CLIFFORD

CHANCE

# CHINA'S BLUEPRINT FOR ITS PHARMACEUTICAL SECTOR

— THOUGHT LEADERSHIP

OCTOBER 2019

# CHINA'S BLUEPRINT FOR ITS PHARMACEUTICAL SECTOR

China has stepped up its legislative reform of the pharmaceutical sector to drive down prices, improve access to new drugs and foster generic competition with brand name drugs. These policies have had a wide-ranging impact on the industry and led many drug companies to restructure their China-based portfolio of drugs, sales model and investment strategy, creating new opportunities for international and domestic players alike. Clifford Chance experts assess the changing regulatory landscape as the Chinese government puts quality and affordability at the centre of its healthcare policy agenda.

## Key issues

The 2018 "Dying to Survive" blockbuster movie heralded a new wave of healthcare reform

- Since 2016, the QCE scheme has been used to mandate pharmaceutical companies to ensure that the quality and efficacy of their generics is on a par with the brand-name drug. Once qualified, QCE-approved generic drugs receive preferential treatment over the originator drug
- Price negotiations in 2018/19 between drug companies and the medical authorities (through volume-based tenders) led to price cuts averaging over 50%
- The "fast-track" approval regime for new drugs introduced in 2016 reduced the number of pending registrations between 2015 and 2018 from 20,000 to 4,000
- In response to these rapid changes, drug companies are overhauling their China drug portfolios and adapting their marketing strategies to meet the new market conditions

## China's regulatory storm

The past few years have witnessed a perfect regulatory storm in China's pharmaceutical sector as the government seeks to implement its dual aims of shifting market demand from highly-priced branded generics to their lower-cost generic alternatives, as well as improving the availability and affordability of essential patented drugs to Chinese patients.

The latest series of reforms began in the summer of 2015. China's State Council issued "Circular 44" which reformed China's drug and medical device approval regime to reduce the backlog of over 20,000 pending drug registration applications. At the same time, the China Food and Drug Administration (CFDA – the predecessor to the National Medical Products Administration or "NMPA") launched its campaign against fake clinical trial data, which resulted in the "voluntary" withdrawal by hundreds of drug manufacturers of their drug registration applications.

Since then, the Chinese government has initiated one reform after another: the generics "quality consistency evaluation" (QCE) reform, the pilot "marketing authorisation holders" regime, and various other policies designed to promote new drug development. Alongside these regulatory reforms, the government has toughened its stance on pricing during market access negotiations; in particular, targeting more expensive drugs.

Industry players have generally applauded these changes and been impressed by the determination of the Chinese government to reform. Clear benefits have been evident. For example, since 2015, the number of pending drug registration applications has been reduced from 20,000 to less than 4,000 in the first quarter of 2018.

That said, challenges remain. In June 2018, Dying to Survive (a blockbuster movie said to be based on the real story of a Chinese leukaemia patient who smuggled cheap but unproven cancer medicine from India into China for cancer sufferers) ignited debate on Chinese social media on issues ranging from the accessibility and affordability of drugs for ordinary Chinese patients to national policies regarding innovative drugs and generics. Perhaps unsurprisingly, the social awareness raised by the movie and subsequent social media chatter set the scene for the Chinese government's strong focus in 2018 on the treatment of cancer and the medicines for treating them. Then came a vaccine scandal later in 2018 which involved a listed Chinese pharmaceutical company and resulted in the arrest of several senior members of management and the resignation of the former head of the CFDA, an official who had been credited with spearheading the reform measures. For people who cared (be it the government, patients, health institutions or market players), it was clear there was still much to be done in order to widen access to affordable, high-quality drugs in China.

A number of reform measures which have been important in changing the regulatory landscape for China's pharmaceutical sector and the evolving role of innovative drug companies. Here are our high-level observations.

## Marking down to stay in: branded generics under pressure to lower prices

Drug prices have always been a sensitive topic in China and the past decade has seen a variety of policies introduced to tackle the issue, ranging from the abolition of the price mark-up by public hospitals, the reform of the public drug procurement tendering system, and the introduction of the two-invoice regime.

Despite these reforms, given most Chinese patients rely on public medical insurance for their healthcare costs, many have still not been able to afford expensive innovative drugs made by international or domestic drug companies. Over the past two years, the government has therefore stepped up pressure to lower the price of branded generic drugs, using a number of regulatory changes to achieve this end.

## Generics quality consistency evaluation (QCE)

The first such initiative has been the generics quality consistency evaluation scheme (or QCE scheme).

The QCE is a mandatory bioequivalence test required by CFDA for the commercialisation of any generic drug in China. First proposed in 2012, as one of the tasks of the Twelfth National Five-year Plan for Drug Safety, and aimed at promoting the quality of China's domestic generic drug industry, the CFDA originally planned to roll out the QCE scheme in 2013 and have it completed by 2020. However, a severe backlog of pending drug registration applications and the outbreak of the tainted drug capsule scandal in mid-2012 diverted the regulator's efforts. In the end, the QCE was formally launched in March 2016, after which the CFDA began implementing it in earnest.

The QCE is carried out primarily by requiring a registered generic drug to pass a test to assess its bioequivalence to a qualified reference drug (typically, the originator drug). The QCE is enforced with both a stick and a carrot. The stick is that under QCE, once a molecule is approved, other versions of the molecule from different manufacturers will also have to apply and obtain approval under the QCE within a three-year time period or be removed from the market. The carrot is that drugs which are QCE-approved can then become preferred candidates for inclusion in the National Essential Drugs List (EDL). Inclusion in the EDL entails a higher reimbursement rate under the public medical insurance system, public hospitals are required to keep EDL products in stock, and physicians are urged to prioritise the prescription of EDL products. QCE-approved generic products thus gain a key, competitive advantage in the market.

At the end of the first quarter of 2019, there were 99 molecules that had passed the QCE, with an additional 157 undergoing QCE registration.

## National drug reimbursement list (NDL)

The second key initiative which has been used to exert downward pricing pressure on drug companies is the national health insurance drug reimbursement list, or NDL.

The NDL is compiled and updated by the central medical insurance authority and serves as guidance to its provincial counterparts on which drug prescriptions to reimburse and at what rate. The government keeps the list open to include innovative, imported drugs that address acute therapeutic needs (such as cancer treatment). However, it also tries to obtain significant price concessions from any drug company whose product is included on the NDL.

The NDL was formally introduced in 2015, and in May 2016 some encouraging results were announced. Innovative drug companies agreed to cut by more than 50% the price of three products (two for treating lung cancer and one for hepatitis B, all of which were either patent-protected or the only generic product available in the market), in exchange for being included on the NDL. Two subsequent rounds of NDL negotiations were held, resulting in 36 products being added to the NDL in July 2017, and another 17 products in October 2018. Of the 53 products added in the second and third rounds of negotiation, 34 were cancer drugs.

Although the NDL may seem to be an attractive opportunity for companies (trading price for volume), it can be a double-edged sword. First, just because a drug is added to the NDL does not necessarily mean that public hospitals will prescribe more of it. This is because reimbursement is paid by each province's own medical insurance fund, and a province may delay the addition of a centrally negotiated drug to its provincial reimbursement list if it considers the negotiated price as still too high a burden on its coffers. Secondly, the corollary of having a drug added to the NDL is that the profit margin that public hospitals will be able to derive from prescribing that product will be reduced to zero, as public hospitals are not allowed to add their own mark-up to the drug price. This can act as a disincentive against prescribing the drug. As a result, some drug companies (following their agreement with the central authority) have reportedly still had to negotiate, on a province-by-province basis, before they have been able to take advantage of the national deal.

## Volume-based tendering

A third important price initiative of the central government has been the increasingly effective use of volume-based public tenders, or "group purchasing" by a collection of local healthcare authorities and hospitals. One recent example of this has been the so-called "4+7" procurement initiative, blessed by the central authorities and launched in 2018 by a coalition of health authorities from 11 major cities (including four cities with the status of a province, and seven cities that are provincial capitals or designated by the central government as economically significant, hence the name "4+7").

As a result of the "4+7" tendering process, 31 molecules were put forward in late 2018 for tendering based not only on price but also purchasing volume. From the perspective of drug companies, the plus side of a group purchasing arrangement, which includes a definite volume commitment, is that once the company's drug is selected, it will enjoy certainty not only of price but also of sales volume during the contract period (of one year). Under the previous system, winning in the provincial tendering process did not automatically translate into hospital prescriptions because hospitals had not committed to purchasing a defined amount of the drug.

The downside of this initiative for drug companies though, has been the even greater pressure to cut prices in order to be competitive. Whilst not excluding off-patent or branded generics, the "4+7" procurement initiative explicitly provides that the candidate molecules should be selected from those that have at least one QCE-approved generic drug, ensuring that there is direct competition between off-patent drugs or branded generics on the one hand, and the QCE-approved generic alternative on the other.

Since the volume commitment made under the tender has typically been determined by each participating city based on 60-70% of the estimated need of their hospitals, this means that a large proportion of patients are ultimately driven to use the QCE-approved generic version of the 31 molecules. Consider this to be a version of the "winner-takes-all" principle. The winning bidder is ensured the largest share of the total market for the tendered molecule in the relevant cities during the contract period in exchange for deep price cuts.

These tender processes also have a ripple effect. Since the provincial medical insurance authority will only reimburse on the basis of the price that the winning bidder has offered with respect to a molecule, companies that offer any other version of the same molecule (be it an off-patent drug, a branded generic, or another QCE-approved generic) find themselves effectively forced to reduce their prices as well, since if they do not, patients who purchase their product will have to pay the price difference out of their own pockets. So, even if you do not win the tender, you are still forced to follow suit with equivalent price cuts.

## Playing to your strengths: accelerated approval of imported drugs

Despite the government's latest price-cutting measures, it has not all been dismal news for innovative drug companies. China continues to see them as playing a critical role in introducing

new, R&D-based medicines and has taken steps to markedly accelerate the approval process for imported drugs which fill a real gap in the market.

For example, in 2016 the CFDA introduced a "fast track" to accelerate the approval of drugs considered to address hitherto unmet market needs. This had an immediate positive impact. According to the Center for Drug Evaluation (CDE) of the CFDA, as at the end of August 2018, there were in total 650 drugs which had been included in the "fast track" process, of which 106 had been approved (some 50% of these were drugs made by international drug companies).

In 2017, the rules were relaxed again so as to make it possible for international drug companies to submit data obtained in overseas multi-centre clinical trials in support of their drug registration applications in China. Historically, the general practice had been to require a drug manufacturer to conduct China-specific clinical trials regardless of the results of any overseas trials.

The Chinese government has been publicising its efforts to accelerate the approval of imported drugs. On 8 August 2018, the CDE published a list of 48 overseas drugs considered to be in acute need in the Chinese market and encouraged the foreign manufacturers of those drugs to apply for registration in China. As a reminder, the notice stated that the drug manufacturers could submit overseas clinical data, together with evidence showing that there was no difference between ethnic groups regarding the effect of the candidate drug.

There is no denying that international drug companies have been major beneficiaries of these measures. Until recently, there was a long gap in time (on average, eight years) between the approval of a drug in a developed market and in China. Since the reforms, however, international drug companies have now been able to bring their blockbuster drugs to China much more quickly than before, especially when they are seen to address an acute therapeutic need (such as cancer treatment).

These new opportunities for international drug companies also bring their own challenges. The accelerated approval process also means that the time between the approval of the new drug and its potential competitors (whether made by other international or domestic players) is also shortened.

Furthermore, whilst the CDE's fast track process helps address the issue of marketing authorisation, that alone does not solve the issue concerning the accessibility and affordability of the drug. Most Chinese patients do not have commercial insurance coverage, which means the affordability of a drug often depends on the local public medical insurance authority's willingness to reimburse its prescription. To overcome this, some drug companies therefore continue to pursue innovative business models, such as partnering with commercial insurers, to make their drugs more affordable.

## Winds of change: healthcare sector reform and its impact on the pharmaceutical ecosystem

Alongside reforms specifically targeting the drug industry, there are policy changes occurring more generally in the healthcare sector which impact the market environment and, indirectly, the drug companies operating in China.

Two such changes are particularly worth noting.

The first is the reform of the hospital system. Traditionally, the sale of medicine has been a critical source of revenue for hospitals which has created an unhealthy dependency on the prescription of drugs for their continued operation. The government is pushing hard to resolve this misalignment of interest by carving out the pharmacy retail operations from the hospital. Other policies have also been introduced with the same aim, for example, by prohibiting any price mark-up to be added by public hospitals (on top of the procurement price) when prescribing drugs to patients, by imposing a cap on the permitted percentage of a hospital's revenue that can be derived from selling drugs, and by encouraging

the sale of drugs by retail pharmacies/ drug stores. Whilst the changes in this area have been gradual to date, it has been reported that some hospitals already are increasingly reluctant to see expensive drugs sold in their hospitals. Drug companies are recognizing that these reforms are changing purchasing behaviour and thus impact their traditional sales model.

A second noteworthy change is the expanding role of the insurance system in purchasing decisions. With the establishment of the National Medical Insurance Bureau, medical insurance funds will likely play a more active role in the drug pricing process in the coming years (unlike in the past, when drug prices were mainly the result of the tendering process at the provincial or local level, and thus driven by the hospitals). Since the medical insurance funds are the ultimate payor of healthcare costs, they are keen to find the most cost-efficient outcome for the money they spend on drugs. Commercial insurance (i.e., policies marketed by insurance companies) will also likely become a major supplement to the public medical insurance system, as patients use (even if only partially) commercial insurance to cover their medical expenditure.

This continuing evolution of the healthcare system means that drug companies must adapt as new stakeholders emerge. Even if they successfully establish a route to market so that their drug is available to the patients who need it, even after the marketing authorisation is granted and tenders are won with the central medical insurance authority, companies still need to consider how best to structure their market access and drug distribution strategy so that it evolves alongside the rapidly-changing healthcare sector. This is the challenge, as well as the opportunity, that faces innovative drug companies operating in China.

# CONTACTS


**Yong Bai**
**Partner**
**Beijing**
T: +86 10 6535 2286
E: yong.bai@
cliffordchance.com

**Richard Blewett**
**Partner**
**Hong Kong**
T: +852 2826 3517
E: richard.blewett@
cliffordchance.com

**Mark Currell**
**Partner**
**Sydney**
T: +61 2 8922 8035
E: mark.currell@
cliffordchance.com

**Emma Davies**
**Partner**
**Hong Kong**
T: +852 2825 8828
E: emma.davies@
cliffordchance.com

**Liu Fang**
**Partner**
**Hong Kong**
T: +852 2825 8919
E: fang.liu@
cliffordchance.com

**Ling Ho**
**Partner**
**Hong Kong**
T: +852 2826 3479
E: ling.ho@
cliffordchance.com

**Tatsuhiko Kamiyama**
**Partner**
**Tokyo**
T: +81 3 6632 6395
E: tatsuhiko.kamiyama@
cliffordchance.com

**Valerie Kong**
**Partner**
**Singapore**
T: +65 6410 2271
E: valerie.kong@
cliffordchance.com

**Glen Ma**
**Head of Corporate, China**
**Shanghai**
T: +86 21 2320 7217
E: glen.ma@
cliffordchance.com

**Natsuko Sugihara**
**Partner**
**Tokyo**
T: +81 3 6632 6681
E: natsuko.sugihara@
cliffordchance.com

**Hong Zhang**
**Partner**
**Beijing**
T: +86 10 6535 2256
E: hong.zhang@
cliffordchance.com

**Yi Yang**
**Counsel**
**Shanghai**
T: +86 21 2320 7201
E: yi.yang@
cliffordchance.com

CLIFFORD

CHANCE

Any advice above relating to the PRC is based on our experience as international counsel representing clients in business activities in the PRC and should not be construed as constituting a legal opinion on the application of PRC law. As is the case for all international law firms with offices in the PRC, whilst we are authorised to provide information concerning the effect of the Chinese legal environment, we are not permitted to engage in Chinese legal affairs. Our employees who have PRC legal professional qualification certificates are currently not PRC practising lawyers. This publication does not necessarily deal with every important topic or cover every aspect of the topics with which it deals. It is not designed to provide legal or other advice.

www.cliffordchance.com

Clifford Chance, 10 Upper Bank Street, London, E14 5JJ



1010191742