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China on the Move: Lesson from China's National Negotiation of Drug Prices in 2022

In January 2023, China's National Healthcare Security Administration (NHSA) published the 2022 National Reimbursement Drug List (2022 NRDL), implementing a comparable level of pricing discounts to those seen in 2021.

This GT Advisory explores the following considerations:

- Out of 147 drugs negotiated, 121 were successfully added to the 2022 NRDL, including 91 with exclusivity. In comparison, 74 were successfully added to the 2021 NRDL. The average price cut of the 121 drugs is 60.1%, close to the figure of 61.7% in 2021.
- Same as 2021, domestic companies are responsible for the majority of newly added medicines, and some multinational companies still struggle to strike a deal with NHSA for their products.
- Just as in 2020 and 2021, seven orphan drugs were included in the 2022 NRDL. However, the reimbursed products could not come close to their prices in other countries, and a substantial level of discount appears to be necessary to be included in 2022 NRDL, for example, a 94% price cut in the negotiation.
- NHSA appears to move into the stage of formalization and finalization of the NRDL based on its learning in past few years. The vision of Chinese government or policy makers to build up a sustainable health care expenditure model without overpromising to the Chinese public has become clear.

Increasing the competition of the product in the same category and permitting commercial insurance to fill the gap of NRDL coverage are the major policy tools to accomplish this objective.

- First-in-class product or the first product for a specific unmet need would not be easily included in NRDL unless the other alternative products or follower candidates would become available soon after.
- A simple renewal mechanism would provide relief to companies with cancer drugs that have multiple indications or products with predictable sale growth against the biannual price negotiation.
- More consolidation among Chinese players and foreign companies' restructuring of their Chinese businesses would likely be the final result of the 2022 NRDL. Chinese players would be motivated to invest in their foreign operation not only through their increasingly prominent partnership practice but also the direct entry model.

1. Delayed Effective Date and Consistent Price Cut Practice

Unlike the 2021 price negotiation and the 2021 version of the National Reimbursement Drug List (NRDL) completed at the end of 2021, the negotiation for the 2022 version of the NRDL was delayed until early January 2023 and was released Jan. 13, 2023, effective since March 1, 2023. The unexpected delay may have been caused by the spread of COVID-19 in China since early December 2022. The 2021 NRDL will therefore still be applicable for the first two months of 2023.

Considering the interference of COVID-19 in early 2020 and late 2022, we expect that, in the following years, the NRDL application may start at the midyear point, and the NHSA will aim to finish the negotiation and release its decision by the end of the year (please find the comparison in Table 1).

Table 1. Comparison of NRDL Timeline

	Application started on	**Application ended on**	**Negotiation started on**	**Negotiation ended on**	**Decision made**
2020	Aug. 21, 2020	Aug. 30, 2020	Dec. 14, 2020	Dec. 16, 2020	Dec. 28, 2020
2021	July 1, 2021	July 14, 2021	Nov. 9, 2021	Nov. 11, 2021	Dec. 3, 2021
2022	July 1, 2022	July 14, 2022	Jan. 5, 2023	Jan. 8, 2023	Jan. 13, 2023

In 2022 NRDL, NHSA received applications for 490 drugs, 344 of which passed the preliminary review before the official negotiation. In comparison, 271 drugs out of 501 applications passed the preliminary review before the 2021 NRDL negotiation. NHSA published the breakdown of such 344 drugs on its site as it did in 2021, disclosing information such as generic names, market authorization holder names, indications, if any patent disputes exist, dosage, and description of effectiveness and safety. NHSA further posted a summary of the 344 drugs prepared by the applicants, and each summary is required to include the basic information, safety information, innovation, economic information, social impact (elaborating on the importance of the drug to public health) and whether the drug is still under exclusivity. The summaries do not include, however, economic information likely due to confidentiality reasons. For example, AbbVie's Venclexta for AML (acute myeloid leukemia) in its summary demonstrated the drug's

clinical value and innovation, and also proves its status of being under exclusivity in China. Venclexta was successfully included in the 2022 NRDL as the first and only drug for acute myelogenous leukemia.

121 drugs are newly included in the 2022 NRDL. The average price cut of such 121 drugs is 60.1%, very close to the 61.7% discount in 2021. It is also noteworthy that this year, seven orphan drugs are included in the NRDL, exactly the same number of orphan drugs included last year.

2. Well-defined NRDL Objectives' Restriction on the Medical Insurance Resource Spending at National Level

The Zero-COVID policy has had a significant impact on basic medical insurance. On one hand, the vaccines, the widely used PCR test, and antigen test were covered by the government (partly with medical insurance and partly with fiscal income) for some time. On the other hand, the lockdowns in the past years may have reduced the contributions to basic medical insurance. With its aging population, the pressure on budget continues. Since the NRDL updates have become annual, the NHSA appears to be particularly mindful of the increasing spending of National Medical Insurance on medicinal products, regardless of the aggressive policy agenda in promotion of life sciences innovation in China. In the past, efforts to make China the next growth engine for foreign companies motivated a large number of companies to provide patient-assistance programs to temporarily "park" their product at the commercial stage in China until the products can be included in the NRDL. Now, policymakers leverage the competition in the same product category or therapeutic area, and intend to leave local authorities to set up commercial insurance or a local government subsidy scheme per each local authority, without expanding NRDL at the same pace, like the regulatory approval of innovative products in China. Based on our analysis, the NHSA appears to be more interested in reimbursing first-in-class product or the first product for a specific unmet need when the agency will get alternative drugs in the same class or the same indication soon following the reimbursement decision of such product.

This approach reflects Beijing's learning from its foreign peers' past and current failures to rein in their public's expectation of the social welfare systems. Considering the deteriorating demographic structure, the significant discrepancies across public finance status of each province, and moderate economic growth in the coming years, NHSA and the other policymakers accordingly aspire to utilize all policy tools in development of its reimbursement practice to contain medical expenditure growth in the long run. These objectives will pretty much define the growth potential of the Chinese market and will set the tone for market access in the next decade. In other words, from our view, the NRDL practice in China is moving from the stage of idea development to the stage of implementation of the idea. This should provide a level of predictability but should also remind the investors or foreign companies to remove their rose-colored glasses.

a) Disciplined Approach in COVID-related Treatment Reimbursement

Before the National Healthcare Security Administration (NHSA), China's payer of public health care security system, published the new NRDL, it announced Jan. 8 that Pfizer did not reach a deal with NHSA over the COVID-19 oral antiviral Paxlovid. The other two domestic drugs for COVID-19, Azvudine of Genuine Biotech and a traditional Chinese medicine made it into the NRDL. According to NHSA, Pfizer's quote of Paxlovid was much higher than NHSA's contemplated price, and Pfizer did not lower the price during the negotiation. The temporary procurement price of Paxlovid is RMB 1,890.

On Jan. 29, the National Medical Products Administration (NMPA) granted conditional approval of another two domestic drugs for COVID-19, Simnotrelvir of Simcere and Renmindevir (known as VV116)

of Junsi Biosciences. Simcere stated to the media that "the pricing of Simnotrelvir, as a drug with the same target (3CL), will be significantly lower than that of Pfizer's Paxlovid." The pricing of VV116 in some countries where it was approved earlier in 2021 was also much lower than that of Paxlovid. Although Simnotrelvir and VV116 are not included in 2022 NRDL, they will be covered together with Paxlovid by the national health care system temporarily until March 31, 2023, according to a payment policy issued by NHSA and other government departments. Fierce competition may emerge in the market of drugs for COVID-19.

b) Gap Between the Ambition and Reality in Rare Diseases Product Reimbursement

NHSA endeavors to include rare disease drugs which were not listed previously. In 2021, BioGen's Spinraza for SMA (Spinal Muscular Atrophy) was included in the 2021 NRDL by offering a 95% discount, giving NHSA a big limelight. Similarly, Takeda's Alglucosidase alfa for Fabry disease, and Pfizer's Vyndamax for ATTR-CM were also known as high-priced drugs for rare diseases but were included at that time by offering a generous discount. This year, NHSA included Takeda's Takhzyro in the NRDL which is the first mAb drug for HAE (hereditary angioedema) in the world.

NHSA also tries to make more rare disease drugs eligible for the negotiation. According to the Work Plan, all rare disease drugs approved before June 30, 2022, are eligible for NRDL adjustment, while for other drugs, only those approved in the past five years are eligible. For example, Treprostinil Injection, included in 2022 NRDL, was first approved in 2013.

On the other hand, NHSA's intent to provide multiple options to rare diseases patients may lead to an unfavorable result for patients. Roche's Risdiplam for SMA, and Biogen's Tecfidera and Novartis's Kesimpta for MS (multiple sclerosis) all earned spots in NRDL. In particular, one year after the 95% discount of Spinraza, its competing product Risdiplam is included, reportedly with a discount of 94%. Biogen's Fampridine for MS was included in 2021. This shows the NHSA's interest in promoting competition between pharmaceutical companies in terms of rare disease drugs. Apart from these two drugs, the Center for Drug Evaluation granted clinical trial approval to Novartis's Zolgensma (also for SMA) in April 2022. The deteriorating pricing for rare disease drugs due to competition may become a concern in the following years.

However, there were a total of 19 rare disease drugs eligible for NRDL negotiation, and less than half of them were included in 2022 NRDL. For example, Roche's Sylvant for Castleman's disease and Takeda's Vpriv for Gaucher's Disease were not included. In 2018, National Health Commission (NHC, as the leading department, together with four other departments including NMPA) published the first batch of rare diseases (121 in total), covering all the rare diseases mentioned in this GT Advisory. The NRDL has hitherto included 52 rare disease drugs for 27 rare diseases. NHC is currently developing the second batch of rare diseases to include on the list. NHC's rare disease list gets a lot of public attention not only because the 2022 Work Plan for the first time explicitly allowed pharmaceutical companies to apply for NRDL inclusion of rare disease drugs (all those approved before June 30, 2022, as mentioned above), but also because certain fast tracks of regulatory approval are available to drugs included in NHC's rare disease list. For example, if a rare disease drug is approved in a foreign jurisdiction and this disease is life-threatening, an applicant may directly apply for market approval with the foreign trial data provided that no racial difference exists. NMPA may also grant conditional approval to rare disease drugs or partly accept the foreign trial data depending on different cases.

Considering the provincial disparity of China and different morbidity of various rare diseases, the combination of nationwide NRDL coverage and provincial critical illness insurance will remain unchanged. The sharp price cut in rare diseases products may discourage companies to launch the product in China. Coverage of rare diseases is still a long way to go in China.

c) Domestic Companies' Continue Dominance in Oncology Product Market

The second approved CAR-T product in China, Carteyva of JW Therapeutics, still walked away without a deal with NHSA. Same as Yescarta of Fosun Kite, it appeared on the short list but was not included in the NRDL. These two CAR-T products cost similarly around 1.2 million RMB per injection. In 2022, more cities introduced inclusive commercial insurance to cover expensive products such as CAR-T. As a general practice, local NHSA coordinated large insurance companies to design the insurance products, determining extra-NRDL drug coverage. Several insurance companies would jointly underwrite the inclusive commercial insurance. The 2022 version of Shanghai inclusive commercial insurance (Huhuibao) offered the maximum insured amount of 500,000 RMB. Other cities such as Beijing, Ningbo, Hangzhou, Changsha and Taiyuan also announced local commercial insurance would cover CAR-T products under their local inclusive commercial insurance.

The PD-1 products of Innovent, Hengrui, Junshi and BeiGene all won new indications in the 2022 NRDL, in addition to the current ones in 2021 NRDL. However, the newly approved PD-1 products, Henlius's Serplulimab and Envafolimab (co-developed by 3D Medicines, Simcere, and Alphamab) failed to get spots in NRDL, likely because the discount offered by these two products could not match the one offered by currently included products from Innovent, Hengrui, Junshi, and BeiGene.

On the other hand, multinational pharmaceutical companies managed to have some innovative anti-cancer drugs included in 2022 NRDL. Innovative drugs such as Pfizer's third-generation ALK inhibitor Lorbrena for lung cancer, and Firmagon for prostate cancer, and Takeda's Alunbrigtm for lung cancer were all included.

Quite a few domestic innovative drugs gave up negotiation. Some PD-1 products, such as Penpulimab by Akeso and Sino Biopharmaceutical, and Zimberelimab by Gloria and Wuxi Biologics, may have ceased negotiations because other PD-1 products included in NRDL had driven down the pricing to such a level that did not meet their expectations. Some other anti-cancer drugs probably gave up due to their confidence that they have no competing products. CSPC Pharmaceutical Group, Innovent, BeiGene, CStone Pharmaceuticals and several biotech companies each had one exclusive product that did not participate in the negotiation. Most of the products were anti-cancer drugs, but one was for rabies (North China Pharmaceutical's Ormutivimab) and another for COVID-19 (Brii Biosciences' Amubarvimab Injection).

3. A Highlight of Simple Renewal Mechanism Introduction

The inclusion of a product in the NRDL is effective for two years. In the past, a company was required to resubmit the application documents to apply for renewal at the end of the two-year period. If a new indication was approved for a marketed product, reapplication was necessary which sometimes leads to significant price revision.

According to the work plan of the NRDL adjustment issued in June 2022 ("Work Plan"), if the past expenditure of a brand name product and its future estimated expenditure during the next two-year period of NRDL inclusion is less than 200% of the estimated expenditure from the national health care insurance fund conceived by the company at the last negotiation (two years ago when the drug was

included in the NRDL), such company may decide whether the renewal should follow a simple renewal mechanism, under which a clear algorithm will be applied to determine the price of renewal (except when there is a major change to the market landscape, e.g., a much lower international reference pricing, or the inclusion of a competitive product). The higher the past two-year total expenditure is, the higher the price reduction (25% at most) for renewal will be.

Additionally, if a new indication is approved for a NRDL-listed drug and the two-year period of NRDL inclusion of the initial indication is going to expire, the company may include the new indication in the simple renewal mechanism together, rather than apply for NRDL inclusion de novo. Re-negotiation may cause uncertainties on the listing decision and result in drastic price reduction, while the simple renewal makes the price concession more predictable to the pharmaceutical companies. This new mechanism may provide more incentive to innovative pharmaceutical companies by limiting the price reduction and also help control the expenditure of drugs that consume "too much" funds of the national health care insurance.

4. New Sentiments Towards Chinese Market

NHSA has held three rounds of NRDL negotiation since 2020. It has become a norm to have NRDL negotiation every year. The pricing methodology and negotiation period have been more established and predictable to pharmaceutical companies.

Indeed, business profit-margins in China have been facing challenges under the current NRDL practice, which will continue to become more and more established over the next decade, which may or may not have high profitability. That said, the current NRDL does continue underscoring the Chinese market's advantage in contribution to the top line product sale data to each company. Trade-off between profitability and sale will be a major product launch decision for each company to make in next decade, in light of the structural constraints of the Chinese market and a clearer healthcare policy agenda.

A more realistic expectation to the growth of Chinese market will highlight the importance of resource efficiency improvement in the Chinese market. We anticipate more consolidation and partnership for commercialization will happen in the Chinese market following the finalization of the NRDL practice. To optimize their portfolio's growth opportunities in China, foreign companies may start contemplating the divestment or spin-off of some their operations and portfolios to their Chinese peers. And Chinese companies may move towards consolidation to improve their competitiveness domestically as well as to secure more resources for foreign expansion, as the Chinese market alone may not be able to be a main contributor to their next-generation growth. It is worth noting that Chinese companies have been exploring options to go global and exploit the value of their innovations through partnerships with multinational pharmaceutical companies. In 2021, Chinese companies have signed at least 12 out-licensing deals for innovative drugs with a median deal value of larger than $900 million. BeiGene, Zailab, HutchMed are also building their commercial presence outside of China. While it remains to be seen how Chinese companies move to appropriate value from China-originated innovations, the Chinese market landscape in the next few years may motivate them to embrace global challenges and work to deleverage their heavy reliance on Chinese market.

The 2022 NRDL may be a catalyst for companies to transform their China strategy and even global strategy, which is the major takeaway we see from the 2022 NRDL negotiation.

GT GreenbergTraurig

Authors

This GT Advisory was prepared by:

- Chia-Feng Lu ‡ | +1 202.331.3184 | ChiaFeng.Lu@gtlaw.com
- Dawn (Dan) Zhang | +86 (0) 21.6391.6633 | zhangd@gtlaw.com
- John Gao | +86 (0) 21.6391.6633 | gaoj@gtlaw.com

‡ *Admitted in The District of Columbia and New York. Not admitted in Japan.*