香港罕見疾病聯盟
RARE DISEASE HONG KONG

Rare Disease Hong Kong[1]

Submission on Optimising and Improving Access Mechanism for Orphan Drugs by Cutting the Red Tape

(April 2022)

For those patients suffering from life-threatening and debilitating rare diseases, their greatest concern is whether they can receive timely treatment. According to the usual process of drug registration and inclusion, patients often have to wait for years before they have the opportunity to take new drugs that have already come onto the market. Fortunately, the Government has begun to recognise and propose new measures dealing with rare diseases in recent years. For instance, since August 2017, eligible patients have been provided with subsidy to purchase ultra-expensive drugs (including those for treating uncommon disorders). Two of the ultra-expensive drugs (Tisagenlecleucel and Tafamidis) currently funded by the Community Care Fund (CCF) were incorporated into the CCF assistance programme in 13 to 14 months on average[2] after registration; whereas Nusinersen was included in the Safety Net in only 4 days after registration[3], so that the patients in need could receive treatment as soon as possible.

As a patient group, RDHK welcomes the flexible approach adopted by the Hospital Authority (HA). The precedent cases in recent years have shown that accelerating the inclusion of orphan drugs in the HA Drug Formulary and Safety Net is feasible. Therefore, RDHK hopes that the Government and the authorities concerned will learn from the successful experience and consider adopting the seven measures recommended below to optimise and regularise the access mechanism for orphan drugs.

1. **Optimise the documentation requirements for registration and registration process of orphan drugs;**
2. **Strengthen collaboration between the Chief Pharmacist's Office (CPO) of the HA and the pharmaceutical industry;**
3. **Omit the non-essential work of the Drug and Therapeutics Committee (DTC) in the drug inclusion process;**
4. **Adjust the schedule and mode of the Drug Management Committee (DMC) meetings ;**
5. **Solve the chicken-and-egg dilemma by coordinating the two mechanisms of medical testing and drug inclusion;**
6. **Adopt early awareness and alert systems (also known as horizon scanning) to set priorities for the allocation of resource in advance; and**
7. **Adopt "Orphan Drug Trial" policy and systematically collect and use real-world data to generate empirical evidence which helps to accelerate patient access to orphan drugs.**

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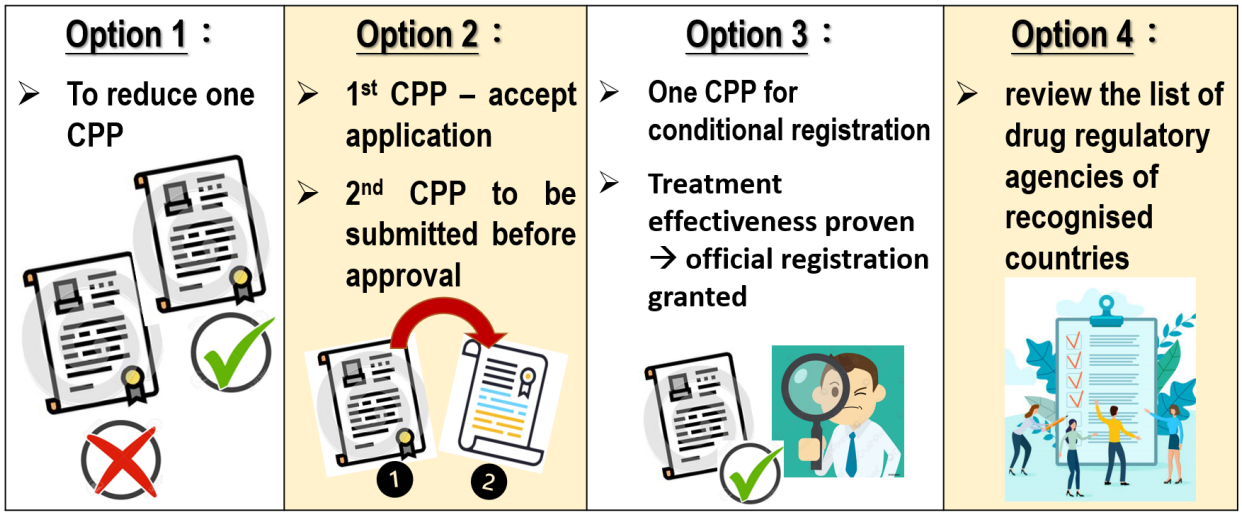
[1] Established in December 2014, Rare Disease Hong Kong Limited (RDHK) is the first patient group in Hong Kong comprising cross-rare disease patients and their families with the support of experts and academics in the field. It is also a charitable institution recognised by the government (ref. no.: 91/16233). Its objectives are to spearhead and improve related policies and services, promote public education on rare diseases, and strengthen the community's support for rare disease patients, in order to ensure equal respect and protection for them in terms of such fundamental rights as healthcare, social support, education, and daily needs.

[2] According to the information available on the website of the Drug Office, the Department of Health (https://www.drugoffice.gov.hk/eps/do/tc/consumer/search_drug_database.html) and the report of "Cumulative approved number of applications & subsidy amount (up to 28 February 2022)" posted on the HA website (https://www.ha.org.hk/haho/ho/ccf/table_eng.pdf), Tisagenlecleucel was registered on 5 Mar 2020 and introduced to the Community Care Fund Medical Assistance Programme (CCFMAP) on 10 Apr 2021; whereas Tafamidis was registered on 28 Oct 2020 and introduced to CCF on 4 Dec 2021.

[3] According to the same sources of information mentioned above, Nusinersen was on 21 Sep 2018 and introduced to the CCFMAP on 25 Sept 2018.

Details of the recommendations are as follows:

1. Optimise the documentation requirements for registration and registration process of orphan drugs



1.1. Although the Government has introduced different measures over the past few years to speed up the registration approval for most pharmaceutical products, there is still room for optimisation of the documentation requirements. Currently, one of the documentation requirements for new drug registration is the submission of proofs of registration and certificates of free sale issued by the drug regulatory authorities of at least two recognised countries, e.g., Certificate of Pharmaceutical Product (CPP). However, the time for approval by a drug regulatory authority varies from country to country, and it takes a long time to obtain two CPPs from two different countries. After obtaining the first CPP, it usually takes at least another three to seven months to obtain the second one. If only one CPP is required, the time for filing an application for drug registration can be significantly reduced.

1.2. If the authorities concerned are worried about whether one CPP is sufficient to prove the safety of the drug, they may refer to the report published by a research team from the Centre for Safe Medication Practice and Research, HKU in the *Orphanet Journal of Rare Diseases*[4] in January this year. The research report points out that the U.S. Food and Drug Administration (FDA) has established some special channels such as "priority review", "accelerated approval pathway" and so on for rare drugs since the last century, which has greatly shortened the time for orphan drug approval. However, the safety of the FDA-approved orphan drugs was found to be similar to the safety data of commonly used drugs collected for post-marketing surveillance. Above all, the benefits of orphan drugs were considered to outweigh the risks[5]。

1.3. If the authorities still consider that CPPs issued by two recognised drug regulatory authorities are necessary, they may consider accepting the registration application upon the receipt of the first CPP, and the second CPP only needs to arrive before the approval of the registration. Such doing can make an early start on the drug registration process.

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[4] *Orphanet Journal of Rare Diseases* is a peer-reviewed open access medical journal covering research on rare diseases. It is an official journal of Orphanet which was established in France in 1997 by the French National Institute of Health and Medical Research, a unique resource to collect and improve knowledge of rare diseases to improve the diagnosis, care and treatment of rare disease patients.

[5] The research report is titled *Postmarketing safety of orphan drugs: a longitudinal analysis of the US Food and Drug Administration database between 1999 and 2018*, which can be downloaded from: https://rdcu.be/cFwi0.

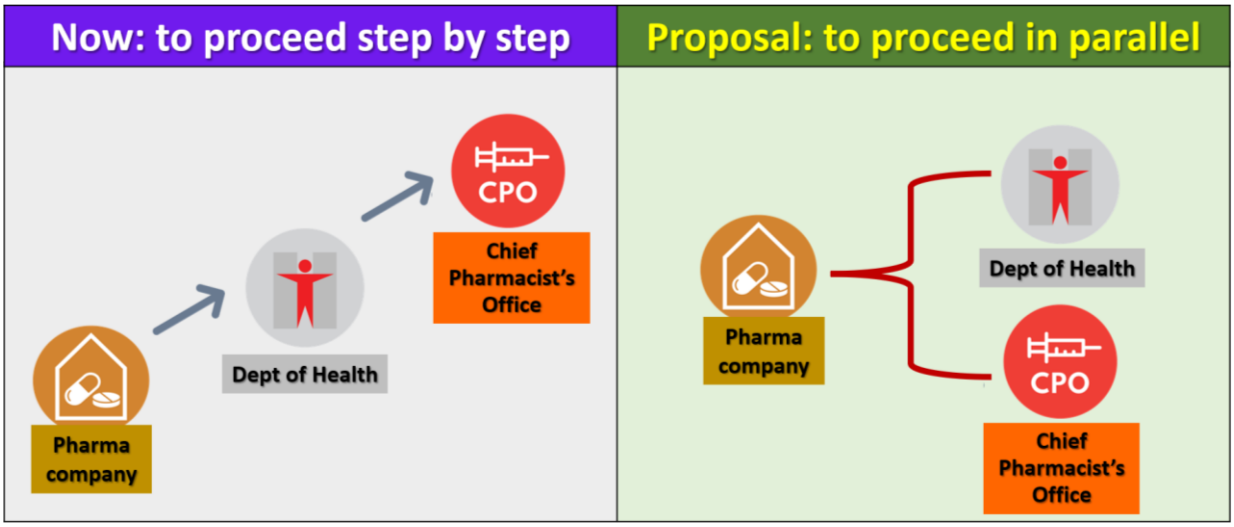
1.4. Another way to consider is to grant a conditional registration lasting for two to three years upon the receipt of one CPP with a detailed medication plan, and before the end of the conditional registration period, a detailed medication report must be submitted for final assessment. If the treatment effectiveness meets the regulatory requirements, official registration in Hong Kong can be granted. Otherwise the registration will be revoked.

1.5. Since patients living with a life-threatening rare disease cannot afford to wait day after day, we sincerely hope that the Government can relax or flexibly deal with the documentation requirements for new drug registration so that the registration process for new orphan drugs in Hong Kong can be expedited. If the accelerated process cannot be fully implemented immediately, it may be first applied to orphan drugs that are registered in Hong Kong for the first time for specific indications as a pilot, and then gradually extended to other orphan drugs.

1.6. In addition, it is time to review the current list of drug regulatory agencies or authorities of recognised countries. For instance, in recent years, the biomedical industry in Mainland China has been rapidly developing, and the research and development capacity of orphan drugs has also been greatly improved. Since Hong Kong has been integrating into the Greater Bay Area gradually, the authorities concerned should promptly consider whether "The National Medicine Product Administration" in Mainland China should be included in the list of recognised drug regulatory authorities.

Actions to be taken by: the Department of Health

2. Strengthen collaboration between the Chief Pharmacist's Office (CPO) of the HA and the pharmaceutical industry

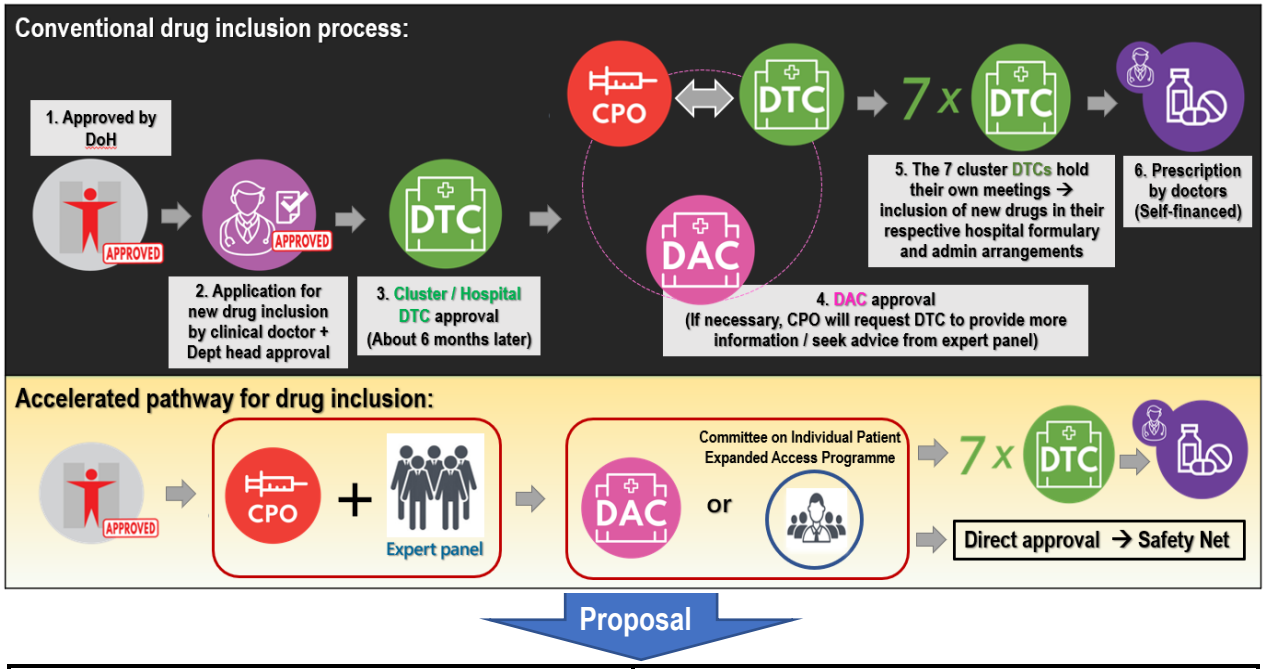


2.1. To start the process of application for including new drugs in the Drug Formulary as early as possible, pharmaceutical companies should take the initiative to contact the CPO before preparing to apply for new drug registration, to provide detailed drug information and negotiate the transaction terms and conditions; whereas the CPO should keep an open mind and respond proactively to the invitation of the pharmaceutical industry by carrying out discussions as soon as possible and strengthening government-business collaboration, with a view to benefiting the people.

2.2. With prior communication and good preparation work, the reviewing and approval procedures for applications for new drug inclusion that follow can go more smoothly and efficiently, which will help improve access to orphan drugs.

Actions to be taken by: the pharmaceutical industry & CPO

3. Omit the non-essential work of the Drug and Therapeutics Committee (DTC) in the drug inclusion process



3.1. Under the current system, applications for inclusion of new drugs initiated by hospital clusters must be reviewed and recommended by the DTC before they can be submitted to the Drug Advisory Committee (DAC) for consideration. However, according to the experience of the pharmaceutical industry, in the past few years, some applications for inclusion of orphan drugs, rare cancer drugs and ultra-expensive drugs were examined by the CPO and the expert panel and then submitted to the DAC without involving the DTC. RDHK strongly agrees with this approach as there may not be experts with in-depth knowledge of rare diseases or rare tumors in the DTC, so DTC participation is not necessary.

3.2. At the symposium held by RDHK in September last year, a guest speaker representing the HA revealed that the "Committee on Individual Patient Expanded Access Programme" (IPEAP Committee) had been set up with the following terms of reference:

- To form a panel of experts on uncommon disorders;
- To develop treatment guidelines for individual uncommon disorders and evaluate the drug efficacy in individual patients according to clinical treatment and scientific evidence; and
- To review and recommend new drugs for treatment of uncommon disorders for inclusion into the CCF Subsidy for Eligible Patients to Purchase Ultra-expensive Drugs (Including Those for Treating Uncommon Disorders) Programme.

Between November 2017 and December 2020, the IPEAP Committee approved the inclusion of drugs for four rare diseases (including rare cancers) into the CCF Medical Assistance Programmes.

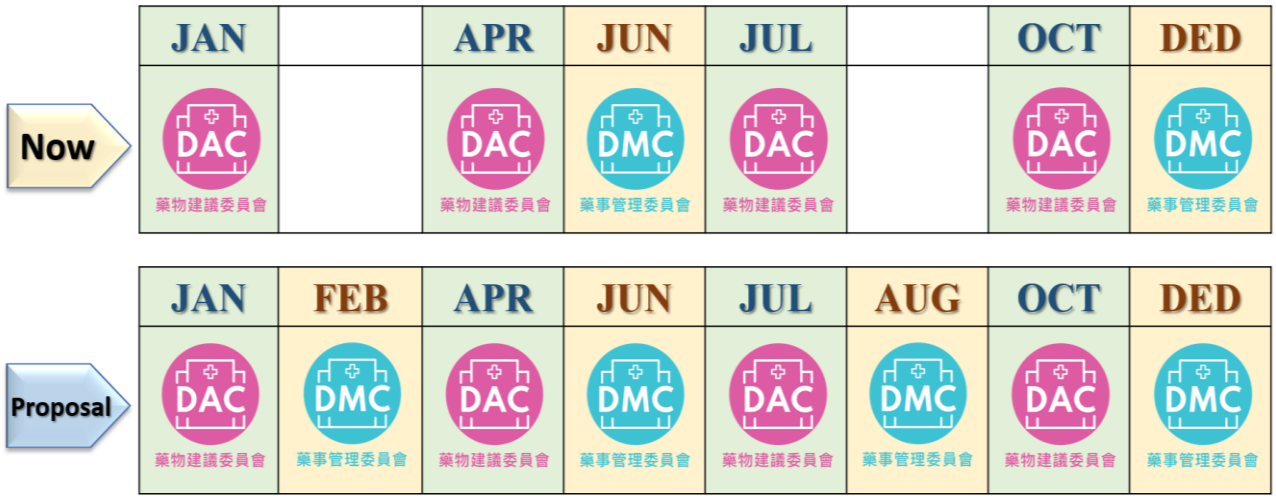
3.3. In view of the above feasible instances, RDHK recommends that the authorities concerned set up a regular process for inclusion of drugs for rare diseases (including rare cancers) and ultra-expensive drugs, in which the CPO and expert panel can directly submit applications to the DAC or IPEAP Committee for approval.

3.4. To carry out the regular process suggested above, it is necessary for the HA to clearly define the terms "drugs for uncommon disorders" and "ultra-expensive drugs" based on the actual operations of the past few years, so as to facilitate compliance by all stakeholders in the process of communication and collaboration.

3.5. In addition, the authorities concerned should also review the procedure of reverting an application for including new drugs for other common diseases approved by DAC to the relevant DTCs again for final approval. By omitting the overlapping duties or taking DTC resolutions by using the email circulation method without physical meetings may help to alleviate the administrative burden on the DTC, and hence enabling early patient access to new medicines.

Actions to be taken by: DTC, CPO, DAC and IPEAP Committee

4. Adjust the schedule and mode of the Drug Management Committee (DMC) meetings



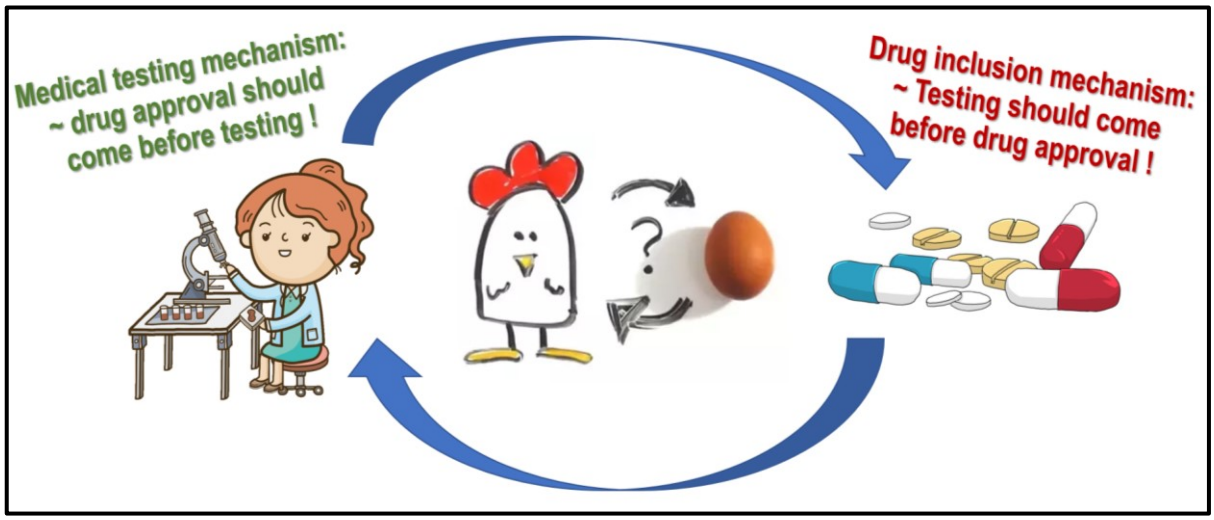
4.1. Due to the high cost of orphan drugs, the general public simply cannot afford them without government subsidies. So, after a new drug has been approved by the DAC, it is still subject to the approval of the DMC before it can be covered by the Safety Net. However, the DMC meets annually in June and December to evaluate new drug applications, which cannot match with the meeting times (January, April, July, and October) of the DAC. As a consequence, the waiting time for including new drugs to the Safety Net has been extended, resulting in longer patients' waiting time for new drugs.

4.2. To shorten the waiting time for an application to be reviewed, it is recommended that the DMC increase the number of meetings to four times a year and hold the meetings one month after the DAC meeting.

4.3. Instead of holding only two meetings per year, the authorities concerned may also consider replacing the DMC's physical meetings with e-mail circulation, which will make the review of applications more flexible and efficient, and hence help to speed up the process of application reviews.

Actions to be taken by: DMC

5. Solve the chicken-and-egg dilemma by coordinating the two mechanisms of medical testing and drug inclusion



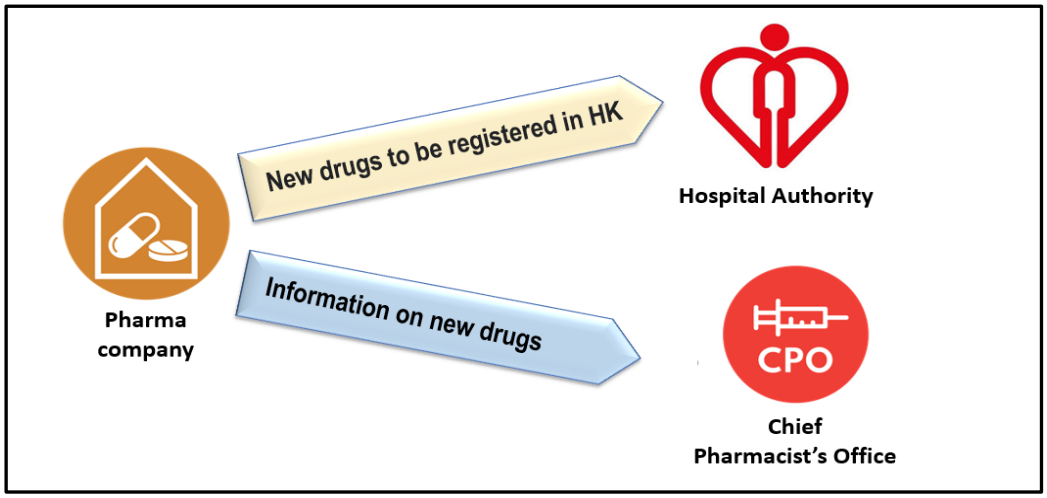
5.1. Precision medicine, which is widely used in developed countries, aims to make patients get more accurate and timely diagnosis, and hence obtain more accurate and appropriate treatment. Diagnosis and treatment are in fact equally important.

5.2. Unfortunately, the HA's internal review of drugs and medical testing are under two different mechanisms handled by two different committees. If the two committees operate in their own way, the public will not be able to benefit from precision medicine. At present, the committee that approves drugs will reject the inclusion of a drug into the HA Drug Formulary or Safety Net because the relevant medical testing has not yet been included in any medical assistance programme; on the other hand, the committee that approves medical testing will reject subsidising certain medical testing because the relevant drug has not been approved, which will cause the chicken-and-egg dilemma.

5.3. To solve the above-mentioned problem, the HA is advised to close the policy loopholes immediately by coordinating the two mechanisms or setting up a Precision Medicine Committee to coordinate the review of precision medicine-related drugs and tests, so as to benefit the patients in need.

<u>Actions to be taken by: HA management</u>

6. Adopt early awareness and alert systems (also known as horizon scanning) to set priorities for the allocation of resource in advance



6.1. Due to the rapid development of health technologies and the ever-rising healthcare costs, horizon scanning has been adopted by many advanced countries such as the United Kingdom, the United States, Canada, Australia, etc. to identify new and emerging health technologies that may have impact on the health system so that policymakers can make prearrangements and early planning for regulatory environment, financial management, workplace preparedness, training and education, ethics and so on. According to the Agency for Healthcare Research and Quality in the United States, horizon scanning aims to identify, differentiate, filter and prioritise new and emerging health technologies in order to assess or predict their potential impact on health, costs, society and the healthcare system.

6.2. In the long run, if horizon scanning is adopted in the Hong Kong healthcare system, the authorities concerned will be able to grasp the information on what new drugs are going to be registered in Hong Kong, specifications and clinical use of the drugs, etc.; and start financial planning early, which will enhance the effectiveness of drug inclusion and funding. Besides, the adoption of horizon scanning can also prompt the pharmaceutical companies to plan in advance and prepare the information and related data required for drug registration as early as possible, which will further accelerate the registration and drug inclusion process. Thus, patients can receive treatment as soon as possible. Isn't it a triple win scenario that will benefit the Government, the business sector and the patients?

Actions to be taken by: the pharmaceutical industry, HA management & CPO

7. Adopt "Orphan Drug Trial" policy and systematically collect and use real-world data to generate empirical evidence which helps to accelerate patient access to orphan drugs

7.1. It is difficult to collect scientific research data on rare diseases because such patients are scarce in number. Unfortunately, the HA often delays the clinical use of new drugs for rare diseases on the grounds of insufficient empirical evidence.

7.2. To overcome this obstacle, the HA may adopt an "Orphan drug trial" policy[6], in which the Government should take the initiative to collaborate with the pharmaceutical industry by discussing the terms of transaction and launch a trial period of 6 to 18 months based on different diseases and drugs, whereas the duration of trial, participation criteria, efficacy indicators, etc. should be mutually agreed by all parties including patient groups. During the drug trial period, real-world data (RWD) can be collected and analysed systematically. If the patient-reported outcomes can be effectively used, more comprehensive and patient-centric reviews can be obtained to evaluate the clinical and quality-of-life benefits of drugs.

[6] Similar orphan drug or rare disease drug trial policies have already been implemented overseas. For example, Managed Access Agreements (MAAs) are signed between the National Health Service in England and manufacturers to enable a drug to become available for a limited time period at a discounted price. This allows patients to access the drug whilst further evidence is gathered on its real-world effectiveness.

7.3. In fact, many countries are stepping up the use of RWD to help optimise drug approvals, regulations, and reimbursement. For example, the government departments of Mainland China and U.S. have issued guidelines to support drug development and review[7]; the **REAL** World Data **I**n A**S**ia for H**E**alth Technology Assessment in Reimbursement (**REALISE**) working group, comprising experts from multiple universities, trade associations and governments in Asia, published a guidance document last year to support drug reimbursement decision making[8]. The HA should draw on the experience of other regions, develop appropriate guidelines for Hong Kong, clarify the scenarios in which RWD are applicable, make specific requirements for the quality and analytical methods of data sources (local, Greater Bay Area, Mainland China, foreign countries), and work with the stakeholders to develop and update an evaluation framework for RWD which can serve as a reference for all parties.

Actions to be taken by: the pharmaceutical industry, HA management & CPO

Conclusion

Xia Baolong, vice-chairman of the National Committee of the Chinese People's Political Consultative Conference and head of the Hong Kong and Macao Affairs Office of the State Council, made it clear at a symposium marking the first anniversary of the enactment of the Law on Safeguarding National Security in the Hong Kong held on 16 July 2021 that Hong Kong leaders should have strategic thinking and a broad vision to effectively solve such tough problems as housing, employment, healthcare, wealth inequity, etc.; ensure that the Government's future work will be closer and more responsive to the aspirations, sentiments and opinions of the community; serve the public with a down-to-earth attitude; solve problems effectively with pragmatic approach; and win the people's trust by governance performance.

The Government has occasionally taken some good measures and steps to deal with rare diseases over the past few years. The most impressive instance was that in September 2018, the Government took the initiative to invite a pharmaceutical company to offer an Expanded Access Programme (EAP) providing patients with Spinal Muscular Atrophy Type 1 with free treatment. Moreover, it took only four days to complete the process of drug registration and introduction to the Safety Net, which demonstrates that the Government is willing to take advice and able to act in an extraordinarily efficient manner.

Of course, we do not expect the Government to reduce the processing time for all orphan drug inclusion to four days. However, if the Government can listen, understand and empathise with the actual needs of rare disease patients, it will realise that early treatment can not only save lives, but also ensure quality of life and dignity of the patients. Therefore, it is hoped that the Government can actively consider the above recommendations. To meet Xia's expectations and be down-to-earth, the Government should give full play to the benefits of tripartite collaboration among the Government, the business sector and the community, as well as continuously optimise and improve the access mechanism for orphan drugs.

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[7] Source of information – (i) Notice of the National Medical Products Administration on Issuing the Guiding Principles (Trial) for Real-World Evidence Supporting Drug Development and Review (2020 No. 1) (https://www.nmpa.gov.cn/directory/web/nmpa/yaopin/ypggtg/ypqtgg/20200107151901190.html); and (ii) Framework for FDA's Real-World Evidence Program (https://www.fda.gov/media/120060/download).

[8] Source of information – REALISE Working Group: Use of real-world data and real-world evidence to support drug reimbursement decision making in Asia (https://hiper.nus.edu.sg/wp-content/uploads/2021/03/REALISE-Full-guidance-post-feedback_20201211-version-1.1.pdf)