law, the Department of Health (DoH) Philippines has integrated public information and screening campaigns in its programs to identify persons afflicted with rare diseases and help the public understand the special needs of such persons.

5.5.2 National Strategy Framework and Policy Shaping

Philippine government has developed the Health Care Financing Strategy for 2023-2028. This strategy aims to enhance the sustainability and efficiency of healthcare financing, ensuring that resources are effectively allocated to meet the population's health needs. Despite government efforts, public health expenditure remains limited, which impacts the ability to provide comprehensive healthcare services to the entire population. This results in reliance on out-of-pocket spending, making healthcare less accessible, especially for low-income groups.

National Plan and Legislation

- The Rare Diseases Act of the Philippines (Republic Act 10747), which was enacted on March 3, 2016, seeks to enhance healthcare accessibility for individuals suffering from rare diseases by focusing on diagnosis, clinical management, and genetic counseling. It mandates PhilHealth to include benefit packages for rare disease patients and provides medical assistance under the Sin Tax Reform of 2012. The DoH was tasked with establishing a Rare Disease Registry to track affected patients. Additionally, individuals with rare diseases are classified as Persons with Disabilities (PWDs), granting them access to priority programs and discounts on healthcare services and medicines, as outlined in Republic Acts 9442 and 7277. The legislation also promotes research and development by offering regulatory and fiscal incentives while facilitating the manufacture and importation of affordable orphan drugs and products [160].
- The Integrated Rare Diseases Management Program Strategic Plan 2022–2026 is the first nationally coordinated effort in the Philippines to address the needs of individuals with rare diseases. Developed through consultations with national government agencies, non-government organizations, medical societies, and patient support groups, the plan aims to provide comprehensive care and support for persons living with rare diseases (PLWRDs) [148].

Programs and Initiatives

- Newborn Screening (NBS) is a method for early detection of genetic and metabolic disorders in infants and is active since 1996. NBS was integrated into the public health delivery system with the passing of the Newborn Screening Act of 2004 or RA 9288[149]. In the initial act newborns were screened only for 6 conditions (NBS 6-test). The facility for NBS is available at > 7000 islands in the country. However, there are only 10 geneticists in the entire Philippines [3] [150].
- In 2017, the DoH collaborated with the University of the Philippines National Institute of Health (UP NIH) to establish a rare disease registry and an effective referral system. This initiative aimed to improve support, treatment, and access to information for rare disease patients. Additionally, a technical group was formed to identify necessary treatments and services, which later integrated into the medical assistance program and the PhilHealth benefits package, ensuring better healthcare access for individuals with rare diseases [151].
- Newborn screening for rare diseases in the Philippines has significantly expanded since its inception in 1996. Initially covering five conditions, the program grew in 2014 to include 21 additional disorders, thanks to advances in mass spectrometry. By 2018, it added even more conditions, including argininosuccinic aciduria, and was fully covered by the Philippine Health Insurance Corporation (PHIC), making it free for parents. As of December 2023, the program screens over 94% of the 1.2 million annual births across more than 7,000 screening centers nationwide. This expansion has led to earlier detection and better management of rare diseases, improving health outcomes for affected infants [152].

5.5.3 Funding and Financial Support

- Since 2007, Philippine Society for Orphan Disorder (PSOD) provide financial assistance through donations for rare disease research, maintaining the Rare Disease Registry, and purchasing orphan drugs or products. Ultimately, this advocacy seeks to enhance healthcare and resources for individuals affected by these conditions. Through its various initiatives, the PSOD plays a vital role in addressing the needs of the rare disease community in the country[153].
- Despite the law's progressive framework, its implementation has faced challenges, particularly concerning funding. It wasn't until 2022 that the law received an initial allocation of PHP104.9 million (USD $1.81 million) in funding to support the implementation of the Rare Diseases Act, aimed at providing services such as diagnosis, treatment, genetic counseling, and access to medications for individuals with rare diseases [154]. However, the budget for the Rare Diseases Law faced a significant reduction in the subsequent year, with funding slashed to PHP28.809 million (USD $0.50 million) in 2023.

- In response to these challenges, the Philippine Health Insurance Corporation (PhilHealth) expanded its coverage in December 2024 to include 10 rare genetic diseases under the "Z-Benefits Package for Rare Diseases." This initiative aims to alleviate the financial burden on families by providing case rates ranging from PHP99,000 to PHP739,000 (USD $1,710.49- $12,754.79) for conditions such as Maple Syrup Urine Disease, Phenylketonuria, and Gaucher Disease [155].

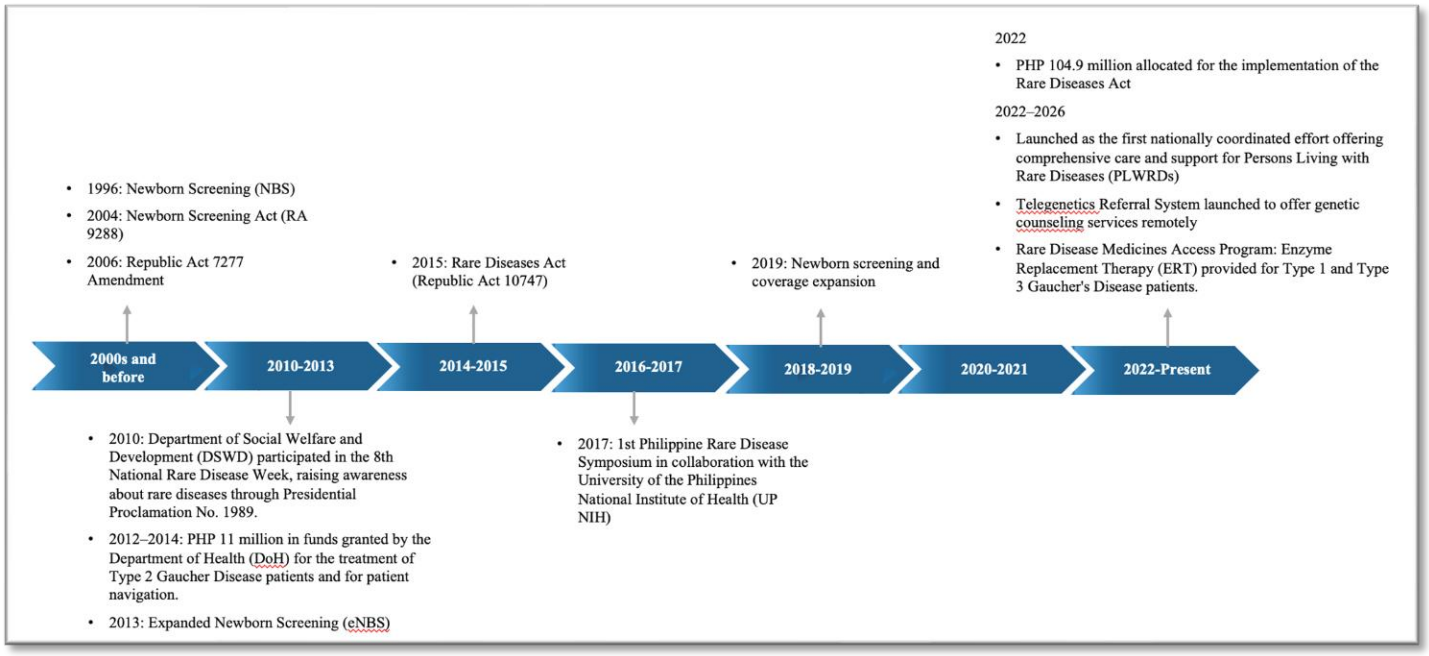
5.5.4 Regulatory and Market Access

- In the Philippines, the Department of Health (DOH), Food and Drug Administration (FDA), and National Institutes of Health (NIH) lead key regulatory and market access initiatives for rare diseases. In 2017, the DOH established the Rare Disease Technical Working Group (RD-TWG), which supports continuity clinics, develops policies for orphan drugs, and updates the list of recognized rare diseases [148]. The FDA works to ensure the availability of orphan drugs and essential medical devices for rare conditions. The NIH offers technical assistance, conducts research, and oversees the Rare Disease Registry, helping monitor and improve care for rare disease patients. These combined efforts aim to streamline access to treatments and strengthen the overall support system.
- Rare Disease Medicines Access Programs (RDMAP) 2018 – DoH aims to provide health care access to patients with rare diseases. The current beneficiaries of this programme are Type 1 and 3 Gaucher’s disease with ERT infusion[156].

5.5.5 Care Pathways and Infrastructure

- In 2015, Philippine Performance Evaluation and Assessment Scheme (PPEAS) significantly enhances both the quality and efficiency of the Philippine Newborn Screening System [157]. This program aims to improve the early detection of rare genetic and metabolic disorders in newborns for early intervention and better health outcomes.
- In 2018, Telegenetics Referral System is designed to provide genetic counseling services in regions of the Philippines where there is a shortage of subspecialists, including geneticists [158]. This program leverages telemedicine to connect patients with genetic counseling services remotely, enabling individuals in rural and underserved areas to access critical genetic consultations. It enhances the diagnosis and management of rare genetic conditions, ensuring that patients across the country can benefit from expert advice even if they are far from specialized centers.
- Strategic plan 2022-2026 has implemented several key initiatives to improve access to treatments and enhance care pathways for rare disease patients. Initiated by the Department of Health (DOH), the Rare Disease Medicines Access Program aims to provide free Enzyme Replacement Therapy (ERT) for patients with Type 1 and Type 3 Gaucher's Disease, a rare genetic disorder [155].

Figure 7. Shows the timeline of the rare diseases progress in Philippines



Abbreviation: NBS = Newborn Screening, RA = Republic act, RDMAP = Rare disease medicine access program, DoH = Department of health, UP NIH = University of the Philippines national institute of health.

5.5.6 Key Organizations Advancing Rare Disease Initiatives in Philippines

Organization Name	Established Year	Description
Department of Health (DoH)	-	- Government body responsible for legislations to support RD patients.
Philippines Society for Orphan Disorders Inc. (PSOD)	2006	- NGO which works for the welfare of rare disease patients in Philippines.
Pharmaceutical & Healthcare Association of the Philippines (PHAP)	1946	- PHAP and its member companies represent the research-based pharmaceutical and health care industry.
National Institutes of Health-University of the Philippines Manila (NIH-UP)	1990	- Dedicated to advancing the understanding and management of genetic disorders in the Philippines. - Aims to increase awareness among the public and decision-makers about rare diseases and their impact on the lives of affected families.
Care-for-Rare Foundation	2009	- Non-profit dedicated to supporting children with rare diseases by providing access to modern genetic diagnostics and innovative therapies.
Philippine Alliance of Patient Organizations, Inc. (PAPO)	2002 - 2007	- Aims to empower Filipino patients through education, networking, policy advocacy and capacity building.
Asia-Pacific Alliance of Rare Disease Organizations (APARDO)	2015	- Regional organization established to amplify the voices of rare disease advocacy groups across the Asia-Pacific region. - Aims to improve the lives of individuals and families affected by rare diseases by fostering collaboration, increasing awareness, and advocating for better healthcare policies and access to treatments.
Rare Diseases International (RDI)	2013	- Advocate for rare diseases as an international policy priority - Empowerment of RDI members through knowledge exchange, networking, mutual support and joint actions
Tzu Chi Foundation	1966	- International humanitarian organization support individuals suffering from rare diseases through its funding assistance and better quality of life

Table 8. Key organizations in the area of rare diseases in Philippines

Abbreviation: RD = Rare disease, NGO = Non-governmental organization

5.6 Thailand

5.6.1 Rare Disease Landscape in Thailand

In Thailand, rare disease is defined as fewer than 10,000 cases per year. According to report published in 2021 indicates that approximately 5% of the Thai population is affected by one of the rare diseases, which translates to about 3 million individuals out of a total population exceeding 65 million. However, only around 20,000 of these individuals are receiving treatment [159]. The true burden of rare diseases in Thailand is likely higher than reported, as many conditions remain underdiagnosed or misdiagnosed due to limited awareness and diagnostic capabilities.

Approximately, **6% (3.5 million)** of the entire Thailand population is affected with rare disease and only 20,000 receiving treatments out of **more than 65 million Thai population** [352]

The financial strain on patients and their families is significant, particularly due to the exorbitant costs associated with treatments for rare diseases. These treatments tend to be costly because of the small patient populations and the extensive expenses linked to research and development. In 2021, Thailand's GDP per capita was USD $7,070.5, with health expenditures constituting

approximately 5.4% of the total GDP, while out-of-pocket expenses accounted for about 9% of total health expenditures. [160]. Although the Thai government implemented a Rare Disease Policy in 2020 to address this issue, challenges persist in providing comprehensive coverage and reducing financial strain. The National Health Security Office (NHSO) has allocated funding for around 24 rare diseases under the Universal Coverage Scheme (UCS). However, only a limited segment of the population benefits from this, as the funding for rare conditions is inadequate, leading many patients to incur high out-of-pocket costs for specialized treatments that may not be covered by the Universal Coverage Scheme (UCS).

Additionally, the country has a National Newborn Screening (NBS) Program operating since 1996, initially covering congenital hypothyroidism (CH) and phenylketonuria (PKU). It is a mandatory program included in the country's universal health coverage, ensuring that all Thai newborns have access to screening. Since 2002, the NBS coverage rate for HC and PKU has been consistently high, exceeding 85% and reaching over 95% in the last decade. In October 2022, the Thai NBS program was expanded to include screening for inborn errors of metabolism using mass spectrometry (MSMS), making it a mandatory part of the NBS as part of universal health coverage [161].

5.6.2 National Strategy Framework and Policy Shaping

Thailand has developed a strong domestic framework to address rare diseases, despite the lack of a formal national action plan. Key initiatives include the Universal Coverage Scheme (UCS), which has covered 24 rare diseases by 2020, including treatments and diagnostics. The Thai government has also implemented frameworks to expedite the registration and approval of orphan drugs, aiming to enhance access to treatments for rare diseases. Moreover, the government has also added 10 orphan drugs to the National List of Essential Medicines in 2022, ensuring free access for patients. A budget of Baht2.85 million (USD $0.37 million) was allocated in 2019 for the treatment of these diseases. The Rare Diseases Committee, established in 2019, advises the government on policy and includes members from various sectors. Additionally, the Genomics Thailand program, launched in 2019, aims to create a database of Thai genetic variations, targeting 100,000 samples to support research and health advances.

National Plan and Legislation

- Even without a legislative framework for rare diseases or orphan drugs, the recognized definition of the disease has led to the inclusion of the Orphan Drug List into Thailand's National Drug List in 2012 [162]. National Drug List consists of 50 orphan drugs. Procurement process of medicines in the country is decentralized and is undertaken by individual health facility or hospital. Only few high-cost and

orphan medicines are centrally supplied and funded by the Government Pharmaceutical Organization (GPO) on behalf of National Health Security Office (NHSO)[163].

- While Thailand may not have a National Action Plan, they have a robust internal framework to set rare disease priorities and agenda. The rare disease committee, active since 2019, advises the government on rare disease policies and comprises 30 members from ministries, clinicians, and genetics patient organizations[164].

Programs and Initiatives

- The country has been an early adopter of sequencing technology for rare diseases. Thailand started sequencing patients' genomes in 2012, and since then Chulalongkorn University has been leading efforts to build knowledge and human resources to accelerate diagnosis of rare diseases[165].
- The Care-for-Rare Foundation, along with the Chulalongkorn University of Bangkok, has initiated a "German-Thai alliance for better care of children with rare diseases" in order to raise more awareness for rare diseases in South East Asia. The foundation hosted its first international "European-South-East-Asian (PID) Meeting: From Bench to Bedside" in January 2015 in the Thai capital[166].
- Thailand Rare Disease Network (ThaiRDN) established as a pilot project in 2016 with aim to develop service platform and share resources to assist the rare disease community.
- Genomics Thailand program initiated in 2019 through a collaborative effort of the Health Systems Research Institute (HSRI), Ministry of Higher Education, Science, Research, and Innovation (MHESI), Ministry of Public Health (MOPH), and Thailand Center for Excellence for Life Science (TCELS) Aims to build a database to capture Thai genetic variations with a target of 100,000 samples[164].

5.6.3 Funding and Financial Support

- Sanofi Genzyme (PAL fund) granted a fund of USD $10,000 to the Genetic LSD Foundation of Thailand to support LSD community especially in the underserved areas of the country. The grant was used to facilitate communication amongst patients, physicians and the advocacy group. Further, these funds allowed LSD foundation to create a database for continuous dissemination of vital information to LSD patients for optimal care [167].
- The Newton Fund by UK, a research fund of £1 million (USD $1.3 million) was awarded for the best research and innovation to promote economic development and social welfare in developing countries. Four countries are eligible for the funds which includes – India, Thailand, Malaysia and Vietnam, respectively. Individual project may receive funds up to £200,000 (USD $261,400) to advance their research.

- The UK-Thailand Research and Innovation Partnership Fund, established in 2017, was the first official research and innovation partnership programme between the UK and Thai government. One of the awarded projects has successfully identified around 100 undiagnosed cases of rare genetic diseases in children. The collaboration aims to speed up the diagnosis of the rare genetic diseases from an average of 7 years to only 2 weeks. Under this partnership both the countries agreed upon five priority area of mutual interest including– health and life sciences, agrotechnology, future cities, environment and energy and digital innovation and creativity. Both countries agreed to invest at least Baht 1,200 million (USD $37 million) from 2014 to 2021[168].
- In 2019, the National Health Security Office (NHSO) initiatives expanded the Universal Health Coverage (UHC) scheme to include 24 rare but severe diseases, allocating an additional budget of Baht 12.85 million (USD $0.37 million) for the treatment [159].
- Universal Coverage Scheme (UCS) in Thailand has made significant strides in providing comprehensive coverage for rare diseases. Since 2020, the UCS has included 24 rare diseases under its coverage, ensuring that patients have access to critical healthcare services [347]. This expanded coverage aims to reduce the financial burden on families affected by rare diseases, improve access to necessary healthcare, and enhance the overall quality of life for these patients.
- In 2022, the government added 10 orphan drugs to the National List of Essential Medicines, ensuring free access for patients with rare diseases [169].

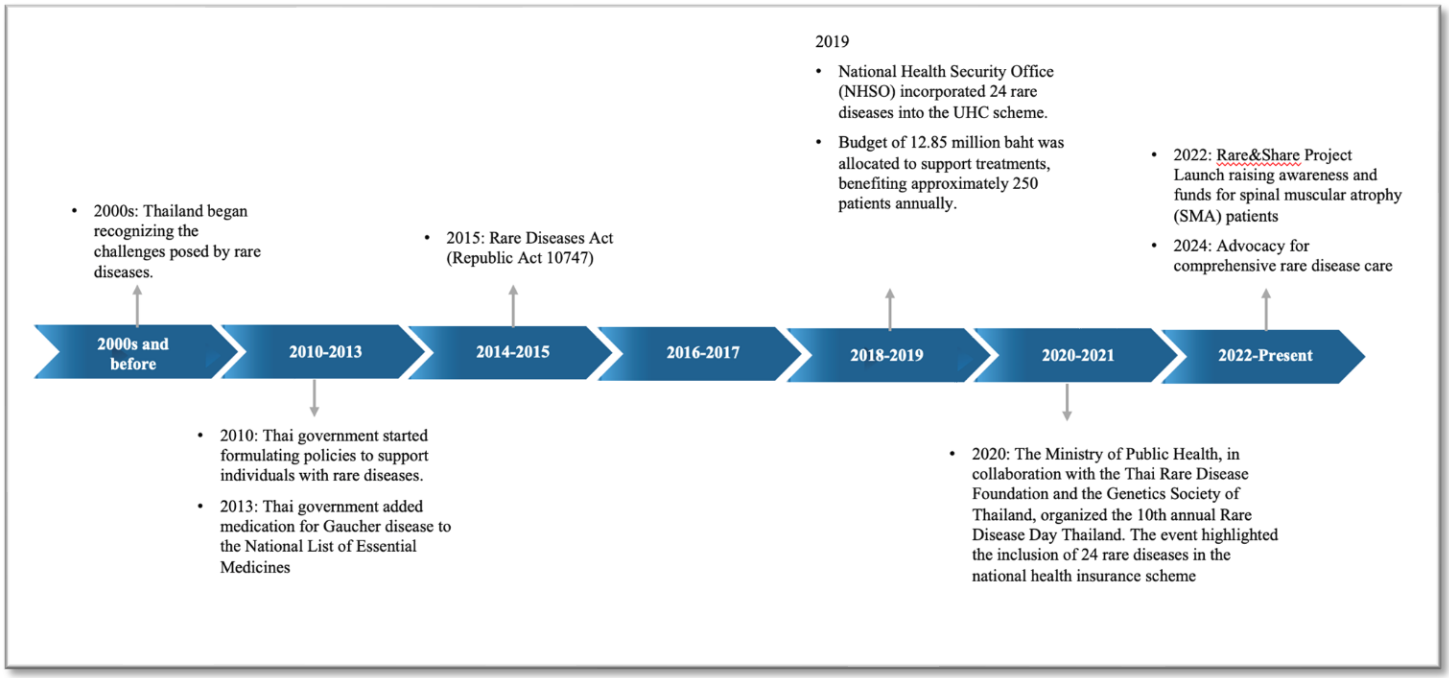
5.6.4 Regulatory and Market Access

- The Thai FDA has made significant changes to clinical requirements concerning orphan drugs (particularly those already sanctioned in benchmark nations like Australia, Canada, the EU, Japan and the U.S.) [170]. This streamlined approach facilitates a quicker marketing authorization process in Thailand; the FDA considers approval from these countries as adequate proof of safety and efficacy. Consequently, the necessity for comprehensive local clinical trials is diminished. The relaxed standards are part of Thailand's initiative to enhance access to life-saving treatments for rare diseases, thus accelerating the availability of crucial therapies. Moreover, orphan drug manufacturers can benefit from incentives such as expedited review and reduced application fees, further encouraging the development of treatments for rare conditions.
- The National Drug Development System Committee (NDDSC) committee establishes median drug prices as the maximum allowable purchase price for hospitals [170]. Although these prices are determined and listed in a notification by the committee, their primary purpose is to ensure that the cost of medications remains affordable for both healthcare providers and patients.

5.6.5 Care Pathways and Infrastructure

- Thailand's healthcare system for rare diseases is supported by a strong referral network, with 7 tertiary hospitals equipped with clinical genetics experts and advanced healthcare technologies. These hospitals, primarily based in Bangkok, serve as key centers for diagnosing and treating rare conditions. Notable hospitals include Chulalongkorn Hospital, Thammasat Hospital, and Siriraj Hospital, all of which offer specialized care for rare diseases [170].
- However, there are significant challenges regarding the availability of specialized personnel. Thailand currently has only 22 geneticists serving a population of 67 million people, creating a disparity in access to genetic counseling and diagnosis for rare diseases [171]. This shortage places considerable strain on the healthcare system, limiting the capacity to deliver timely and accurate genetic testing and diagnosis for patients, especially in rural areas.

Figure 8. Shows the timeline of the rare diseases progress in Thailand



Abbreviation: ThaiRDN = Thailand rare disease network.

5.6.6 Key Organizations Advancing Rare Disease Initiatives in Thailand

Organization Name	Established Year	Description
Thalassemia Foundation of Thailand	1989	- Foundation to support thalassemia patients and support funding for research.
Thai Rare Disease Foundation (Thai RDF)	2016	- An umbrella organization to help and support patients with different rare diseases.
Genetic LSD Foundation	2009	- Advocacy and support group for LSD patients and their families
Thailand Center of Excellence for Life Sciences (TCELS)	2004	- To support and promote life sciences, research and innovation etc.
Care-for-Rare Foundation	2009	- Non-profit dedicated to supporting children with rare diseases by providing access to modern genetic diagnostics and innovative therapies.
Rare Diseases International (RDI)	2013	- Advocate for rare diseases as an international policy priority

		- Empowerment of RDI members through knowledge exchange, networking, mutual support and joint actions
Foundation to Eradicate Neuromuscular Diseases of Thailand (FEND)	2015	- Non-profit help children suffering from the effects of neuromuscular disease. - Aim to raise awareness and aid affected individuals.
Asia-Pacific Alliance of Rare Disease Organizations (APARDO)	2015	- Regional organization established to amplify the voices of rare disease advocacy groups across the Asia-Pacific region. - Aims to improve the lives of individuals and families affected by rare diseases by fostering collaboration, increasing awareness, and advocating for better healthcare policies and access to treatments.
National Health Security Office (NHSO)	2002	- Government agency responsible for managing the country's Universal Health Coverage (UHC) system - Raise public awareness, build networks among patient groups, and engage directly with government agencies to monitor policy progress in rare disease care systems.

Table 9. Key organizations in the area of rare diseases in Thailand

Abbreviation: LSD = Lysosomal storage disorder.

5.7 Vietnam

5.7.1 Rare Disease Landscape in Vietnam

6 million people in Vietnam are affected by around 100 rare diseases

In Vietnam, currently there is no official definition of rare disease. However, it is estimated that approximately 6 million people in Vietnam are affected by around 100 rare diseases, with 58% of these patients being children [9]. Many of these conditions are genetic, and early diagnosis is crucial for effective management. However, limited awareness and access to specialized care remain significant challenges. Vietnam is one of the Southeast Asian regions with low GDP per capita of USD $4,086 as of 2022 and low health expenditure per capita of USD $172.55 (2021) [172]. The treatment costs for the rare diseases remain high and unaffordable to most of the patients, has very limited healthcare benefits for the population with no rare disease and orphan drug policy, especially for prolonged treatment.

Moreover, newborn screening for rare diseases is currently focused on a limited set of conditions, primarily including Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, congenital hypothyroidism, and congenital adrenal hyperplasia, with the government aiming to screen 90% of newborns for at least five common congenital diseases by 2030 [173], however, the program is still developing and faces challenges in expanding to include a wider range of rare disorders due to resource constraints typical of low and middle-income countries like Vietnam.

5.7.2 National Strategy Framework and Policy Shaping

Vietnam's approach to rare disease management is evolving, despite the lack of comprehensive legislation and a formal national plan. The Ministry of Health (MoH) is improving access to treatments by regularly updating a list of 214 rare disease drugs and recently, in January 2025, introduced a new list of 62 rare and severe diseases eligible for full insurance coverage, without the need for referral documentation. This initiative aims to prioritize critical medications and enhance treatment access at specialized medical facilities. These efforts are part of a broader strategy to address challenges in diagnosis, treatment, and awareness of rare diseases in Vietnam.

National Plan and Legislation

- In 2000, Vietnam joined the World Federation of Hemophilia (WFH) as a national member organization (NMO) and in 2001, the bilateral cooperation began to expand the limited bleeding conditions treatment and care services in the country.
- To further improve rare disease management, the Advisory Council on Rare Disease Management was established in 2018. Composed of 20 members, including representatives from the Ministry of Health (MoH) and hospital directors, the council focuses on improving healthcare practices and expanding access to treatment for rare diseases. [9].
- Although Vietnam lacks a comprehensive legislation and formal national plan for rare diseases, they issued a list of Rare Drugs in 2019 to ensure access to essential medications for patients with rare conditions [174].

Programs and Initiatives

- Deputy Minister of Health Tran Van Thuan said the Ministry of Health has put in place several policies and solutions to better manage the rare diseases. These include forming a task force in 2014, establishing an advisory council on rare disease management, and participating relevant forums within the Asia-Pacific Economic Cooperation (APEC) forum and the World Health Organization (WHO)[175].

Additionally, efforts are being made to establish a national registry for rare diseases, which can aid in better understanding the prevalence and patterns of rare diseases in Vietnam.

5.7.3 Funding and Financial Support

- In Vietnam, funding for rare diseases is primarily supported through out-of-pocket payments, private insurance, and pharmaceutical assistance. The reimbursement system is decentralized, with hospitals managing their own lists of reimbursable rare disease treatments, leading to inconsistent access across the country[176] [174].
- Since January 2025, Vietnam's health insurance has covered 100% of treatment costs at any hospital for patients with rare or severe diseases, complex surgeries, or advanced procedures, without requiring referral documents [177]. This is a key provision of the amended Health Insurance Law recently passed by the National Assembly. The change aims to expedite patient care, eliminate lengthy referral processes, and reduce treatment time and costs.

5.7.4 Regulatory and Market Access

- The Law of Pharmacy (2016) emphasizes the necessity for policies that ensure the availability of orphan drugs at reasonable prices. This legislation aims to balance the incentives for pharmaceutical companies to develop these drugs while addressing the affordability and accessibility challenges faced by patients [178].
- Effective from 2017, Vietnam's New Pharmacy Law, which was approved by the National Assembly is an effort to bring real change in Vietnam's local healthcare market. Key initiatives under this law includes: 1) removal of the country's local clinical trial requirement, 2) introduction of patient assistance programs and 3) prioritization of orphan drugs. Amongst Association of Southeast Asian Nations (ASEAN) countries, it takes the longest time for a new molecule to enter into Vietnam market which is around ~ 5.4 years after their global introduction. This when compared with Malaysia (3.2 years) and the Philippines (3.3 years) is still longer. New Pharmacy Law will enable high quality treatment and improved access to healthcare for Vietnamese rare disease patients [179].
- On April 20, 2018, Medical Services Administration of MoH and Shire Singapore signed a joint MoU to collaborate on improving the diagnosis, treatment, therapy access and management of rare diseases in Vietnam until 2023. In addition, MoU will help support education programme for medical professionals and develop a management programme for rare diseases. Hemophilia and primary immune deficiency (PID) are complex rare disorders with need for continuous research efforts and innovative treatment for positive impact on rare disease patients [180].

- Circular No. 26/2019/TT-BYT establishes a formal list of orphan drugs and outlines the regulatory framework for their designation, marketing authorization, and importation[181]. The Ministry of Health's emphasis on diagnostic tools under Circular No. 26/2019/TT-BYT highlights the critical role of effective diagnostics in healthcare management [181]. The Drug Administration of Vietnam's management of applications without a defined timeline raises concerns about the efficiency and accessibility of these tools, potentially delaying diagnosis and treatment initiation.
- Sanofi's International Charitable Access Program (ICAP) has been providing free enzyme replacement therapy to patients without access to necessary medications since 1997. Over the past 27 years, ICAP has supported 59 Pompe disease patients, 11 Gaucher disease patients, 10 MPS I (Mucopolysaccharidosis I) patients, and 16 MPS II (Mucopolysaccharidosis II) patients in Vietnam. This initiative reflects Sanofi's commitment to improving access to vital treatments for patients suffering from rare genetic disorders in the country [182].

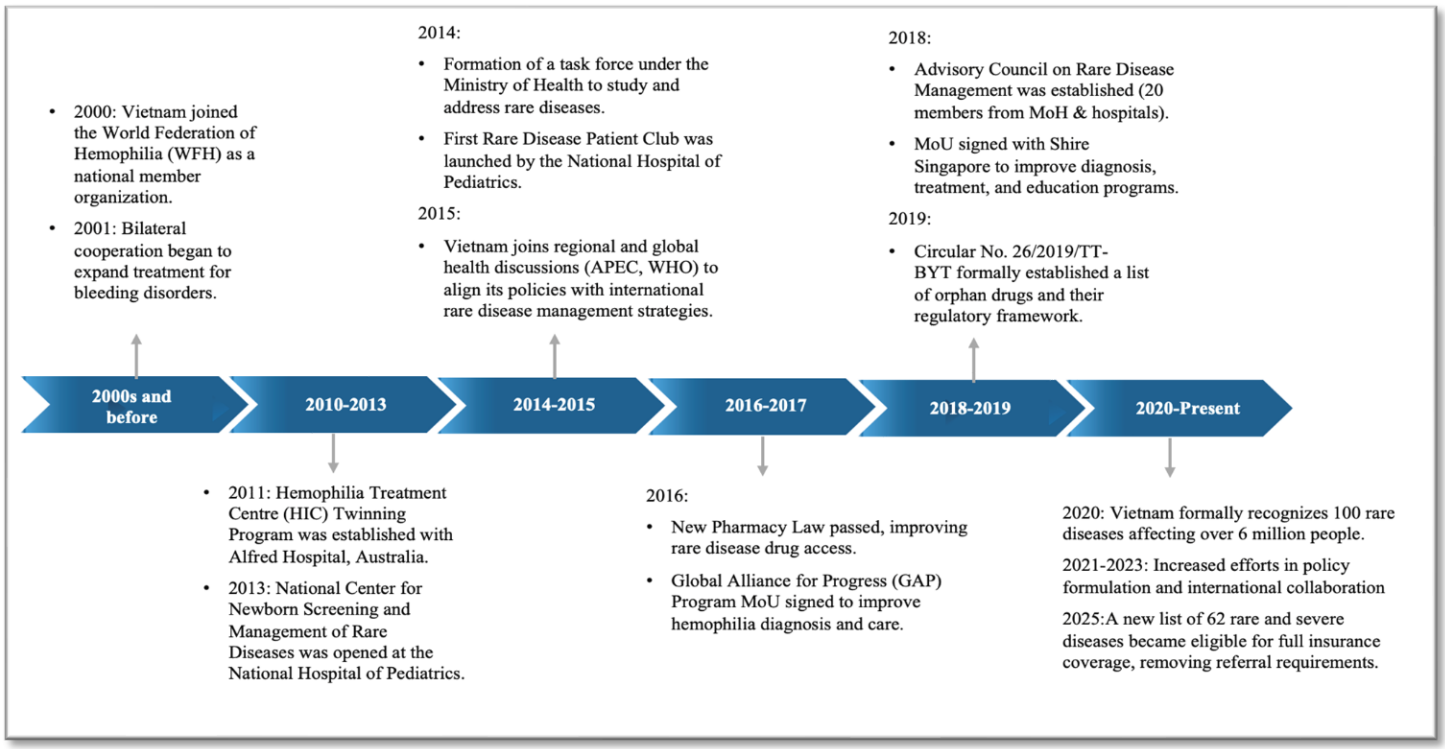
5.7.5 Care Pathways and Infrastructure

- In 2011, the Hemophilia Treatment Centre (HIC) Twinning Program of the WFH was established between the National Institute of Hematology and Blood Transfusion (NIHBT) and Alfred hospital, Australia. Australian HTC helped establish a NIHBT comprehensive care team to attend patients from Hanoi and northern provinces along with raising awareness about the disease across the country. Another Twinning Program by WFH was undertaken to support the Vietnam Hemophilia Association (VHA) in partnership with the Irish Haemophila Society[183].
- In 2013, the National Center for Newborn Screening and Management of Rare Diseases was opened at the National Hospital of Pediatrics. Currently, 31% of the newborns are screened in Vietnam. The screening is done for free and is funded by government.
- In November 2014, a major milestone was achieved by the community of rare disease patients in Vietnam, with the launch of the country’s first Rare Disease Patient Club by the NHP. NHP is the only hospital in the country which provides LSD treatments in the northern provinces [183].
- In Thanh Hóa, Vietnam, on September 21, 2016, Global Alliance for Progress (GAP) Program (2016-19) a MoU was signed between the MoH of the Socialist Republic of Vietnam – NIHBT and the WFH. Before 2001, very few hospitals in Vietnam (Hanoi, Ho Chi Minh city and Hue) provided basic care for hemophila patients. The estimated prevalence of Hemophilia in the country is around 6000 patients and until 2016, only 2400 patients were identified.
- The main objective of GAP program is to identify 1000 new patients with hemophilia and related bleeding disorders. In addition, the program aims to establish a national registry supported by MoH in 2016. The program will also help to expand the care services of the network of seven HTCs in Hanoi,

Ho Chi Minh City, Hue, and Can Tho through staff training. In addition, 10 satellite HTCs and ten VHA chapters will help provide basic care, help procure factor concentrates through a national tender, and reduce state insurance co-payments for factor concentrates. The GAP program is funded by companies such as Bayer, Biogen, Biotest, CSL Behring, Grifols, Kedrion, Novo Nordisk, Pfizer, Shire and Swedish Orphan Biovitrum [184] [185].

- In Vietnam, misdiagnosis and delays in diagnosis are common, with only 27% of patients able to access necessary diagnostic equipment. This results in delays of up to 10 years before receiving an accurate diagnosis. Furthermore, only around 5% of rare diseases in Vietnam have specific treatments available, and 9% of patients face significant challenges in accessing the care they need[175].
- The Ministry of Health is working to address these issues by regularly updating a list of 214 rare disease drugs, which helps improve access to essential treatments[181].
- Key healthcare facilities like the Vietnam National Children's Hospital (VNCH) in Hanoi, which serves as a major pediatric referral center, and the three Centers of Excellence, including the National Hospital of Pediatrics with its Center for Rare Diseases and Newborn Screening, are playing a crucial role in improving the diagnosis and treatment of rare diseases in the country [186]. Despite these efforts, the healthcare system in Vietnam still faces significant barriers, including socio-economic factors that disproportionately affect poorer populations, leading to worse health outcomes.

Figure 9. Shows the timeline of the rare diseases progress in Vietnam



Abbreviation: VT = Vietnam, NHBT = National institute of hematology and blood transfusion, VHA = Vietnam hemophila association, RD = Rare disease, NHP = National hospitals of pediatrics, GAP = Global alliance program, MoU = Memorandum of understanding.

5.7.6 Key Organizations Advancing Rare Disease Initiatives in Vietnam

Organization Name	Established Year	Description
Vietnam Hemophilia Association (VHA)	2007	- Voluntary socio-professional organization comprising doctors, medical staff, patients, and individuals dedicated to the care and treatment of hemophilia and related bleeding disorders in Vietnam.
National Hospitals of Pediatrics (NHP)/Vietnam National Children's Hospital	1969	- Healthcare institution involved in diagnosing and treating rare genetic diseases in children. - Raise awareness through counseling and diagnostic services, research support and preventative, vaccination and early detection programs
Vietnamese Organization for Rare Diseases (VORD)	2021	- Non-profit social enterprise dedicated raising awareness, promoting diagnosis and treatment, building patient communities, connecting local and global networks, and influencing policies for people living with rare diseases (PLWRD)
World Federation of Hemophilia (WFH)	1963	- Global nonprofit organization dedicated to improving the care and treatment of individuals with hemophilia and other inherited bleeding disorders. - Support advocacy, education, partnerships, and humanitarian aid
Department of Medical Services Administration of the Ministry of Health	2015	- Part of Ministry of Health in Vietnam responsible for ensuring the quality of healthcare services, regulating healthcare professionals, and implementing national health programs. - Focus on improving healthcare access and quality related to rare diseases, infrastructure, and medical workforce development
Cures Within Reach	2005	- Philanthropic foundation accelerating the discovery of new treatments to improve the quality of life for people with catastrophic diseases
Vietnam Academy of Science and Technology (VAST)	1975	- National research institute in Vietnam to promote sustainable development and n rare disease research and healthcare innovation in Vietnam. - By focusing on genetic research, biotechnology, policy advocacy, and international collaboration, VAST contributes significantly to improving the diagnosis, treatment, and care of individuals with rare diseases in the country.

Table 10. Key organizations in the area of rare diseases in Vietnam

Abbreviation: HOD = Head of the department, NHP = National Hospital of Pediatrics, RD = Rare disease.

5.8 Hong Kong

5.8.1 Rare Disease Landscape in Hong Kong

1 in 67 individuals affected by rare diseases

Hong Kong has one of the world-renowned public health policies and a healthcare system of high standard. However, the government does not have a clear definition or national policy for rare diseases, classifying them instead as uncommon diseases. Although the rare diseases impact relatively small number of patients, a study conducted in 2018 by the University of Hong Kong estimated that 1 in 67 individuals approximately 1.5% of the city's 7.5 million population—are impacted [19]. In recent years, Hong Kong's healthcare expenditure has significantly increased, reaching HK$284.1 billion (USD $36.36 billion) in 2022-2023, which reported for 10% of the GDP, with per capita spending at HK$38,670 (USD $4974.31) [19] [187] .

Due to the rarity of these conditions, there is a lack of comprehensive evidence on the epidemiology and economics of rare diseases, as well as a comprehensive integrated patient registry. This limits the scientific

knowledge and awareness among healthcare professionals, patients often experience prolonged diagnostic journeys, sometimes spanning several years. This delay is further exacerbated by the insufficient focus on clinical genetics, which is not a recognized specialty by The Medical Council of Hong Kong, and the absence of designated departments for rare diseases at universities or the Hospital Authority[188] [189].

Another challenge is the high cost of rare diseases medication and inadequate financial support mechanisms place an unbearable burden on patients and families in Hong Kong. In Hong Kong, patients seeking financial support for RD drugs undergo an annual evaluation by the Expert Panel on Rare Metabolic Diseases before receiving government funding [190]. However, most orphan drugs are not included in the Hospital Authority Drug Formulary (HADF), meaning they are not covered by financial assistance programs like the Samaritan Fund or Community Care Fund (CCF) [190]. As a result, many patients receive no financial aid and must pay exorbitant out-of-pocket expenses for medication.

The Hong Kong government's "case-by-case" approach to managing rare diseases leads to inconsistencies in access to treatment, financial support, and diagnostics, creating uncertainty for patients. The lack of a standardized policy results in disparities in care, particularly for costly treatments like gene therapies. Without a centralized rare disease registry, early diagnosis and research are hindered, and medical professionals may struggle with limited guidelines. Meanwhile, the Hospital Authority provides medical services for patients with genetic diseases, and to prevent severe complications, the Department of Health and the Hospital Authority launched the Pilot Study of Newborn Screening for Inborn Errors of Metabolism in October 2015. The number of metabolic disorders covered under the study increased from 21 to 24 in April 2016 [191]. However, compared to regions with structured rare disease policies, Hong Kong may need reforms to ensure equitable and efficient care.

5.8.2 National Strategy Framework and Policy Shaping

Hong Kong lacks a comprehensive rare diseases strategy and policy. Compared to countries like Singapore and Japan, Hong Kong lags in rare disease prevention and treatment. While the Hong Kong government is addressing rare diseases through various measures, including developing databases for specific uncommon disorders, improving drug registration processes, and enhancing public awareness. The Hospital Authority (HA) has been providing drug subsidies, such as through the Community Care Fund and the Samaritan Fund, to support patients. Long-term strategies involve promoting clinical research, improving treatment access, and collaborating internationally. Further efforts are needed to enhance definitions, diagnostic processes, and treatment accessibility.

National Plan and Legislation

- The Hong Kong Alliance for Rare Diseases (HKARD) or Rare Disease Hong Kong (RDHK), established in December 2014, is the first patient group in Hong Kong that brings together individuals affected by various rare diseases and their families, with support from experts and academics in the field. In 2016, the Hong Kong Alliance for Rare Diseases (HKARD) advocated for comprehensive support measures to enhance the quality of life for rare disease patients. Their proposals included the introduction of case managers to assist patients, optimization of the Comprehensive Social Security Assistance (CSSA) scheme to allow patients to receive support while living with their families, and other supportive incentives [192].
- In 2019, the Hong Kong Legislative Council introduced the Draft Rare Diseases Bill, aiming to establish a comprehensive framework for rare disease management [193]. This initiative aims to enhance the well-being of individuals affected by rare diseases and align with international standards, such as the United Nations Convention on the Rights of Persons with Disabilities. The proposed legislation includes:
    - Commission on Rare Diseases Policy: Advises the government on strategic development and monitors policy implementation.
    - Evaluative Committee on Rare Diseases: Evaluates diseases for rare disease status and maintains a register of related drugs and treatments.
    - Subsidy Scheme: Provides financial assistance for patients' expenses on rare disease drugs and treatments.
- Rare Disease Information System: Collects data on rare diseases, including prevalence and treatment usage.
    - Several of Rare Diseases Hong Kong's (RDHK) recommendations have been addressed or are in progress. In 2024, the Hong Kong government announced plans to establish a rare disease center in collaboration with Mainland China, which will be located at the Hong Kong Children's Hospital and will focus on rare disease expertise. This initiative aligns with RDHK's recommendation for a centralized facility to support patients with rare diseases. rThere has also been significant focus on improving clinical services for rare disease patients. The Hong Kong Children's Hospital will expand its integrated paediatric services, improving healthcare access for children with rare diseases, addressing RDHK's call for specialized clinical care. The government's initiatives to enhance healthcare collaboration with the Greater Bay Area further support RDHK's recommendation for regional cooperation on rare disease treatments.rHowever, some of RDHK's recommendations are still pending or unclear. For example, there has been no specific update regarding the removal of age restrictions for drug subsidies, particularly for treatments for spinal muscular atrophy. Similarly, the inclusion of

Herpes Zoster vaccination in subsidy schemes has not been confirmed. While significant progress has been made in certain areas, more work is needed to fully address all of RDHK's proposals.

- The Hong Kong government's 2024 Policy Address presents a comprehensive strategy aimed at improving both public and private healthcare services. Notable initiatives encompass a review of the Hospital Authority's fee structure, the centralization of drug procurement, enhancements in the diagnosis of rare diseases, the integration of pediatric services, the progression of hospital development projects, the establishment of specialized centers for stroke and chest pain, the refinement of specialist outpatient referrals, and a 20% increase in the capacity for cataract surgeries [194].

Programs and Initiatives

- Since 2014, awareness of rare diseases in Hong Kong has grown significantly, marked by the establishment of Rare Disease Hong Kong (RDHK) (formerly HKARD), the first patient organization in Hong Kong and discussions in the Legislative Council in 2016 on support measures for patients. RDHK has played a crucial role in advocacy, raising public awareness, and pushing for better healthcare policies. While Hong Kong still lacks a formal Rare Disease policy, increased attention has led to gradual improvements in drug accessibility, financial support, and medical services for rare disease patients [188].
- In October 2015, the Department of Health and the Hospital Authority launched the Pilot Study of Newborn Screening for Inborn Errors of Metabolism to prevent and reduce severe complications from these conditions. The study initially covered 21 types of inborn errors of metabolism, with the scope expanding to 24 types in April 2016, enhancing early detection and intervention efforts[191] [188].
- Currently, there is a lack of national level rare disease registry, however, all the universities, medical departments and patients' group have their own sets of data, making it difficult to estimate the overall medical and social burdens of rare diseases on patients. This underscores the soaring need on governments part to make allocation of resources in the next fiscal year 2016-2017 to enable the Children's Hospital (managed by the HA) to take the lead in coordinating a joint effort by the two medical schools in Hong Kong, in collaboration with the other hospitals, to pilot a rare-disease patients registry for selected rare diseases. Further, effective use of an electronic health-record sharing platform to gradually build a comprehensive rare-disease patients registry is a necessity of the hour.
- The Hong Kong Genome Institute (HKGI) was established in May 2020 by the former Food and Health Bureau (now the Health Bureau) of the Hong Kong Special Administrative Region. It was founded to implement the Hong Kong Genome Project (HKGP) with the vision of "genomic medicine for all for

better health and well-being" [195]. It conducted WGS for 20,000 cases in accelerating the clinical application of genomic medicine to more accurately diagnosis and tailor the treatment of patients and their families. Given the success of the project, in 2022, expanded eligibility to cover other hereditary diseases and research cohorts related to genomics and precision health.

- In the 2024 Policy Address, the Chief Executive announced plans to develop a directory for inherited and rare diseases utilizing genomic data from the Hong Kong Genome Institute. This initiative aims to facilitate early diagnosis and treatment, as well as support related research and clinical trials to advance precision medicine [194].

5.8.3 Funding and Financial Support

- Since the 2008-2009 period, the Hong Kong government has subsidized enzyme replacement therapy (ERT) for patients diagnosed with 6 specific types of lysosomal storage disorders (LSDs) who meet certain clinical criteria[191].
- The Chinese University of Hong Kong (CUHK) launched the territory's first screening program for inborn errors of metabolism (IEM) with a funding received from Joshua Hellman Foundation for Orphan diseases worth HK $1 million. The departments of Chemical Pathology, Obstetrics and Gynecology, as well as Pediatrics jointly launched the first newborn metabolic screening program in Hong Kong. The program can test 30 kinds of IEM. CUHK established the Centre of Inborn Errors of Metabolism in July 2013 to offer the screening program[196].
- The Comprehensive Social Security Assistance (CSSA) Scheme is designed to provide financial assistance to individuals and families in need so as to bring their income up to a prescribed level to meet their basic needs. From 1 February 2017 onwards, the amount of assistance payable per month of Normal Disability Allowance and Higher Disability Allowance is HK$1695 and HK$3390 (USD $ 217.60- $435.20) respectively [197].
- In past, government subsidized patients suffering from 6 specified types of lysosomal storage disorder and meeting specific clinical criteria to obtain enzyme replacement therapy. From 2016-2017, Government provided drug subsidies to eligible patients suffering from specified rare diseases (e.g. Paroxysmal Nocturnal Haemoglobinuria) through the Community Care Fund [191].
- In 2017, the government and the Hospital Authority (HA) introduced the Community Care Fund (CCF) Medical Assistance Programme to subsidize eligible patients in purchasing ultra-expensive drugs, including those for rare diseases. Since its inception, the program has approved 77 applications, resulting in a total of HK$259.5 million (USD $33.33 million) in subsidies granted to eligible patients.

[198]. The program plays a critical role in ensuring that patients who require high-cost treatments can still access them despite financial limitations.

- In Hong Kong, patients who receive subsidies for rare disease drugs are assessed and evaluated annually by the Expert Panel on Rare Metabolic Diseases, after which they may receive additional recurrent funding from the government [199].However, many drugs for rare diseases are not included in the Hospital Authority Drug Formulary (HADF)system, meaning they are not covered by the Samaritan Fund or the Community Care Fund (CCF) [188]. As a result, most patients do not have access to financial support through these mechanisms and are left to bear the high costs of these medications out-of-pocket.
- Since the 2021 Policy Address, financial support for rare disease patients has improved through expanded drug coverage under the Samaritan Fund and CCF Medical Assistance Programmes [190].
- To further support patients, the government increased recurrent funding by HK$25 million (USD $3.22 million) from the 2021-22 financial year onwards[198]. This funding aims to enhance services at the Hong Kong Children's Hospital, including bolstering clinical genetic services, launching a case manager programme for coordinated care, and expanding genetic and genomic testing capabilities.

5.8.4 Regulatory and Market Access

- In March 2018, a scheme was initiated by the HKARD and other non-profit groups, respiratory specialists and a pharmaceutical company to provide free drugs for idiopathic pulmonary fibrosis, Nintedanib. The drug was registered in Hong Kong since 2016 but was not listed in the HA Drug formulary. Until now, the drug costed HK $20,000 (USD $2,550) a month. However, the patients still need to pay for the first two years for the treatment and afterwards free medication will be offered until patient’s physician changes the prescription. While private patients can get the drugs from their own specialists, public patients have to bring the prescription and visit any one of the designated community pharmacies under the three charities involved, namely the Hong Kong Pharmaceutical Care Foundation, HKSKH Lady MacLehose Centre and St James’ Settlement[200].
- In 2017, the government and the Hospital Authority (HA) introduced the Community Care Fund (CCF) Medical Assistance Programme to subsidize eligible patients in purchasing ultra-expensive drugs, including those for rare diseases. As of March 2021, the programme covered 37 drugs, reflecting a commitment to expanding access to necessary medications [198].
- The government introduced pilot programs like the Pilot Scheme for Supporting Patients in the Greater Bay Area, which began in 2020, allowing rare disease patients to access specialized services at subsidized costs [188].

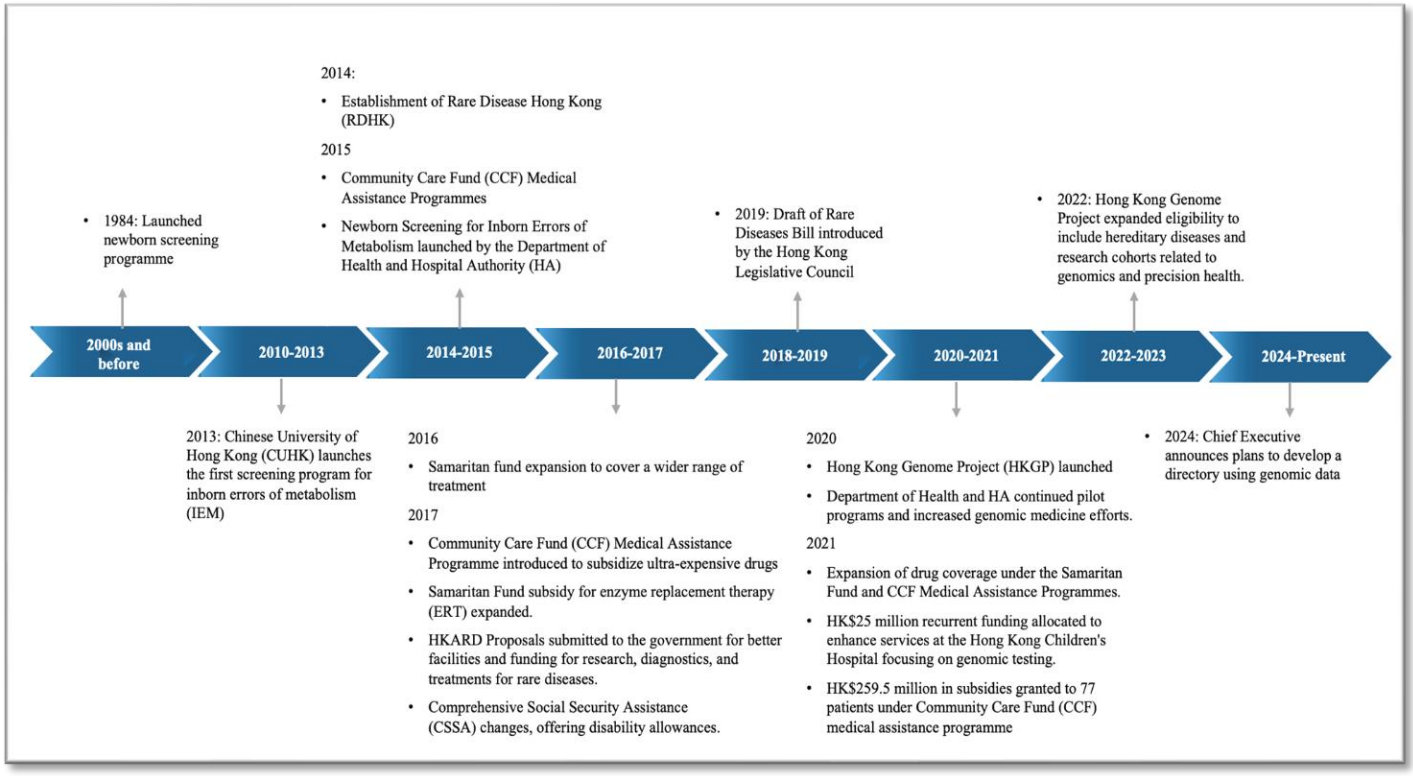
- The Ultra-expensive Drugs Programme has subsidized costly treatments, and the Hospital Authority Drug Management Committee continues to enhance drug accessibility in 2021 [188]. Additionally, the government has increased funding to strengthen services at the Hong Kong Children's Hospital, improving genetic testing and newborn screening to facilitate early diagnosis and treatment.

5.8.5 Care Pathways and Infrastructure

- The Chinese University of Hong Kong (CUHK) launched the territory's first screening program for inborn errors of metabolism (IEM). The departments of Chemical Pathology, Obstetrics and Gynecology, as well as Pediatrics jointly launched the first newborn metabolic screening program in Hong Kong. The program can test 30 kinds of IEM. CUHK established the Centre of Inborn Errors of Metabolism in July 2013 to offer the screening program[196].
- In 2015 Policy Address, the launch of pilot screening programme for newborn babies for inborn errors of metabolism (IEM) was announced. The scheme was launched in October 2015 and was available only at Queen Elizabeth Hospital and Queen Mary Hospital. During the first 6 months (the first phase of the scheme), 21 kinds of IEM were tested, and 3 more were included in the second phase.
- The Hospital Authority (HA) has not established a specialized department for rare diseases, but various hospitals may have specialists who treat individual aspects of rare diseases. However, treatment often requires visiting multiple specialists, and diagnosis may involve sending specimens to overseas laboratories. The HA Drugs Formulary does not include many medications for rare diseases, which leads to challenges in accessing necessary treatment. However, some efforts have been made to bring more drugs into the formulary, and discussions are ongoing regarding how to improve access [188].
- Clinical genetics is not recognized as a registered specialty by the Medical Council of Hong Kong, and there is no specific department dedicated to the treatment of rare diseases in universities or within the Hospital Authority (HA) reported in 2019 [201]. Due to limited attention and focus on rare diseases among medical professionals, there is a lack of research and development in this area, as well as a shortage of experienced medical staff. As a result, patients often have to consult multiple specialists and send their samples to overseas laboratories for diagnosis [202]. This leads to a prolonged delay between the onset of symptoms and diagnosis, which in turn causes delays in accessing timely clinical interventions, ultimately affecting the potential for optimal patient outcomes.
- In 2020, the Hong Kong Genome Project was launched by the Hong Kong Genome Institute to conduct large-scale genome sequencing, focusing on undiagnosed genetic diseases and hereditary cancers [188]. The project began with a pilot phase involving 2,000 eligible volunteers with undiagnosed disorders and hereditary cancers from Hong Kong Children's Hospital, Prince of Wales Hospital, and Queen Mary

Hospital. The second phase, which will expand to include additional hereditary diseases and 18,000 more cases, is set to launch in the future. The project collaborates with the Department of Health, the Hospital Authority, and local universities, aiming to advance genomic medicine and cultivate talent in Hong Kong.

Figure 10. Shows the timeline of the rare diseases progress in Hong Kong



Abbreviation: NBS = Newborn Screening, RA = Republic act, RDMAP = Rare disease medicine access program, DoH = Department of health, UP NIH = University of the Philippines national institute of health.

5.8.6 Key Organizations Advancing Rare Disease Initiatives in Hong Kong

Organization Name	Established Year	Description
Hong Kong Alliance for Rare Diseases (HKARD)	2014	- To promote public education on RDs, policy advocacy and support and assistance of patients, families and carers.
Samaritan Fund	1950	- Provides financial assistance for needy patients for special needs which are not covered by the standard fees and charges in public hospitals and clinics.
Hong Kong Rett Syndrome Association	2013	- Provides support to parents of young patients of Rett syndrome.
Hong Kong Angelman Syndrome Foundation (HKASF)	2016	- NGO to support patients with Angelman syndrome, their families.
Tuberous Sclerosis Complex Association of Hong Kong (TSC)	2015	- To promote mutual and community support by fostering public understanding of the little-known disorder of TSC.
Hong Kong Neurofibromatosis Association	2016	- To support neurofibromatosis patients and families.
Hong Kong Spinocerebellar Ataxia Association (HKCAA)	2007	- Dedicated to support individuals affected by Spinocerebellar Ataxia (SCA) and other related neurodegenerative disorders in Hong Kong. - Raising awareness, provide patient support, and promote research to improve diagnosis, treatment, and care for those living with SCA.
Hong Kong Red Cross John F. Kennedy Centre Alumni Association	2011	- To support individuals affected by rare diseases.

		- Collaborates with various patient support groups to enhance advocacy, awareness, and resources for those living with rare conditions.
Hong Kong Mucopolysaccharidoses & Rare Genetic Diseases Mutual Aid Group (HKMPS)	2005	- To support and educate families and patients about MPS and other RDs. To advocate for RDs and assist in R&D and other therapies.
The Hong Kong Society for Rehabilitation	1959	- They promote rehabilitation and empowerment of people with disabilities or health conditions through innovations.
Joshua Hellman Foundation for Orphan Disease	2008	- To advance the awareness, diagnosis, treatment and research of RDs, and improve the welfare of children with RDs.
Hong Kong Credible Care Volunteers Association Limited	2013	- Aims to gather nurses, professionals from various sectors, and volunteers willing to provide voluntary services to the Hong Kong community.
Sudden Arrhythmia Death Syndromes (SAD) Foundation	1991	- Dedicated to increasing public awareness of the warning signs of heart rhythm abnormalities that can cause sudden death in the young. - Provides information, resources, and support to assist patients and families in making informed medical decisions and living with the challenges of these conditions.
Seoul National University Hospital's Center for Rare Diseases	2010	- Actively working towards establishing a comprehensive Rare Disease Center to better serve individuals with rare diseases - Involved in Rare Disease Research Center Project, aimed at advancing research in rare diseases, and the Genetic Diagnosis Program, which focuses on offering genetic testing and precise diagnosis for patients with rare conditions.
Hong Kong Genetic Association (HKGA)	2010	- Promoting genetic research, education, and clinical services in Hong Kong. - To advance the understanding and application of genetics in healthcare, fostering collaboration among professionals and the public.
Rare Disease Hong Kong (RDHK)	2014	- First patient group in Hong Kong comprising individuals affected by various rare diseases and their families. - Aiming to improve policies and services related to rare diseases, promote public education, and strengthen community support for patients to ensure equal respect and protection in areas such as healthcare, social support, education, and daily needs.

Table 11. Key organizations in the area of rare diseases in Hong Kong

Abbreviation: RDs = Rare diseases, MPS = Mucopolysaccharidosis

5.9 Indonesia

5.9.1 Rare Disease Landscape in Vietnam

Indonesia, as the largest country in Southeast Asia with a population of over 270 million, faces significant challenges in addressing rare diseases.

Indonesia lacks formal definition of rare diseases and is one of the countries in the APAC region which is lagging far behind in healthcare system. Rare diseases, while individually infrequent, collectively impact a significant number of individuals affecting 12.5 million in 2018, often leading to substantial morbidity and mortality [16]. Patients with rare diseases lack access to proper medication and treatment in the region, which occasionally leads to premature death. Healthcare financing in Indonesia has undergone significant transformation in recent years, driven by the introduction of universal health coverage (UHC) and the establishment of the Jaminan Kesehatan Nasional (JKN) program in 2014. Despite several decades of efforts to improve health equity, an estimated half of the world's 7·3 billion people still do not have access to essential health services and more than half a billion people who seek health care are forced into poverty every year due to out-of-pocket payments as per the study in 2023[203] . Additionally, Indonesia initiated a national new-born screening program for congenital hypothyroidism (CH) in 2014, yet logistical issues, cultural barriers, and insufficient healthcare infrastructure hinder its effectiveness.

5.9.2 National Strategy Framework and Policy Shaping

Indonesia does not have a specific, comprehensive national policy solely dedicated to rare diseases. However, efforts are integrated into broader health policies, with the Badan Penyelenggara Jaminan Sosial (BPJS) Kesehatan system offering coverage for some rare disease treatments, though access remains limited. The government has focused on improving early detection through newborn screening programs, raising awareness among healthcare professionals, and negotiating for affordable orphan drugs. Collaboration with international organizations and medical research initiatives is also increasing. However, challenges remain, including the absence of specific legislation for rare diseases, limited diagnostic infrastructure, and high treatment costs.

National Plan and Legislation

- In January 2014, the Indonesian government launched a new healthcare system policy, *Badan Penyelenggara Jaminan Sosial (BPJS Kesehatan)* under which all Indonesians intend to be covered by 2019. The program recognizes the need that a quarter billion of the population will need advanced medical technologies for diagnosis and treatment [204].
- Indonesia currently lacks specific national legislation or a formal definition for rare diseases. Unlike countries such as Japan, South Korea, and Singapore, which have established laws and policies to address rare diseases and orphan drugs, Indonesia has not implemented similar measures[205].This absence makes it challenging to address the full spectrum of needs related to rare disease care, from diagnosis to treatment and patient support.

Programs and Initiatives

- While many countries have implemented nationwide newborn screening programs to detect genetic and metabolic disorders early, Indonesia has not established a comprehensive policy. The only screening program currently in place is for congenital hypothyroidism, which limits early identification and intervention for other rare diseases [206].

5.9.3 Funding and Financial Support

- There is no formal governance structure in Indonesia specifically dedicated to rare diseases [205]. This means there is no central authority responsible for coordinating care, ensuring the availability of treatments, or implementing policies that could improve outcomes for rare disease patients.

- There is a significant lack of government funding and support for rare diseases, with no dedicated financial resources for treatment or research. Rare diseases are not covered by the national health insurance system, BPJS Kesehatan, leaving patients without access to necessary treatments. Current policies fail to address the high costs of rare disease care, which often involves expensive therapies and long-term management that patients cannot afford. As a result, individuals with rare diseases face considerable financial barriers, often relying on out-of-pocket expenses or charity organizations for assistance [205].

5.9.4 Regulatory and Market Access

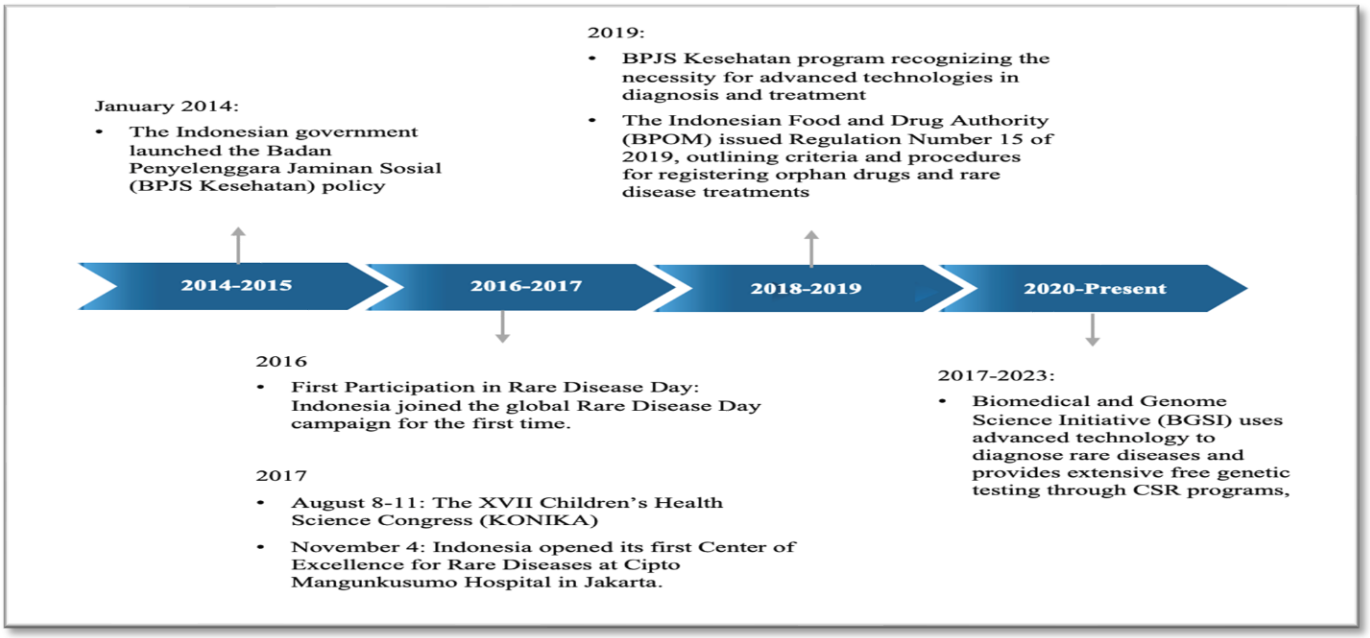
- The regulatory framework and governance for rare diseases are lacks formal governance structure for rare diseases, though Centre of Excellence exists at Cipto Mangunkusumo Hospital, in collaboration with key research institutions, provide specialized care and research opportunities [16]. However, there is no dedicated Rare Diseases and Orphan Drug Act to establish a clear policy or legal framework for the management and treatment of rare diseases [384]. The registration of orphan drugs is managed under Ministerial Decree No. 1379A/Menkes/SK/XI/2002, but the process lacks a specific legislative focus on rare diseases. While rare disease treatments face limited coverage and government support, the government has made efforts to facilitate market access by ensuring that imported medicines for rare diseases are tax-free and by streamlining the registration process.
- Indonesian Food and Drug Authority (BPOM) has outlined criteria and procedures for registering drugs related to rare diseases under Regulation Number 15 of 2019, which includes requirements for justification and supporting documents [207]. This aims to speed up the process of registering drugs that might be key to treat conditions with limited available treatments, although it remains part of a broader, less specialized framework for rare diseases in the country.

5.9.5 Care Pathways and Infrastructure

- On November 4, 2017, Indonesia opened its 1st Center of Excellence for Rare Diseases in Cipto Mangunkusumo Hospital. The center aims to provide its services in the form of multidisciplinary team, diagnostic laboratory in conjunction with Human Genetic Research Center and Indonesia Medical Education and Research Institute Universitas Indonesia (IMERI UI), and patient organization to support rare disease affected families[208].
- New drug registrations for rare diseases require justification and documentation. Off-label drugs, like sildenafil, are used for rare conditions due to the lack of registered options, driven by economic disincentives[209]. Biomedical and Genome Science Initiative (BGSI) uses advanced technology for

rare disease diagnosis and offers extensive free genetic testing through CSR programs[207] . Accurate diagnosis is difficult, causing treatment delays; CSR programs like Prodia's provide record setting free genetic tests to address this issue [210].

Figure 11. Shows the timeline of the rare diseases progress in Indonesia



Abbreviation: VT = Vietnam, NHBT = National institute of hematology and blood transfusion, VHA = Vietnam hemophila association, RD = Rare disease, NHP = National hospitals of pediatrics, GAP = Global alliance program, MoU = Memorandum of understanding.

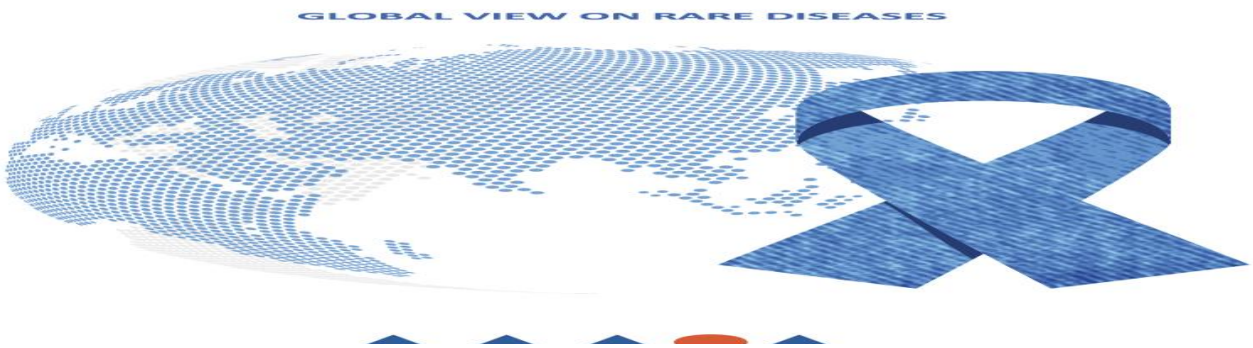
5.9.6 Key Organizations Advancing Rare Disease Initiatives in Indonesia

Organization Name	Established Year	Description
Indonesia Rare Disorders (IRD)	2015	- Community with aim to support patients and families with RDs. - Increases awareness about RD via information, cooperation, advocacy and procurement of activities.
Indonesian MPS and Rare Disease Foundation / Yayasan MPS & Penyakit Langka Indonesia	2016	- Non-profit provides support to rare disease patients and is a bridge between patients with rare diseases and the right health workers.
Asia-Pacific Alliance of Rare Disease Organizations (APARDO)	2015	- Regional organization established to amplify the voices of rare disease advocacy groups across the Asia-Pacific region. - Aims to improve the lives of individuals and families affected by rare diseases by fostering collaboration, increasing awareness, and advocating for better healthcare policies and access to treatments.
Indonesia CARE for RARE Diseases		- Focuses on supporting and educating families with special needs, particularly those affected by rare diseases, through an online parents' support group.
Yayasan MPS dan Penyakit Langka Indonesia	2010	- Focused on providing support and advocacy for individuals affected by Mucopolysaccharidosis (MPS). - Aims to raise awareness, provide resources, and aid patients and their families facing these conditions. - Promote research and healthcare access for rare diseases in Indonesia.
Indonesian Community of Rare Disorders (ICORD)	2013	- Non-profit organization in Indonesia that aims to raise awareness, provide support, and advocate for individuals and families affected by rare disorders. - Bridge the gap in healthcare access, diagnosis, treatment, and social support for those living with rare diseases in Indonesia.

Faculty of Medicine, University of Indonesia - Cipto Mangunkusumo National General Hospital (FMUI-RSCM)	1851	- Provide educational opportunities for medical students and a range of healthcare services to the public. It is a key institution for medical education, research, and clinical care in Indonesia.
Cipto Mangunkusumo National Referral Hospital	1919	- Government-run district general hospital offers comprehensive diagnostic and therapeutic services, offering some of the first and only medical and surgical services

Table 12. Key organizations in the area of rare diseases in Indonesia

Abbreviation: RD = Rare disease.



5.10 NEW ZEALAND

5.10.1 Rare Disease Landscape in New Zealand

In New Zealand, a disease is considered rare when it affects fewer than 1 in 2000 people or less. An ultra-rare disease affects fewer than 1 in 50,000 people or less [211]. More than 7,000 different rare diseases have been identified, and about half of people with rare diseases are children. About 80% of rare diseases are genetic[212]. Despite their name, rare diseases are not uncommon and collectively affect about 300,000 New Zealanders[15] [15]. Although these diseases occur individually in very small numbers in the population, those affected share the same systemic challenges and barriers in our health system: lack of rapid diagnosis, poor access to treatment, lack of care coordination, isolation and, for many, loss of support in the system.

In 2020, New Zealand's healthcare spending was about USD $3,929 per capita on health, or about 10.05% of the country's gross domestic product (GDP) significantly lower than comparable countries such as Canada and Australia, which spent USD $6,215 and USD $5,802 per capita respectively [212] [213]. Despite this, New Zealand stands out as one of the few countries offering universal healthcare coverage and subsidized medicines for its residents, with a low patient co-payment of just USD $5, and free care for

children. These efforts are managed by the Pharmaceutical Management Agency (PHARMAC), a government agency established in 1993 to oversee the funding and supply of medicines. PHARMAC plays a critical role in New Zealand's healthcare system, balancing cost-effectiveness with access to essential medicines. Although its model is internationally recognized, challenges remain predominantly around access to high-cost medications and ensuring equity. In 2019, only 348 patients with rare diseases had their specialist drugs funded by PHARMAC, while it is estimated that between 2,000 and 15,000 people in this country are living with a rare and treatable disease [214]. Another barrier that rare disease patients face in accessing care in New Zealand is the lack of coordination within the health system. The old District Health Boards (DHBs) were highly fragmented and, while some steps were taken to encourage information sharing, they were still very fragmented. However, there is a huge opportunity for integration and coordination of care with the new single national DHB (Health NZ) introduced in July 2022.

New Zealand does not have a national registry of diagnosed rare diseases, limiting the ability to understand the collective needs of people with rare diseases [15]. The lack of data on rare diseases in New Zealand not only presents a challenge for estimating prevalence, but also for improving diagnosis, treatment and research. As a small country, New Zealand relies heavily on international partnerships for research and, without using the internationally recognized rare disease classification system, Orphanet, partnerships are limited.

Additionally, Newborn metabolic screening programme is in place in New Zealand for last 40 years. This programme screens newborns for free to identify metabolic disorders. When diagnosed early, treatment can be started at an early stage and helps prevent the permanent damage or debilitating effects on children. Current programme screens newborns for 20 conditions. The National Screening Unit (NSU) of the Health ministry holds the responsibility for the funding, monitoring and strategic direction of the screening programme.

5.10.2 National Strategy Framework and Policy Shaping

In New Zealand, the primary legislation addressing rare diseases is the Aotearoa New Zealand Rare Disorders Strategy published in 2024[215]. This strategy provides a comprehensive framework aimed at improving healthcare access and support for individuals living with rare disorders. This strategy also provides insights on the data collection, early diagnosis, coordinated healthcare pathways, equitable access to treatments, and training healthcare professionals specifically on rare disorders. Additionally, the strategy is being implemented by various agencies, including the Ministry of Health, Health New Zealand, PHARMAC, and the Health Quality & Safety Commission. Rare Disorders New Zealand (RDNZ) is actively involved in the implementation process, working with these agencies to ensure the strategy delivers meaningful change for individuals living with rare disorders.

National Plan and Legislation

- In July 2024, the Ministry of Health released the Aotearoa New Zealand Rare Disorders Strategy. This strategy outlines a framework and long-term priorities to improve health and well-being outcomes for individuals with rare disorders over the decade from 2024 to 2034[215]. It aims to address significant barriers to timely and effective healthcare faced by patients and challenges encountered by healthcare providers in diagnosing and supporting rare disorders.
- The Ministry of Health plans to build national datasets on rare disorders as part of its 10-year strategy to improve health and better support people living with rare disorders [216]. Currently, limited data available to precisely estimate people living with rare disorders and support care planning. Besides data collection, New Zealand is also enhancing health data sharing by coming up with the NZ Core Data for Interoperability, which will serve as the standard for the most shared health data in clinical workflows and consumer access to data.

Programs and Initiatives

- New Zealand Organisation for Rare Disorders (NZORD), established in 2001 is a non-profit organization that advocates for the needs of people living with rare diseases. In an effort to identify the challenges faced by the people suffering or related to rare disorders several programmes were initiated by NZORD. In September 2015, the Patient Support group survey was launched, and the General Practitioner Survey commenced in February 2016. Outcome of both surveys was that improvements are highly sought, especially there is a need to improve educational resources which could benefit both patients and medical clinicians[217].
- During Rare Disease Day 2016 event, NZORD launched a support group named “Syndrome without a name” (SWAN) which aims to support the patients and families affected by unknown genetic conditions [218].
- New Zealand Neuromuscular Disease Registry established in 2012 and is part of the TREAT NMD Alliance, an international network. It was funded by the research trust of the Muscular Dystrophy Association of New Zealand, Neuromuscular Research New Zealand [15]. After five years, it had enrolled 1,019 people with 70 different diagnoses and has acted as a conduit for many global prevalence, treatment and genomic sequencing projects for rare neurological disorders (Rodrigues et al 2017). The registry has since been renamed Pūnaha Io Neuro-Genetic Registry and BioBank. It continues to provide access to subjects primarily for research and clinical trial purposes [219].
- Biobanks collect, process and store tissues and cells (including blood, muscle, nerves and cerebrospinal fluid) for ethically approved research studies (Hudson et al 2016). Te Ira Kāwai - Auckland Regional

Biobank opened in 2016 and is part of the Faculty of Medical and Health Sciences at the University of Auckland. Te Ira Kāwai uses OpenSpecimen, a specialist biobank database, which allows to efficiently track the storage locations of individual samples to ensure that stored tissue can be monitored at all times to minimise the risk of loss [15].

- Founded in September 2000 as the New Zealand Organization for Rare Disorders (NZORD) and renamed in 2019, as Rare Disorders NZ (RDNZ) is the national organization for rare diseases [220]. It provides a central point of contact for patients and families affected by rare diseases, helping them find essential information and support groups. RDNZ also advocates for equitable health services for the approximately 300,000 New Zealanders living with a rare disease.
- In 2024, New Zealand's Ministry of Health is planning a routine collection of rare disorders data as part of a 10-year strategy to improve outcomes for affected individuals [221]. This initiative aims to enhance clinical classification systems, integrate rare disorder data with national health datasets, and support research using de-identified data. With an estimated 300,000 people in New Zealand living with rare disorders, the project seeks to address gaps in diagnosis, care, and monitoring to enable better-informed health services.

5.10.3 Funding and Financial Support

- The Pharmaceutical Management Agency (PHARMAC) made provisions to spend NZ$25 million (USD $15.25 million) over 5 years under a pilot commercial project which improved access to 9 medicines (1 more drug is under consideration) [222].
- According to NZORD recent reports in 2018, the government has decided to reduce the organization funding’s which is threatening to the existence of this organization. During the election, then contesting party and now the government had promised to establish a separate fund of NZ$ 20 million (USD $14.6 million) for 4 years to allow rare disease patients access to vital and life-saving medicines [217].
- The New Zealand Government invested up to $35 million for a period of 2017-2024 in Genomics Aotearoa, a new collaborative science organization supporting advanced genomics research across health, environment and primary production – covering all life sciences of relevance to New Zealand's economic, environmental and social wellbeing [15] [223].
- In 2025, X4 Pharmaceuticals announced that its Marketing Authorization Application (MAA) for mavorixafor, a treatment for WHIM syndrome, has been validated for review by the European Medicines Agency's CHMP [224]In April 2024, mavorixafor (branded as XOLREMDI®) was approved by the U.S. FDA as an oral, once-daily treatment for patients aged 12 and older with WHIM

syndrome. Norgine is working with X4 to enable access to mavorixafor for patients in Europe, Australia and New Zealand and achieving regulatory milestone.

5.10.4 Regulatory and Market Access

- PHARMAC is an agency on behalf of district health boards which decides on which drugs are to be subsidized for community use. In July 2018, PHARMAC published an updated policy for assessing medicines for rare conditions and established a commercial process seeking funding applications from pharmaceutical suppliers specifically for medicines for rare disorders[225].
- PHARMAC also decided to widen access to previously funded ERT for the treatment of Gaucher's disease. Tagliglucerase is to be introduced in the system from August 1, 2018, and will replace the current funded treatment of imiglucerase.
- PHARMAC, New Zealand's pharmaceutical regulatory agency, has been actively updating its policies and initiatives to improve access to medicines for rare diseases. Recent initiatives in October 2024 include a call for applications for funding for rare disease drugs in its Rare Diseases Policy and the establishment of the Rare Diseases Advisory Committee (RDAC) to provide expert advice on funding decisions [226]. PHARMAC also engages patients, families and healthcare professionals to inform its decision-making process and ensure that treatments meet unmet need. While advocacy groups, such as Rare Disorders NZ, have welcomed the increase in drug funding, concerns remain about the transparency and timeliness of funding decisions, highlighting the need for continued collaboration and clarity.

5.10.5 Care Pathways and Infrastructure

- New Zealand is enhancing research efforts to better understand and treat rare diseases. The University of Otago, for example, has received backing from the European Union, uniting over 170 organizations with more than €150 million (USD $159 million) in funding for rare disease research [227].

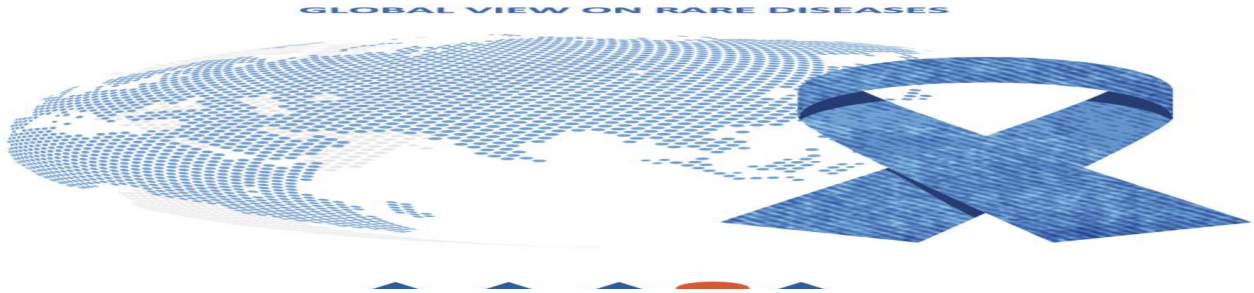
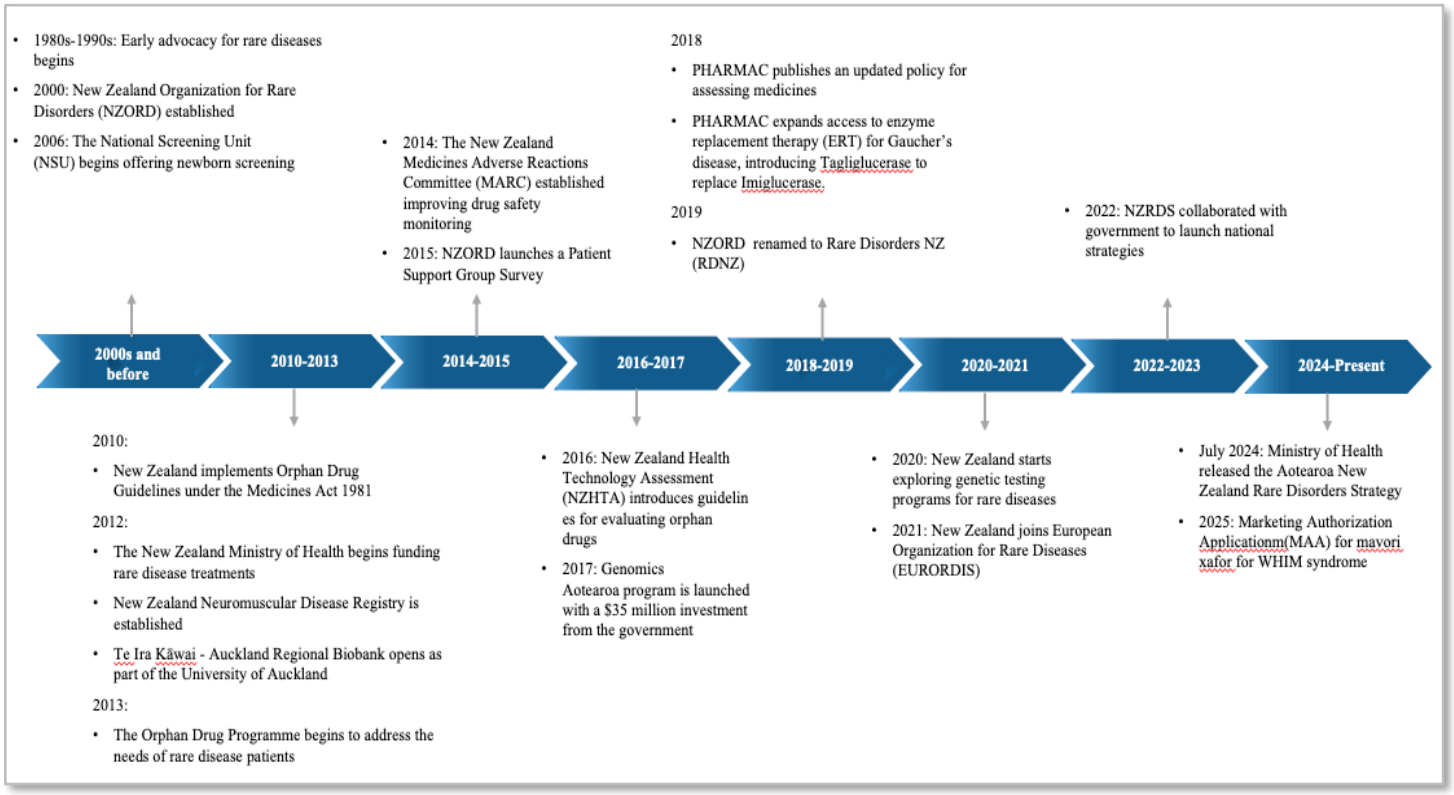


Figure 12. Shows the timeline of the rare diseases progress in New Zealand



Abbreviation: PHARMAC = Pharmaceutical management agency, NZORD = New Zealand organization for rare disorders, SWAN = Syndrome without a name, NZ = New Zealand, RD = Rare disease, ERT = Enzyme replacement therapy.

5.10.6 Key Organizations Advancing Rare Disease Initiatives in New Zealand

Organization Name	Established Year	Description
New Zealand Organization for Rare Disorders (NZORD) / Rare Disorders NZ (RDNZ)	2000	- National organization which supports New Zealanders living with rare diseases and their families.
Lysosomal Disease New Zealand (LDNZ)	2000	- A charitable trust dedicated to improve contact between families affected by LSDs within NZ, and supporting research into the causes and treatment of LSDs and improvements in the clinical care of affected people.
Syndromes Without a Name (SWAN)	2016	- Support group for NZ patients and families affected by an undiagnosed genetic condition. - Launched by NZORD.
Pharmaceutical Management Agency (PHARMAC)	1993	- Entity which decides on behalf of District Health Boards, which medicines and pharmaceutical products are subsidized for use in the community and public hospitals.
AFT Pharmaceuticals	1997	- Pharma company focuses on developing and distributing a range of medical treatments, advocate access to treatment including those for rare diseases.
One Percent Collective	2011	- Subscription-based model encourages individuals and businesses to donate at least 1% of their income to charity. - Focused on fostering a culture of giving and supporting a variety of causes, including rare diseases and other health-related issues, environmental sustainability, education, and social welfare.
MPS Society New Zealand	1974	- Non-profit organization dedicated to acting as a support group for families affected by mucopolysaccharidoses (MPS), mucolipidoses (ML) and other related disorders - Increasing professional and public awareness; and raising funds to further research into such disorders.

Cystic Fibrosis New Zealand (CFNZ)	1968	- Non-profit dedicated to supporting and improving the quality of life for people with Cystic fibrosis and their families. - Raising awareness, financial support, research innovation and advocacy for improved healthcare services
Muscular Dystrophy New Zealand (MDANZ)	1950	- Non-profit support people with muscular dystrophy and their families, including practical support, counseling, and referrals to specialists and healthcare services.
IDFNZ and the Kids Foundation	1989	- Dedicated to providing New Zealand families struggling with chronic illness relating to Primary Immune Deficiency (PID) - Provide financial and emotional support, raising awareness, and advocating for better access to healthcare and treatment options.
Friedreich Ataxia Research Association NZ (FARA NZ)	2014	- Dedicated to advocating for and supporting individuals with Friedreich Ataxia, aiming to provide the best care, treatment, and quality of life.

Table 13. Key stakeholders in the area of rare diseases in New Zealand

Abbreviation: NZ = New Zealand, LSDs = Lysosomal diseases

5.11 Australia

5.11.1 Rare Disease Landscape in Australia

In Australia, a disease is considered rare if it affects fewer than 5 in 10,000 people. Despite their individual rarity, rare diseases present a significant public health challenge, affecting about 8% of the population, or roughly two million [228]. These conditions are frequently life-threatening or debilitating, with common obstacles such as delays in accurate diagnosis, limited care and support, and insufficient research, despite acknowledged gaps in knowledge. In the 2022–23 period, Australia allocated an estimated USD $252.5 billion for health goods and services, averaging USD $9,597 per person, which accounted for 9.9% of the nation's gross domestic product (GDP) [229]. However, despite this substantial healthcare expenditure, 15% of healthcare costs are borne directly by individuals, creating a significant financial strain on those living with rare diseases and their families [220]This financial burden includes out-of-pocket expenses for care and support, as well as income loss associated with caregiving duties, which exacerbates the difficulties faced by this population.

Affects fewer than 5 in 10,000 people

5.11.2 National Strategy Framework and Policy Shaping

National Plan and Legislation

- Rare Voices Australia (RVA) was established in 2012 following the "Awakening Australia to Rare Diseases" symposium in Fremantle, which highlighted the need for better support and policy for Australians living with rare diseases. RVA advocates for a National Strategic Action Plan to improve awareness, healthcare access, and research, aiming to address the unique challenges of rare disease patients. The organization works with stakeholders such as patients, healthcare providers, and policymakers to drive change in the healthcare system, ensuring rare diseases are recognized and supported. RVA also provides resources like the RARE Portal and RARE Helpline to offer information and assistance to those affected by rare conditions.
- In 2014, RVA undertook initiative and principles and objectives to progress a national plan were presented at the National Rare Disease Summit in 2015. The collaborative outcome of the Summit was a Communiqué to progress a National Rare Disease Plan that listed key principles and objectives. The Communiqué was subsequently endorsed by more than 170 organizations and individuals in the rare disease community and was key to RVA's advocacy for a coordinated national response to rare diseases.
- In June 2017, the themes of the Communiqué were further developed into the key advocacy and policy document, Call for a National Rare Disease Framework: 6 Strategic Priorities. This made the case for a nationally coordinated approach to effective rare diseases policy and was presented to the Minister for Health, the Hon Greg Hunt MP. This was critical in creating momentum in rare diseases policy reform, particularly around reforms to the Life Saving Drugs Program (LSDP); Medical Research Future Fund (MRFF) grant opportunities targeting rare diseases (Rare Cancers and Rare Diseases and Unmet Needs competitive grant program); and fee exemptions in relation to the Therapeutic Goods Administration (TGA) reforms to Orphan Drug Designation.
- The Australian Government has also made significant investments into genomics, a health technology with great potential for rare diseases. This was done through Australia's first National Health Genomics Policy Framework 2018–2021
- In November 2018, the Federal Minister for Health, the Hon Greg Hunt MP, announced, with bipartisan support, funding for RVA to collaboratively develop and deliver the Action Plan, the first nationally coordinated effort to address rare diseases in Australia. Collaborative work towards the development of the Action Plan began immediately at the 2018 National Rare Disease Summit, which brought all key stakeholders in the rare disease sector together, including rare disease organization leaders, clinicians, researchers, government and industry.

- In Febraury 2020, Australia initiated the National Strategic Action Plan for Rare Diseases representing the first nationally coordinated effort to address rare diseases. The Action Plan aligns with, and expands on, the Call for a National Rare Disease Framework: 6 Strategic Priorities, which was published by RVA in June 2017. Additionally, it aligns with the National Strategic Framework for Chronic Conditions, the National Aboriginal and Torres Strait Islander Health Plan 2013–2023 and the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases. Crucially, it also aligns with the Asia-Pacific Economic Cooperation (APEC) Action Plan on Rare Diseases. Covering a wide scope, the Action Plan is comparable to other international rare disease plans and strategies, including those in Europe, the United Kingdom (UK), Canada and the United States (US). The Action Plan is comprised of three core Pillars, with each Pillar outlining priorities, actions and implementation areas. The Pillars are: 1. Awareness and Education 2. Care and Support 3. Research and Data [230].

Programs and Initiatives

- Rare Cancers, Rare Diseases and Unmet Need Clinical Trials initiative: The Clinical Trials Activity initiative in Australia focuses on addressing the challenges faced by individuals with rare diseases, rare forms of cancer, and health conditions with unmet medical needs. Originally established to fund clinical trials exploring new drugs, devices, and treatments for these areas, the initiative continues under the support of the Medical Research Future Fund (MRFF). People living with rare diseases or cancers often encounter significant hurdles, including delays in receiving a diagnosis, limited treatment options, difficulties in accessing appropriate care, and poor health outcomes. Unlike common cancers, survival rates for rare cancers have not seen the same level of improvement. Additionally, for many patients with unmet medical needs, existing diagnostic and treatment options are insufficient, leaving critical gaps in their care. This initiative plays a vital role in fostering research to address these challenges. Its primary objectives include increasing the number of clinical trials conducted in Australia, developing innovative drugs, devices, and treatments, and providing more opportunities for patients to participate in clinical trials. A key focus is also on strengthening Australia's position as a preferred location for conducting clinical trials on a global scale. The initiative is funded through the MRFF, with the National Health and Medical Research Council (NHMRC) administering grants. It remains active, continuing to support research and clinical trials aimed at improving outcomes for individuals affected by rare diseases, rare cancers, and other serious health conditions where effective solutions are currently lacking [231].
- The Life Saving Drugs Program (LSDP) in Australia provides fully subsidized, life-saving medicines for patients with ultra-rare and life-threatening diseases. This program is separate from the Pharmaceutical Benefits Scheme (PBS), meaning LSDP medicines are not subject to PBS co-payments.

Instead, the Australian Government covers the entire cost of these medications, ensuring they are available at no charge to eligible patients. The LSDP supports medicines that meet specific criteria. These medicines must be clinically effective but not cost-effective enough to qualify for PBS listing. They must also treat ultra-rare conditions, defined as affecting fewer than 1 in 50,000 people in the Australian population. Pharmaceutical companies, referred to as sponsors, must apply for a listing under the LSDP for their medicines to be included. While the medicines themselves are fully subsidized, pharmacies may charge patients a fee for handling and cold transport, if required. Pharmacies are obligated to inform patients of these costs upfront and secure their agreement before dispensing the medicines. Importantly, pharmacies cannot impose any other co-payments or additional fees on LSDP medicines. The LSDP is a critical initiative ensuring that individuals with rare and life-threatening conditions can access vital treatments without financial burden [232]

- Procedure guidance for medicines funded through the Life Saving Drugs Program (LSDP): To be eligible for listing on the Life Saving Drugs Program (LSDP), medicines must meet specific criteria outlined in the LSDP Procedure Guidance. The medicine must be approved by the Therapeutic Goods Administration for treating an ultra-rare disease, defined as having a prevalence of 1:50,000 people or fewer in Australia, which is roughly 500 individuals. Additionally, treating physicians should be able to diagnose the disease with reasonable accuracy, and evidence must show that the disease reduces life expectancy. The guidance document includes detailed information on the application process, pricing, deeds of agreement, and treatment guidelines. Sponsors are required to submit their applications to the LSDP Expert Panel secretariat. The panel reviews each application and advises the Chief Medical Officer (CMO), who then makes the final decision on whether the medicine should be subsidized. When reviewing applications, the panel considers the proposed price of the medicine in comparison to similar medicines available in overseas markets and assesses whether the cost is reasonable compared to other medicines already subsidized under the LSDP. However, the program only covers the cost of the medicine itself, excluding transport, storage, administration fees, hospital or medical expenses, and other costs related to disease management [233].
- National Disability Insurance Scheme: It has been a lifesaver for many individuals with rare diseases, offering comprehensive support packages that include everything from early intervention to vocational assistance[234]

5.11.3 Funding and Financial Support

- The Australian Government is committed to promoting health and medical research, recognizing its essential role in developing a world-class health system. Through the Medical Research Future Fund

(MRFF), the government provides funding to improve health outcomes, enhance quality of life, and support the sustainability of the healthcare system. Under the 2nd MRFF 10-Year Plan, introduced in the 2022-23 Budget, $750 million has been dedicated over ten years to the Clinical Trials Activity Initiative. This initiative focuses on three key areas: Rare Cancers, Rare Diseases, and Unmet Need (RCRDUN); International Clinical Trials Collaborations; and Effective Health Interventions. The RCRDUN grants specifically target clinical trials exploring new treatments, devices, or medications for rare diseases, rare cancers, or areas with unmet medical needs, addressing significant gaps in healthcare.

- In addition, the MRFF Genomics Health Futures Mission represents a groundbreaking investment in precision medicine. With $500 million allocated over a decade (2018-19 to 2027-28), this mission drives genomics research, enabling the development of personalized, targeted treatments and transforming healthcare in Australia.
- Additionally, a structured framework has been implemented to transform research opportunities identified through Health Technology Assessment (HTA) into competitive grant opportunities supported by the MRFF. A total of $100 million has been allocated for this research over a ten-year period, from 2022-23 to 2031-32.
- The Australian Government has also approved an annual horizon scanning forum, organized by Medicines Australia, involving stakeholders from the innovator medicines sector. This forum aims to identify significant therapeutic advancements expected to enter regulatory and/or reimbursement systems.
- The National Strategic Action Plan for Rare Diseases provides a framework to guide key priorities and goals for Australians living with rare diseases, as well as their families and carers. To support these objectives, the Australian Government has allocated $3.3 million over three years (2020-21 to 2022-23) for initiatives aimed at raising awareness and providing education about rare diseases. This funding supports the development and delivery of educational resources for healthcare professionals and activities to assist individuals living with rare diseases.
- Additionally, the government has committed $28.1 million through to 2026 to establish a new national body that will shape the future of genomic health and medicine in Australia. This investment aims to advance genomic research and innovation, ensuring its integration into healthcare delivery to improve outcomes for patients with rare and complex conditions over the coming decade [235].
- A national single-payer funding system, Medicare serves as the publicly funded universal health insurance scheme in Australia, supplemented by the Pharmaceutical Benefits Scheme (PBS), which aids in covering expenses for certain medications and treatments. Accordingly, Australia established the LSDP in 1995 as a complementary initiative to the PBS. The LSDP aims to broaden access to high-

cost drugs intended for treating rare diseases, acknowledging the unique challenges posed by such medications within the healthcare landscape. As of 2023, 17 medicines are subsidised via the LSDP.

- In 2022, Zolgensma® was approved for SMA by listing under the PBS, saving approximately 20 patients AUS$ 2.5 million (USD $1.6 million)[236]. In the following year, the scheme was expanded to include pre-symptomatic babies as well, thus extending the subsidy to an additional 15 babies. An outcome-based risk sharing agreement was also established, which encompassed an unspecified rebate on the cost over at least 5 years, following circumstances of a patient's death and the failure to meet certain developmental milestones

5.11.4 Regulatory and Market Access

- Australia's Orphan Drug Program, established by the Therapeutic Goods Administration (TGA) in 1997, aims to facilitate the development and market access of treatments for rare diseases that would otherwise be commercially unviable due to the small patient population. The program addresses the high costs of drug development and marketing, offering incentives to manufacturers to ensure that patients with rare diseases have access to necessary treatments.
- Key features of the orphan drug policy include a legal framework for orphan drug designation, waivers of application and annual registration fees, and a 5-year exclusivity period for approved drugs. The program underwent significant reforms in 2017, with the rare disease prevalence threshold expanded from fewer than 2,000 individuals in Australia to fewer than 5 in 10,000 individuals. However, the validity of orphan drug designation was shortened from the product's lifetime to six months post-approval, with the option to extend for another six months.
- One of the key financial incentives for sponsors is the waiver of TGA evaluation and registration fees, which are substantial—$217,598 for a new chemical entity and $129,091 for an extension of indication in the 2023/24 financial year. Additionally, sponsors can receive a fee waiver for their first Health Technology Assessment (HTA) submission to the Pharmaceutical Benefits Advisory Committee (PBAC) for reimbursement under the Pharmaceutical Benefits Scheme (PBS) or the Life Saving Drugs Program (LSDP). This waiver covers fees ranging from $197,930 to $252,540, depending on the submission category [237].
- The designation process, governed by regulation 16J of the Therapeutic Goods Regulations 1990, determines whether a medicine qualifies for orphan drug status. This status is granted to new treatments for rare diseases and is part of a program that waives application fees to help offset the costs of developing orphan drugs. The program aims to facilitate faster access to the Australian marketplace for these medicines, ensuring they reach the patients who need them. By providing a consistent and

transparent process for assessment against eligibility criteria, the program supports the development of therapies for conditions that affect small patient populations [238]

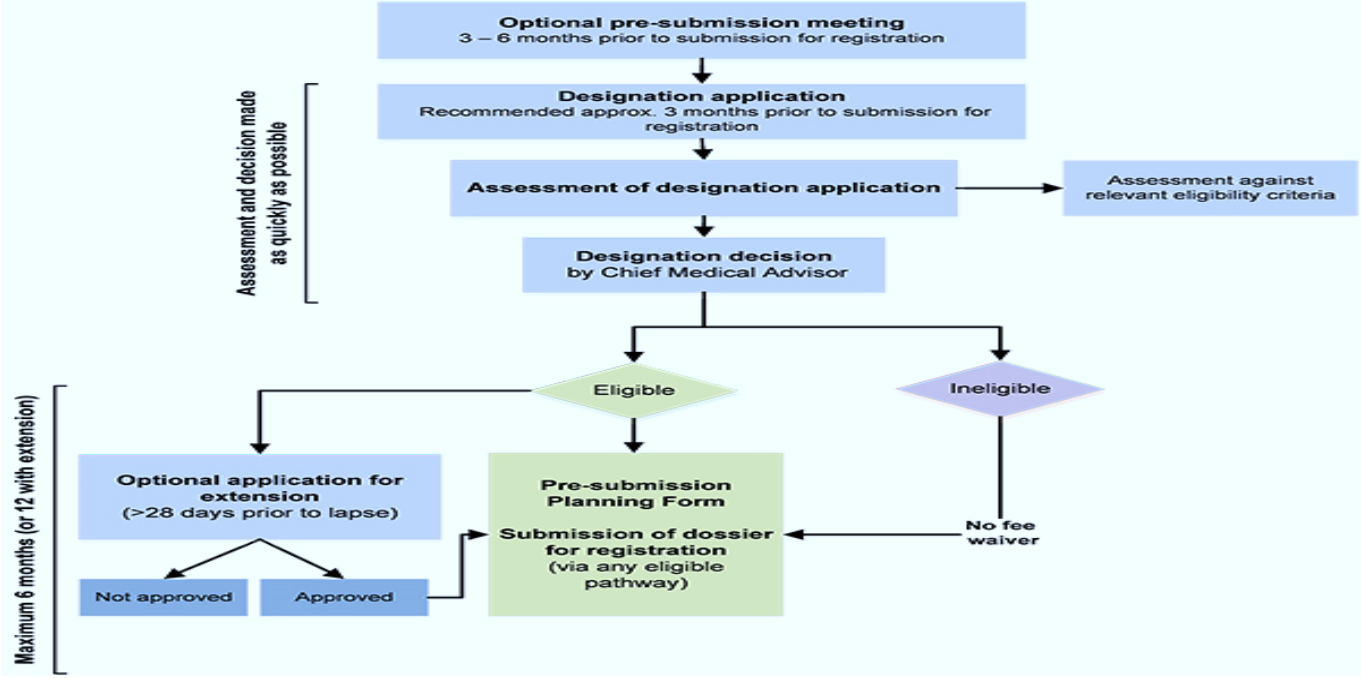


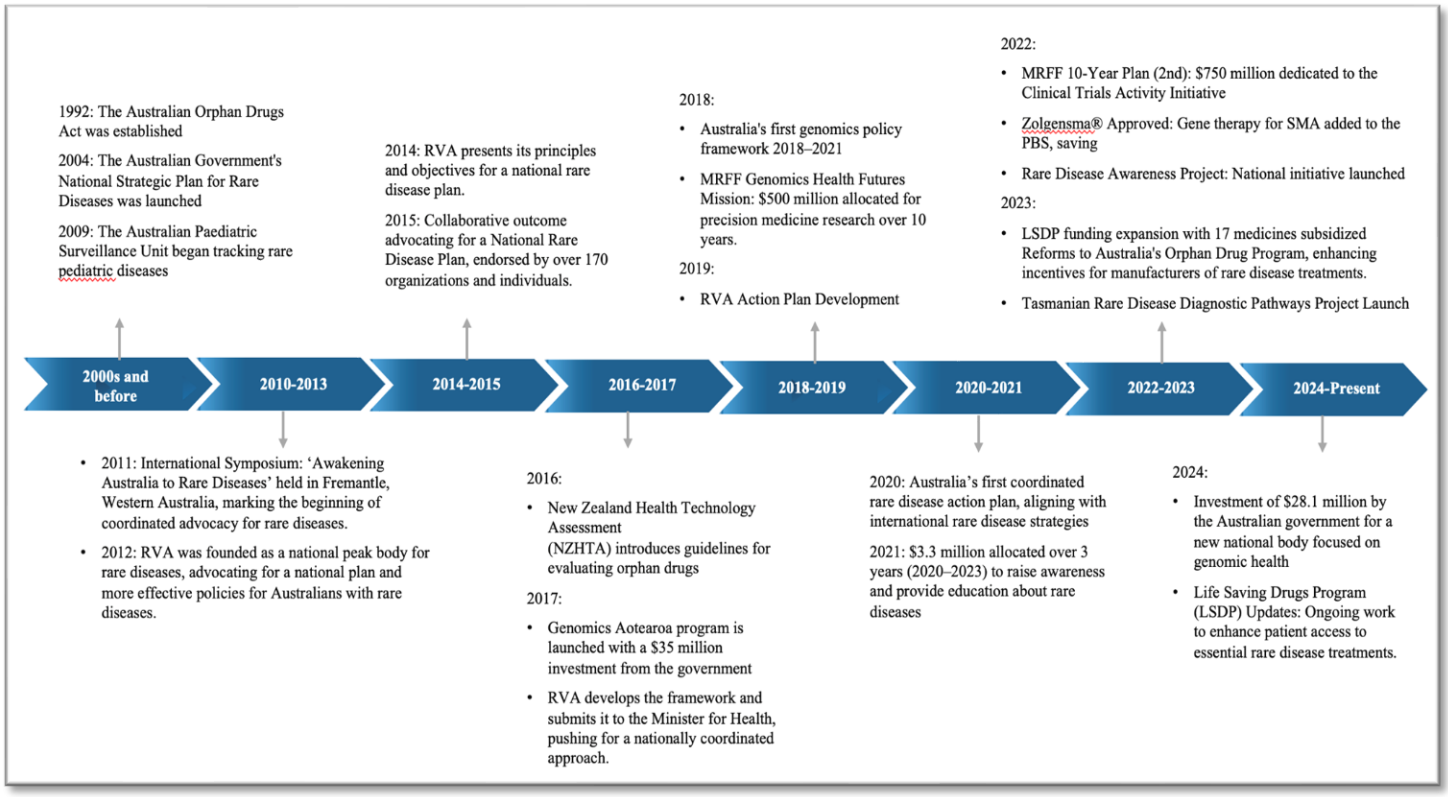
Figure 12: The image shows a flowchart depicting the process for submitting an application for registration, with various steps and decision points [502].

5.11.5 Care Pathways and Infrastructure

- The Western Australian Undiagnosed Diseases Program (UDP-WA) was launched in March 2016 as a collaborative effort between clinicians from Genetic Services WA and policymakers from the Office of Population Health Genomics. Established as a clinical service program within the WA public health system, the UDP-WA was designed to enhance existing genomic diagnostic workflows and multidisciplinary clinic services. The program specifically targets paediatric patients and those transitioning from paediatric to adult care, addressing the unique challenges faced by these age groups. By focusing on undiagnosed diseases, the UDP-WA aims to improve diagnostic accuracy and provide better care pathways for individuals with rare and complex conditions [239]
- The Tasmanian Rare Disease Diagnostic Pathways Project was launched to address challenges in diagnosing rare diseases, which affect 6–8% of Australians, including 35,000–45,000 Tasmanians, with 80% being genetic. These conditions contribute to 20% of Tasmania's hospital costs, worsened by delays, misdiagnoses, and gaps in rural care. Funded by Australian Genomics, the project aims to map diagnostic pathways, identify barriers, understand community needs, and develop innovative models to improve access to genetic testing, expert care, and efficient rare disease diagnosis in Tasmania [240].

- The Rare Disease Awareness Education Support and Training (RArEST) Project, to improve awareness, knowledge, clinical care and support for people living with a rare disease. HealthCare professionals can effectively collaborate with the rare disease community by adhering to the clinical practice guidance outlined in the National Recommendations for Rare Disease Health Care, which aims to enhance the quality of clinical care. Additionally, generating robust data and evidence is crucial for improving best practices in care and treatment, ensuring better outcomes for individuals living with rare diseases [241].

Figure 13. Shows the timeline of the rare diseases progress in Australia



Abbreviation: RD= Rare disease, LSDP= Life-saving drugs program, RVA= Rare voice Australia

5.11.6 Key Organizations Advancing Rare Disease Initiatives in Australia

Organization Name	Established Year	Description
Rare Voices Australia (RVA)	2012	RVA is an advocacy, education, public awareness group.
Australian Pompe's Association	1997	Supports the needs of Australian Pompe patients, families and carers.
Genetic Alliance Australia	1988	Charity for peer support group and connects other families. Educational resources and counselling services.
Centre for Genetics Education	-	Provides education information and resources. Information about newborn screening and genetic testing. List of genetic services and counselling.
Steve Waugh Foundation	2005	Grant support for children and families suffering with RDs. Fundraising and networking events.
Australian Paediatric Surveillance Unit (APSU)	1993	Responsible for active surveillance of uncommon, rare childhood diseases, complications and adverse effects of treatment.
HCU Network Australia	2014	Health Promotion Charity aim is to improve individual outcomes through education, research and support.

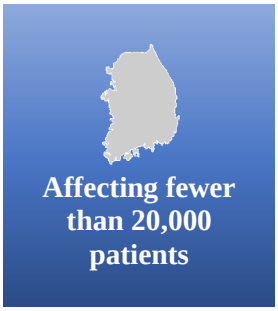
Australian Genomics	2016	Help bridge the gap between basic genomic research and its clinical application by building the evidence to inform national health policy as genomic medicine becomes standard of care in Australia.
Genetic Support Network of Victoria (GSNV)	1997	Committed to long-term sustainability and value of support strategies and systems including genetic, undiagnosed and rare disease patient support groups. Collaborative effort by Genetic Support Network Victoria (GSNV), Genetic Alliance Australia (GAA), and Syndromes Without A Name (SWAN) Australia, GUARD focuses on a unified approach to genetic, undiagnosed, and rare diseases
Cystic Fibrosis Australia (CFA)	1971	National organization aimed at raising awareness and education of cystic fibrosis through advocacy and research
Leukaemia Foundation	1975	National charity dedicated to helping people diagnosed with leukemia, lymphoma, myeloma, and related blood disorders.
MS Australia	1956	Non-profit organization conducting research and advocacy in support of individuals affected by Multiple Sclerosis (MS).
SWAN Australia (Syndromes Without A Name)	2012	National organization providing information, support, connection and advocacy to families caring for a child with an undiagnosed or rare genetic condition.
Rare Cancers Australia (RCA)	2012	Focuses on raising awareness, advocating for patients' rights, funding research, and providing support to individuals and families affected by rare cancers. Aims to improve access to treatments, healthcare services, and resources for those impacted by rare cancer types.
Lysosomal Diseases Australia (LDA)	2010	National umbrella organization formed to represent the interests of people effected by lysosomal storage disorders including their families and carers, to maximize resources available for support services, treatment and research.
Cure for MND Foundation	2014	Dedicated to raising funds for research aimed at finding a cure for motor neuron disease (MND) Provides support services for individuals affected by MND, helping them access equipment and care. Increasing awareness of MND and advocates for advancements in research and treatment options for the disease.
Rare Voices Australia (RVA)	2012	Advocacy on behalf of the Rare Disease Community Awareness raising campaigns
Rare Voices Australia (RVA)	2012	Advocacy on behalf of the Rare Disease Community Awareness raising campaigns
Australian Pompe's Association	1997	Supports the needs of Australian Pompe patients, families and carers.
Genetic Alliance Australia	1988	Peer support and linkage with other families Educational resources and opportunities Group and individual counselling services
Centre for Genetics Education	1989	Educational resources for families, including disease fact sheets, pamphlets and other publications Information regarding newborn screening and genetic testing List of genetic services List of genetic counselling services
Steve Waugh Foundation	2005	Grant support for children and families living with rare diseases Fundraising and networking events The SNUG (Special Needs Unlimited Group) program provides retreats for families caring for a child with a rare health condition- Fundraising and networking events
Australian Paediatric Surveillance Unit (APSU)	1993	Responsible for active surveillance of uncommon rare childhood diseases, complications and adverse effects of treatment.
Variety – The Children's Charity	1975	Equipment, medical assistance, and supporting children in educational, sporting, or artistic endeavours and experiences

Table 14. Key organizations in the area of rare diseases in Australia

5.12 South Korea

5.12.1 Rare Disease Landscape in South Korea

In South Korea, rare diseases are defined as conditions affecting fewer than 20,000 patients or diseases with undetermined prevalence due to diagnostic challenges. To address the needs of these patients, South Korea introduced legislation regarding orphan drugs in 2003, followed by the Rare Disease Management Act in 2016. 1,248 diseases are recognized as rare in Korea [242]. According to the 2019 Annual Report on Rare Disease Patients in Korea by the Korea Disease Control and Prevention Agency, 55,499 patients were diagnosed with 636 different rare diseases. Of these, 47.1% were male and 52.9% female[243]



South Korea's healthcare expenditure has grown steadily, reaching USD 135 billion in 2021, with a per capita health expenditure of USD 4,190, accounting for approximately 9.3% of the country's GDP. However, the limited coverage provided by the National Health Insurance system has led to a significant

rise in private healthcare spending, which now accounts for 40% of total health expenditures. The growing burden of rare diseases on families, coupled with insufficient resources, limited information, and inadequate funding, continues to pose a major challenge for the South Korean healthcare system [244]

5.12.2 National Strategy Framework and Policy Shaping

National Plan and Legislation

- Rare Disease Management Act 2015: The Rare Disease Management Act, established in South Korea in 2015, aims to alleviate the individual and societal burden associated with rare diseases while improving public health and welfare. The Act provides a framework for comprehensive policies addressing various aspects of rare disease management, including prevention, diagnosis, treatment, and research. It emphasizes the importance of ensuring access to adequate medical services for individuals affected by rare diseases and mandates efforts by both the state and local governments to support these initiatives. To foster awareness and enhance public understanding of rare diseases, the Act designates May 23 each year as Rare Disease Day. This annual observance serves as a platform to encourage societal engagement and reinforce the commitment to preventing, treating, and managing rare diseases. Recognizing the need for long-term planning, the Act requires the Minister of Health and Welfare to develop a comprehensive rare disease management plan every five years. These plans focus on promoting projects related to research, medical technology development, and supportive measures essential for rare disease management.
- To further streamline efforts in addressing rare diseases, the Act stipulates the establishment of a rare disease support center within the Korea Centers for Disease Control and Prevention. This center serves as a hub for research, resource allocation, and strategic planning, ensuring a coordinated approach to addressing the challenges posed by rare diseases. Through these provisions, the Rare Disease Management Act underscores South Korea's commitment to reducing the burden of rare diseases and improving the quality of life for affected individuals [245]

Programs and Initiatives

- Korean Undiagnosed Rare Disease Diagnosis Research Program: Seoul National University Hospital’s Centre for Rare Diseases, designated by the Ministry of Health and Welfare in 2017, leads the Korean Undiagnosed Rare Disease Diagnosis Research Program (K-UDP). This program helps patients with unexplained conditions by conducting advanced clinical and family trio genetic tests to identify causes and develop treatment plans. Once diagnosed, patients are referred to regional rare disease centres for long-term follow-up care [246]

- Comprehensive Rare Disease Management Plan: A specialized insurance program now covers 90% of medical expenses, requiring patients to pay only 10%. Additionally, a genetic diagnosis support program assists those suspected of having ultra-rare diseases. To enhance medical services and enable earlier diagnoses, South Korea implemented the 1st Comprehensive Rare Disease Management Plan (2017–2021), followed by the 2nd Comprehensive Plan (2022–2026), which is currently in progress [247]
- Rare Disease Program for Pediatric Cancer: The initiative seeks to advance global healthcare and improve the quality of life for paediatric patients with rare diseases through research-driven diagnosis and treatment. A key objective is to establish a robust genomic research infrastructure to facilitate the identification and diagnosis of newly discovered or previously undiagnosed rare diseases. Additionally, the program aims to develop and apply therapeutic substances by leveraging mechanistic research in basic life sciences. By building and disseminating standardized clinical genomic databases, the initiative contributes to the advancement of precision medicine. Furthermore, it emphasizes the training of specialists in rare paediatric diseases, ensuring the continued development of expertise in this critical area of healthcare [248]
- Korean Undiagnosed Diseases Program (KUDP): The Korean Undiagnosed Diseases Program (KUDP) was launched as a pilot project in 2017 to support undiagnosed patients and initiate RD research. aimed to solve the problem of undiagnosed patients throughout the country and develop infrastructure, including a data management system and functional core laboratory, for long-term translational research [249]
- South Korea's Rare Disease Medical Expenses Support Program: South Korea's Rare Disease Medical Expenses Support Program seeks to ease the financial strain on low-income families by covering copayments for individuals with rare diseases who meet designated income and property requirements under the special health insurance co-payment system. In 2025, the program expanded its coverage to 1,338 rare diseases, an increase of 66 conditions from 2024. The income eligibility criteria were broadened to support more families, particularly paediatric patients, by raising the threshold to 130% of the median income. The program also streamlined its application process by accepting medical certificates that mention a rare disease, whether listed as a primary or secondary diagnosis [250]
- Korean Genetic Diagnosis Program for Rare Disease: Started in 2013, the Korean Genome Diagnosis Project (KGDP) in its first phase supported the genetic diagnosis of 18 rare diseases. With the commencement of phase two in 2017, it expanded to provide diagnostic services for ultra-rare diseases. KGDP operates through 51 clinical sites across the country and works closely with the Korean Undiagnosed Diseases Program to offer comprehensive analysis of undiagnosed cases. By 2023, it had diagnosed 629 positive patients, identifying 297 genes [251]

5.12.3 Funding and Financial Support

- The National Health Insurance Service (NHIS), managed by the Ministry of Health and Welfare, operates as a single-payer system in which individuals with sufficient income contribute to their own insurance coverage. Participation in NHIS is mandatory for all hospitals and clinics. Currently, South Korea does not have a dedicated fund for rare disease medications, though certain conditions and treatments are covered under NHIS [252] .For hospitalization, rare disease and cancer patients have a reduced copayment rate of 10 %, compared to the standard 20% required for other patients [253]
- Rare Disease Subsidy Project: The Republic of Korea initiated the Rare Disease Subsidy Project to financially assist low-income patients through a national fund-holding system. In 2021, 1,086 rare diseases and 24 severe intractable diseases qualified for support. Applicants must renew enrollment biennially after income and property assessments. That year, Moyamoya disease had the most beneficiaries, while Hurler syndrome received the highest average financial aid [254]

5.12.4 Regulation and Market access

- The market entry of orphan drugs in South Korea follows a structured process governed by the Korea Ministry of Food and Drug Safety (MFDS), which sets criteria for designation, regulatory approvals, pricing, and reimbursement mechanisms. To qualify as an orphan drug, a medication must either treat a disease affecting 20,000 or fewer patients or provide a treatment option where no adequate alternatives exist. Additionally, drugs that significantly improve safety or efficacy compared to existing treatments can also be designated as orphan drugs. If a drug is still in the clinical or non-clinical trial stage and intended for a disease with fewer than 20,000 patients, it can be classified as an under-development OD receiving regulatory support in the form of clinical trial documentation, patient recruitment, and facilitation of international trials.
- South Korea provides regulatory incentives to accelerate the approval process for orphan drugs. These drugs may receive priority approval over non-orphan drugs, ensuring faster market entry. Once approved, they benefit from an extended validity period of ten years, twice the standard five-year period granted to non-orphan drugs. Market exclusivity is also extended to ten years, compared to the four- to six-year period for regular drugs. Additionally, if an orphan drug receives approval for paediatric indications, it is eligible for a one-year extension of its exclusivity period.
- Pricing and reimbursement decisions for orphan drugs in South Korea follow the Health Technology Assessment (HTA) framework, which evaluates new drugs based on the availability of alternatives. When an alternative treatment exists, decisions on pricing and reimbursement are based on

pharmacoeconomic (PE) studies or a weighted average price (WAP) model. However, if no alternative treatment is available, the drug undergoes one of three specialized review pathways: designation as an Essential Drug (ED), a Pharmacoeconomic Study Waiver (PEW), or inclusion in a Risk Sharing Agreement (RSA). The final reimbursable price is determined through negotiations between the National Health Insurance Service (NHIS) and the Health Insurance Review and Assessment Service (HIRA), ensuring that the financial impact on the healthcare system is considered.

- Under the South Korean National Health Insurance (NHI) system, patients diagnosed with specific rare diseases benefit from reduced copayment rates. While general patients are required to pay between 20% and 60% of treatment costs, rare disease patients only bear a 10% copayment for inpatient care, significantly reducing their financial burden.
- To assess the cost-effectiveness of orphan drugs, South Korea employs an incremental cost-effectiveness ratio (ICER) threshold set at one gross domestic product (GDP) per capita, equivalent to $22,727 per quality-adjusted life year (QALY). However, for innovative treatments that address severe diseases and carry significant social impact, the threshold can be increased to two times the GDP per capita, amounting to $45,454 per QALY. This flexible approach allows greater access to groundbreaking treatments while maintaining cost-effectiveness within the healthcare system [255]

Pathway	Criteria	Notes
When no alternatives		
Essential Drug	• No alternatives • Treat life threatening conditions • Treat small patient groups • Significant improvement in clinical efficacy or patient survival	*Life threatening*- 2 years or less of life expectancy Unclear definition of small groups
Risk Sharing Agreement	• No alternatives • Anticancer agent or serious life-threatening diseases • Should be approved via drug review committee on severity, social and ethical influences	*Refund based* RSA most used (mandatory PE evidence) *Contract term*- 4 years can't be extended if alternatives exist. *No expansion* of indications for P&R
Pharmacoeconomic evaluation exemption	• Rare disease and rare cancers • Clinically effective proven by single arm RCT or phase -II trial. • Drugs to be listed in at least three of A7 countries	*Expenditure cap RSA*- with the pharmaceutical sector *Price*- based on lowest adjusted list price from A7 countries.
Price negotiation waiver	• If pharmaceutical companies accept the weighted average price, it is allowed to pass the negotiation	-

Figure 13: Image: Criteria for P&R pathway for drug with no alternative [256]

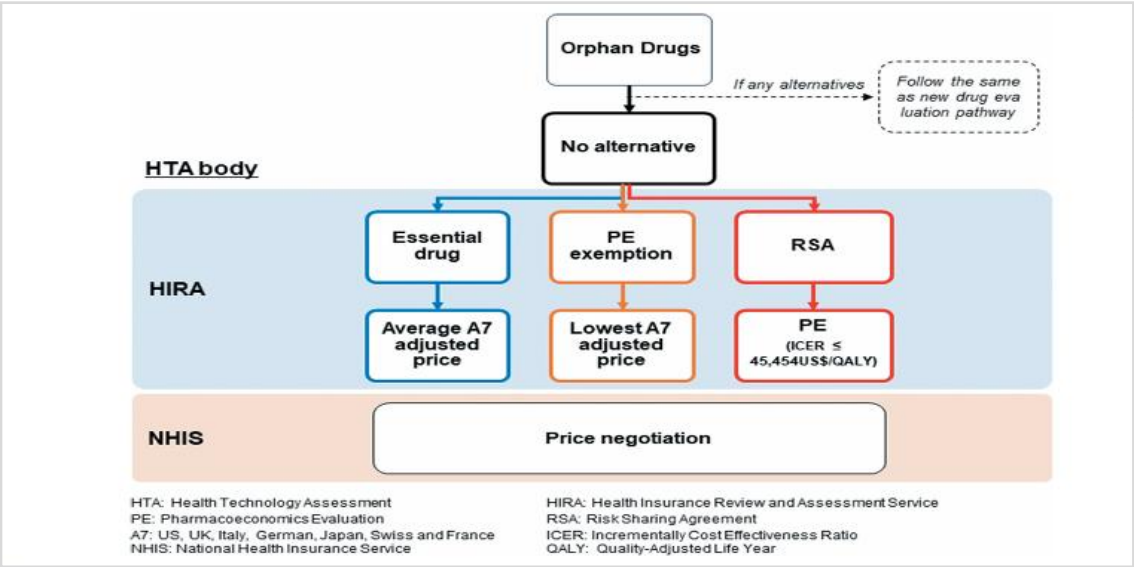
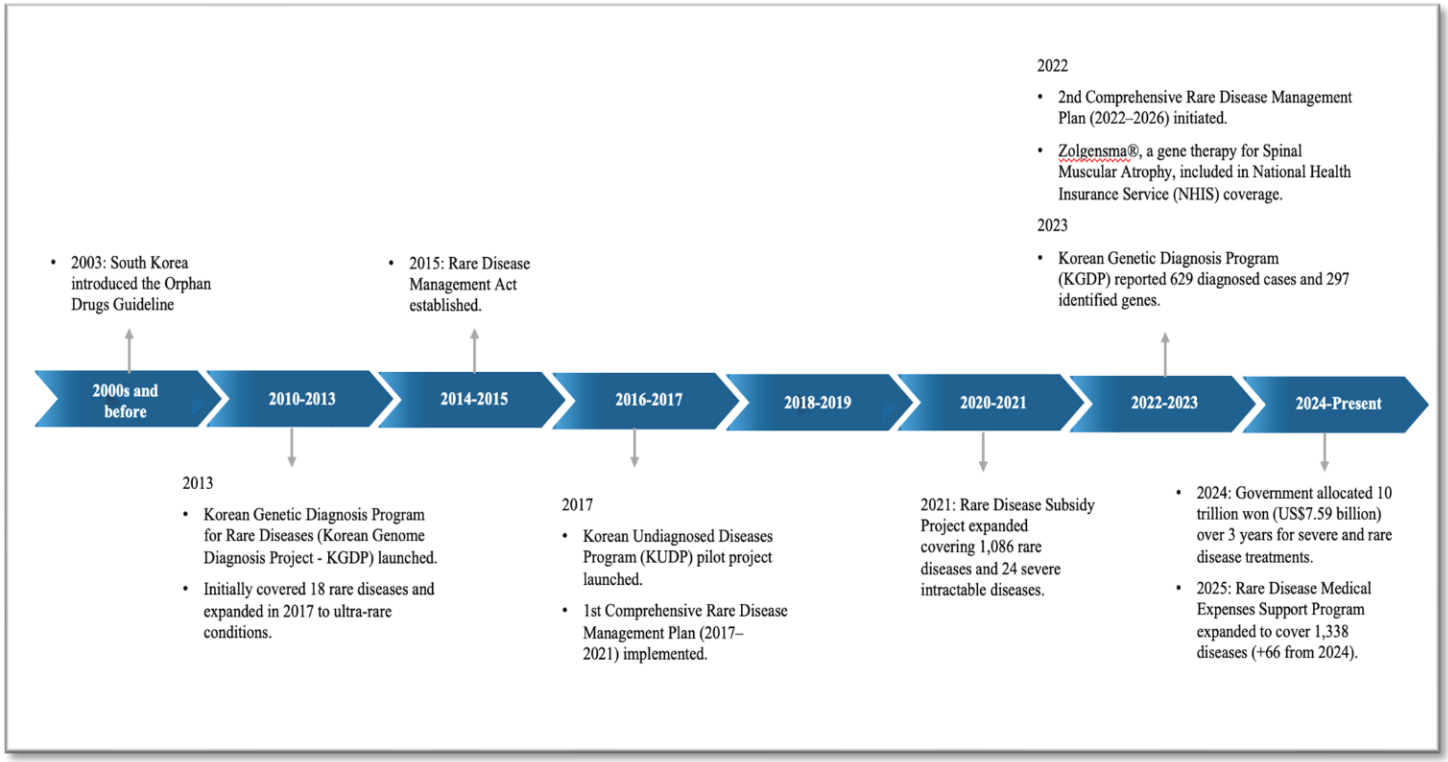


Figure 14: Evaluation pathway for the reimbursement of new orphan drugs in the South Korean national health insurance service.[255]

5.12.5 Care Pathways and Infrastructure

- Rare and Incurable Diseases Patient Support System: Due to limited awareness and challenges in diagnosing rare diseases, patients often face difficulties in accessing proper treatment. To address this, the Republic of Korea government established the Rare and Incurable Diseases Patient Support System, which aims to alleviate patient suffering and provide the necessary assistance [257]
- Korea Orphan and Essential Drug Center: The Korea Orphan Drug Center (KODC) serves as a critical component of South Korea's healthcare system, ensuring access to essential medications for patients with rare diseases. By securing and distributing orphan drugs, KODC addresses supply shortages and facilitates timely treatment. Additionally, it strengthens collaboration between pharmaceutical manufacturers and healthcare providers, optimizing drug availability. Beyond individual patient care, KODC enhances public health by maintaining emergency stockpiles and reinforcing pharmaceutical stability. Through these efforts, KODC plays a fundamental role in improving treatment accessibility of medicine for rare diseases and wellbeing of the patients [258]

Figure 15. Shows the timeline of the rare diseases progress in South Korea



Abbreviation: NBS = Newborn Screening, RA = Republic act, RDMAP = Rare disease medicine access program, DoH = Department of health, UP NIH = University of the Philippines national institute of health.

5.12.6 Key Organizations Advancing Rare Disease Initiatives in South Korea

Organization Name	Established Year	Description
Korean Organization for Rare Disorders (KORD)	2001	- Social welfare organization which promotes rights and welfare of RD patients - Shares information with RD community about national policy development and overseas programs
Korea Hemophilia Foundation (한국혈우재단)	1991	- Supports and educates patients to get correct treatment - Develop their quality of life
ALS (amyotrophic lateral sclerosis, 근위축성 측색 경화증) Association (루게릭 협회)	2001	- Educates and supports patients financially - Provides inputs and assists on policies formulation by communicating with government - Encourages communication with doctors for better research and for access to novel treatments
Korea Haemophilia Foundation	1991	- Supports and educates patients to get correct treatment - Develop their quality of life
ALS (amyotrophic lateral sclerosis-Association	2001	- Educates and supports patients financially - Provides inputs and assists on policies formulation by communicating with government - Encourages communication with doctors for better research and for access to novel treatments
Korean Rare and Incurable Disease Association	-	- Provide direct assistance to patients and their families - Effort to improving positive social awareness - Policy Advocacy-Developing laws and systems to protect and support those with rare and incurable diseases.
Rare Genomics Korea (RG Korea)	2011	- Offering support to individuals with rare diseases. - Assists patients and families in raising funds and creating personalized research projects based on genome sequencing

Table 15. Key organizations in the area of rare diseases in South Korea

5.13 Taiwan

5.13.1 Rare Disease Landscape in Taiwan

Taiwan has become the fifth nation in the world to enact legislation protecting rare disease patients through the introduction of the Rare Disease and Orphan Drug Act. This landmark law provides legal, social, and financial protection to rare disease patients, establishing a comprehensive care model. As defined by the Act, a rare disease is one with a prevalence rate lower than 1 in 10,000 individuals[259] [260]. According to the current public notice. By 2024, the Ministry of Health and Welfare has recognized 246 rare diseases and registered 22,059 rare disease patients, with Taiwan offering 140 kinds of orphan drugs for their treatment [261]. Taiwan's approach to rare disease care and treatment has become a global model, incorporating the enforcement of rare disease prevention laws, medical subsidies for rare diseases, and orphan drug research and development. However, despite these advancements, Taiwan still faces challenges such as low awareness, delays in diagnosis and treatment, and limited drug options and effectiveness[262].

Taiwan has made significant progress in rare disease management, becoming one of the leading countries in Asia with a well-structured policy framework. With a strong healthcare system and government support, Taiwan provides rare disease patients with better access to diagnosis, treatment, and financial assistance compared to many other countries in the region.

5.13.2 National Strategy Framework and Policy Shaping

National Plan and Legislation

- Taiwan promulgated the Rare Diseases and Orphan Drug Act on February 9, 2000, to strengthen the prevention, diagnosis, and treatment of rare diseases. The Act aims to facilitate patient access to essential drugs and special nutritional foods critical for sustaining life. It mandates the central, county, and municipal governments to ensure effective implementation and establishes the Review Committee for Rare Diseases and Orphan Drugs to oversee the designation and registration of rare diseases, the approval and marketing of orphan drugs, and the provision of subsidies to support drug development. Furthermore, by classifying rare diseases as notifiable conditions, the Act ensures that the central competent authority provides patients with comprehensive consultation and psychosocial support services.

Programs and Initiatives

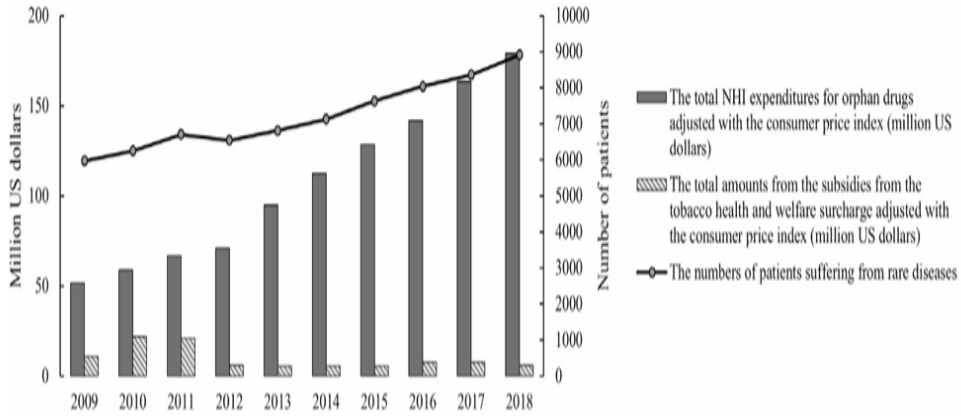
- Paediatric and Rare Diseases Priority Review Voucher Program: In 2019, the Taiwan Food and Drug Administration (TFDA) launched the PRD Priority Review Voucher Program to accelerate the evaluation of innovative drugs aimed at addressing unmet medical needs, particularly for serious paediatric conditions or critical diseases with a prevalence of fewer than five cases per 10,000 people. This program offers a significant advantage by shortening the review period for new drug applications (NDA) to 240 days, compared to the standard 360-day timeline. Between 2020 and 2023, 49 drugs applied for PRD designation, with the majority targeting rare diseases (90%), followed by paediatric diseases (6%), and a combination of both (4%) [263].
- Regulations on Medical Subsidization for Rare Diseases: Under this regulation, patients with rare diseases can apply for subsidies to cover medical expenses that are not included under other grants. These subsidies encompass costs related to diagnostics, treatment, medications, and specialized nutritional foods essential for sustaining life. Additionally, they cover laboratory fees, nutritional counselling, and laboratory testing for diagnosing relatives of patients with rare diseases [264]

5.13.3 Funding and Financial Support

- Taiwan's National Health Insurance (NHI) covers nearly 99% of the population and provides comprehensive coverage for prescription medications, as well as inpatient and outpatient medical services. Between 2003 and 2014, total health expenditures for rare disease treatment increased

significantly from USD 18.65 million to USD 137.44 million, accounting for approximately 0.68% of Taiwan's total health expenditure in 2014. Drug expenditures for rare diseases also saw a sharp rise, growing from USD 13 million in 2003 to USD 121.98 million in 2014, representing 71% and 88.75% of total rare disease health expenditures for those respective years [265].

- To further support patients, the National Health Insurance Administration (NHIA) established a special rare disease fund in 2005. By 2020, a total of 12,524 rare disease patients held a catastrophic illness card, allowing them access to essential healthcare support. As the demand for rare disease treatment continues to grow, the allocated fund has increased over the years, reaching NT$8.775 billion in 2022 [266].



5.13.4 Regulation and Market access

- The following regulations fall under the Rare Disease and Orphan Drug Act and govern the entry, research, manufacturing, supply, and subsidy provisions related to orphan drugs in Taiwan: The Rules Governing the Awards for Orphan Drug Research provide incentives to encourage research on orphan drugs. The Enforcement Rules of the Rare Diseases and Orphan Drugs Act outline the procedures for implementing the Act. The Rules Governing the Awards for Orphan Drug Research, Manufacturing, and Supply extend incentives to drug manufacturing and supply. The Regulations for Registration of Orphan Drugs set the criteria for official orphan drug registration. The Rules Governing Orphan Drugs Import Application regulate the process for importing orphan drugs. The Regulations on Medical Subsidization for Rare Diseases establish financial support mechanisms for patients with rare diseases.
- Process of Orphan Drug Registration: The process of orphan drug registration in Taiwan is governed by the Rare Disease and Orphan Drug Act and follows a structured multi-stage evaluation by the Health Promotion Administration (HPA) and the Taiwan Food and Drug Administration (TFDA). The first

stage involves the designation of a disease as rare, which is determined by the Review Committee (Medical) under the HPA. The committee evaluates diseases based on criteria such as rarity, hereditary nature, and diagnostic and treatment challenges. However, diseases caused by human factors, acquired conditions, and cancer-related illnesses are excluded from this classification. If a disease meets the required criteria, it is officially designated as a Rare Disease, allowing for further regulatory processes to begin.

- Following the rare disease designation, pharmaceutical companies can apply for orphan drug designation, which is reviewed by the Review Committee (Drug) under the TFDA. The evaluation focuses on several key factors, including the drug's indication for the specific rare disease, its mechanism of action, safety and efficacy data, and the availability of alternative treatments. This phase of designation typically takes between six to twelve months. Once a drug receives orphan drug designation, pharmaceutical companies proceed with the orphan drug registration process, which involves submitting a New Drug Application (NDA). Upon approval, the orphan drug is granted specific permissions for import and manufacturing, along with approval for drug pricing and reimbursement under Taiwan's healthcare system. Additionally, the HPA provides financial subsidies to support patient access to these essential medications [267].
- After obtaining approval through the registration process or receiving specific permission for import, orphan drugs become eligible for listing under the NHI Pharmaceutical Benefits and Reimbursement Scheme. To promote the availability of orphan drugs, the central competent authority imposes a ten-year exclusivity period, during which applications for pharmaceuticals of the same kind are not accepted. Additionally, financial support is provided to encourage research on the prevention and management of rare diseases. To further incentivize orphan drug development, application fees for marketing registration and related processes are significantly reduced. For instance, the registration fee for a new orphan drug is approximately US$341, whereas the fee for a non-orphan new chemical entity is significantly higher at US$51,181 [268].

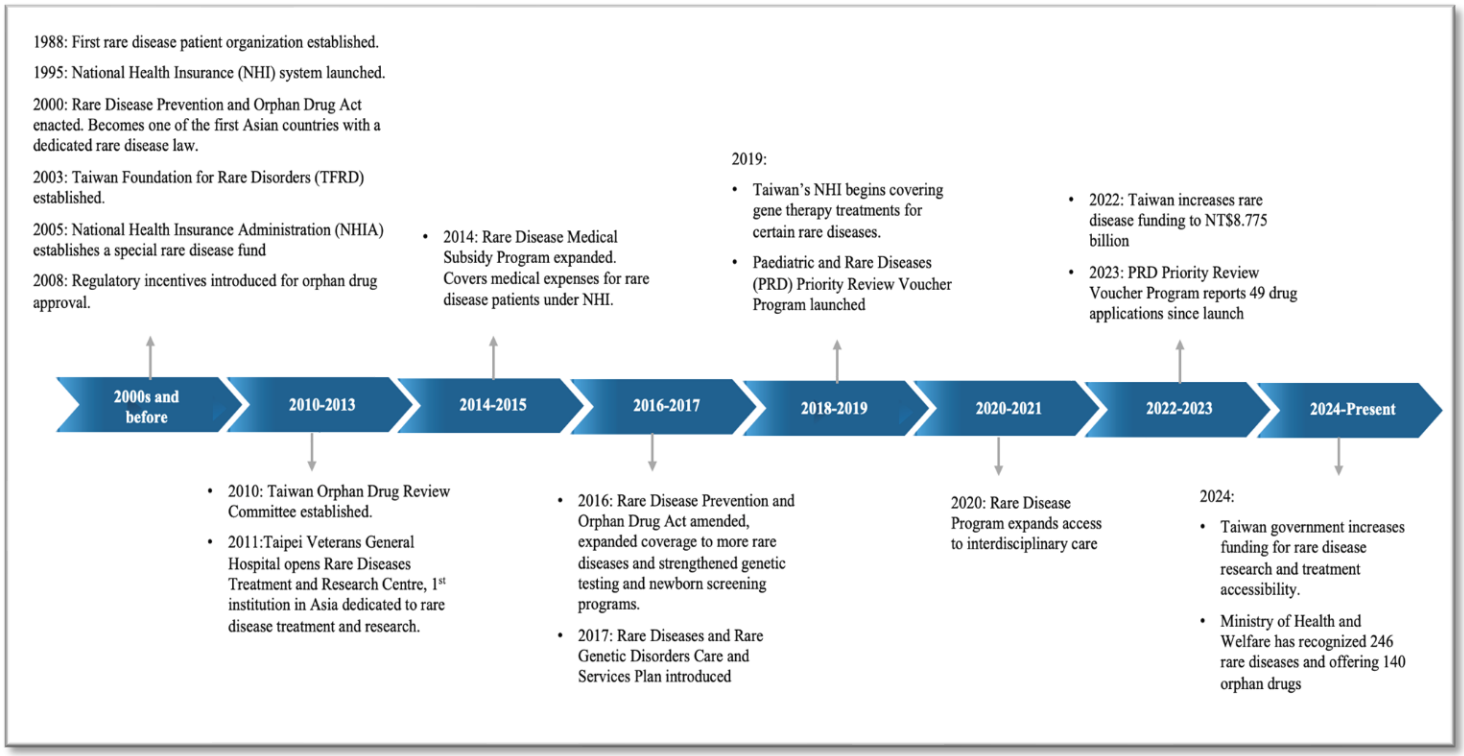
5.13.5 Care Pathways and Infrastructure

- Rare Diseases Treatment and Research Centre: On March 11, 2011, Taipei Veterans General Hospital established the Rare Diseases Treatment and Research Centre, making it the first institution in Asia dedicated to the treatment, care, and research of rare diseases. The centre consists of two divisions. The first is the Rare Disease Treatment Center, which includes a specialized team of medical professionals and a dedicated treatment ward, providing a high-quality and patient-centred medical environment tailored to individuals with rare diseases. The second division is the Rare Disease Research and Testing Laboratory, offering a range of specialized diagnostic services, including genetic testing, enzyme

analysis, gene analysis, organic acid analysis, and amino acid analysis, to support the diagnosis and study of rare diseases. Additionally, the center introduced Taiwan's first multidisciplinary outpatient clinic specifically for rare diseases. The center is equipped with a joint outpatient clinic, enabling interdisciplinary care and reducing the need for patients to visit multiple departments [269]

- Rare disease program: Beginning in 2017, the Health Promotion Administration partnered with medical institutions to deliver a rare disease program, ensuring accessible and interdisciplinary care across Taiwan. Core services include care consultation, guidance on the impact of diseases on daily life, psychological support, and fertility care. The initiative also connects patients to National Health Insurance home-based care, long-term care, social welfare, and support groups, forming a comprehensive care network to reduce the physical and emotional strain on families. By January 2023, more than 7,000 families had received support through these services[270]

Figure 13. Shows the timeline of the rare diseases progress in Taiwan



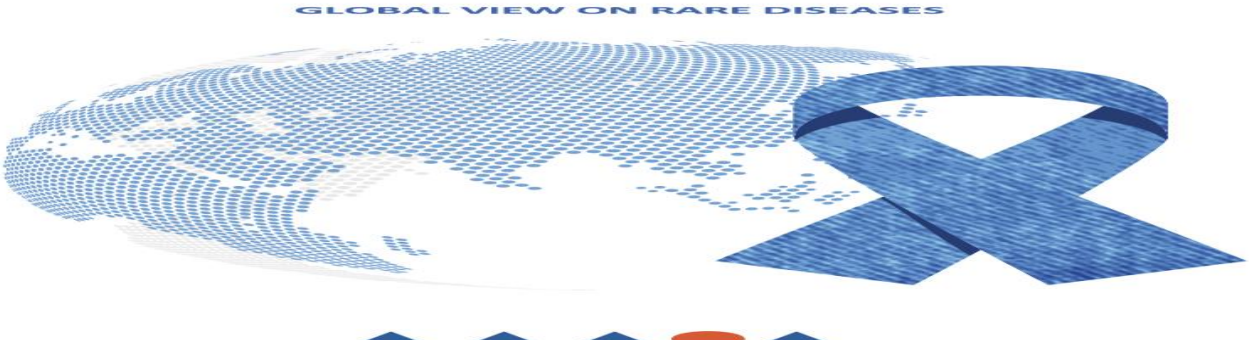
Abbreviation: NBS = Newborn Screening, RA = Republic act, RDMAP = Rare disease medicine access program, DoH = Department of health, UP NIH = University of the Philippines national institute of health.

5.13.6 Key Organizations Advancing Rare Disease Initiatives in Taiwan

Organization Name	Established Year	Description
Taiwan Foundation for Rare Disorders (TFRD)	1999	- Support rare disease patients to receive medical treatment and rehabilitation, securing orphan drugs and special nutrients. - Provides education, employment and long-term care to patients.
Debra International	2009	- Provides support, resources, and advocacy for those living with Epidermolysis bullosa (EB)

Taiwan Organization for Disadvantaged Patients	1999	- Support individuals with rare diseases and disabilities including medical care, educational support, employment assistance, and family support programs, aiming to enhance the quality of life for disadvantaged patients and their families.
Taiwan Foundation for Rare Disorder	1999	- Provide care and home visits, support patient groups, and promote rare disease research. - Collaborate with geneticists and medical institutions to strengthen the global rare disease network. - Raise awareness, advocate for government policies, and foster cooperation with medical institutions. -

Table 16. Key organizations in the area of rare diseases in Taiwan



6 Best Practices: How some Countries Effectively Manage Rare Diseases

Country	Rare diseases Act/Policies	Defining Rare Diseases	Funding policies	Drug Approval and Reimbursement Criteria	Market Exclusivity	Care Pathway
 **United States of America**	Orphan Drug Act (1983)- Rare Disease Act (2002)	Fewer than 200,000 cases	Private insurance, Medicare & Medicaid	Fee waivers, 50% tax credit on clinical expenditure, and grants for clinical research. The FDA approves drugs and can grant orphan drug status for rare diseases. Pricing & Reimbursement Influence by negotiations among pharmacy benefit managers insurers, and healthcare-providers pharmaceutical companies.	7-year market exclusivity.	The Genetic and Rare Diseases (GARD) Information Centre [271]
 **Canada [476]**	Health Canada's Special Access Program National Strategy for Drugs for Rare Diseases 2023	<50 cases per 100,000 population [[272]	Publicly funded	Priority-Review policy has a review performance standard of 180 days. The Special Access Programme (SAP) authorizes a manufacturer to sell a drug that cannot otherwise be sold or	8 years of market exclusivity for drugs, if they meet the definition of an innovative drug. Certificates of Supplementary Protection(CSP) additional period of protection of up to 2 years	CRDN (2024)

				distributed in Canada. Fee mitigation or deferral [273]		
 **United Kingdom**	UK Strategy for Rare Diseases 2013 Early Access to Medicines Scheme (EAMS)-2014 Ultra-orphan medicines pathway (Scotland)-2018	Affects less than 1 in 2,000 people	Publicly funded (NHS)	Full or partial refunds of marketing authorization fees Medicine listed Orphan Register. [274] NICE evaluates for cost-effectiveness and clinical benefit, uses HST criteria for rare diseases	Up to 10 years of Market exclusivity	Rare Disease Collaborative Networks
 **Japan**	Act on Medical Care for Patients with Intractable/Rare Disease 2015 [275] Pharmaceutical Affairs Law (1993) Revision of Specified Disease Treatment Research Program 1972	Fewer than 50 000 affected individuals in Japan [275]	Publicly funded	Orphan drug as a drug for a disease Receive subsidies Priority review for marketing authorization [276] Regulatory fee waivers, clinical and non-clinical study grants, 15% tax credits and up to 14% tax reduction Protocol assistance and fast track approval	Extension of re-examination period- drugs will be extended up to 10 years for drugs and up to 7 years for medical devices	IRUD

European Union	Orphan Medicinal Product Regulation (EC) No. 141/2000 (1999) Rare Disease National Plan (EUROPLAN) Compassionate Use Programs (CUPs) The Seventh Framework Program (FP7) Horizon Europe (2021-2027)	Fewer than 5 cases per 10,000 people	Publicly Funded	Regulatory fees reduced or waived Access to centralized procedures, Protocol assistance	Market exclusivity for 10 years; 6 years if drug criteria not met	European Reference Networks (ERNs)
Germany	National Action Legue for people with Rare Diseases (Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen (NAMSE)	Fewer than 5 cases per 10,000 people	Publicly Funded	Central EU authorization COMP OD Designation [277]	Market exclusivity for 10 years; 6 years if drug criteria not met	Centres for Rare Diseases (Zentren für Seltene Erkrankungen)
France	National plan for Rare Diseases	Fewer than 5 cases per 10,000 people	Publicly Funded	Central EU authorization COMP OD Designation [277]	Market exclusivity for 10 years; 6 years if drug criteria not met	BNDMR (National Rare Disease Registry)
Brazil	Brazilian policy of Comprehensive care for people with Rare Diseases 2014	No more than 65 cases per 100,000 people.	Publicly Funded (Specialized Component of Pharmaceutical Services (CEAF) [278]	Fast Track Registrations (Resolution number 205/2017) [279]	-	Brazilian Rare Disease Network (Centers for Comprehensive Care & Training in Rare Diseases (Casa dos Raros)
Colombia	Law 1392 (2010)	1 case per 5,000 people	Publicly Funded (EPS part SGSSS social security scheme) [280]	Exempt from the cost-effectiveness analysis [281]		Reference Centers for Diagnosis, Treatment, and Pharmacies

				International reference pricing methodology [282]		for the Comprehensive Care of Orphan Diseases
Argentina	Law 26.689 (Comprehensive Healthcare of People with Diseases of Low Prevalence 2011)	Fewer than 5 cases per 10,000 people (EU Definition)	Publicly Funded (m (Sistema de Tutelaje de Tecnologias Sanitarias Emergentes)	centralized purchasing, and new medicine evaluation (Not specific to Orphan drugs) [283]	-	-
Mexico	Article 224 revision (2012) No specific Plan	Fewer than 5 cases per 10,000 people (EU Definition) [284]	Publicly Funded (Seguro Popular- Public Health Insurance)	Accelerated review available Process in place for OD classification [55], [285], [286], [287]	-	Mexican Network of Rare Diseases (ReMexER)

7 Recommendations and the way forward

In recent years, there have been notable advances in the understanding and treatment of rare diseases, with patient advocacy playing a central role in these developments. Despite this progress, much work remains to address the unmet needs of patients and their families. Many policymakers are unaware of the challenges rare disease patients face in obtaining a diagnosis or adequate treatment, making awareness-raising efforts crucial to establishing rare diseases as a key public health priority. Access to treatment remains a significant issue globally, requiring stakeholders to collaborate in making rare diseases a global priority and ensuring equitable access to care. Existing knowledge must be shared, and collaboration across sectors is essential to maximize understanding and avoid duplicating efforts. The unique expertise and insights of patients should be integrated into research and policies to ensure their needs are met. Enabling legislation for orphan drug development must continue, alongside efforts to improve regulatory processes and reduce inequalities in access to treatment and care. Based on our insights and discussions with experts in the field of rare diseases, we are putting forth recommendations for a next generation of rare diseases policies :[55] [285] [286] [287]

Global collaboration among various stakeholders is essential for advancing rare disease treatment and improving the quality of life for patients. The below Figure 24 shows the key stakeholders involved with rare diseases and the need for collaborative efforts aimed at patient centric partnerships for the evolution of better treatment, quality life for rare disease patients and to mitigate the obstacles faced by these patients. Patient involvement, which is prominent in regions like Europe and the US, is also gaining traction in Japan through organizations like the Japan Agency for Medical Research and Development (AMED) and the Pharmaceuticals and Medical Devices Agency (PMDA). Implementing regional network of Centers of Excellence and international collaboration to facilitate the exchange of best practices, clinical guidelines, and innovative approaches to rare disease care, and patients may be able to move between centers across borders or access virtual consultations for diagnosis and treatment recommendations.

Figure 14. Partnerships and coordinated efforts essential between different stakeholders involved in the health and welfare of patients with rare disease

Source: [288]

Harmonizing policy to develop an adaptive and inclusive definition of rare diseases is crucial for encouraging policymakers to establish orphan drug legislation and national rare disease plans. To create a robust policy framework, countries must align their rare disease definitions with international standards. A globally standardized definition will ensure transparency in setting regulations and facilitate harmonization in orphan product designation and approval processes. Establish a consistent and transparent procedure in close collaboration with a diverse array of stakeholders, including health professional organizations, academic institutions (researchers, clinicians, etc.), industry representatives, civil society, non-governmental organizations, and patient advocacy groups. This process should focus on reviewing (1) the definition of rare diseases, (2) the corresponding list of recognized rare diseases, if applicable, and/or (3) the designation process, considering new insights, treatments, and real-world evidence. Ensure that all stakeholders are given sufficient time to contemplate potential modifications and provide feedback and facilitate this process through a dedicated cross-agency working group or public forum.

Information and knowledge sharing, which makes it difficult for rare disease patients, families, caregivers and clinicians to identify the signs and symptoms at an early stage of the disease. Efforts must be made to ensure that groups have adequate access to essential resources, including financial support and in-kind contributions, to bolster their advocacy and outreach initiatives. Furthermore, collaboration with pertinent authorities to simplify registration procedures and alleviate administrative challenges faced by patient organizations. It has been observed that numerous countries have made significant strides in this area. For instance, various organizations in the United States, such as the National Institutes of Health (NIH), the National Organization for Rare Disorders (NORD), and the Food and Drug Administration (US FDA), along with the European Organization for Rare Diseases (EURORDIS), ORPHANET, and the European Platform for Patient's Organizations, Science and Industry (EPPOSI), have advanced efforts to enhance the collection and dissemination of information related to rare diseases. ORPHANET has been active on an international scale, successfully registering a total of 5,954 rare diseases. These organizations have played a crucial role in supporting patients, facilitating access to information, and promoting networking opportunities, which can significantly enhance research and development in the field of rare diseases. Moreover, there is a pressing need for greater media representation through both public and private funding for initiatives, films, and digital content that raise awareness about the challenges associated with rare diseases.

Promote continued research and development by implementing robust governance and capacity-building measures for managing and storing rare disease patient data, fostering scientific discovery, innovation, and societal benefits. There is a need to focus on the seed funding initiatives aimed at supporting early-stage research and the development of orphan products, encouraging collaboration between industry stakeholders and civil society. Moreover, aligning funding strategies with the unique strengths of each economy, enhancing support for academic institutions, and fostering partnerships among public, private, and patient entities to propel research forward. Furthermore, necessity of providing financial and non-financial incentives to facilitate the commercialization of domestic research on rare diseases, including tax incentives for clinical trials and centralized efforts for commercialization. To enhance the efficiency of research processes, harmonization of ethical review protocols and the implementation of policies designed to shorten approval timelines for clinical trials, thereby ensuring a more rapid and effective research and development landscape for rare diseases. Additionally, APEC advocated for developing a national rare disease registry based on observations, success stories, and outcomes of the Rare Diseases Registry and Analytics Platform (RD-RAP). The development of a Rare Disease registry based on global standards will help in the timely collection of

standardized and high-quality clinical data to support the development of orphan drugs, design and conduct of clinical trials, and regulatory decision-making.

Ensuring sustainable access to diagnosis, treatment, and care for rare diseases requires improving healthcare infrastructure, training specialized professionals, and strengthening legislation for orphan drug availability. Enhancing genetic testing and diagnostic capabilities by capitalizing on the distinct advantages of each economy is essential. The APEC initiative advocates for the revision of trade policies to enable the seamless transfer of anonymized patient data and tissue samples, while fostering advancements in diagnostic techniques. The strategy aims to create a regional genetic reference sequence database accessible to researchers and clinicians. Further implement reimbursable newborn screening programs for rare diseases, thereby ensuring accessibility, early intervention, and ongoing evaluations. Furthermore, it encourages regional cooperation in genetic counseling and interpretation services. Additionally, establishing domestic referral networks to direct newly diagnosed individuals toward suitable healthcare services, employing digital technologies and trained personnel to enhance patient care, especially for adults or those diagnosed later in life.

Engage in enhancing the integration of healthcare systems with social welfare programs to guarantee that patients suffering from rare diseases and their families receive vital support. Implementing programs to harmonize social protection initiatives across various ministries and funding bodies to optimize resource allocation and operational efficiency. Furthermore, policies must be designed to promote

innovative private insurance solutions, enhancing inclusivity within employment and educational frameworks for individuals with rare diseases. There is a need to emphasis on anti-discrimination initiatives, psychosocial support, and specialized education or skills training, particularly targeting vulnerable populations including women, the elderly, and individuals with disabilities, to bolster economic security and accessibility. Ensuring that diagnostic tests and treatments for rare diseases are included in both public and private insurance coverage will aid in removing financial obstacles. Additionally, increasing subsidies, grants, and financial incentives for orphan drugs will help mitigate their high costs, while advocating for fair reimbursement policies will enable patients to access the most advanced treatments, particularly when options are limited.

Establish streamlined regulatory, pricing and reimbursement policies. To ensure a smooth and efficient regulatory system, it is important to establish policies that promote evidence generation throughout the entire life cycle of a product or technology, as well as the patient journey from diagnosis to treatment access. For instance, these policies should also ensure a fair and transparent decision-making process for assessing orphan products. One way to achieve this is by implementing an accelerated regulatory framework with clear eligibility criteria. This framework should accept international data, waive local manufacturing and testing requirements, and be applicable to all orphan products. It should be implemented by trained regulators and should also streamline review timelines, allow exemptions from certain dossier requirements, and provide easily accessible submission guidelines for manufacturers without any discrimination based on disease area. To enhance harmonization and facilitate faster registration processes, it is recommended to promote mutual reliance on regulatory decisions among countries. Additionally, it would be beneficial to establish or collaborate with a regional network that can share best practices in policy, regulation, and reimbursement decisions specifically for rare diseases.

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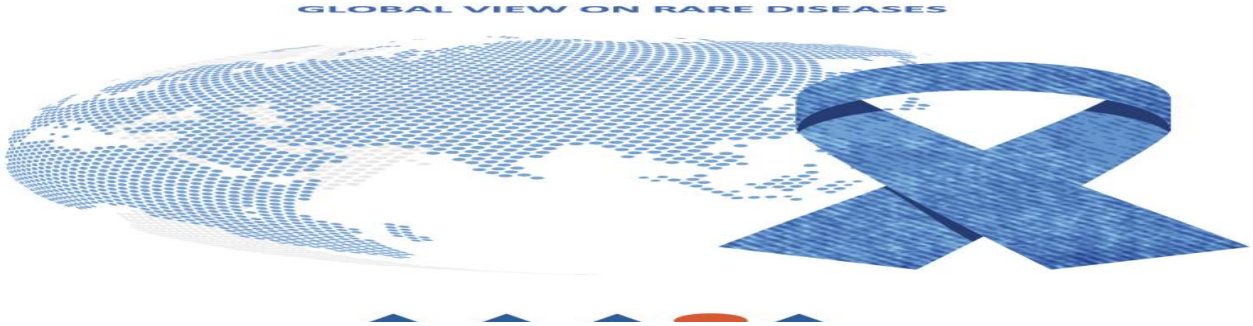

8 APPENDIX

No.	Diseases	No.	Diseases
1	21-Hydroxyulase Deficiency	27	Fabry Disease
2	Albinism	28	Familial Mediterranean Fever
3	Alport Syndrome	29	Fanconi Anemia
4	Amyotrophic Lateral Sclerosis	30	Galactosemia
5	Angelman Syndrome	31	Gaucher's Disease
6	Arginase Deficiency	32	General Myathenic Gravis
7	Asphyxiating Thoracic Dystrophy (Jeune Syndrome)	33	Gitelman Syndrome
8	Atypical Hemolytic Uremic Syndrome	34	Glutaric Acidemia Type I
9	Autoimmune Encephalitis	35	Glycogen Storage Disease (Type I, II)
10	Autoimmune Hypophysitis	36	Hemophilia
11	Autoimmune Insulin Receptopathy (Type B Insulin Resistance)	37	Hepatolenticular Degeneration (Wilson disease)
12	Beta-Ketothiolase Deficiency	38	Hereditary Angioedema (HAE)
13	Biotinidase Deficiency	39	Hereditary Epidermolysis Bullosa
14	Cardic Ion Channelopathies	40	Hereditary Fructose Intolerance
15	Carnitine Deficiency	41	Hereditary Hypomagnesemia
16	Castleman Disease	42	Hereditary Multi-infarct Dementia (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalqpathy, CADASIL)
17	Charcot-Marie-Tooth Disease	43	Hereditary Spastic Paraplegia
18	Citrullinemia	44	Holocarboxylase Synthetase Deficiency
19	Congenital Adrenal Hypoplasia	45	Homocysteinemia
20	Congenital Hyperinsulinemic Hypoglycemia	46	Homozygous Hypercholesterolemia
21	Congenital Myasthenic Syndrome	47	Huntington Disease
22	Congenital Myotonia Syndrome (Non-Dystrophic mytonia, NDM)	48	Hyperornithinaemia-Hyperammonaemia-Hhomocitrullinuria Syndrome
23	Congenital Scoliosis	49	Hyperphenylalaninemia

24	Coronary Artery Ectasia	50	Hypophosphatasia
25	Diamond-Blackfan Anemia	51	Hypophosphatemia Rickets
26	Erdheim-Chester Disease	52	Idiopathic Cardiomyopathy
53	Idiopathic Hypogonadotropic Hypogonadism	85	Ornithine Transcarbamylase Deficiency
56	IgG4 related Disease	86	Osteogenesis Imperfecta (Brittle Bone Disease)
57	Inborn Errors of Bile Acid Synthesis	87	Parkinson Disease (Young-onset, Early-onset)
58	Isovaleric Acidemia	88	Paroxysmal Nocturnal Hemoglobinuria
59	Kallmann Syndrome	89	Peutz-Jeghers Syndrome
60	Langerhans Cell Histiocytosis	90	Phenylketonuria
61	Laron Syndrome	91	POEMS Syndrome
62	Leber Hereditary Optic Neuropathy	92	Porphyria
63	Long Chain 3-hydroxyacyl-CoA Dehydrogenase Deficiency	93	Prader-Willi Syndrome
64	Lymphangioleiomyomatosis (LAM)	94	Primary Combined Immune Deficiency
65	Lysine Urinary Protein Intolerance	95	Primary Hereditary Dystonia
66	Lysosomal Acid Lipase Deficiency	96	Primary Light Chain Amyloidosis
67	Maple Syrup Urine Disease	97	Progressive Familial Intrahepatic Cholestasis
68	Marfan Syndrome	98	Progressive Muscular Dystrophies
69	McCune-Albright Syndrome	99	Propionic Acidemia
70	Medium Chain Acyl-CoA Dehydrogenase Deficiency	100	Pulmonary Alveolar Proteinosis
71	Methylmalonic Academia	101	Pulmonary Cystic Fibrosis
72	Mitochondrial Encephalomyopathy	102	Retinitis Pigmentosa
73	Mucopolysaccharidosis	103	Retinoblastoma
74	Multi-Focal Motor Neuropathy	104	Severe Congenital Neutropenia
75	Multiple Acyl-CoA Dehydrogenase Deficiency	105	Severe Myoclonic Epilepsy In Infancy (Dravet Syndrome)
76	Multiple Sclerosis	106	Sickle Cell Disease
77	Multiple System Atrophy	107	Silver-Russell Syndrome
78	Myotonic Dystrophy	108	Sitosterolemia
79	NAGS Deficiency	109	Spinal and Bulbar Muscular Atrophy (Kennedy Disease)

80	Neonatal Diabetes Mellitus	110	Spinal Muscular Atrophy
81	Neuromyelitis Optica	111	Spinocerebellar Ataxia
82	Niemann-Pick Disease	112	Systemic Sclerosis
83	Non-Syndromic Deafness	113	Tetrahydrobiopterin Deficiency
84	Noonan Syndrome	114	Tuberous Sclerosis Complex
115	Tyrosinemia	119	X-linked Agammaglobulinemia
116	Very Long Chain Acyl-CoA Dehydrogenase Deficiency	120	X-linked Adrenoleuko Dystrophy
117	Williams Syndrome	121	X-linked Lymphoproliferative Disease
118	Wiskott-Aldrich Syndrome		

Table 17. List of rare diseases from the Notice on the First National List of Rare Diseases in China. The following list was jointly issue by five bodies including the National Health Commission

Source:[289]

ATC code	Generic name	Brand name	Manufacturer or import status	Strength	Per strength price	Average unit price of drug procurement (USD)*	Number of procurement provinces	EM
					Average (M in-Max) (USD)			Y/N
A01AB18	Clotrimazole	Empecid	M and I	10g:300mg	0.13（0.08，0.22）	0.0004/mg	11	N
A03AB02	Glycopyrrolate	Cuvposa	M	0	0	0	0	N
A05AA02	Ursodeoxycholic Acid	URSO	M and I	50mg	0.03（0.001，0.04）	0.0007/mg	11	Y
A07AA11	Rifaximin	Normix	M and I	200mg	0.48（0.29，1.68）	0.002/mg	5	N

A07EC02	Mesalazine	PENTASA	M	25mg	0.24（0.24，0.24）	0.001/mg	4	N
A12AA12	Calcium acetate	Phos-Lo	M	66.7mg	10.39（8.23, 13.30）	0.001/mg	4	N
A16AA01	Levocarnitine	Carnitor	M and I	5ml:1000mg	5.63（1.59，9.49）	0.006/mg	5	N
A16AA03	Glutamine (L)	Nutrestore	M and I	100ml:20000mg	21.01（13.50, 24.36）	0.001/mg	8	N
A16AB02	Imiglucerase	Cerezyme	I	0	0	0	0	N
A16AX07	Sapropterin dihydrochloride	Kuvan	I	0	0	0	0	N
B01AC11	Iloprost inhalation solution	Ventavis	I	0	0	0	0	N
B01AC19	Beraprost Sodium	DORNER	I	20ug	0.79（0.78，0.82）	0.04/mg	5	N
B01AE03	Argatroban Hydrate	Novastan	M and I	20ml:10mg	23.01（11.88, 25.58）	2.30/mg	5	N
B02AB01	Aprotinin	Trasylol	M	0	0	0	0	N
B02BD04	Coagulation Factor IX (recombinant)	Benefix	I	0	0	0	0	N
B02BD05	Coagulation Factor VIIa (Recombinant)	Novoseven	I	1.2mg(60KU)	1057.57（1057.45, 1057.69）	881.31/mg	3	N

B02BD08	Eptacog Alfa (Activated) (Genetical Recombination)	NovoSeven	I	0	0	0	0	N
B02BD09	Nonacog Alfa (Genetical Recombination)	BeneFIX	I	0	0	0	0	N
B03XA01	Epoetin alfa	Epogen	M and I	1ml:1000IU	1.67（1.14，18.59）	0.0027/ IU	8	N
C01BD01	Amiodarone HCl	Cordarone	M and I	200mg	0.13（0.003, 0.40）	0.0007/mg	15	Y
C01CA17	Midodrine HCl	ProAmatine	M and I	2.5mg	0.38（0.32，0.43）	0.15/mg	3	N
C02KX01	Bosentan	Tracleer	I	125mg	56.96（56.96, 56.96）	0.46/mg	1	N
C02KX02	Ambrisentan	Letairis	I	5mg	51.13（51.13, 51.13）	10.22/mg	1	N
C07AA07	Sotalol HCl	Betapace	M	80mg	0.18（0.19，0.21）	0.002/mg	5	N
C09AA16	Imidapril Hydrochloride	Tanatril	M	5mg	0.26（0.25，0.27）	0.05/mg	2	N
D06BX01	Metronidazole	Metrogel	M and I	300mg:10000mg	0.68（0.68，0.68）	0.002/mg	1	N
G03AC05	Megestrol acetate	Megace	M	160mg	1.55（1.46，1.64）	0.01/mg	5	N

G03DA03	Hydroxyprogesterone caproate	Makena	M	0	0.00	0	0	N
G03GA04	Urofollitropin	Metrodin	M	75IU	22.70（21.88, 23.52）	0.30/IU	3	N
G03GA05	Follitropin alfa, recombinant	Gonal-F	I	100IU	266.71（55.87, 66.05）	2.67/IU	5	N
G03XB01	Mifepristone	Korlym	M	25mg	0.56（0.53，0.61）	0.02/mg	9	Y
G03XC01	Raloxifene	Evista	M and I	60mg	1.39（1.09，1.84）	0.02/mg	4	N
G04BE08	Tadalafil	Adcirca	I	20mg	17.85（17.06, 18.11）	0.89/mg	4	N
H01AC01	Somatropin (rDNA origin)	Saizen	M and I	10IU	52.88（22.05, 977.24）	5.29/IU	10	N
H01AC01	Somatropin	Genotropin	M and I	0	0	0	0	N
H01AC01	Somatropin	Norditropin，Norditropin SimpleXx	M and I	30IU	182.93（181.97, 184.13）	6.10/IU	7	N
H01BA02	Desmopressin acetate	n/a	M and I	1ml:1ug	0.90（0.70，1.09）	0.90/ug	6	Y
H01CA01	Gonadorelin acetate	Lutrepulse	M	0.1mg	2.03（1.92，2.25）	20.29/mg	4	N
H01CB02	Octreotide	Sandostatin Lar	M and I	1ml:0.1mg	8.52（1.46，19.08）	85.20/mg	6	N

H01CB03	Lanreotide	Somatuline Depot	I	40mg	550.97（510.21, 577.62）	13.77/mg	4	N
H02AB09	Hydrocortisone	Plenadren	M	2ml:10mg	0.03（0.02，0.06）	0.003/mg	12	Y
H05AA02	Teriparatide	Parathar	I	2.4ml:20μg:80μl	1106.25（1106.25, 1106.25）	55.31/ug	1	N
J01EC02	Sulfadiazine	n/a	M	500mg	0.01（0.01，0.02）	0.00003/mg	6	Y
J01FA09	Clarithromycin	Clarith	M	125mg	0.13（0.10，0.32）	0.001/mg	5	Y
J01FA10	Azithromycin Hydrate	Zithromac	M and I	250mg	0.36（0.04，1.70）	0.001/mg	13	Y
J01MA01	Ofloxacin	Tarivid	M	100mg	0.04（0.01，0.25）	0.0004/mg	4	Y
J01XA01	Vancomycin Hydrochloride	Vancomycin	M	500mg	16.10（13.69, 22.30）	0.03/mg	7	N
J02AA01	Amphotericin B lipid complex	Abelcet	M and I	10mg	22.23（22.16, 22.42）	2.22/mg	7	N
J02AA01	Liposomal amphotericin B	Ambisome	M and I	10mg	22.23（22.16, 22.42）	2.22/mg	7	N
J04AB02	Rifampin(Rifampicin)	Rifadin I.V.	M	5ml:300mg	4.46（4.15，4.96）	0.015/mg	6	N
J04AM05	Rifampin, isoniazid, pyrazinamide	Rifater	M	450mg	0.11（0.06，0.22）	0.0002/mg	3	N

J04AB04	Rifabutin	Mycobutin	M	150mg	2.56（2.41，2.64）	0.017/mg	5	N
J04AB05	Rifapentine	Priftin	M	150mg	0.14（0.11，0.17）	0.0009/mg	7	N
J04BA01	Clofazimine	Lamprene	M	50mg	2.23（2.23，2.23）	0.04/mg	1	N
J05AB04	Ribavirin	Rebetol	I	100mg	0.02（0.0007，0.05）	0.0002/mg	11	N
J05AB14	Valganciclovir Hydrochloride	Valixa	I	450mg	40.50（38.05，42.95）	0.09/mg	2	N
J05AD01	Foscarnet Sodium Hydrate	Foscavir	M	250ml:300mg	15.78（12.50，21.47）	0.005/mg	5	N
J05AE01	Saquinavir Mesilate	Invirase	M	0	0	0	0	N
J05AE02	Indinavir Sulfate Ethanolate	Crixivan	M	0	0	0	0	N
J05AE03	Ritonavir	Norvir	I	0	0	0	0	N
J05AE08	Atazanavir Sulfate	REYATAZ	I	0	0	0	0	N
J05AF01	Zidovudine	Retrovir	M	0	0	0	0	N
J05AF02	Didanosine	Videx EC	M and I	0	0	0	0	N
J05AF06	Abacavir Sulfate	Ziagen	I	0	0	0	0	N
J05AF07	Tenofovir	Viread	M and I	0	0	0	0	N
J05AF09	Emtricitabine	Emtriva	M and I	0	0	0	0	N

J05AG01	Nevirapine	Viramune	M and I	0	0	0	0	N
J05AG03	Efavirenz	Stocrin	M and I	0	0	0	0	N
J05AG04	Etravirine	Intelence	M	0	0	0	0	N
J05AG05	Rilpivirine Hydrochloride	EDURANT	I	0	0	0	0	N
J05AR10	Lopinavir, Ritonavir	Kaletra	I	0	0	0	0	N
J05AX08	Raltegravir Potassium	ISENTRESS	I	0	0	0	0	N
J05AX09	Maraviroc	Celsentri	I	0	0	0	0	N
J06BB04	Hepatitis B immune globulin (human)	Hepagam	M	200IU	47.76（35.77, 52.88）	0.24/IU	2	N
L01AA01	Cyclophosphamide Hydrate	Endoxan	M and I	200mg	2.08（0.55，4.53）	0.01/mg	9	Y
L01AA03	Melphalan	Alkeran For Injection	I	0	0	0	0	N
L01AA06	Ifosfamide	Ifex	M and I	1mg	21.02（8.57, 42.92）	21.02/mg	10	N
L01AB01	Busulfan	Busulfex	I	10ml:60mg	269.39（269.39, 269.39）	4.49/mg	1	N
L01BA01	Methotrexate sodium	Methotrexate	M and I	10ml:1000mg	2.91（2.52，3.29）	0.003/mg	5	Y
L01BA04	Pemetrexed disodium	Alimta	M and I	500mg	647.98（549.20, 821.79）	1.30/mg	8	N

L01BB02	6-mercaptopurine monohydrate	Xaluprine	M	50mg	0.07（0.07，0.07）	0.001/mg	1	Y
L01BB04	Cladribine	Leustatin	M	10ml:10mg	1068.43（1068.11,1068.75）	106.84/mg	3	N
L01BB05	Fludarabine phosphate	Fludara	M	50mg	218.49（174.66,367.31）	4.37/mg	5	N
L01BB05	Fludarabine phosphate oral tablets	n/a	I	10mg	71.03（71.03,71.03）	7.10/mg	1	N
L01BC01	Cytarabine	Cylocide N	M and I	100mg	2.92（1.20，8.18）	0.03/mg	6	Y
L01BC05	Gemcitabine Hydrochloride	Gemzar	M and I	200mg	55.20（27.19,72.79）	0.28/mg	5	N
L01BC08	Decitabine	Dacogen	M and I	50mg	1667.47（1662.74,1670.51）	33.35/mg	6	N
L01CB02	Teniposide	Vumon	M and I	5ml:50mg	21.83（18.99,25.14）	0.44/mg	7	N
L01CD01	Paclitaxel	Taxol	M and I	5ml:30mg	30.87（18.75,59.59）	1.03/mg	3	Y
L01DB01	Doxorubicin liposome	Doxil	M and I	10ml:20mg	1058.65（836.22,1245.83）	52.93/mg	4	N

L01DB03	Epirubicin	Ellence	M and I	5ml:10mg	47.57（15.39, 108.88）	4.76/mg	10	N
L01DB06	Idarubicin HCl for injection	Idamycin	M and I	10mg	475.91（381.19, 623.08）	47.59/mg	5	N
L01DB07	Mitoxantrone	Novantrone	M	5mg	6.02（5.37，7.53）	1.20/mg	5	N
L01DC03	Mitomycin-C	Mitosol	M	10mg	11.45（6.47, 12.92）	1.14/mg	7	Y
L01XC02	Rituximab	Rituxan	I	50ml:500mg	2892.55（2884.62, 2900.48）	5.79/mg	6	N
L01XC03	Trastuzumab	Herceptin	I	440mg	3638.46（3604.62, 3660.32）	8.27/mg	6	N
L01XC06	Cetuximab	Erbitux	I	20ml:100mg	730.77（692.31, 740.38）	7.31/mg	8	N
L01XC07	Bevacizumab	Avastin	I	4ml:100mg	843.40（843.40, 843.40）	8.43/mg	1	N
L01XE01	Imatinib	Gleevec	M and I	100mg	29.45(31.25,33.65)	0.29/mg	7	N
L01XE04	Sunitinib Malate	Sutent	I	12.5mg	73.16（70.89, 74.11）	5.85/mg	7	N
L01XE05	Sorafenib Tosylate	Nexavar	I	200mg	65.70（62.18, 67.08）	0.33/mg	5	N
L01XE06	Dasatinib	Sprycel	M and I	0	0	0	0	N

L01XE08	Nilotinib	Tasigna	I	200mg	53.17（52.08, 54.29）	0.27/mg	5	N
L01XE10	Everolimus	Afinitor	I	0	0	0	0	N
L01XE16	Crizotinib	Xalkori	I	0	0	0	0	N
L01XX03	Altretamine	Hexalen	M	50mg	0.88（0.88，1.05）	0.02/mg	8	N
L01XX14	Tretinoin	Vesanoid	M	0	0	0	0	N
L01XX24	Pegaspargase	Oncaspar	M	5ml:3751IU	727.36（691.29, 772.44）	0.2/IU	7	N
L01XX27	Arsenic trioxide	Trisenox	M	5ml:5mg	37.90（37.90, 37.90）	7.59/mg	1	Y
L01XX32	Bortezomib	Velcade	I	1mg	809.15（792.81, 825.48）	809.15/mg	9	N
L02BA02	Toremifene	Fareston	M and I	60mg	1.75（1.74，1.75）	0.032/mg	6	N
L02BG06	Exemestane	Aromasin	M and I	25mg	5.20（1.69，8.59）	0.21/mg	7	N
L03AB03	Interferon Gamma-1a(Genetical Recombination)	Imunomax®-γ	I	2Mill IU	8.14（7.44，8.94）	0.041/IU	7	N
L03AB04	Interferon alfa-2a (recombinant)	Roferon-A	M and I	6Mill IU	7.69（5.77，9.71）	0.013/IU	3	N

L03AB05	Interferon alfa-2b (recombinant)	Intron A	M and I	5Mill IU	8.57（5.77，11.54）	0.017/IU	8	N
L03AB08	Interferon beta-1b	Betaseron	I	0.3mg	131.89（131.89, 131.89）	439.64/mg	1	N
L03AB10	Peginterferon alfa-2b	Sylatron	I	100ug	212.58（210.38, 214.76）	2.13/ug	2	N
L03AX03	Freeze-dried BCG Vaccine(Japanese Strain)	Immunobladder	I	0	0	0	0	N
L04	Anti-human T-Lymphocyte Immunoglobulin, Rabbit	Zetbulin	M and I	5ml:100mg	604.65（604.65, 604.65）	6.05/mg	1	N
L04	Mycophenolate Mofetil	CellCept	M and I	250mg	1.23（1.02，1.48）	0.005/mg	5	N
L04AA04	Anti-human Thymocyte Immunoglobulin, Rabbit	Thymoglobuline	I	5ml:25mg	462.06（462.00, 462.00）	18.48/mg	1	N
L04AB01	Etanercept	Enbrel	I	25mg	378.93（375.64, 382.21）	15.16/mg	5	N

L04AB02	Infliximab	Remicade	I	100mg	981.64（938.78, 1025.64）	9.82/mg	5	N
L04AB04	Adalimumab	Humira	I	0	0	0	0	N
L04AC02	Basiliximab (Genetical Recombination)	Simulect	I	20mg	1356.86（1345.35, 1368.36）	67.84/mg	5	N
L04AD01	Ciclosporin	Sandimmun	M and I	5ml:250mg	22.96（15.72, 26.89）	0.09/mg	5	N
L04AD02	Tacrolimus	Prograf	M and I	0.5mg	1.91（1.57，2.23）	3.82/mg	6	N
L04AX02	Thalidomide	Thalomid	M	25mg	0.36（0.35，0.37）	0.01/mg	1	N
L04AX04	Lenalidomide	Revlimid	I	0	0	0	0	N
M01AC06	Meloxicam	Mobic	M and I	7.5mg	0.23（0.04，0.45）	0.03/mg	7	N
M03AX01	Botulinum toxin type A	Botox	I	0	0	0	0	N
M03BX01	Baclofen	Lioresal Intrathecal	M and I	10mg	0.27（0.21，0.49）	0.03/mg	7	N
M04AC01	Colchicine Tablets	Colcrys	M and I	10mg	1.19（0.60，3.54）	0.12/mg	18	Y
M05	Etidronate disodium	Didronel	M	200mg	0.33（0.24，0.42）	0.002/mg	5	N

M05BA07	Sodium Risedronate Hydrate	Actonel,Benet	M	5mg	0.86（0.67，1.35）	0.17/mg	6	N
N02CX02	Clonidine	Duraclon	M	0	0	0	0	N
N03AX09	Lamotrigine	Lamictal	M and I	25mg	0.26（0.18，0.34）	0.01/mg	8	N
N03AX11	Topiramate	Topamax	M and I	25mg	0.26（0.22，0.30）	0.01/mg	6	N
N03AX12	Gabapentin	Gralise	M and I	100mg	0.11（0.08，0.16）	0.001/mg	7	N
N04BC07	Apomorphine HCl	Apokyn	M	0	0	0	0	N
N04BD01	Selegiline HCl	Eldepryl	M and I	5mg	0.51（0.48，0.53）	0.10/mg	3	N
N05CA24	Phenobarbital Sodium	Nobelbar	M	1ml:100mg	0.07（0.05，0.10）	0.0008/mg	4	Y
N06BC01	Caffeine Citrate	Cafcit	I	0	0	0	0	N
N07BC01	Buprenorphine hydrochloride	Subutex	M	0	0	0	0	N
N07XX02	Riluzole	Rilutek	M and I	50mg	5.63（4.01，5.52）	0.11/mg	8	N
P01AB02	Tinidazole	Tindamax	M	500mg	0.03（0.01，0.05）	0.00007/mg	13	Y
P01BC01	Quinine Sulfate	n/a	M	0	0	0	0	N
P01BF01	Artemether 20mg /lumefantrine 120mg	Coartem	M	80mg	1.28（1.28，1.28）	0.02/mg	2	N

P02CA03	Albendazole	Albenza	M	100mg	0.02（0.0014, 0.05）	0.0002/mg	12	Y
P02CF01	Ivermectin	Stromectol	M	0	0	0	0	N
R05CB12	Tiopronin	Thiola	M	2ml:100mg	1.74（1.89，2.80）	0.02/mg	5	N
R07	Poractant Alfa	Curosurf	M and I	3ml:240mg	1050.63（1032.45, 1065.71）	4.38/mg	8	N
S	Tacrolimus Hydrate	Talymus	I	0	0	0	0	N
S01AD09	Ganciclovir Ophthalmic Gel	Zirgan	M	5g:7.5mg	3.83（3.62，3.96）	0.51/mg	5	N
S01GX05	Lodoxamide tromethamine	Alomide Ophthalmic Solution	M	0	0	0	0	N
S01LA04	Ranibizumab (Genetical Recombination)	Lucentis	M	0	0	0	0	N
S02AA16	Ofloxacin	Ocuflox Ophthalmic Solution	M and I	3.5g:10.5mg	3.33（2.25，4.17）	0.32/mg	6	N
V03AB23	Acetylcysteine	Acetadote	M	20ml:4000mg	5.03（4.87，5.27）	0.001/mg	4	N
V03AB33	Hydroxocobalamin	Cyanokit	M	0	0	0	0	N
V03AC02	Deferiprone	Ferriprox	I	500mg	2.97（2.84，3.04）	0.006/mg	2	N

V03AC03	Deferasirox	Exjade	I	125mg	11.59（11.59, 11.59）	0.09/mg	1	N
V03AF01	Mesna	Mesnex	M and I	4ml:400mg	2.26（1.75，3.68）	0.006/mg	6	Y
V03AF02	Dexrazoxane	Zinecard	M	250mg	71.39（66.67, 74.84）	0.29/mg	8	N
V03AF03	Leucovorin	Leucovorin Calcium	M and I	10ml:100mg	54.71（32.31, 90.40）	0.55/mg	7	Y
V03AF05	Amifostine	Ethyol	M	500mg	58.16（46.79, 76.92）	0.12/mg	8	N

Table 18. List and situation of 165 orphan drugs marketed in China

Source: [290]

(M = a drug manufactured in China; I = a drug imported by China; EM = Essential medicine; Y = Yes, N = No; n/a = not available) *Procurement prices were obtained from the centralized pharmaceutical bidding system of government web-platforms of 31 province in 2011

Country	Orphan drug legislation	National plan/strategy for RD or RD act	Neonatal screening	Market exclusivity	Financial incentive	Non-financial incentive	Reimbursement	Public advocacy groups	Highlights
US [33] [291]	Orphan drug act (1983)	Rare disease act (2002)	Yes	7 years	50% tax credits, FDA fee waivers, grants	Scientific advice, protocol assistance, pre-licensing access	95% covered under Medicare-prior authorization needed after a co-payment of USD $4350	NORD, Genetic alliance	Center of excellence: CNRDI; Registry: RaDaR program; NIH funded research programs
Canada [33] [292] [291]	No	Proposed National Strategy launched with Rare Alliance Canada	Yes	No	Tax incentive, marketing authorization fee reduction	Protocol assistance, regulatory assistance	Covered under Public Service Health Care Plan, increased from 80% to 100% after patient copayment reaches	CORD, Rare Alliance Canada	Health Canada special access program; Centers of Expertise; Canadian Institutes for Health; Formal inclusion of RD in

							threshold of Can$3000		CIHR is proposed
UK [153, 154, 293] [293] [33] [294]	Yes (as in EU)	UK strategy for rare diseases. Plan adopted for all 4 UK countries; ongoing implementation	Yes (as in EU)	10 years	No	Ongoing debate on pre-licensing access	Given for approved ODs given they meet ICER criterion of £20,000-30,000 per QALY (it can be higher than ODs)	Rare disease UK and specialized healthcare alliance	UK 10K project on RD genetics to build RD registry; specialist centers
EU [33]	1:2000	Regulation (EC) No. 141/2000 (1999)		10 years	Different in participating countries; Centralized drug approval				
France [33] [294] [295] [296] [297]	As in EU	First NP (2005-08), Second NP (2011-14), Third NP (2018-22)	Yes	10 years	Tax exemptions	Scientific advice, protocol assistance, pre-licensing access	65-100% reimbursement for ODs. Additional, co-payments are covered by health insurance	Alliance Maladies Rares, French Foundation for Rare Diseases	Early access program; Hospital clinical research programmes;131 reference centers and 501 centers of competence; Launch of Maladies Rares national database
Germany [154, 293, 294, 297]	As in EU	NAMSE	Yes	10 years	No	Pre-licensing access	Fully reimbursed based on benefit analyses by IQWiG. Fixed co-payment of €10/drug, annual threshold cut-off at 2% of individual annual income	ACHSE	RD expert centers; Genetic diagnosis act, proposal for disease-specific registries of RDs; cross-border healthcare
Greece [154, 293, 294, 298]	As in EU	National plan for RDs (2008-12) proposed; not implemented yet	Yes	10 years	No	Pre-licensing access (granted compassionate use)	Listed ODs reimbursed via public insurance system, fixed co-payment of 50% of the	PESPA	No official RD expert centers but specialized services are provided for some conditions; proposed creation of

							reference drug price		national registry
Italy [154, 293, 294, 299]	As in EU	National plan for RDs under Ministerial Decree n. 279/2001 (2013-16)	Yes	10 years	Specific cost exemption	Off-label, compassionate procedure (Law 648/96)	Reimbursement for licensed drug under different categories, special service support	UNIAMO FIMR	Volpi amendment for neonatal screening will include more conditions; National register for RDs; no renewal of NRDP; dedicated funding for research, regional service networks
Portugal [154, 293, 300]	As in EU	National strategy (2008-15)	Yes	10 years	No	Early access programs, specialization authorization of use	Drugs reimbursed through National programmes for RDs; National Health Services	The Portuguese National Alliance	6 centres of expertise; personal card for RD patients for better care and continuity of treatment
Spain [154, 293, 301]	As in EU	National plan (2010)	Yes	10 years	Reduced rebates (4% instead of 5% and 7.5%)	Pre-licensing access (compassionate use and temporary authorization of use)	100% reimbursement for approved drugs. Covered in National Health System coverage	FEDER	SpainRDR (registry); Spain UDP; Royal Decree 1015/2009-improved procedure for faster access to drugs for compassionate use or temporary authorization
Bulgaria [154, 293, 302]	As in EU	National plan for RDs (2009-13); second plan to be officialized by 2014	Yes	10 years	No	Pre-licensing access	ODs are reimbursed by NHIF	NAPRD	National registries for 10 conditions are active; no integrated national registry so far; no expert centres for RDs

Czech Republic [154, 293, 303]	As in EU	Czech National Strategy (2010-20); National plan (NAP) for RDs: NAP1-2012-14 via Decree 633 and NAP2-2015-17	Yes	10 years	No administrative fees for application	Compassionate use, individual patient reimbursement scheme	In-patient case drugs are fully reimbursed, variable for out-patients based on negotiation between market authorization holders and payers (insurance funds) along with healthcare professional	ČAVO	In process of establishing national registry; The Act on social services for people with disabilities (2007)
Lithuania [154, 293, 304]	As in EU	National plan for RDs (Order No V-938) (2012)	Yes	10 years	No	Patient basis	Reimbursed from the Compulsory Health Insurance Fund budget	No alliance for RDs; Council of representatives of Lithuanian patient organizations	No official centres of expertise and national registry; implementation of E-Health project (2013-15); Lithuanian R&D priorities (2007-10) and several other academic research project on genetic diseases
Slovenia [154, 293, 305, 306]	As in EU	Nation plan for RDs	Yes (limited)	10 years	Reduced fees for marketing authorization	No	Reimbursed by compulsory health insurance and partly by complementary health insurance	Slovenian rare disease association	Planning for national registry for RDs
Slovakia [154, 293, 307]	As in EU	National strategy for RD (2012)	Yes	10 years	No	Pre-licensing access, individual basis	Authorized ODs are reimbursed with a co-payment ranging between 1.51% to 20.61% of the total drug price	Slovak rare disease alliance	No national registry or centres of expertise

Cyprus [33],[294] 308]	As in EU	CNSPRD (2012)	Yes (limited)	10 years	No	Several ODs available on patient name basis	No	CARD	No national registry or centres of expertise; no dedicated research funds for RDs
Latvia [33], [294] [309]	As in EU	National plan (2013)	Yes (limited)	10 years	Fee exemption or reduction	Scientific advice and free protocol assistance	Some ODs covered under "Medical treatment of RDs for children", reimbursement for drugs in positive reimbursement list, 2% reimbursement budget for every patient	Latvian rare disease organization Caldrius	Planning for national plan (2017-20) ongoing; no official centres of expertise and national registry; funding available for RD projects but not specific for RD research
Netherlands [33],[294] 310]	As in EU	Nation plan for RDs (2013)	Yes	10 years	Registration fee waiver	No obligation for pharmacoeconomic data in case of no alternative treatment	100% reimbursement for approved ODs. Addition rules for "too expensive" ODs	VSOP	No national registry; planning for centres of expertise; several research programmes (eg. ZonMw with a funding of €13.4m; €22.5m funds for national biobanking infrastructure); tax reductions for R&D
Belgium [33],[29] 311]	As in EU	Belgian plan for RDs	Yes	10 years	Tax exemptions	Compassionate use programs, Medical Need programs,	Fully reimbursed (for some may require specialist prescription from recognized centre), Special Solidarity Fund for some non-	RaDiOrg	Centres of expertise with funding; national registry; RD related research funding

							reimbursed drugs		
Austria [33],[29] , 312, 313]	As in EU	Austrian national action plan for RDs (NAP.se) (2014-18)	Yes	10 years	Fee waiver for marketing authorization, tax exemptions	No	Physicians are entitled to prescribe drugs in the EKO	Pro Rare Austria (Allianz für seltene Erkrankungen)	No designated centers of expertise; no national registry; genetic testing facility available with reimbursement; no dedicated research funds
Sweden [33],[29] [314]	As in EU	Strategy exists but not adopted	Yes	10 years	Fee waiver for clinical trial	Scientific advice, Compassionate use, Named patient prescription	Full reimbursement by social insurance for ODs positively recommended by the Dental and Pharmaceutical Benefits Agency	Rare Diseases Sweden (Riksforbundet Sallsynta diagnoser)	Centres of expertise; National patient registry exists however not dedicated to RD; Parts of national strategy are implemented; decent prerequisites for innovation in the field of RD
Malta [33], [294] 315]	As in EU	No plan or strategy	Yes (limited)	10 years	No	Scientific advice, free protocol assistance, Compassionate use programmes	Full reimbursement for ODs via National Health Scheme which are either on national government formulary list or approved via Exceptional Medicines Treatment policy	National Alliance for RDs Support Malta	Planning for Malta RD national register; limited initiatives; No specific research programmes for RD but several projects underway with funds from University of Malta and EU
Poland [33], [294]	As in EU	National plan for RDs- the roadmap completed but not	Yes	10 years	No	No	Reimbursement for approved drugs. For some drugs reimbursem	National forum for the therapy of	No official centres of expertise; no national registry; some

316]		implemented yet					ent via therapeutic programmes	RDs - ORPHAN	training and education initiatives in place; No specific RD research programmes but 10% funding from Polish Ministry allocated for RD research
Hungary [33], [294] 317]	As in EU	National plan for RDs- approved	Yes	10 years	No	Off-label use possible but difficult	Reimbursement at different levels under special equity procedure as per law	HUFERDIS	Specific budget for RD national plan; no officially approved centres for expertise but 8 informally recognized centres; initiation of RDs register by NRDC; training and education initiatives; research funds available
Croatia [33], [294] 318, 319]	As in EU	National programme for RDs (2015-20)	Yes (limited)	10 years	No	Compassionate use possible	Available ODs are fully reimbursed by the Croatian health insurance fund ("expensive drug fund")	Croatian Society of Patients with Rare Diseases	3 Referral Centres for RDs; no national registry; 40 projects on genetic diseases funded by Ministry
Estonia [33], [294] 320]	As in EU	ERTA or Estonian National Health Plan (2009-20)	Yes	10 years	No	No	100% reimbursement for children under 4 years of age; reimbursement from Estonian Health	ECDP	No national registry; Tartu University Hospital serves as Centres of expertise; special courses for physicians on RDs

							insurance funds		
Luxembourg [33], [294] 321]	As in EU	National plan (2018-22)	Yes (limited)	10 years	No	Off-label use	Full reimbursement for approved ODs	ALAN absl.	No centres of expertise or national registry
Romania [33], [294] , 322]	As in EU	PNBR (2013-20)	Yes (limited)	10 years	No	Compassionate use and off-label use of ODs	Reimbursement via National Programme for RDs	RONARD	No. of centres exist but no official centres for expertise and registry; training and education provided; no specific RD research funding
Finland [33], [294] 323]	As in EU	Finnish National Programmer for RDs (2014-17)	Yes	10 years	No	Free administrative and scientific advice	Basic reimbursement of 35% of purchase price, special reimbursement of 65%-100% available	HARSO	No national registry but 2 legal RD registries: the Finnish register of congenital anomalies and the Finnish register of visual impairment; no specific research funds
Denmark [33], [294] 324]	No official definition; Danish Health and Medicines Authority (500-1000 patients, 1-2/10,000 in the Danish	National strategy for RDs (2015-20)	Yes	10 years	No	Free scientific advice, Compassionate use of drugs	All ODs dispensed at hospitals are free; on needs-based co-payment when dispensed from pharmacy	RDD	2 centres of expertise; no national registry or specific research funding; 2 rare diseases centres to educate healthcare professionals, families and caretakers

	population)								
Mexico [[33], [293] 325]	As in EU	Article 224 revision (2012)*	Yes (limited)	No	N/A	N/A	Some reimbursement via Seguro Popular (public health insurance policy)	N/A	Few to no national initiatives for research; academic or private support for research
Argentina [33], [293] 325]	As in EU	National legislation -Law No. 26.689 (2011)*	Yes	No	N/A	N/A	N/A	N/A	Few to no national initiatives for research; academic or private support for research; ongoing legislation project for creation of specific funds for RDs
Colombia [[33], [293] 325]	1/5000 people	Orphan disease law - Law 1392 (2010)	Yes	N/A	N/A	N/A	N/A	N/A	
Brazil [33], [293] 325]	65/100,000 people	National Policy for RDs (2014)	Yes (limited)	N/A	N/A	N/A	ODs included in SUS are fully reimbursed	N/A	Few to no national initiatives for research; academic or private support for research; no national registry; call for reference treatment centre establishment
Chile [[33], [293] , 325]	As in EU	Ricarte Soto Law (2015)*	Yes	N/A	N/A	N/A	N/A	N/A	The law provides funding for RD patients; allotment of 200 bn pesos grant

									over 4 years
Peru [[33], [293] 325]	Not defined	Law 29698 (2011)*	Yes	N/A	N/A	N/A	N/A	N/A	The law promotes national strategy for RDs
Japan, [33], [293] 217	1:2500	Orphan Drug Amendment to the Pharmaceutical Affairs Law (1993)	Yes	10 years	Waived consultation fee ($20k USD), up to 50% of development costs, 12% tax exemptions, 14% corporate tax, ~25% reduction in review fees	Pre-licensing access, scientific advice and free protocol assistance	Fully reimbursed for approved ODs with 30% contribution from insurance companies and 70% from government		Specified disease treatment research program (1972); National registry of designated intractable diseases
Korea [217, 235, [33],[293]	1:2500	Orphan drug act (1998)	Yes	6 years	May get 50% price reduction for application fee	No	Reimbursed by NHI with a co-payment of 10%, low income families 100% covered	KORD	Research centres and dedicated research funding for RDs; Korean Biobank Project; MoHW announced 4-year roadmap for national system to tackle RD
Taiwan [217, 238, [33], [293]	1:10,000	Rare Diseases Control and Orphan Drug Act (2000)	Yes	10 + 2 years	Fee reductions; copay can be waived	Regulatory and protocol assistance	RD patients can get 80% reimbursement, low income patients can get 80-100%	TFRD	Universal health coverage of 99.9% citizens
Australia 202, 217, [33], [293]	1:2000	Australian orphan drugs program (1997	Yes	5 years	Fee reduction for market authorization of ODs	Pre-licensing access, regulatory assistance	Fully reimbursed by LSDP programme	AVA	Western Australia Rare Diseases Strategic Framework 2015-18; dedicated

									WGS programme
New Zealand [153, 154, 217, 292]	1:2000	N/A	Yes	No	No	NPPA	Reimbursed for drugs on Pharmaceutical Schedule	NZORD	Universal health coverage; limited research funding
China [153, 217, [33], [293]	1:50,000	No	Yes	No	Value added tax reduction on ODs from 16% to 3% (80% reduction)	Can be allowed for smaller CTs or waiver of CTs if required	Often paid by patients as OOP; ODs on NRDL are 100% reimbursed and inclusion based on cost-effectiveness and low pricing	CORD and others	CRDPTA launched national research program (2013); no national registry but planning ongoing; proposal for improvement of drug exclusivity; several initiatives in different provinces; inclusion of 121 drugs in rare disease list
Hong Kong [33], [293] [153, , 217,	N/A	N/A	Yes	No	No	No	Several subsidized ODs by Hospital Authority	HKARD	Social support provided to RD patients
Singapore [33], [293] [153, 217,	< 20,000	Orphan Drug Exemption to the Medicines Act (1991)	Yes	10 years	N/A	N/A	Medishield Life covers congenital diseases; decision to reimburse made by CDA	RDSS, RAB	Orphan drug legislation not activated yet; RD funds requested with initial corpus of SGD $200mn
Malaysia [33], [293]	1:4000	In progress	Yes	No	N/A	EPP	ODs included in national medicine formulary are free with a co-	MRDS	3 Centres of expertise; EPP status to pharma's

[153, 217,							pay of RM5		
Indonesia [33], [293] [153, 217,	1:2000	No	No	No	No	Off-label drug use, expedited review	OOP	N/A	Launch of *BPJS Kesehatan* (new healthcare policy*)* to cover all citizens by 2019; Centre of excellence to support RD patients
India [109, 217] [33],	1:5000	National policy for treatment of RDs[a]	No	N/A	N/A	Compassionate use or named patient programme	Usually self-funded or via NGO's, pharmaceutical companies	I-ORD and others	No dedicated funds for research and innovation; RD policy recently revoked

Philippines [153, , [33], [293] 217	1:20,000	Rare Diseases Act - Republic Act no. 10747 (2016)	Yes	N/A	N/A	Expedited review of ODs, Compassionate use scheme	N/A
Vietnam [33], [293] [153, 217,	1:500 – 1:2000	N/A	Yes	N/A	N/A	Compassionate use of drugs possible	N/A
Thailand [33], [293] [153, , 217,	1:2500	In planning stage	Yes	N/A	N/A	Treatment for Gaucher disease provided	Few ODs centrally supplied and funded by the GPO; OOP

Table 19. Summary of rare disease policies, regulations, laws and initiatives in countries across globe

Abbreviation: RDs = Rare diseases; ODs = Orphan drugs; NAMSE = *Nationales Aktionsbündnis für Menschen mit Seltenen Erkankungen;* IQwiG = Institute for Quality and Efficiency in Healthcare; ACHSE = Alliance of Chronic Rare Diseases; PESPA = Greek Alliance for Rare Diseases; SpainRDR = Spanish Rare Diseases Registries Research Network; SpainIDP = The Spanish Undiagnosed Rare Diseases Program; FEDER = the Spanish Rare Disease Federation; NHIF = National Health Insurance Fund; NAPRD = The National Alliance of People with Rare Diseases; ČAVO = The Czech Association for Rare Diseases; CNSPRD = The Cyprus National Strategic Plan for Rare Diseases; CARD = Cyprus Alliance for Rare Disorders; VSOP = Dutch national alliance of patients organization for rare and genetic disorders; ZonMw = The Netherlands Organization for Health Research and Development; RaDiOrg = Rare Diseases Organization Belgium; EKO = Austrian Reimbursement Code; NRDC = National Rare Diseases Centre; HUFERDIS = Hungarian Federation of People with Rare and Congenital Diseases; ERTA = Eesti Rahvastiku Arengukava; ECDP = Estonian Chamber of Disabled People ; ALAN = Luxembourg Association for Neuromuscular and Rare Disorders; PNBR = National Plan for Rare Diseases; RONARD = Romanian National Alliance for Rare Diseases; HARSO = HArvinainen (rare) Sairauksien (diseases) Organisaatio (organization); RDD = Rare Diseases Denmark; SUS = Unified Health System; LSDP = Life-saving drug programme; AVA = Rare Voices Australia; WGS = Wide genomic sequencing; CTs = Clinical trials; NRDL = National ; CORD = Chinese Organization for Rare Disorders; OOP = Out of pocket; NPPA = Named Patient Pharmaceutical Assessment; NZORD = New Zealand Organization for Rare Disorders; RDSS = Rare Disorders Society Singapore; RAB = Rainbows Across Borders; CDA = Centre for Drug Administration; MRDS = Malaysian Rare Disorders Society; EPP = Early Point Project; BPJS Kesehatan = *Badan Penyelenggara Jaminan Sosial* ; I-ORD = Indian Organization for Rare Diseases; PSOD = Philippines Society for Orphan Disorders; HKARD = Hog Kong Alliance for Rare Diseases; TFRD = Taiwan Foundation of Rare Diseases; KORD = Korean Organization for Rare Disease; MoHW = Ministry of Health and Welfare; NHP RD club = National Hospitals of Pediatrics; GAP = Global Alliance for Progress; GPO = Government Pharmaceutical Organization; ThaiRDN = Thailand Rare Disease Network; N/A = Not available; No = Does not exist

(*) = currently are either law or legislation but not national plan or strategy

(°) = temporarily withdrawn

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