CHINA'S AMBITIOUS PATH TOWARDS UNIVERSAL HEALTH COVERAGE (UHC)

INTRODUCTION

In the last publication of CSOFT's series on China's healthcare reforms, the topic of how China's radical regulatory makeover is shaking the entire pharmaceutical industry, both globally and domestically, was discussed. In this latest piece, another significant aspect of China's healthcare reform will be looked at: how China is dramatically improving the accessibility and affordability of treatments, aiding to realize the country's eventual ambition – Universal Health Coverage (UHC).

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BACKGROUND

In 2018, China launched its Healthy China 2030 campaign, aiming to build a **patient-centered, value-based, evidence-supported** healthcare system. In pursuit of its own universal health coverage (UHC), China has since adopted the following 4-part initiatives:

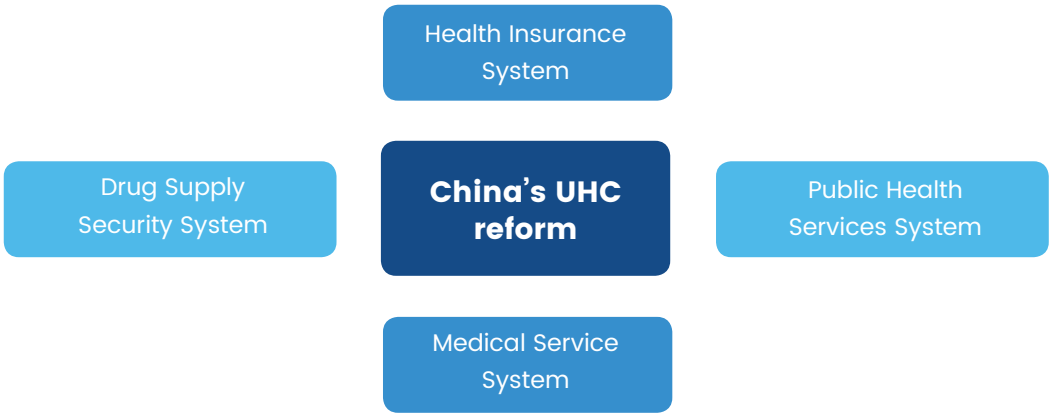


Figure 1: China's 4-part initiatives towards Universal Health Coverage (UHC)

The reform of the drug supply and security system led by the country's rebranded regulatory agency – the National Medical Products Administration (NMPA) – has been in the spotlight for the last five years. The agency has been taking multiple ground-breaking measures to improve the availability of high quality and cost-effective drug products, such as conducting major updates on the National Reimbursement Drug List (NRDL), establishing '4+7' centralized procurement, introducing urgently needed new overseas drugs in clinical practice, and promoting the national adaptation of the Market Authorization Holder (MAH) policy.

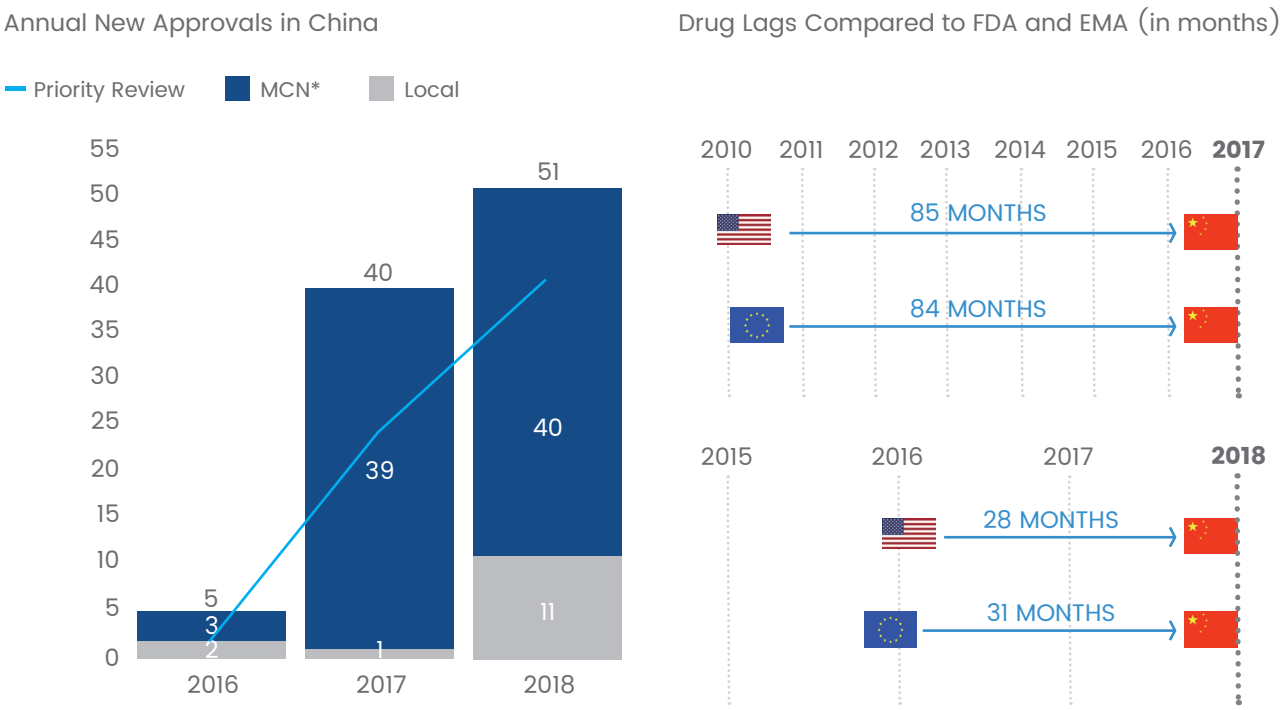
IMPROVING DRUG ACCESSIBILITY

Access to new drugs has, in the past, long been a source of pain for patients in China, impacting not only their life expectancy, but also their quality of life (QoL). The **drug lag** in China, which measures the delay in drug accessibility in a particular market, was previously measured in years, and as a result has caused millions of patients and their families unmeasurable pain and suffering.

To this end, the regulatory authority has undertaken three major actions:

- Introducing urgently needed new drugs overseas in clinical practices
- Fast tracking review and approval programs
- Updating the Essential Drug List (EDL)

As a result, China has reduced the drug lag period by two-thirds.



*MCN: Multinational pharmaceutical company.
Source: Deloitte LLP, 2018.

Figure 2: China's decrease in drug lag (Credit: Deloitte)

Introduction of urgently needed new drugs overseas in clinical practices

To encourage pharmaceutical companies to bring the latest breakthrough treatments that have been approved in the U.S., European Union, and Japan to China, the NMPA has introduced two batches of urgently needed overseas new drugs in clinical practices that comply with one of the following three criteria:

1. Address an identified rare disease;
2. Attend to a life-threatening medical condition without any current approved treatment;
3. Demonstrate a significant clinical advantage compared to the current Standard of Care (SoC).

These two batches of drug lists, in total amounting to 78 drugs, seek to grant people in China access to the newest drug development products in the shortest possible time. By March 2020, 20 of the listed drugs were already approved in China, with an additional 10 candidates in the pipeline that are close to receiving approval from the NMPA. So far, the shortest approval time is just **82** days.

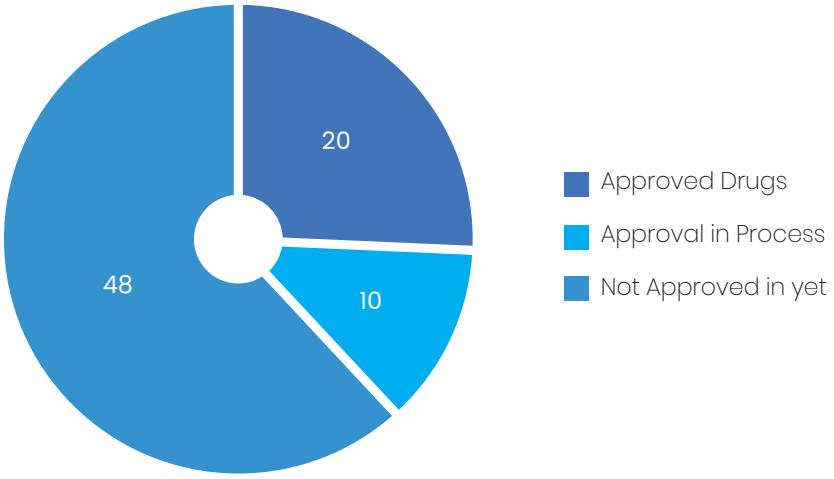


Figure 3: Approval status of 78 urgently needed new overseas drugs in clinical practices (as of March 2020)

Fast Track Review and Approval Programs

China's NMPA has largely copied the FDA's fast track review and approval program structure while also taking the country's healthcare situation into consideration. The specific issue China is facing is to ensure that patients can gain access to innovative foreign drugs approved in the U.S. and/or Europe for many years. For the first time, the Drug Administration Law, which was officially put forward in 2020 by China, lays out four fast track review and approval programs that serve different purposes:

	Breakthrough Program	Conditional Approval Program	Priority Review Program	Special Approval Program
Applying Stage	Clinical Trial Stage	Clinical Trial Stage	Marketing Authorization Stage	Clinical Trial Stage
Applying Scenario	· **Innovative** or **improved** new drugs · Used for life-threatening medical condition without any current approved treatment or, compared with existing measures of treatment, there is sufficient evidence proving the **obvious clinical advantages**	· Drugs that treat life-threatening injuries with no effective treatment, and **early trial data indicates efficacy and potential clinical value** · Urgently needed drugs for the **public health** with clinical trial data that indicates efficacy and potential clinical value · **urgently needed vaccines** for major public health emergencies	· Urgently needed drugs in short supply, and innovative drugs and improved new drugs for serious **infectious and orphan diseases** · New varieties of paediatric drugs that meet the physiological characteristics of **children** · urgently needed and innovative **vaccines** · Drugs approved under the **breakthrough or conditional approval programs**	Applies when there is a **public health emergency**
Process	Applicants may request **communication with CDE**, and CDE reviewers will provide comments on the applicant's **development strategy**	· Potential path of **clinical trial waiver** · NMPA will place **post-marketing conditions** on drugs under this program and **a timeline** for completion.	CDE evaluates priority review drugs for marketing approval on an **expedited timeframe** and priority review drugs receive **priority for other procedures**, i.e., inspection, registration testing, and approval of non-proprietary names	NMPA may legally decide to implement special approvals of drugs needed for the prevention and control of such public health emergency
Noticeable Case(s)	First approved case: **Legend Biotech's** Anti-B-cell maturation antigen CAR-T therapy: LCAR-B38M (Aug. 05, 2020)	In 2018, **Merck's** HPV vaccine **Gardasil 9** received conditional approval from NMPA to market with just **9** days, setting an unprecedented record	On June 5th, 2020, **BeiGene's** cancer therapy zanubrutinib gained market approval from NMPA via priority review program, having claimed the place of **the first Chinese cancer therapy being granted breakthrough treatment status by FDA**	During COVID-19 pandemic, **Gilead's** remdesivir received special approval from NMPA for clinical trial with just 3 days

Figure 4: Four priority review and approval programs under China's new Drug Administration Law

The most impressive case that the NMPA has achieved is the approval of **Merck's** HPV vaccine Gardasil 9 in just **9** days under the conditional approval program in 2018. The vaccine was originally approved in the U.S. in 2014. However, for a total of **4** years, people in China were unable to receive the vaccine that could most effectively prevent a life-threatening condition. Indicating the demands for the vaccine, Merck reported a **55% increase in sales** over the same period last year following the approval.

Update of Essential Drug List (EDL)

The Essential Drug List (EDL) should include all drugs that must be available at all primary care institutions, making the expansion of the list a vital step in fully addressing basic healthcare needs. In the latest update of the EDL, 12 oncology drugs and 22 urgent drugs for children have been among the latest additions to the ever-growing list.

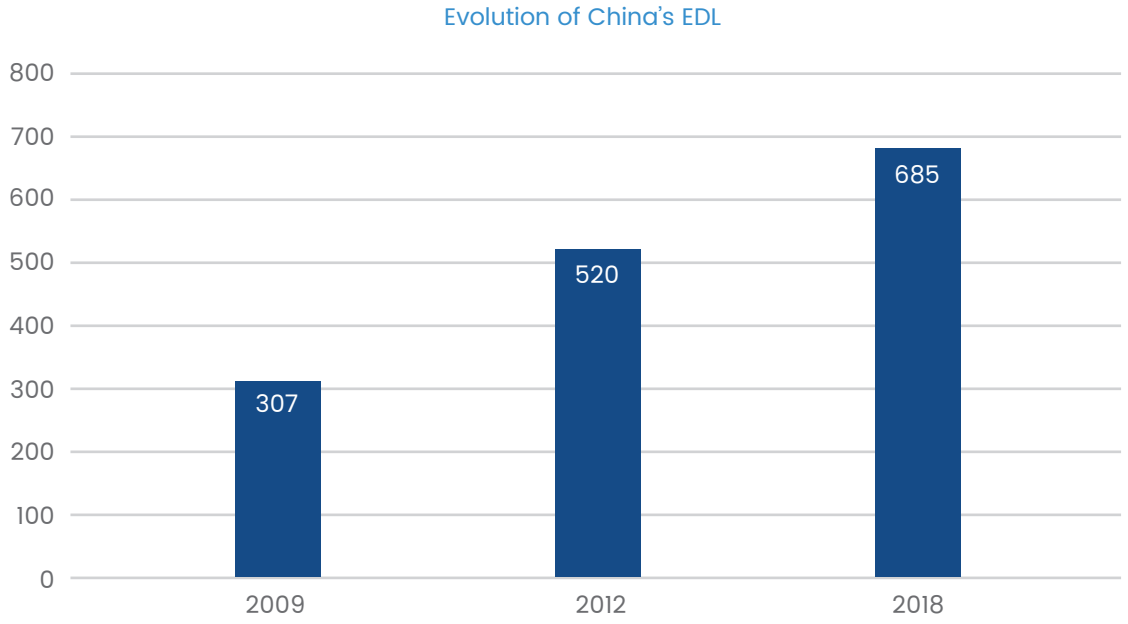


Figure 5: Evolution of China's Essential Drug List (EDL)

ENSURING DRUG AFFORDABILITY

In the past, China's drug procurement and reimbursement system suffered from the lack of a centralized system for coordination and quality control, resulting in domestic local manufacturers producing low quality drugs, disincentivizing global pharmaceutical companies from entering the market. Consequently, patients in China were forced to pay excessive costs for sub-par treatment. In response to the situation and to dramatically improve the drug affordability in China, the government has taken two major steps towards ensuring quality drugs at affordable costs for its growing middle-class population.

Major updates on National Reimbursement Drug List

In 2017, after a long 8-year wait, China made its first consequential update to the National Reimbursement Drug List (NRDL), which mainly focused on **innovative** but **premium priced** drugs. This would signal the start of the country's effort to fundamentally transform the pricing and reimbursement processes in China, introducing the pilot practices of price negotiations in exchange for inclusion and value-based, evidence-supported evaluation for the first time.

2017: price negotiation in exchange for inclusion

During the 2017 update, a total of 339 drugs were added to the existing list from 2009, with a heavy focus on cancer, HIV, and rare diseases. Among the newly added drugs, 36 were innovative patent drugs. By introducing price negotiation in exchange for inclusion, the price for these premium priced drugs witnessed an average **44%** drop. The same practice would continue to yield positive results into late 2018, when 17 cancer drugs were also added to the NRDL given the provision of significant price cuts.

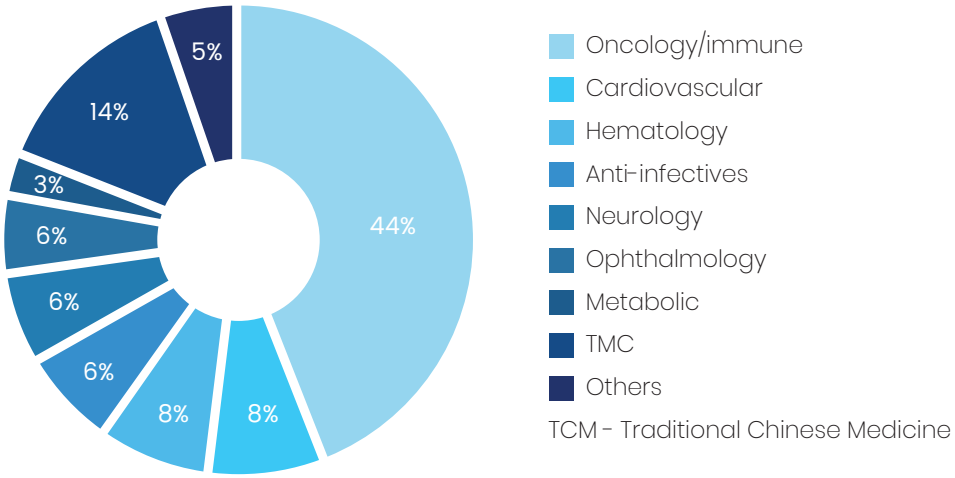


Figure 6: Breakdown of Therapeutic Areas of Newly Listed Drugs in 2017 (credit: PPD)

2019: introducing health technology assessment (HTA)

In 2019, health technology assessment (HTA) before price negotiation was adopted to further support the process. The HTA for innovative patent drugs includes:

1. Evaluation of clinical necessity (e.g., urgent, unmet need);
2. Safety profile;
3. Clinical effectiveness;
4. Reasonable pricing for drugs with the same indications.

Under this rigorous new procedure, 148 new drugs were added to the list while the 150 existing drugs were removed due to the existence of better alternatives. This was the first time in China's healthcare reform history that a value-based, evidence-supported evaluation model was adopted as part of a health outcome assessment.

Result of the National Reimbursement Drug List Updates

Under the new HTA system and dynamic price negotiation for inclusion, the long unmet needs of patients in China have been relived dramatically. For example, **Roche**, whose oncology drugs were among those added to the NRDL, reported a **53%** of revenue growth in China for Q3, 2018, even though the company agreed to significant price cuts of more than 60% in exchange for inclusion. Similarly, **AstraZeneca** also reported a **40%** growth in China's revenue after accepting a **71%** of price cut to be included in NRDL. The robust growth in sales testified to the urgent needs of the country's patients. Thanks to the new HTA system and dynamic price negotiation, drug prices are much lower than before. With this lower drug price cost, life-saving drugs are more accessible to Chinese patients, resulting in more patients able to purchase the drugs they need, thus leading to the increased revenue growth. Overall, the NRDL updates haven proven to be crucial in meeting the needs of Chinese patients, and large numbers of people have benefitted from the government's efforts.

'4+7' Centralized Procurement: trading volume for price

To tackle the existing procurement challenges of variable quality in domestically produced generic drugs, as well as the high autonomy of public hospitals and poor coordination of various payment policies, China launched its newest round of drug pricing and procurement reform that would pilot in **4 municipalities** (Beijing, Shanghai, Tianjin and Chongqing) and **7 cities** (Guangzhou, Shenzhen, Xi'an, Dalian, Chengdu, Xiamen) in 2018. Thus, the term '4+7' procurement was coined. In total, these 11 regions make up roughly 30% of the country's total drug sales.

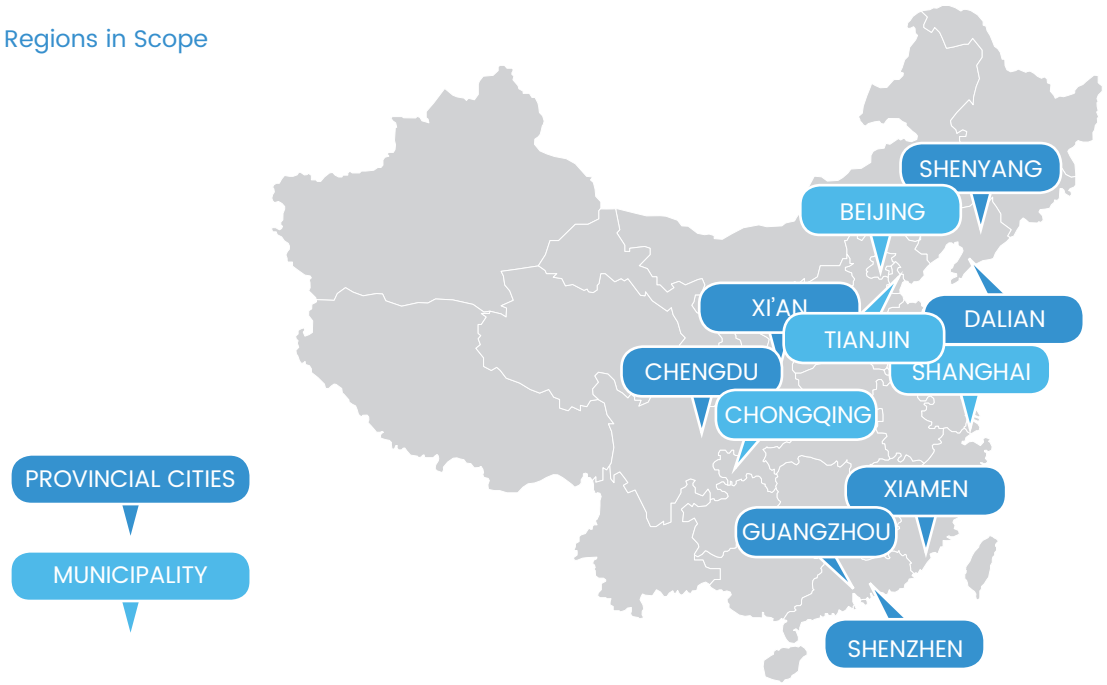


Figure 7: '4+7' pilot reform map

This newest reform would differ from previous efforts in several major aspects, which are detailed below in Table 1:

	The "4+7" Reform	Previous Pilots
Leadership	The State Council	Municipal/provincial government, or regional government alliance
Scale	Nationwide	Municipal/ provincial/regional level
Initiator	Payers, with support of regulators, health administrators	Local/provincial/national health authorities
Implementers	All the public hospitals at primary, secondary and tertiary level	All the public hospitals at primary, secondary and tertiary level
Price	Huge price reduction based on the guaranteed national purchasing	Moderate price reduction, and sometimes price rising after procurement
Quantity	Predefined national minimum quantity, and quota for public hospitals	Quantity depends on the specific facility
Payment	Minimum 30% prepayment by the payer	Varied depend on the local budget
Incentives	Compensation, performance assessment	Compensation, performance assessment
Implementation	Procurement and facility-level purchasing is unified in the same process; payment tariff is the same as the procurement price	Procurement and facility-level purchasing is separate; hospitals can decide if they will purchase the product

Table 1: Comparison of the "4+7" reform and the previous reforms (credit: China National Health Development Research Center)

Additionally, the '4+7' procurement reform is a coordinated effort among three major agencies: the National Health Insurance Bureau (NHIB) for coordination and payment, the National Health Commission (NHC) for provider behaviors, and the National Drug Administration (NDA) for drug quality.

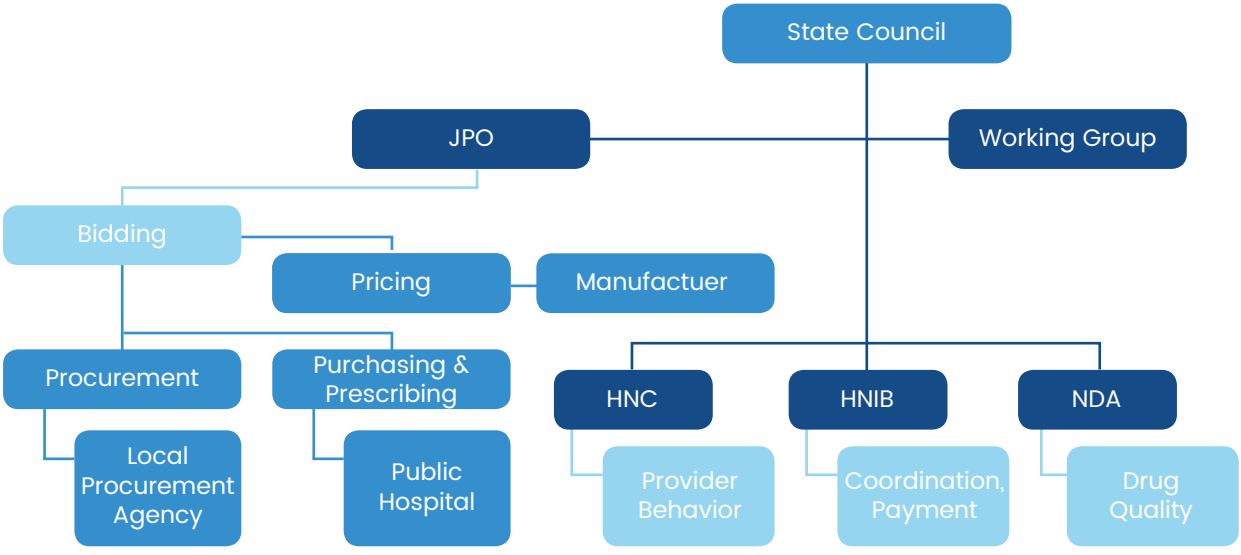


Figure 8: Organizational structure of the "4+7" reform (credit: China National Health Development Research Center)

Result of the '4+7' Centralized Procurement

As a result of the coordinated efforts, out of the 25 drugs that were selected, an average price cut of 52% was achieved, with some cuts going as high as 96%.

*Domestic Manufacturer

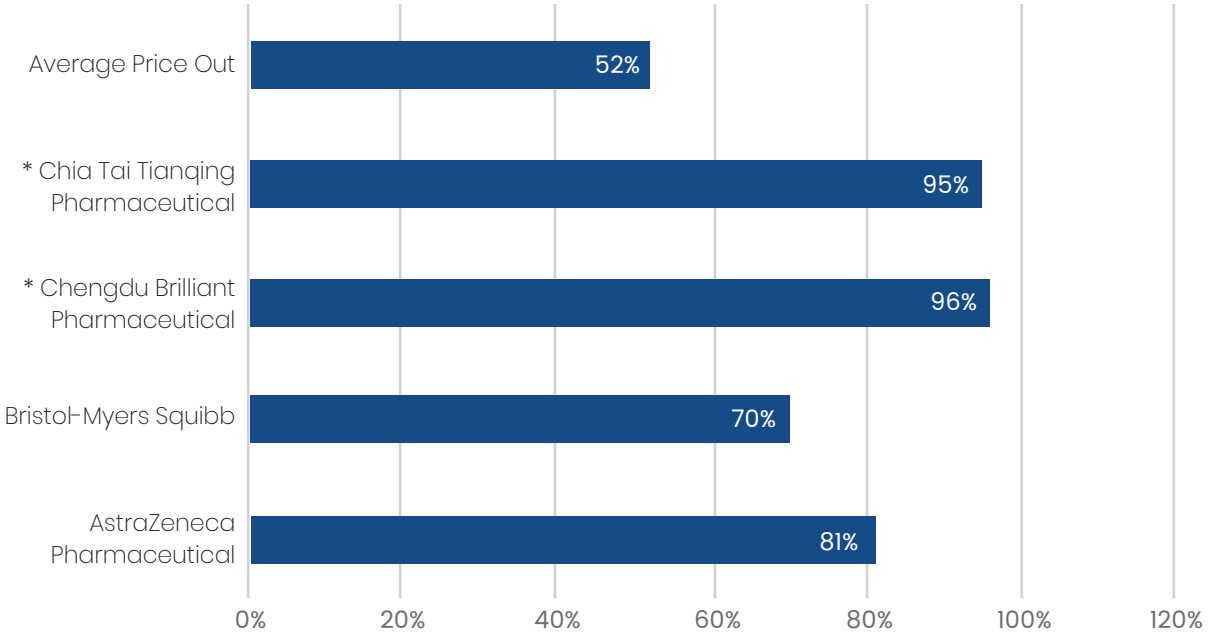


Figure 9: Result of the '4+7' centralized procurement (selected)

OUTLOOK FOR THE INDUSTRY

As China continually makes progress in healthcare reforms to further its efforts in providing affordable, accessible and high-quality drugs for the biggest population in the world, **global pharmaceutical companies** must develop their market access strategies to keep up with the country's ever-changing healthcare market landscape. Adaptation of health economics modeling tools, collaboration with local healthcare payment data providers, and now even consideration of real-world evidence (RWE) will be crucial to gain market access for their innovative patent drugs.

For **domestic companies**, to survive in this increasingly challenging market, research and development capacities are shifting from 'nice-to-have' to 'must-have' as China tightens its control on the generic drug market and eliminates unreasonable price premiums that have burdened patients in the past.

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R & D

2015.11
Published 'Opinions on Product Registration' (Draft was published in July); Reform of drug and medical device regulation

2016.02
Published the 'priority approval' policy to address the backlog of drug registration and set up **priority review**

2016.03
Published policy on **generic drug consistency** evaluation

2017.06
China becomes a member of **ICH**

2017.10
Published opinion on strengthening the reform and approval process to **encourage drug and medical device** innovation, covering clinical trial management, review process acceleration, life cycle management and innovator's rights protection

2017.12
Published standard for generic products

2018.03
CFDA renamed as **NMPA**

2018.06
Published the first national list of 121 **rare diseases**, introducing incentives for R&D of orphan drugs

2018.07
Published policy on **generic drug consistency** evaluation

2019.05
eCTD implementation

2019.05
Published 'Key Considerations in Using **Real-World Evidence (RWE)** to Support Drug Development' Set up Hainan medical tourism zone allowing in-zone collection of RWEs on imported drugs and devices that have not been approved

2019.07
Published **National Regulation on the Management of Human Genetics Resources**, specifying the collection, preservation and using of a range of genetic materials and prohibiting foreign organizations/individuals from collecting or preserving China's human genetic resources

2020.01
Published **Guidelines for Real World Evidence to Support Drug Development and Review**, to further guide and standardize the use of **RWE** in drug R&D and review, and ensure the quality and efficiency of drug R&D

2020.04
Published the new Drug Administration Law, which officially took effect on July 1st

Market Access

2015.06
Announcement on instructions for improving **public hospital centralized procurement**

2016.05
Announcement on advancement of **central procurement for negotiation**

2016.06
Marketing Authorization Holder (MAH) pilot scheme

2017.02
Published 'Opinions on Further Reform and Improvement of Drug Manufacturing and Distribution Policies', tightening regulation on **medical representatives** and enforcing **drug launch price**

2017.03
New National Reimbursement Drug List (NRDL) updates and 44 products entering negotiation

2017.10
Beijing proposes Healthy China 2030, putting health at the center of the country's agenda

2018.10
Update of **Essential Drug List (EDL)**, including 12 oncology drugs and 22 urgent drugs for children

2018.11
Commencement of **'4+7' centralized procurement** reform trial in 4 municipalities and 7 cities

Announcement of the First batch of **urgently needed overseas new drugs in clinical practices:** 48 products

2019.01
Update of **NRDL** and introducing the dynamic method of **trading volume for price**

2019.03
Introducing the 60**-day IND review system for medical device**

2019.04
Increase **reimbursement of major and critical disease** from 50% to 60%

2019.05
Announcement of the Second batch of **urgently needed overseas new drugs in clinical practices:** 30 products

Other Healthcare Policies

2015.09
Implement of **tiered healthcare system**

2016.06
Contracted service of **general physicians** implemented

2017.04
Announcement of policy on advancing the building up and development of **medical partnership**. Forum of pricing reform of medical service ('**Zero mark-up**')

2018.12
Policy on governance of **modern comprehensive medical** services, and selected hospitals for trials