Recent Pricing Negotiations on Innovative Medicines Pilot in China: Experiences, Implications, and Suggestions

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ABSTRACT

The China National Formulary (CNF) for reimbursable drug use, also known as the National Reimbursement Drug List (NRDL), was formally established in 2000, revised in 2004 and 2009, and covers 52% of China’s population under the government urban health insurance programs. A third major and long-awaited update to the formulary was completed in February 2017 based on intensive reviews by a group of experts in medicine, pharmacology, health economics, and health policy. Shortly after this major update, a pilot project at the central government level was implemented for negotiations mainly on innovative but expensive medicines that were still outside the National Formulary. The pilot, conducted between March and July 2017, eventually reached an overall agreement rate of 81.8% regarding approved indications and drug prices between China’s government and the pharmaceutical companies. This pilot showcased numerous leading edge features including a working definition of innovative medicines and opportunities to submit dossiers on drug clinical and economic information. This pilot covered 44 medications for negotiations in a breakthrough attempt to increase the appropriate access to innovative but expensive medicines. The implications to the future of the CNF go beyond the drugs included in the pilot. This paper describes the background of the CNF and the negotiation pilot. In addition, authors of this paper make six recommendations critical to CNF future developments, including enhancing criteria and process for evaluations, standardizing the dossier format, specifying data requirements, refining pricing calculation, and cultivating evaluation professional development.

Keywords: China, formulary, innovative medicines, pricing negotiations.

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Introduction

In a country with a health technology assessment (HTA) in place, a drug formulary represents a list of preferred medicines under certain medical policies within the health care system. The decision regarding which drugs to include on this list is made according to clinically sound and cost-effective principles to promote best medical practices given a limited health care budget [1]. The China National Formulary (CNF) for the government medical insurance program was formally established in 2000. Since then, there have been three updates to the CNF, with the most recent one at the end of 2016. Included in this update was a pilot project at the central government level for a new approach to pricing negotiations with selected innovative medicines, still not on the CNF. This pilot had substantial implications for the future development of the CNF. This article describes the background of the CNF and this pilot project. It also offers six suggestions for the future evolution of the CNF.

Background on the China National Formulary

The public medical insurance offered by the Chinese government contains three programs: 1) the urban employee basic medical insurance, 2) the urban resident basic medical insurance, and 3) the new rural cooperative medical insurance [2]. As of 2016, more than 95% of the Chinese population was covered by one of these three programs [3,4]. Established formally in 2000, the CNF contains a list of preferred medicines for government medical insurance programs for urban employees and residents, who make up about 52% of the Chinese population [5]. The original intent was to provide major updates to the formulary every 2 years. However, only three major updates have appeared since its
creation: the first in 2004, followed by one in 2009, and then the most recent one between the end of 2016 and February 2017 [6].

As of the 2017 update, there are now 2535 medicines (under chemical names) in the CNF: 1297 are Western medicines and the remaining 1238 are Chinese traditional medicines. In comparison to the 2009 version of the CNF, the 2017 version added 339 new medications, or an increase of 15.4%, with special attention to the areas of serious diseases, pediatric medications, medications for work-related accidents, and Chinese traditional medicines. For example, of the 339 newly added medications, 91 are for pediatric patients.

The review and update to the CNF in 2016 were completed by experts in the fields of medicine, pharmacology, health economics, and health policy. These experts were selected from a national pool of more than 20,000 based on recommendations from the professional community and individuals’ reputations in the fields. The updates of the CNF are made in accordance with the following six principles: 1) preserving the Essential Medicine List’s (adapted from World Health Organization) balance of local economic development and cultures, 2) maintaining stability and consistency of medication use based on the Formulary, 3) reflecting cutting-edge clinical and drug developments for evolving unmet medical needs, 4) conducting the evaluations by experts in a scientific and authoritative way, 5) keeping the principles of transparency, fairness, and judiciary in a comprehensive review process, and 6) maintaining a national formulary in a uniform manner [7].

Pilot Project Negotiations on Innovative Medicines

Although the review and subsequent update to the 2017 CNF is comprehensive and well balanced, a few innovative medicines, especially for oncology, are still excluded from this formulary mainly because of their relatively high costs, despite their recognized clinical benefits. Exclusion of these drugs from the CNF creates access issues for patients who because of financial strain cannot obtain the medicine and its benefits. This is certainly a less ideal situation to promote the national goals described in the national plan for Healthy China 2030, such as the focus on health for all people in China [8].

Before this pilot, pricing negotiations were underway among the National Health and Family Planning Commission, local governments, and pharmaceutical and medical device companies. However, the scope of those early negotiations was relatively small in terms of the number of medicines on the negotiation table. In addition, most of the process was closed to the pharmaceutical suppliers; for example, no formal submissions with information on clinical or economic from pharmaceutical companies were allowed.

The design of the recent pilot project was different. Forty-five medicines were chosen, based on thorough reviews of market sales data in the country, and 35 pharmaceutical companies were invited by the government to participate in the initial negotiation. Although there may be some debate as to whether these medicines were really the most “innovative” ones at present, it is notable that for the first time in the history of the CNF a working definition of innovative medicines was created: “innovative medicine of clearly proven clinical outcomes for urgent unmet medical needs but expensive” [9]. In addition, the pilot also formally opened an unprecedented submission window before the final negotiations that allowed pharmaceutical companies to submit evidence dossiers. Countries such as the United Kingdom, Australia, South Korea, and those with HTA systems all accept external dossiers. For China, however, this is a break from convention because the current CNF negotiation system excludes external submissions of drug information.

The selection of experts for this pilot project was similar to that for the selection of CNF reviewers. These experts then provided their professional comments on the externally submitted materials including the evidence dossiers. Members of the negotiation committees were chosen separately, and four different teams conducted the negotiation for different medicines in one day. Figure 1 represents the pilot program as an addendum process under the context of the current CNF system.

This pilot commenced in February 2017 and was completed by the end of July 2017 [9]. As a result, agreements were successfully reached for 36 of the 44 medicines on the initial list, in both approved indications and prices. These 36 medicines cover some important disease areas, such as hematology, cardiology, oncology, immunology, neurology, and Chinese traditional medicines for cancer therapy. Although operational and other challenges are likely to arise in further processes, a successful agreement rate of 82% indicates that this pilot has been a positive, win–win project for the government, companies, patients, and health care providers.

Pros and Cons of the Pilot

The pilot project was an important attempt to provide access to innovative medicines that were still outside the CNF at the time of the negotiation, thus opening accessibility to these drugs and reducing the financial pressure on patients at the same time.
Rather than undergoing another round of negotiations below the central level, the Chinese government at this point made it clear that the agreed on medications from this pilot will be in the CNF throughout the country without any modification at the provincial level. In China, conducting a pilot project before establishing a national policy is a common practice. From this perspective, the scope of this pilot went beyond just pricing negotiation; it can be considered as a test of a mini-process for formulary inclusions of a subset of medicines that were outside the CNF. In addition, the government is currently considering transforming the fixed-period update of the CNF to a dynamic update process. If so, this pilot might have served as a prologue that provides valuable experience for future development, not just affecting a small group of drugs at this time.

As expected, this pilot also came with some limitations. For example, the invitations to pharmaceutical companies to participate in the negotiation included requests for pharmacoeconomic analysis. However, there were no requirements regarding the format. Some companies presented copious materials whereas others brought almost nothing. When economic data were evaluated, criteria for evaluation were not well defined into implementable details. The number of pharmacoeconomics experts was far from enough to conduct sufficient evaluations during the review process. These named limitations of the pilot are consistent with key findings from the recent literature [10,11].

**Suggestions for Future Enhancements of the CNF**

For the HTA system, the focus on evaluating innovative medicines is often the primary purpose. The valuation of medicines is then defined in a comprehensive framework, which incorporates the clinical and humanistic benefits such as quality of life, alongside the drug prices that impact both patients and third-party payers, some of which may include the government [12]. From this perspective, the value of an innovative medicine can be measured and evaluated in a robust manner. This is the ideal direction for the future development of the CNF. To this end, the authors of this article offer the following six suggestions:

1. Need for clearly defined and measurable criteria for health economic evaluations to promote HTA development for more efficient health policy decision making in China. The Chinese Guidelines for Pharmacoeconomic Evaluations and Manual published in 2015 [13] needs to be operationalized through the CNF review and update. Criteria should be value based and involve multiple aspects including clinical, economic, and humanistic [14]. In addition to the principal criteria for general evaluations, disease-specific criteria (e.g., for oncology) should also be considered, as evaluations would vary when different diseases are evaluated; examples of disease-specific evaluations can be found on the webpage of the National Institute of Clinical Excellence (NICE) of the United Kingdom [15]. These criteria should also include not only methodology and results, but also ways to report and interpret the findings and implications [16], for example, showing the method used and the rationale for its use. Overall, setting up these criteria would provide an opportunity for analyzing what measures would provide the best fit for China.

2. Need to standardize a dossier formation for submission. It has been a common practice to have a submission dossier with well-designed sections to have a logical flow of the information regarding the drug under review. Such a dossier would include clinical sections on efficacy and safety, not only during clinical studies before the products are launched but also incorporating results from real-world studies, economic analysis, and budget impact analysis. In a well-structured dossier, even the page limitations are specified, although flexibility may be limited. Examples in this regard can be found in Australia, South Korea, Taiwan, and the United States [17-20]. Having such a standardized dossier format will help ensure transparency of the evaluation process and assist in preparing the necessary evidence.

3. Need to specify the details of the process. These include the pathway, the time associated with each step in the process, and the accountability attending each step. The process may also establish the frequency of submissions and reviews throughout the year. There is no uniform model for submission frequency. For example, in Australia, three submission rounds per year are scheduled and companies can send in submissions accordingly. In the United States, there is no specific timeline for submissions. In Taiwan, there is a time window for submissions every month. How frequently a review should take place depends on several factors, including the infrastructure for conducting the reviews.

A good process should provide transparent information and include public monitoring. In addition, the process may include an option to appeal the initial decision to finalize a formulary inclusion and/or pricing on a medicine is exhaustive. There is no obvious uniform system in the world, as there is variability even in Europe, where HTA is well established [21]. The HTA systems in South Korea and Japan experienced many challenges before their systems matured [18,22]. Therefore, the process in China needs to evolve gradually based on the unique situation and the needs in the country.

4. Need to specify exact information from randomized clinical trials and/or real-world studies. For newly approved products introduced to the Chinese market, it would be appropriate to present clinical studies, including the ones conducted in China if the data are available. However, for products that have been marketed in China, it would be reasonable to request information from real-world studies in the country. For real-world studies on a database, justifications for choosing the data should be specified [23].

Besides the needs for local clinical data, we should also expect health economic and quality of life data, including patients’ value propositions, either before or after the product is launched in China. Demand for local data is on the rise [24] despite the challenges of tracking them down. Data requirements are an evolving situation and the requirement for local data may be an obstacle at this point in time. However, making this requirement clear now will be of benefit in the future in many ways. We should keep in mind that HTA evaluations should be a scientific data-driven process for rigorous reviews and evaluations aimed at enabling more efficient decision making. In this regard, high-quality data, including local data, are an important cornerstone for good analysis, and eventually lead to better decision making.

5. Need to properly enhance methods to calculate prices based on the drug’s life cycle stage. These include drugs that have just been launched or that have been marketed in the world, including China, for some time. Price estimation may vary in different circumstances. Detailed examples in this regard can be found in Australia, Germany, and Taiwan [25-27]. It is important for both the company and the payer (e.g., the government) to have realistic expectations before the review and negotiation. In China, the
government’s health insurance programs certainly have a strong purchasing power in any drug pricing negotiation. However, the engagement on pricing negotiation (and formulary inclusions eventually) between the Chinese government and the pharmaceutical industry should result in a win-win situation, reflecting appreciations of growth and investment in innovation in the pharmaceutical industry. This innovation is through pharmaceutical research and development, the clinical benefits to patients, and the budgetary effect on the government’s programs.

6 Need to develop professional evaluation teams for the CNF, especially when a dynamic review process is established. There are several models for conducting formulary review in the world. The National Institute of Health and Care Excellence (NICE) in the United Kingdom and Pharmaceutical Benefits Scheme (PBS) in Australia outsource reviews of submitted dossiers to external designated academic centers. These external reviews only provide professional comments and make recommendations (i.e., the assessment phase). The internal teams of NICE and PBS evaluate these reviews and then conduct negotiations with the submitting party (i.e., the appraisal phase). In this regard, NICE and PBS are the authorities for the final decisions. In the United States, reviews on submissions and decisions are likely to be made by an internal professional team of a health insurance organization (such as Aetna or Kaiser Permanente) or a health care system (such as the Veterans Health Administration). Therefore, the review model of NICE or PBS may be a good reference for the Chinese government if creating a relatively large and comprehensive internal team is perceived as too challenging. Adoption of the NICE or the PBS model in China would increase the technical capacity of internal teams within the Chinese government at various levels. In addition, the NICE and the PBS models would also cultivate HTA professional education programs in universities in China.

Besides these foregoing six suggestions, there are other key issues to consider for improvement of patient access under the CNF. For example, it is important to set up criteria and processes to evaluate candidate medicines to be considered by the CNF. In the meantime, it would be equally vital to have criteria and processes for an exit mechanism for the CNF to evaluate products that have been in the formulary for some time. Based on the international experiences of delisting medicines from national formularies, no drug—even one of the innovative medicines with patent expiration—should stay in a national formulary forever, nor should the price stay unchanged over time. This is because of the evolution of medical technology, the status of a drug’s life cycle, and the aggregated budget impacts [28,29]. Another important issue beyond the scope of this article is how to help patients better access innovative medicines that are still outside the CNF.

Conclusions

China continues to make significant progress in improving public health insurance coverage. Along with this progress, the CNF is also becoming more wide ranging. The recent pilot of negotiations for innovative drugs has been successful, although with some limitations, including innovative medicines in the CNF, thus benefiting patients in China. Even though this is the first such pilot in China, the positive outcomes suggest a promising direction for future CNF development. More pilots can be expected before the evaluation system becomes finalized.

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REFERENCES


