

An Overview of China's Market Approval Policy and Medical Insurance Payment System for Rare Disease Drugs

»» Yajie Li
Vice President Technical
Parexel Regulatory and Access Consulting

Gary Cheng
Vice President
Health Advances

Eric Woo
Senior Analyst
Health Advances

Jinchuan Guo
Director of Information Research
Illness Challenge Foundation

>>> Index

I. Relevant Policies on Expedited Approval of Rare Disease Drugs

- (1) Regulatory Incentives for Rare Disease Drugs in Countries/Regions Including Japan, Europe, and the US
- (2) China's Policies for Accelerating Development and Approval of Rare Disease Drugs
- (3) Development Strategies for Imported Rare Disease Drugs in China
 - a. Drugs Already Launched in Foreign Markets
 - b. Conducting Clinical Trials in China in Parallel with Foreign Markets
 - c. Approval for Use Granted Upon Filing in Specific Regions
- (4) Development Strategies for Domestic Rare Disease Drugs in China

II. An Overview of China's Multi-Layered Reimbursement System for Rare Disease Drugs

- (1) Basic Medical Insurance
- (2) Supplemental Medical Insurance
- (3) Inclusive Commercial Health Insurance
- (4) Non-governmental charitable donations

Parexel's Advantages in Rare Disease Drug Development Consulting



The term rare disease refers to a group of diseases with extremely low prevalence. Rare diseases are generally considered severe chronic diseases, which often lead to poor quality of life and may even be life-threatening to patients. According to the World Health Organization, there are around 5,000 - 8,000 rare diseases that have been recognized across the world. In China, rare diseases are recognized in the National Rare Diseases List. In May 2018, the National Health Commission of China published the List of Rare Diseases (First List), covering 121 indications that affect up to three million patients¹ to provide a reference for the rare disease drug review. Since 2021, the compilation of the second list of rare diseases is also in progress under the guidance of the National Health Commission. Additionally, in September 2021, at the 3rd China Multi-Disciplinary Symposium on the Definition of Rare Diseases/Rare Disease drugs - which was jointly organized by the Joint Meeting of Chairpersons of National Rare Disease Academic Groups, the Shanghai Foundation for Prevention and Control of Rare Diseases, and the Rare Diseases Branch of the Shanghai Medical Association - *The China Research Report on The Definition of Rare Diseases 2021* was published. Lin Wang, Secretary-General of the Joint Meeting of Chairpersons of National Rare Disease Academic Groups, provided the latest academic definition for rare disease in China. It is defined as a disease with an incidence of less than 1 in 10,000 newborns, or prevalence of less than 1 in 10,000 in the general population or affecting less than 140,000 people. According to official estimates, there are 20 million rare disease patients in China. Considering the low diagnosis rate and lack of disease awareness, this number is likely underestimated.

Rare disease patients in China face many challenges. Rare diseases can be challenging to diagnose. Even when patients are diagnosed, they cannot get access to efficacious treatment as there are no available drugs in China, or the approved drugs are not intended for rare disease treatments. Moreover, patients cannot afford approved drugs due to their lack of reimbursement coverage. Among them, inaccessibility and unaffordability are the most prominent causes, making more than half of patients unable to receive timely and sufficient treatment.



》》》 I. Relevant Policies on Expedited Approval of Rare Disease Drugs

(1) Regulatory Incentives for Rare Disease Drugs in Countries/Regions Including Japan, Europe, and the US

In Europe, the US, Japan, and other countries or regions, regulators have introduced their own criteria for orphan drug designations and formulated a series of incentive policies from drug development to commercialization^{2,3} to accelerate the approval of rare disease drugs.

- ▶ In 1983, US Congress passed the Orphan Drug Act and initiated the Orphan Drug Designation program. Later, the US Food and Drug Administration (FDA) revised orphan drug rules in 1991, 1992, 2011, and 2013, adopting a series of incentive policies for designated orphan drugs, including accelerated approval, market exclusivity rights, and financial support. By February 2021, the FDA has granted 5,808 orphan drug designations and approved 952 drugs for orphan indications.
- ▶ In the EU, EMA launched the orphan designation program in 2000 to encourage research and development for rare disease medicines. Companies can benefit from incentives such as access to scientific advice during development, shortened approval timelines, and market exclusivity protection after launch.
- ▶ In 1993, Japan introduced the Orphan Drug Amendment to the Pharmaceutical Affairs Law, which established three criteria for orphan designation, and provided financial incentives (subsidies, lower application fees, and tax credits) as well as regulatory support, including guidance and consultation on research and development

activities, priority review, and market exclusivity. So far, Japan has more than 300 drugs with orphan designation.

In summary, regulators in Japan, the US, and Europe have introduced similar regulatory incentives since the 1980s to encourage the development of rare disease drugs. Combined with pharma investments in this area, these policies have reached a level of maturity that has correspondingly allowed increased numbers of rare disease drugs to be approved through fast-track review, and in turn, allowed patients to receive treatment quicker. The pharmaceutical companies also benefited greatly.

(2) China's Policies for Accelerating Development and Approval of Rare Disease Drugs

Rare disease drug development in China has been impeded by high costs and execution difficulties in clinical trials. Before the reform of the drug review and approval system was introduced in 2015, few global pharmaceutical companies would consider developing or launching rare disease drugs in China, and few domestic pharmaceutical companies engaged in the development of rare disease drugs. Consequently, there were limited treatment options for a large number of rare disease patients.

Since 2015, the Chinese government has adopted a series of policies to encourage the import, development, and manufacturing of rare disease drugs and accelerate the regulatory review and approval of these products.

- › In August 2015, the State Council issued *Opinions on the Reform of the Review & Approval System for Drugs and Medical Devices* (State Council [2015] No. 44). In October 2017, the General Office of the CPC Central Committee and the General Office of the State Council released the *Opinions on Deepening the Reform of Review and Approval System and Encouraging the Innovation of Drugs and Medical Devices*, providing a firm stance on expedited application review for rare disease drug to foster development.
- › In December 2017, the National Medical Products Administration (NMPA, formerly known as the China Food and Drug Administration) published the *Opinions on Priority Review & Approval to Address the Application Backlogs*, which explicitly grants priority review and approval for rare disease drugs and allows applicants to request a smaller enrollment size in clinical trials or even a trial waiver.
- › In May 2018, the NMPA and the National Health Commission published the *Announcement on Optimizing Drug Review & Approval*. For rare disease drugs already launched in foreign markets and proven to have no ethnicity-based difference in treatment response, applicants can directly apply for China market authorization by submitting data from clinical trials conducted abroad.
- › In October 2018, the NMPA and the National Health Commission issued the *Working Procedure for the Review and Approval of Overseas New Drugs Urgently Needed in Clinical Settings*. It grants a special channel to speed up the review and approval of new drugs that have been launched in foreign markets but not approved in China. Additionally, the document requires that technical reviews should be finished within 70 working days after acceptance of new drug applications.
- › In July 2020, the State Administration for Market Regulation published the amended version of *Regulations on Drug Registration* which specifies that applications of innovative drugs for rare diseases can be granted with priority review and provided shorter review timelines to reduce the time to market.

According to the *Drug Evaluation Report 2020* published by the Center for Drug Evaluation (CDE) in June 2021, from 2016 to 2020, rare disease drugs granted with priority review experienced a year-on-year increase in their proportion of total new drug applications and in the number of their approvals (see Table 1)⁴. Statistics by Pharnexcloud⁵ show that NMPA approved 18 rare disease drugs in 2021. As of today, the NMPA has published three lists of overseas new drugs launched in foreign markets that are urgently needed in clinical settings. Of the 40

rare disease drugs included in the list, 21 have been launched in the Chinese market, covering 15 types of rare diseases such as Mucopolysaccharidosis, Huntington’s Disease, Multiple Sclerosis, and Spinal Muscular Atrophy. However, drug development is a process with long cycles, and China still lags

far behind Japan and other Western countries in this regard despite the help of priority review and approval. A concerted effort by both regulators and pharmaceutical companies is pivotal to promote rare disease drug development in China.

Table 1. Overview of Applications and Approvals of Rare Disease Drugs Granted with Priority Review

	2016		2017		2018		2019		2020	
	Quantity	Proportion	Quantity	Proportion	Quantity	Proportion	Quantity	Proportion	Quantity	Proportion
NDAAs	8	4.1%	11	5.0%	28	8.9%	28	11.1%	21	14.6%
Approvals	-	-	-	-	3	3.6%	6	7.5%	11	9%

(3) Development Strategies for Imported Rare Disease Drugs in China

Rare disease drugs developed by foreign pharmaceutical companies can be classified into two categories, namely drugs which have already been launched in foreign markets, and drugs with ongoing clinical trials or in the clinical trial preparation stage in foreign markets. Foreign pharmaceutical companies can choose one of the following strategies to accelerate the development and launch of rare disease drugs in China.

a. Drugs Already Launched in Foreign Markets

Today, a considerable number of rare disease drugs have already been launched in Europe, the US and Japan. These drugs are critical to address the availability and accessibility of drugs urgently needed by Chinese patients in clinical settings. In China, the CDE formulated the *Technical Guidance for Accepting Drug Data from Overseas Clinical Trials* and the *Clinical*



Technical Requirements for Drugs Marketed Overseas but Not Marketed in China, respectively, in July 2018 and October 2020, to support the launch of these drugs in China. The document suggests that regulators support the development and commercialization of rare disease products and conduct reviews and approvals on the premise of increasing their accessibility for the public.

Pharmaceutical companies can submit the clinical data used for marketing approval in foreign markets and the post-launch data. The CDE can reference the inspection results of foreign regulators for evaluating the quality of such data. A drug can be exempted from clinical trials and get directly authorized for marketing in China once it has been assessed to be safe and effective and has been shown by evidence to have no ethnic difference in response. If it is safe and effective but lacks ethnic sensitivity data, relevant bridging trials need to be carried out. If global data cannot support the evaluation of safety and efficacy, and there is a continued wish to register and market the drug in China, necessary exploratory and confirmatory clinical trials should be carried out according to the requirements for new drug approval.

b. Conducting Clinical Trials in China in Parallel with Foreign Markets

To reduce unnecessary duplicated clinical trials and shorten the delay of product launch between different countries, CDE encourages applicants

to simultaneously conduct clinical trials in China for rare disease drugs which have not yet been launched in foreign markets. Foreign pharma can adopt the strategy of having China be part of global, international, multi-center clinical trials based on early-stage data, ethnic sensitivity analysis, and the requirements of different regulatory agencies, to accelerate, or even achieve the goal of simultaneously listing rare disease drugs in China and other countries.

c. Approval for Use Granted Upon Filing in Specific Regions

Apart from the strategies mentioned above, foreign applicants can also introduce rare disease drugs directly into the market after filing with regulatory agencies in specific regions in China.

Hainan Boao Lecheng International Medical Tourism Pilot Zone

In December 2018, the State Council published the *Decision on Temporary Adjustment of the Regulations on Implementation of the Drug Administration Law of China at the Hainan Boao Lecheng International Medical Tourism Pilot Zone*. According to the document, the People's Government of Hainan Province is responsible for approving applications for importing a small number of medicines (excluding vaccines) for urgent clinical uses by medical institutions in the pilot zone. After approval, the imported drugs

must be used for special medical purposes within designated medical institutions. In November 2020, the Research Base for Supervision of Drugs and Medical Devices under the National Medical Products Administration was established in the Pilot Zone. Hainan will accelerate the construction of a real-world data platform through the research base construction, establish and improve data standards for real-world research, speed up the process of real-world research pilot work, expand the influence of real-world research and applications in the registration and listing of imported drugs and medical devices, and finally attract more international, advanced pharmaceutical and medical device R&D and production enterprises to participate in follow-up pilots.

Adopting this policy can somewhat improve drug accessibility for rare disease patients. For example, Pralsetinib, developed by Blueprint Medicines Corporation, which is used for treating adult patients with locally advanced or metastatic RET fusion-positive non-small cell lung cancer (NSCLC) after platinum-based chemotherapy, was prescribed in the Boao Lecheng International Medical Tourism Pilot Zone, marking the world's first prescription of Pralsetinib outside the country of approval. Pralsetinib was also the first truly innovative medicine to be marketed and used simultaneously in the international market. In March 2021, Pralsetinib, with a priority review designation, received conditional approval from NMPA, making it the first innovative drug in China to use Lecheng real-world data to assist in its evaluation and conditional approval⁶.

Some rare disease drugs approved in foreign markets can be directly launched in the Boao Lecheng International Medical Tourism Pilot Zone. The real-world evidence obtained can also be used to support subsequent new drug applications or post-launch studies.

Guangdong-Hong Kong-Macao Greater Bay Area

In November 2020, with the approval of the State Council, eight ministries, including the State Administration for Market Regulation and the National Medical Products Administration, jointly issued the *Work Plan for Regulatory Innovation and Development of Pharmaceutical and Medical Device in Guangdong-Hong Kong-Macao Greater Bay Area*. According to the document, Guangdong Provincial Food and Drug Administration will review and approve drugs that are urgently needed in clinical settings which have already been launched in Hong Kong or Macao, and clinically advanced medical devices that are urgently needed in clinical settings which have been purchased by public hospitals in

Hong Kong and Macao. After approval, they can be used by designated medical institutions in the nine inland cities of GBA. This policy underwent a trial stage from April to July 2021, during which time nine imported drugs and two imported medical devices urgently needed for clinical settings were approved, benefiting 150 patients⁷.

Rare disease drugs developed by foreign pharmaceutical companies available in Hong Kong or Macao can be authorized for use in designated hospitals in the GBA after fulfilling simplified approval procedures designed by the Guangdong Provincial Food and Drug Administration. The real-world data (RWD) obtained from GBA can support the subsequent NDA for these drugs in China.

(4) Development Strategies for Domestic Rare Disease Drugs in China

Further improvement on the efficiency of research and development for rare illness drugs is needed to match the needs of rare disease patients. To incorporate characteristics of rare diseases in providing scientific advice and references for the research and development of rare illness drugs and trial design, China CDE published a draft for commentary of the *Technical Guidelines for Clinical*

Development of Rare Illness Drugs in October 2021, and issued the official version on January 6, 2022.⁸ Due to the absence of a clear definition for rare diseases in China, the Guidelines adopts the term Rare Illness (罕见疾病, Hǎnjiàn Jíbìng) to avoid confusion with the term Rare Diseases (罕见病, Hǎnjiàn Bìng) defined by the Rare Diseases List.

The guidelines clearly state that in addition to following the general drug research and development rules, clinical R&D of rare illness drugs should also consider the characteristics of the disease. While highlighting the importance of scientific rigor, the guidelines encourage the adoption of a flexible trial design and making full use of the limited available patient data to obtain scientific evidence for risk-benefit evaluation which can support regulatory decision-making. The guidelines also provide a recommended clinical development plan for rare illness drugs shown as a flowchart in Figure 1. Adopting the official version will further promote rare disease drug development by domestic pharma, thus offering more treatment options to rare disease patients.

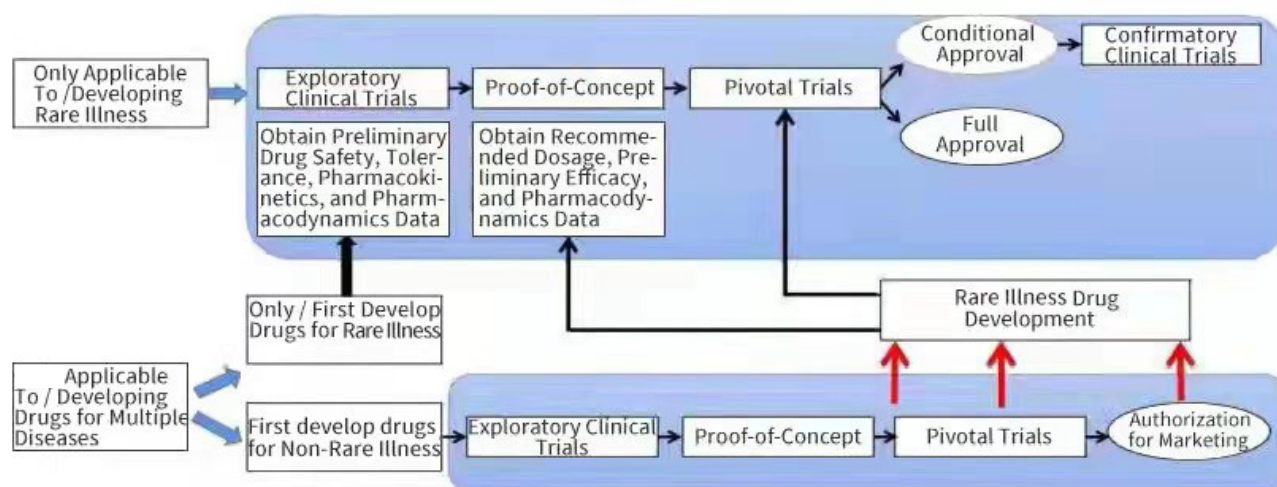


Figure 1: Clinical Development Program for Rare Illness Drugs

II. An Overview of China's Multi-Layered Reimbursement System for Rare Disease Drugs

Rare disease drugs are typically more expensive than ordinary drugs, and the financial burden for patients is enormous. Once diagnosed with a rare disease, a patient may be forced into a life of hardship. Currently, these patients primarily rely on basic medical insurance, critical illness medical insurance, supplementary medical insurance, medical aid, and charitable donations to alleviate their drug cost burden.

(1) Basic Medical Insurance

Basic medical insurance, designed by the government and jointly contributed by employers and employees, is a crucial component of China's social security system. Established in 2018, the China National Healthcare Security Administration has updated

the National Reimbursement Drug List (NRDL) for three consecutive years, bringing considerable benefits to Chinese people by creating a dynamic updating mechanism to include drugs for prevalent diseases, critical illnesses, and rare diseases in the reimbursement system.⁹ As the most influential catalog with nationwide coverage, the NRDL has become more open and inclusive toward rare disease drugs.

- ▶ In 2019, nine rare disease drugs were included in the NRDL, covering a series of rare diseases such as pulmonary hypertension, multiple sclerosis, and Niemann-Pick disease.¹⁰
- ▶ In 2020, six additional rare disease drugs were incorporated into the NRDL to treat pulmonary

hypertension, idiopathic pulmonary fibrosis, amyotrophic lateral sclerosis, systemic sclerosis-related interstitial lung diseases, and Huntington's disease. In particular, Austedo, developed by Teva Pharmaceuticals, and Mayzent, developed by Novartis, were included in the list seven months after being approved for marketing in China.¹¹

- › In 2021, seven rare disease drugs were included in the NRDL following successful drug price negotiations.¹² Apart from previously covered indications such as pulmonary hypertension and multiple sclerosis, the list also incorporated Biogen's nusinersen (Spinraza) for SMA and Takeda's agalsidase alfa (Replagal) for Fabry disease, giving patients much broader access to efficacious treatments and offering great benefits.

According to the Illness Challenge Foundation, 32 rare disease drugs were authorized for marketing in China from 2019 to 2021. Thanks to the efforts by the National Healthcare Security Administration and other stakeholders, 12 rare disease drugs were included in the NRDL to increase the accessibility of the rare disease drugs launched in China. On average, it only took around 14 months for the 12 drugs to go from getting approved for marketing to getting included in the NRDL. In recent years, the Chinese government has attached greater importance to rare disease drugs by bringing most of the rare disease

drugs launched in China into the reimbursement list. However, considering the budget constraints of basic medical insurance funds and factors such as social equity and pricing strategies of pharmaceutical enterprises in the Chinese market, there are still many difficulties to overcome before all high-value rare disease drugs are included in the NRDL. For some rare disease drugs which have not yet been included in the NRDL, it is necessary to adopt other approaches, such as multi-payer co-payment, to ensure drug accessibility for patients.

(2) Supplemental Medical Insurance

Due to the considerable treatment cost, many rare disease drugs have yet to be incorporated into the NRDL, such as those for treating lysosomal storage diseases, Cerezyme for treating Gaucher disease, alglucosidase α for treating Pompe disease, laronidase, idursulfase β , and elosulfase α for treating Mucopolysaccharidoses (Type I, Type II and Type IVA). Some provinces and cities seek to bring high-value rare disease drugs into their local reimbursement system through special funds for rare diseases, critical illness insurance, and medical aid.

Foshan City

Foshan City carried out an innovative restructuring of its existing medical security system, which resulted in including rare disease drugs into the Medicaid

system. More specifically, the city incorporated rare diseases as a special medical aid item into its Medicaid Measures and specified the qualifications for aids.¹³ Foshan also issued the first reimbursement list for rare disease drugs in China, which includes 124 rare disease drugs which have been approved in China for treating 61 types of rare diseases.¹⁴

Chengdu City

Leveraging the *Supplementary Insurance Funds for Mutual Assistance in Medical Treatment of Critical Illness*, Chengdu City seeks to mitigate the catastrophic health expenditures imposed on rare disease patients. To facilitate this purpose, the city set up an access program for rare disease drugs that features the goal of keeping costs at a controllable level and utilizing co-payment, which helps to bring medicines for treating seven rare diseases (tetrahydrobiopterin deficiency, Spinal Muscular Atrophy, mucopolysaccharidosis, Gaucher Disease, Transthyretin Amyloid Cardiomyopathy (ATTR-CM), pulmonary hypertension and Pompe Disease) into the scope of critical illness insurance. In this way, the annual cost of treatment faced by rare disease patients will be shared by the critical illness insurance and pharmaceutical companies (or suppliers). Based on an upper limit of 400,000 RMB per year for payers and 60,000 RMB per year for patients, pharmaceutical companies are encouraged to figure out an innovative payment scheme in collaboration with other social organizations to ensure that the ceiling insured amount offered by the plan is satisfactory that patients can have continued access to treatment.¹⁵

Zhejiang Province

Zhejiang province also restructured its existing medical security system, which is highlighted by the establishment of a rare disease drug access

program. It is the first region in China to implement medical insurance funds pooling for rare diseases at the provincial level. In 2019, Zhejiang Medical Security Administration and three other departments in Zhejiang Province jointly issued the *Notice on Establishing a Rare Disease Drug Access Program in Zhejiang*. The document proposes appropriating 2 RMB per year (per insured person) from the critical illness insurance fund to set up Zhejiang Special Fund for Rare Disease Drugs. The annual cost of drugs will be reimbursed cumulatively, with a reimbursement ratio between 80 - 100 percent.¹⁶ As of now, four types of rare diseases (Gaucher Disease, phenylketonuria, Pompe disease, and Fabry disease) have been incorporated into the reimbursement list.¹⁷ Additionally, Zhejiang province has also delivered excellent performance in screening rare diseases. Of the 26 diseases to be screened for newborn babies, six are rare diseases: Phenylketonuria, Maple Syrup Urine Disease, Citrullinemia, Methylmalonic Acidemia, Propionic Acidemia, and Isovaleric Acidemia.¹⁸

(3) Inclusive Commercial Health Insurance

Commercial health insurance has been in China for several decades, and there are a wide variety of options available in the market. Apart from traditional commercial health insurance, which provides coverage for rare diseases, inclusive commercial health insurance (Inclusive Insurance) has begun to emerge and is gaining strong momentum in different cities in recent years.

Unlike traditional commercial health insurance, inclusive insurance has a low premium. It can accept individuals with pre-existing conditions, making it an essential component of the multi-layered medical security system the government is striving to build. Some cities (such as Foshan, Guangzhou, Shanghai,

Hangzhou, and Jinan) have included high-value rare disease drugs into the specialty drug list of their local inclusive insurance plan, providing a claim limit of 100,000 RMB - 300,000 RMB or even more. Rare disease patients can alleviate their cost burden by

enrolling in inclusive insurance plans in different cities.¹⁹

The table below shows rare disease drugs included in the specialty drug list of inclusive insurance in selected cities.

Table 3. Rare Disease Drugs Included in Selected Chinese ‘Cities’ Inclusive Insurance Specialty Drug List

City	Insurance Plan	Rare Disease Drugs Covered by Insurance Plan	Coverage %: Without Rare Disease Diagnosis before Insurance Enrollment (Specified by Insurance Plan)	Coverage %: With Rare Disease Diagnosis before Insurance Enrollment (Specified by Insurance Plan)	Coverage Amount (RMB)
Guangzhou	Guangzhou City Insurance	Drugs included into the NRDL through successful price negotiations; innovative medicines that meet the specified scope of indications		60%	300,000
Hangzhou	Hangzhou City Insurance	Spinal Muscular Atrophy (SMA): Nusinersen Sodium Injection Mucopolysaccharidosis (MPS) IVA: Elosulfase Alfa Fabry Disease: Agalsidase Alfa		60%	100,000
Jinan	Jinan City Insurance	SMA: Nusinersen Sodium, Risdiplam MPS II: Idursulfase Beta MPS IVA: Elosulfase MPS I: Laronidase Hypophosphatemic Rickets (X-linked Hypophosphatemia): Burosumab Transthyretin Amyloid Cardiomyopathy (ATTR-CM): Tafamidis Soft Capsules		70%	300,000
Chengdu	Chengdu City Insurance	Idiopathic Pulmonary Hypertension: Iloprost Inhalation Solution Acromegaly (not included in the 121 rare diseases): Lanreotide Acetate for Injection		75%	1 million
Shenzhen	Supplemental Insurance for Critical Illness	SMA: Nusinersen Sodium Injection Pompe disease: Alglucosidase Alfa for Injection Fabry Disease: Agalsidase Beta for Injection MPS: Laronidase Concentrated Solution for Injection		70%	150,000

Fujian	Fujian Province (excluding Xiamen) Inclusive Insurance	Idiopathic Pulmonary Hypertension: Iloprost Inhalation Solution Hemophilia: Emicizumab Injection Acromegaly: Lanreotide Acetate for Injection Homozygous Familial Hypercholesterolemia: Evolocumab Injection	80%	Rare diseases (as described) diagnosed before the first insurance enrollment will not be covered	1 million
Deyang	Deyang City Insurance	Hemophilia A: Emicizumab Injection Phenylketonuria: Infant formula powder for particular medical purpose Phenylketonuria formula; amino acid metabolism disorder formula for special medical purpose; non-full nutritional formula powder for special medical purpose Phenylketonuria formula Crohn's Disease: Ustekinumab Injection SMA: Nusinersen Sodium Injection Idiopathic Pulmonary Hypertension: Treprostinil Injection Multiple Sclerosis: Fampridine Extended-Release Tablets, Dimethyl Fumarate Capsules MPS IVA: Elosulfase Alfa Injection Fabry Disease: Agalsidase Beta for Injection Pompe Disease: Alglucosidase Alfa for Injection Gaucher Disease: Imiglucerase for Injection	Plan A (59 RMB): 60% Plan B (99 RMB): 100%		1.2 million
Zhenjiang	Zhenjiang City Insurance	SMA: Nusinersen Sodium Injection Gaucher Disease: Imiglucerase for Injection Pompe Disease: Alglucosidase Alfa for Injection Fabry Disease: Agalsidase Alfa, A Beta for Injection MPS IVA: Elosulfase Alfa Injection	Basic plan: 15% Upgraded plan: 60%		Basic plan: 500,000 Upgraded Plan: 1 million

Dongying	Dongying City Insurance	SMA: Nusinersen Sodium, Risdiplam MPS II: Idursulfase Beta, MPS IVA: Elosulfase, MPS I: Laronidase Hypophosphatemic rickets (X-linked Hypophosphatemia): Burosumab Hereditary Angioedema: Lanadelumab Adult Wild-type or Inherited Transthyretin Amyloid Cardiomyopathy (ATTR-CM): Tafamidis Soft Capsules Homozygous Familial Hypercholesterolemia: Evolocumab	70%		300,000
Heyuan	Heyuan City Insurance	SMA: Nusinersen Sodium ATTR-CM: Tafamidis Soft Capsules X-linked Hypophosphatemia: Burosumab	80%	30% for ATTR-PN drugs if the rare disease is diagnosed before the insurance enrollment	1.5 million
Zhaoqing	Zhaoqing City Insurance	Pompe Disease: Alglucosidase Alfa for Injection ATTR-PN: Tafamidis Meglumine Soft Capsules ATTR-CM: Tafamidis Soft Capsules Gaucher Disease: Imiglucerase for Injection MPS: Laronidase Concentrated Solution for Injection Fabry Disease: Agalsidase Beta for Injection	80%	Rare diseases (as described) diagnosed before the insurance enrollment will not be covered	1 million
Yantai	Yantai City Insurance	SMA: Nusinersen Sodium, Risdiplam MPS II: Idursulfase Beta, MPS IVA: Elosulfase, MPS I: Laronidase Hypophosphatemic Rickets (X-linked Hypophosphatemia): Burosumab Hereditary Angioedema: Lanadelumab Adult Wild-type or Inherited Transthyretin Amyloid Cardiomyopathy (ATTR-CM): Tafamidis Soft Capsules Homozygous Familial Hypercholesterolemia: Evolocumab for Injection	70%		300,000

Wuxi	Wuxi City Insurance	<p>Noonan Syndrome Types 1-6: Recombinant Human Growth Hormone Injection</p> <p>MPS I: Laronidase Concentrated Solution for Injection</p> <p>MPS II: Idursulfase Beta Injection</p> <p>ATTR-PN : Tafamidis Meglumine Soft Capsules</p> <p>Hyperphenylalaninemia: Sapropterin Dihydrochloride Tablets</p> <p>Pulmonary Hypertension: Treprostinil</p> <p>Hemophilia: Emicizumab</p> <p>ATTR-CM : Tafamidis Soft Capsules</p> <p>Homozygous Familial Hypercholesterolemia: Evolocumab for Injection</p> <p>MPS IVA: Elosulfase Alfa Injection</p> <p>Pompe Disease: Alglucosidase Alfa for Injection</p>	50%	20% for the rare disease drugs (as described) if the rare disease is diagnosed before the insurance enrollment	800,000
Xuzhou	Xuzhou City Insurance	<p>Multiple Sclerosis: Teriflunomide, Fingolimod, Siponimod</p> <p>Niemann -Pick disease type C: Miglustat</p> <p>Hemophilia (Type A): Recombinant Human Coagulation Factor VIIa, Human Coagulation Factor VIII</p> <p>Hemophilia (type B): Recombinant Human Factor VIIa, Human Prothrombin Complex, Recombinant Human Factor IX</p> <p>Pulmonary Hypertension: Selexipag, Ambrisentan, Bosentan, Macitentan, Riociguat</p> <p>Amyotrophic Lateral Sclerosis: Edaravone Sodium Chloride Injection</p> <p>Idiopathic Pulmonary Fibrosis: Pirfenidone, Nintedanib</p> <p>Chorea or Tardive Dyskinesia in Adults: Tetrabenazine</p> <p>Acromegaly: Octreotide, Lanreotide</p>	45%		200,000

Source: Illness Challenge Foundation

(4) Non-governmental charitable donations

In addition to the government and the market as payers for high-value rare disease drugs, some non-governmental charitable organizations also provide medical aid to patients with rare diseases.

- › The *Medical Aids for Rare Diseases Project* sponsored by the Beijing Illness Challenge Foundation provides financial aid of up to 10,000 RMB (through national programs) or up to 50,000 RMB (through local subsidy programs offered in Zhejiang, Shanxi, and Shandong) to patients and families having financial difficulties. In particular, the establishment of local special subsidy programs serves as an excellent complement to existing insurance coverage, helping patients facing high out-of-pocket medical costs by providing financial assistance for their co-payments, coinsurance, deductibles, and other health-related expenses, helping to solve the last mile problem for medicine for patients, enhancing drug access to offer real benefit to patients.²⁰
- › The China Primary Care Foundation has pioneered many rare disease initiatives and patient assistance programs, including those for patients with multiple sclerosis, which has led to a 40 percent reduction in drug costs for most patients, and to access to free medicine for qualified low-income patients.²¹

Parexel's Advantages in Rare Disease Drug Development Consulting

Parexel's Experience in Rare Disease Clinical Research

Parexel has managed approximately 400 rare disease clinical studies over the past five years that contributed to 17 FDA drug approvals. At Parexel, field-leading experts understand the nuances of rare disease studies. We combine scientific rigor and patient-community engagement to ensure that every patient is identified. We have the knowledge to decide if the trial is the best treatment option for the patients; and is retained throughout the duration of the trial. Given that most rare diseases have a genetic cause, Parexel's rare disease capability is led and underpinned by expertise in precision medicine and translated into study delivery.

At Parexel, we adopt an integrated, cross-functional model which is distinguished by

- › Lean, nimble delivery teams complemented by broader access to organizational expertise through customized innovation teams (medical, scientific, regulatory)
- › Data-driven insights and innovation applied from study design through implementation
- › Delivery focused on protecting the clinical study endpoints
- › Customized use of patient innovation tools and tactics to enhance patient and caregiver journey

[Health Advances](#), a strategy consulting firm owned by Parexel, has built and maintained a strong understanding of the different development and commercialization challenges companies face targeting rare disease markets. Our involvement in the rare diseases field dates to the late 1990s when the area was still nascent. To assist clients in developing strategies to succeed in rare diseases, Health Advances leverages its vast project experience and key relationships with industry and patient advocacy organizations. Health Advances has access to top key opinion leaders across global markets as well as payers to provide insights into treatment and diagnostic paradigms, unmet needs, and pricing and reimbursement considerations. Health Advances' consultants are thought leaders in the rare area through their publications, moderation of panel discussions, and participation at top rare disease drug and biopharma events.

Parexel's Patient-Centric Approach

Focusing on the Chinese market, Parexel has been strategically deploying a patient-centric approach since 2018. In 2020, Parexel introduced its patient advisory council in China to acquire insights from patients, patients' family members, and patient advocacy groups, to facilitate the design of future clinical trials. In July 2021, Parexel and Beijing Illness Challenge Foundation entered a strategic partnership to jointly plan and implement support and education programs for rare disease patients. This innovative collaboration aims to gain direct insights from rare disease patients to improve their access to clinical trials.

1. Wenbin Shao, Yangyang Li, Fei Wang, Yijing Zhu, Lei Xiao, Rufang Huang (2019) *Current Status and Solutions on the Accessibility of Rare Diseases Drugs in China*, China Food and Drug Administration
2. http://www.360doc.com/content/21/0227/08/72280700_964192693.shtml
3. <https://site.douban.com/277144/widget/notes/191786382/note/580579131/>
4. <https://www.cde.org.cn/main/news/viewInfoCommon/876bb5300cce2d3a5cf4f68c97c8a631>
5. Pharnexcloud database
6. <http://www.cnpharm.com/c/2021-03-25/782757.shtml>
7. <https://baijiahao.baidu.com/s?id=1709255659629686524&wfr=spider&for=pc>
8. <https://www.cde.org.cn/main/news/viewInfoCommon/c4e1ef312a0a0c039a7a4ca55b91d4e8>
9. <http://health.people.com.cn/n1/2021/0930/c14739-32243187.html>
10. http://www.nhsa.gov.cn/art/2019/8/20/art_37_1666.html
11. http://www.nhsa.gov.cn/art/2020/12/28/art_37_4220.html
12. http://www.nhsa.gov.cn/art/2021/12/3/art_37_7429.html
13. http://www.foshan.gov.cn/zwgk/zcwj/gfxwj/szfbgsgfxwj/content/post_4201833.html
14. http://www.foshan.gov.cn/fsybj/gkmlpt/content/4/4363/post_4363536.html#1555
15. http://cdyb.chengdu.gov.cn/yfbzj/c128998/2021-03/18/content_ebb0abea709e46999e3bdd5b24834d1.shtml
16. http://ybj.zj.gov.cn/art/2019/12/31/art_1229113757_601196.html
17. http://ybj.zj.gov.cn/art/2020/6/24/art_1229225636_1914586.html
18. Ziqi Wang, Lianxing Min, Xingjun Tian, Li Luo, Yulian Liu (2021). *The Status Quo and Optimization Path of China's Medical Insurance Policy for Rare Diseases*, Health Economics Research.
19. Jinchuan Guo, Zhengning Ding (2021). *A Study on Supplementary Commercial Insurance Coverage for Rare Disease*, Beijing Illness Challenge Foundation
20. <http://www.chinaicf.org/category/news/id/107>
21. <https://www.simon-kucher.com/en/blog/embracing-change-accessing-rare-disease-patients-china>



*With Heart*TM

»»» We're always available
for a conversation

Parexel International Corporation
275 Grove Street, Suite, 101C, Newton, MA 02466, USA
+1 617 454 9300

Offices across Europe, Asia, and the Americas
www.parexelbiotech.com

© 2022 Parexel International Corporation.

parexel[®]
BIOTECH