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RARE DISEASES ARE NOT RARE IN CHINA

What can be done more for this Special Category of Patients

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Currently there is no official definition in China in terms of prevalence or absolute number patients[13]. The national rare disease academic group proposed a new definition in the China rare disease definition Research Report 2021[14]. It is suggested that the disease with "neonatal morbidity less than 1/ million, incidence rate less than 1/ million and disease number less than 140 thousand" should be included in rare diseases.[15] There are debate, but we do not think this is the point. What is needed is to have one clear definition in order to

conditional-marketing authorization (CA).[20] Beyond regulatory, Japan also subsidizes the cost of clinical and non-clinical research during all research periods. [21]

1.3. Social protection

Medical insurance is a key component of healthcare system in order to ensure access to medicine and treatments. It is even more important for rare diseases as the number of patients is limited and there is not enough reward to the companies for the development of suitable drugs.
Globally there are many different models of medical insurance systems, but in essence, it is dominated by the government and supplemented by insurance and co-payment by patients.

Often patients suffering from rare diseases are very vulnerable and benefit from full or almost full reimbursement, like in most of Europe. When there is

It is reported that the selection of the diseases in this catalogue was based on following factors: 1) There is evidence that the incidence rate or prevalence rate is low; 2) Great harm to patients and families; 3) There are clear diagnostic methods; 4) Treatment or intervention means are available and affordable, or there is no effective treatment or intervention means, but it has been included in the national scientific research project. This list lacks a standard definition.

In 2021, a second list has been prepared and it is said to be announced soon[24]. According to the working procedure for the formulation of rare disease catalogue issued by NHC, the list should be dynamically updated and the update time should not be less than 2 years in principle. Up to the reply time, NHC has successively received more than 200 applications for increasing diseases and these materials are currently in the stage of review.

2.2. Regulatory approval

The Chinese regulatory agency NMPA (National Medical Products Administration) has now established four special review channels to accelerate registration of drugs against rare diseases, including breakthrough therapeutic drugs, conditional approval, priority review and approval and special approval procedures, so as to improve the review and approval efficiency of innovative drugs at different stages and accelerated the process of drug R & D and listing.

Before 2018, there was no special process in China to register drugs to cure rare diseases. From 2018 to 2020, NMPA has issued three lists of *overseas new drugs in urgent clinical need*, involving a total of 73 drugs and 39 drugs for rare diseases[25]. It was pointed out that a special channel would be established to review and approve overseas new drugs urgently clinically needed.

Since 2019, taking the first list as the definition basis, NMPA has newly approved 14 rare disease drugs, involving 9 rare disease indications, opening the door to new rare disease drugs.

On February 26, 2021, the NHC further open the door by listing 121 rare diseases. China is the only country in the world that issues a rare disease catalogue. Based on the 121 rare diseases in the First List of Rare Diseases, 86 rare diseases have drugs available worldwide, 77 of them have drugs available in China, and 9 rare diseases face the dilemma of "drugs available outside China but not inside". In China, there are 87 drugs with clear indications for rare diseases, covering 43 rare diseases, of which 58 drugs have been included in the NRDL after the national medical insurance negotiations in 2021, covering 29 rare diseases[26].

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[24] See National Health Commission 's reply to the Fourth Session of the Thirteenth National People's Congress http://www.nhc.gov.cn/wjw/jiany/202202/6ac97171a1d54f2dad97c6088f2ea080.shtml

“ ⅃ ” (“First, on the expansion of health insurance coverage, as soon as possible to introduce the second batch of rare disease catalog.”)

[25] According to Center for Drug Evaluation, NMPA
List1: 19/40. Source: https://www.cde.org.cn/main/news/viewInfoCommon/21de8acd6c395746b041b2ad93eb5c43

List2: 17/26. Source: https://www.cde.org.cn/main/news/viewInfoCommon/82f3bf94dc2c38d1a24d851f0e44914b

List3: 3/17. Source: https://www.cde.org.cn/main/news/viewInfoCommon/08818b168ccc85db9a42a0f6623b5688

[26] https://m.nbd.com.cn/articles/2022-02-27/2141619.html China Rare Disease Industry Trend Watch Report 2022 ʁ 2022

2.3. Social protection

In parallel, since 2018, China has issued a number of policies to improve the accessibility of drugs for rare diseases and improve the level of protection for patients with rare diseases. It includes the establishment of national patient registration system for rare diseases[27], diagnosis and treatment norms and networks (324 hospital networks) but also some the tax reduction etc. T*he notice on the value added tax policy for drugs with rare diseases* issued by the Ministry of Finance in 2019, reduced value-added tax to 3% on the first batch of 21 drugs with rare diseases and 4 APIs with reference to anticancer drugs[28].

This administrative activity is improving the situation, but what really matter is the accessibility of drugs. Since 2017, the NRDL process has been gradually normalized, and progressively rare disease drugs have been included in NRDL. As of December 2021, 58 rare disease drugs have been included in the NRDL while the total number of drugs reimbursed is 2,860.

3. WHY IT IS IMPORTANT TO DO MORE IN CHINA

Looking at the big picture, China has seen a robust improvement since 2018. But the actual coverage is limited (only a few rare diseases are recognized as such) and they are almost not part of the social protection system. In a simplistic way, China is not “playing in its league” here. Second pharmaceutical market in value, and first in volume, China is one of the last markets in middle-income market in the area of rare diseases. It is time now to review this first step and find way to scale -up. There are several reasons to do so. First, the patients with rare diseases should benefit from fair treatments. Second, beyond this moral argument, China could use this opportunity as a leverage of innovation in drug development. Rare diseases are not rare in China.

3.1. Patients with rare diseases should receive fair and accessible treatments

In public circles, we often hear that common diseases are concerning masses and they should be the priority of the medical insurance. Not patients suffering from rare diseases as they are a minority. But if we compare the diseases we can also say that the nature of rare diseases is very special. They are very often genetic based, while more common diseases are sometimes due to lifestyle and lack of public awareness. In other terms, the impact and development of general diseases could be reduced if the society and individuals do something in term of prevention and management. But it is not the case of rare diseases who are very often genetic based. Treatment of rare diseases and access to them are the moral responsibility of the society as a whole. This principle being recognized, implementing universal healthcare coverage requires a pragmatic and step-by-step process starting with the big masses. The issue with rare diseases is that it is sometimes difficult to understand one's

for human beings to live in dignity. Every

For business value, the field of global rare diseases has spawned a number of blockbuster drugs, which are popular for investment thanks to supportive policies and thus have a high market value. For example, in December 2020, AstraZeneca acquired Alexion for $39 billion. In April 2018, Takeda pharmaceutical acquired Shire with $65 billion, becoming the largest M&A in the pharmaceutical field in that year. The US pharmaceutical industry association has recently issued a report celebrating “a decade of innovation” that enable to create 600 orphan drugs[30]. BCG predicts that by 2024, the global sales of drugs for rare diseases such as cystic fibrosis, hemophilia A and myasthenia

accelerate diagnosis[34]. The focus on “acceleration of diagnostic” supported by digital tools would have the additional benefit to increase awareness on rare diseases.

4.2. Accelerate & facilitate more registration

We saw that accelerated registration is critical or the development of drugs against rare diseases.

With its first list of rare disease, NMPA has started the fight but is far away to have a significant impact. Looking at the current pipeline of clinical trials of rare diseases registered in China, there is

enlarged by prescribers and patients. In the case of rare diseases, prescription are backed by specific and scientific diagnostic. Over prescription is limited. Thus the situation is manageable due to the limited number of patients who need these specific drugs. The individual financial risk is limited. The cumulative risk, or collective cost of orphan drugs, is significant[41]

It would also enable to get more interest and support from charity organizations to donate and support patient associations and organisations fighting rare diseases. Raising the attention of the public and medical workers to rare diseases would unleash the financial power of elites and give full play to the power of charity.

In summary, China has made a lot of progress in terms of treating rare diseases. Before 2018, there was no specific Government policies in terms of definition, registration and drug access. The Last 5 years have seen the creation and improvement of many needed policies and tools. Thisc Government policies n5 ny5(