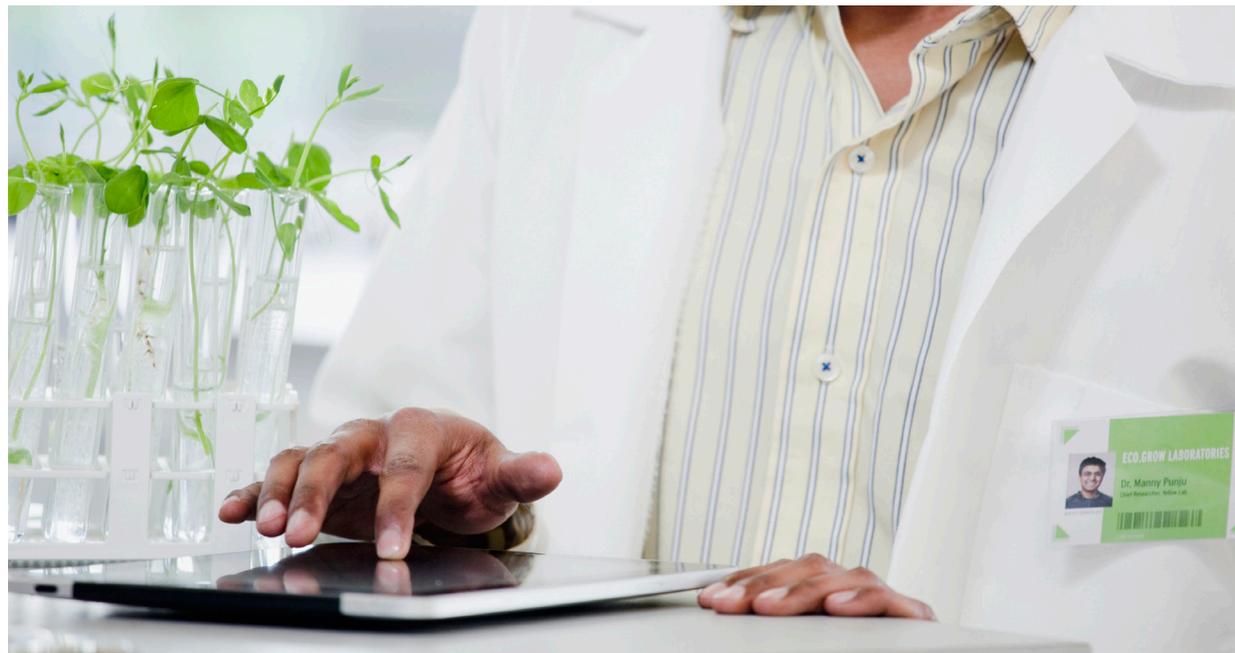


Fortune Favors the Bold Unlocking Access across China



Foreword

As Deloitte reported in *The Next Phase: Opportunities in China's Pharmaceuticals Market* (November 2011), China will soon be the Asia Pacific region's leading market for health care — a widely anticipated result given the country's unrelenting socioeconomic growth trends. However, the past 24 months have seen a rapid acceleration in the development of the life sciences and health care market in China. With this acceleration comes rising uncertainty about where the market is headed and how it will impact the companies that operate within the health care system. This uncertainty comes from the unprecedented demographic changes and continued experimentation from the government as it seeks to expand the quality of care while also controlling expenditures.

Many pharmaceutical companies are now looking at China's health care market and asking themselves, where next? The opportunities that drive growth are less clear now than in the previous decade and the risks in the market are substantially higher than ever before. Finding a path forward that delivers the returns and performance companies want will not be easy in this environment.

This report highlights major events of the past 24 months in the health care market and explores one of the key questions facing pharmaceutical companies as they think about their future in China: How can we ensure market access at the provincial and hospital level?

The answers to this question will impact the success of pharmaceutical companies moving forward and help determine who wins and who loses in China's health care market. The opportunity is large but so is the challenge.

We believe that fortune favors the bold in China and those companies who take decisive action today will be the ultimate winners, while companies who seek gradual change will be left behind as the market passes them by.

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Unlocking Access across China

China's market access system is constantly evolving, presenting unique opportunities and challenges for companies seeking entry. Driven by multiple cost control measures, a wide range of decision makers and continued national focus on reducing health care cost, the past 18 months have seen the emergence of numerous programs that may offer greater access, but also bring with them a degree of uncertainty. As a result, the single most pressing challenge for companies in China is managing this highly complex and challenging market access environment.

To be more effective, companies must better understand incentives for each stakeholder, adopt an approach that creates real value for the health care system and be willing to make substantive trade-offs. Companies must be willing to experiment with innovative approaches to market access to move forward successfully.

Recent changes offer hope for greater access in China

Over the past 5 years, China's access environment has moved from a system driven primarily by self-pay or private institutions to one offering a myriad of access opportunities. The environment is changing — shifting from limited to increased access, but only for therapies that demonstrate appropriate value to the health care system and patients. With this scenario, strategies that work elsewhere in the world will likely not be feasible in China. Thus, businesses will need new and innovative approaches to access.

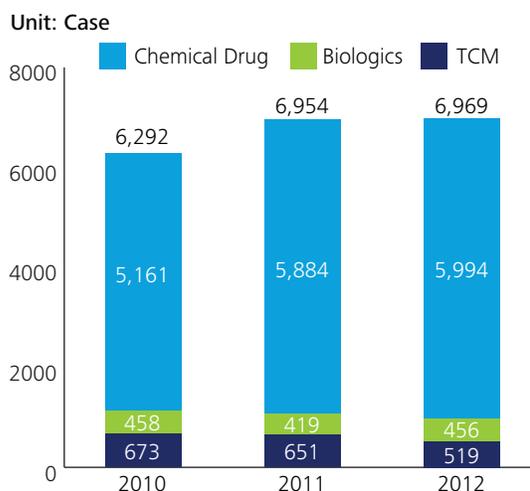
Several positive developments have taken place in the past two years. Significant changes include streamlining of the regulatory process, reimbursement expanded to several different diseases and therapies and increasing focus on creating more access opportunities. These changes create greater opportunity for life sciences companies.

Streamlining the regulatory process

The first component of access for any company is to obtain regulatory approval. In most countries, these processes are generally straightforward, but in China, the complex process, conservative attitude toward clinical trials of innovative drugs and large numbers of domestic generic drug applications have overburdened the system, resulting in substantial approval delays.

The Center for Drug Evaluation (CDE) at the China Food & Drug Administration (CFDA, formerly State Food & Drug Administration) receives an overwhelming number of applications for both generic and innovative drugs (numbering around 7,000 applications in 2012) for its 150-member review staff (Figure 23)³⁶. Consequently, application and registration processes require an average of more than 2 years to complete³⁷. Particularly for innovative drugs, CFDA has an attitude of "stringent in, easy out," meaning increased approval time for Clinical Trial Application (CTA) compared with other markets (Figure 24)^{38,39,40}.

Figure 23: Total Applications Received by CDE (2010-2012)



Note: Includes CTA, NDA, formulation change, bioequivalent studies, etc; both innovative and domestic drugs

Source: Center for Drug Evaluation, 2012 Annual China Drug Review Report, 2013

³⁶ Center for Drug Evaluation, 2012 Annual China Drug Review Report, 2013.

³⁷ Monitor Deloitte analysis.

³⁸ Chang, M., 2010 Multi-regional Clinical Trials Seoul Workshop, Regulation & Expectation on MRCT in China — the Perceptive of MNCs, 2010.

³⁹ Korean Food & Drug Administration 2010 report.

⁴⁰ Downing et al, New England Journal of Medicine, Regulatory Review of Novel Therapeutics — Comparison of Three Regulatory Agencies, 2012.

Figure 24: General Range of Approval Time for CTA and NDA in China vs. Major Countries

Unit: Month

| | China | US | EU | Korea | Taiwan | India |
|-----|-------------|------|-------|-------|--------|-------|
| CTA | 8–18 | 1–2 | 1–2 | 1–2 | 3–4 | 3–4 |
| NDC | 4–15 | 6–10 | 10–15 | ~4 | N/A | 12–18 |

Note: Clinical Trial Application; New Drug Application
 Source: Chang, M., 2010 Multi-regional Clinical Trials Seoul Workshop, Regulation & Expectation on MRCT in China — the Perceptive of MNCs, 2010; Downing et al, New England Journal of Medicine, Regulatory Review of Novel Therapeutics — Comparison of Three Regulatory Agencies, 2012

Changes to the regulatory processes and increasing cooperation between the CFDA and biopharma companies, however, are building momentum for reducing approval time. The CFDA is implementing a series of national reforms and pilot programs aiming to shorten approval lead times (Figure 25). In addition to these national-level changes, the CFDA introduced pilot programs to delegate parts of the workload to provinces. For instance, the CFDA authorized the Guangdong FDA to conduct evaluations and review drugs manufactured locally. Distributing the review workload across multiple departments should reduce review time for any one product.

Supplementing this effort, companies are working closely with the local Chinese regulators by including them in the trial design process early on and adding a China component in earlier phases of trials, such as Phase II or even Phase I (Figure 26). These actions appear to be working as approval timelines for some compounds are being reduced.

The CFDA highly emphasizes that actual value to Chinese patients is a key lever for expediting the approval process. Therefore, addressing critical unmet clinical needs in China is a prerequisite for fast-track approval. Superior clinical results from mainland Chinese trials, backed up by data from Asian-population or global trials, make convincing cases that can expedite approval from CFDA⁴¹. For instance, many cancer or hepatitis therapies were launched in China less than 2 years after their global launch, while many other therapies experience 5 to 8 years of “drug lag.” Xalkori, the first personalized medicine for lung cancer, received speedy approval when the minimum cohort size requirement was waived (Figure 27).

While the full impact of these reforms is yet to be seen, some positive momentum is evident. Given the size, scale and scope of the system involved, hurdles remain, but thanks to government ambitions we can expect continued reforms.

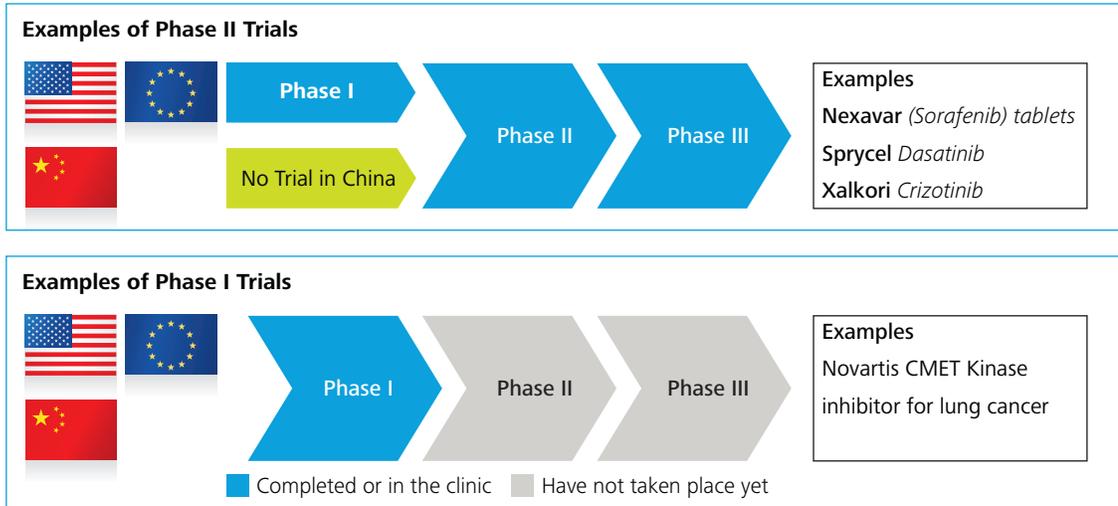
Figure 25: Reformative Approaches to Expedite Drug Approval

- 1** Established fast-track channel for drugs that address critical unmet needs in China
- 2** Set rolling submission mechanism for innovative drugs to shorten waiting times
- 3** Initiated open-door consultation to improve communication efficiency
- 4** Invested in capability improvement to smooth the review process

Source: Center for Drug Evaluation, 2012 Annual China Drug Review Report, 2013

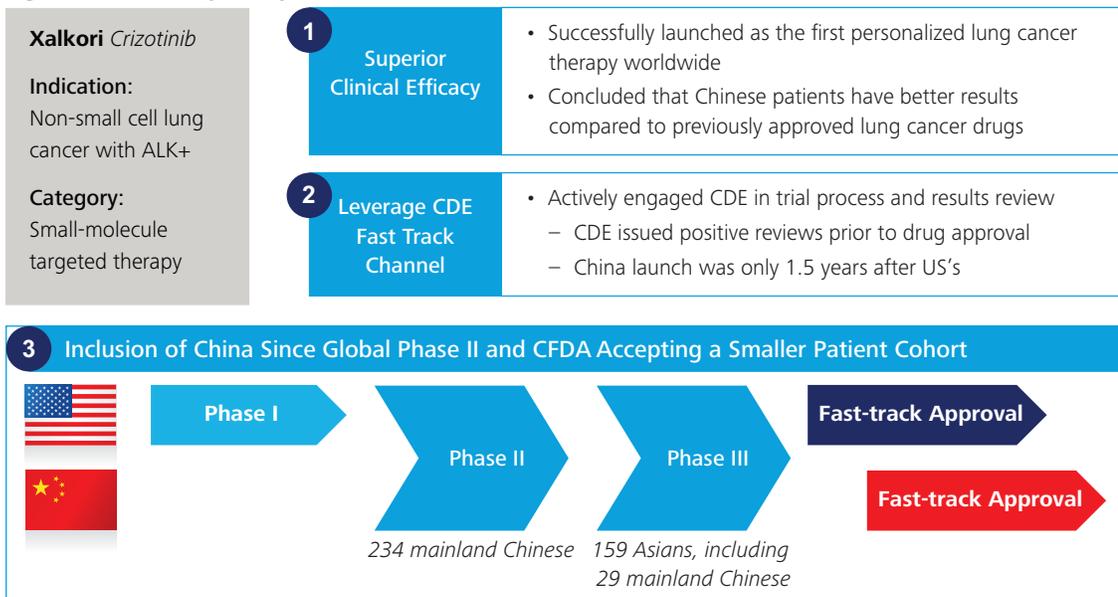
⁴¹ China Food and Drug Administration, Drug Registration Guidelines, 2007.

Figure 26: Examples of China Included in Phase II or I Global Trials



Source: clinicaltrials.gov; Monitor Deloitte analysis

Figure 27: Case Study — Key Success Factors of Xalkori’s Fast Launch in China



Note: Anaplastic lymphoma kinase

Source: Clinicaltrials.gov; Pfizer press release; FDA press release; Monitor Deloitte analysis.

Broader reimbursement coverage

Reimbursement opportunities have grown following the introduction of Essential Drug List (EDL). Drugs can now be reimbursed under one of three lists — the EDL, the National Reimbursement Drug List (NRDL) and the Provincial Reimbursement Drug List (PRDL). Although reimbursement opportunities have increased, so has the complexity of obtaining reimbursement approval. Frequently, the price associated with reimbursement is substantially less than that in the private market, thus forcing companies to make a difficult choice about their strategies for gaining access. Yet, in this difficult environment, many new therapies have received reimbursement approval over the past 18 months.

Former Health Minister Chen Zhu announced several measures in late 2012 and early 2013 that will directly and indirectly change the make-up of the different lists and improve the overall quality of reimbursable drugs.

EDL: Recent EDL changes have broadened the number of therapies available and improved overall access. Previously focused on reimbursing generics in basic disease areas, the 2013 EDL revision included a number of major branded generics and extended its coverage into cancer diseases with the addition of 14 oncology drugs. In addition, EDL prescriptions at clinics will provide patients with higher reimbursement rates versus larger hospitals. This will likely alter patient flows, driving more patients and prescriptions through smaller clinics and hospitals. In the meantime, the National Health and Family Planning Commission (NHFPC, formerly Ministry of Health) intends to expand sales of EDL drugs at urban hospitals, aiming to cover up to 25-30% of drug usage for Class III hospitals and 40-50% for Class II hospitals⁴².

While these developments are a plus for patients, many multinational companies will see their products facing greater price pressure as the EDL lowers price points and incorporates intense generic competition. For drugs listed on the EDL, this results in an even higher level of price cuts, particularly for branded generics. Compared to the 40-50% average price cuts in the 2009 EDL listings, branded generics saw reductions as high as 95% for Bristol-Myers Squibb's Capoten and 93% for Roche's Rocephin. While the 2012 EDL revision has yet to release maximum price limits for the listed drugs, a similar impact may occur for drugs on the list. The future of the EDL remains relatively uncertain as the government works to refine one of its key policy initiatives.

NRDL A & B: The NRDL has not seen any changes since 2009, however, it is widely expected that its upcoming revision will follow the lead of the EDL in expanding its size and improving treatment quality. The introduction of the Critical Illness Insurance Program (CIIP) in late 2012 hints at the direction the NRDL's changes will take. The CIIP pledges to reimburse at least 50% of all medical costs related to its 20 most catastrophic diseases like gastric cancer and child leukemia⁴³. The NRDL will likely include more high-value treatments in these therapeutic areas to help the CIIP achieve this goal. However, we have yet to see how these programs will affect price points and access conditions for life sciences products.

PRDL: Some provinces are actively addressing local medical needs by expanding NRDL to PRDL. PRDL could be adjusted with shorter intervals than NRDL, but the timing is unpredictable and varies among provinces. The drugs added to PRDL are normally innovative drugs of three major types (Figure 28): expensive therapies, those launched after the 2009 NRDL and innovative drugs manufactured locally.

⁴² Ministry of Health, National Health Work Conference, 2013.

⁴³ Ministry of Health, Policy Briefing on China's Health Reform, 2013.

Figure 28: Examples of PRDL Drugs

| Categories | Examples | Provinces Adopted |
|---------------------------------------|------------------------|---|
| Expensive Therapies | Herceptin (Trasuzumab) | Jiangsu |
| | Tarceva (Erlotinib) | Anhui |
| | Mabthera (Rituximab) | Heilongjiang, Shandong, Guizhou, Jiangxi, Guangxi |
| Launched after 2009 NRDL | Ezetrol (Ezetimibe) | Jiangsu, Jilin, Heilongjiang, Hainan, Shaanxi, Qinghai, Yunnan, Hebei |
| Innovative Drugs Manufactured Locally | Conmana (Icotinib) | Zhejiang |

Source: Press releases

The PRDL typically only offers partial reimbursement, but still substantially expands coverage. Some provinces are willing to cover more expensive therapies for outstanding local needs that cannot be paid for nationally, creating opportunity for innovative or biologic products. Additionally, the PRDL is more flexible, offering a faster time to reimbursement than national coverage. Therapies typically must wait several years for an NRDL review to obtain listing, but in some provinces, PRDL listing could be as early as 6 months after launch. Finally, listing on the PRDL provides a stronger case for listing in other provinces and nationally. This helps therapies or companies build the necessary body of evidence to gain greater support for coverage at the national level.

Commercial insurance: The continued growth of commercial insurance will broaden overall coverage and may supplement public coverage for expensive therapies. Recent actions to improve reimbursement have shed light on the government’s intentions to further enhance overall coverage quality. Because budgetary constraints persist, reimbursement inclusions will likely be limited to therapies that offer proven, real-world value in the health care system. Many recent inclusions on the EDL are proven products with substantial data in the Chinese market, reflecting the government’s desire to provide coverage for therapies that improve overall health of the population. Given an ongoing emphasis on value, companies must present a clear, data-driven value story that emphasizes the real-life impact therapies have on patient health, and on health care budgets.

Despite positive progress, uncertainty remains

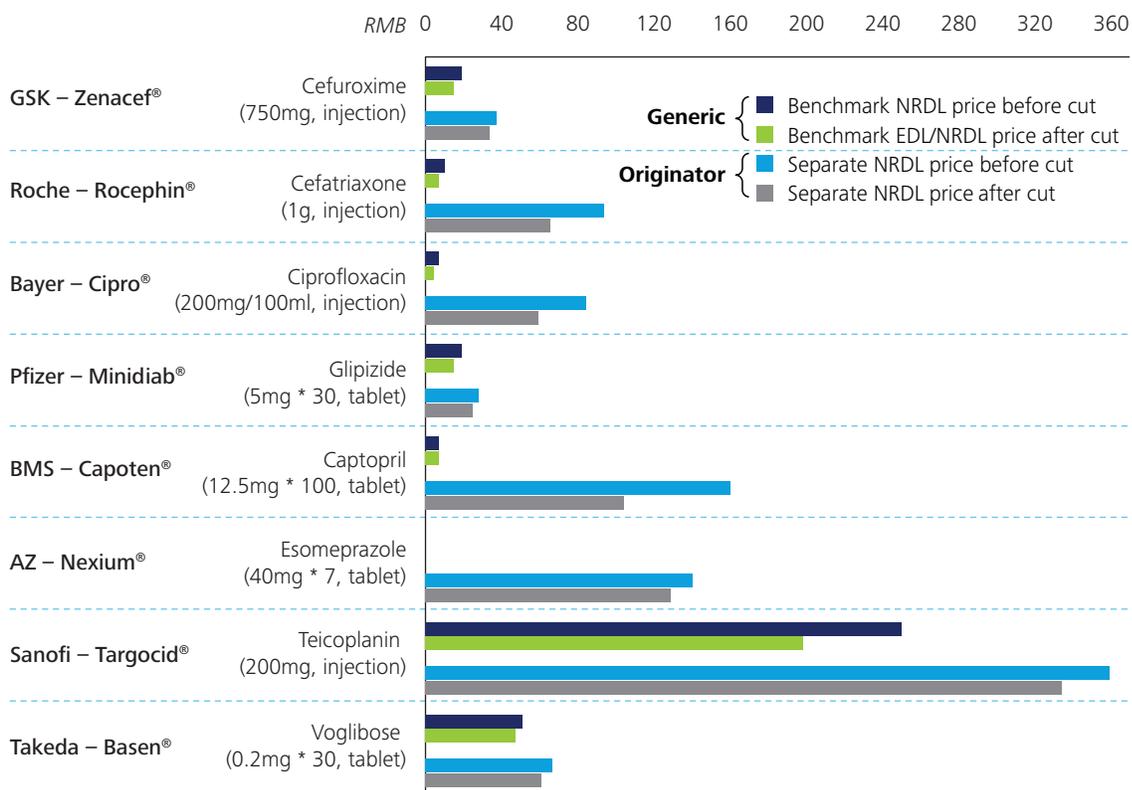
Drug pricing changed substantially in recent years on the national, provincial and hospital levels. While all drugs are affected, MNCs continue to be a critical focus of the government’s cost control efforts. Positive steps have been taken, but several recent actions have created uncertainty about the direction pricing and access will take at the national, provincial and hospital levels.

National pricing pressure

The National Development and Reform Commission (NDRC) has issued five rounds of price cuts since 2010. Consistent with the NDRC’s objective to reduce the separate pricing premiums enjoyed by multinationals by 30-100%⁴⁴, these price cuts have disproportionately affected branded generics. This is demonstrated by the “double price cut” schedule implemented for selected drugs, such as Sanofi’s Taxotere and GlaxoSmithKline’s Hycamtin, in the September 2012 price cut (Figure 29). These price cuts seem likely to continue until branded generics compete at price points close to the next available generic therapy.

⁴⁴ National Development and Reform Commission, National Pharmaceutical Pricing Policy Draft, 2011.

Figure 29: Selected Examples of Recent NDRC Price Cuts Affecting MNCs



Source: National Development and Reform Committee press releases regarding drug cuts

Provincial pricing pressure

Provincial governments continue to take a stronger stance in controlling prices. Historically, local governments acted to reduce pharmaceutical prices beyond the national cap price. However, over the past 18 months governments have worked to eliminate separate pricing for branded generics and more broadly adopt the Anhui model, which aims to aggressively lower drug pricing by minimizing profits.

As an example, Guangdong province announced plans in late 2012 to revamp its pricing policies for branded generics. In its pilot program, Guangdong proposed to eliminate premium pricing for all branded generics that

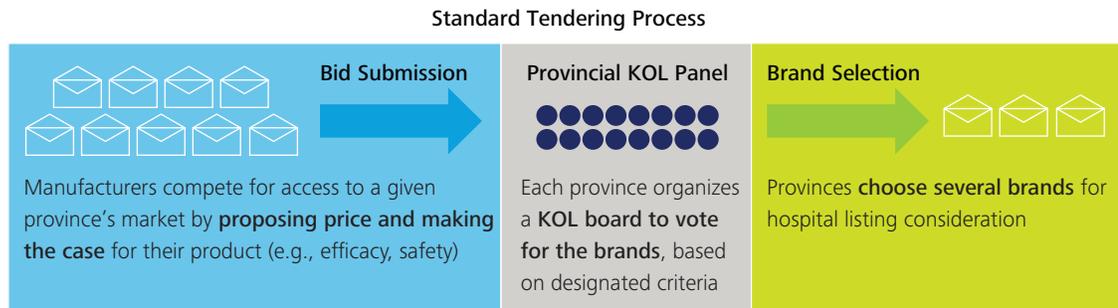
compete with more than 3 generics in the market. For branded generics with less than 3 generic competitors, the province will evaluate the appropriate level of premium on an individual basis.

In addition, provincial tendering processes have further restricted price points. The Anhui tendering model, known for its “double-envelope” system and low-cost focus (Figure 30), has expanded well beyond the its originating province. As of 2012, 18 of China’s 23 provinces have adopted all or part of the Anhui model⁴⁵. The Anhui model has resulted in a 53% average price reduction creating concern about its impact moving forward⁴⁶.

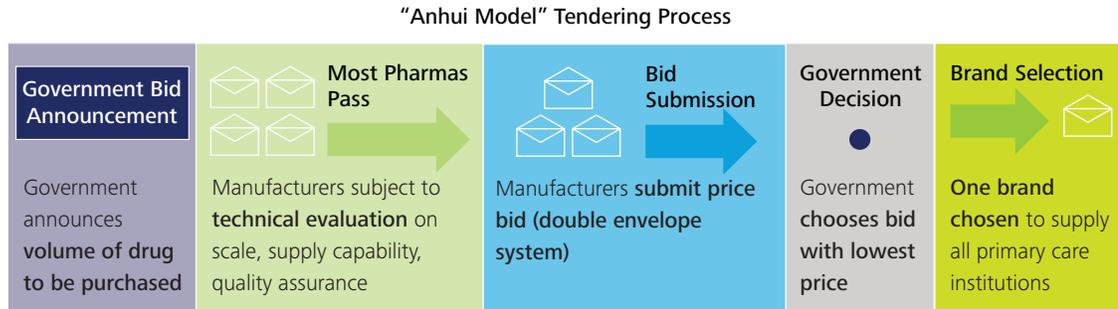
⁴⁵ Shobert, B., Anhui Medicine Wrong for China, 2012.

⁴⁶ Taylor, L., Pharmatimes, Drugmakers’ Fury as China Plans to Widen Price-Cutting System, 2012.

Figure 30: Comparison of Anhui Model vs. Standard Tendering Processes



Source: Monitor Deloitte analysis



Source: Monitor Deloitte analysis

Hospital pricing pressure

Hospitals are also seeking ways to lower health care expenditure through experiments with point-of-care restrictions. For example, Shanghai City Med Insurance Bureau piloted a program that limits budgets for hospitals and takes a stronger role in determining how budgets are allocated among diseases and therapies. In Beijing, the City Med Insurance Bureau will determine the appropriate budget for certain diseases using Diagnosis Related Groups (DRGs). These pilots restrict both the prices associated with therapies and the overall volume at which a therapy can be prescribed.

Building a successful access program in China

Despite the uncertainty, companies exploring innovative approaches to access are seeing substantial success at both the national and provincial levels. Many companies, such as Roche and Bristol-Myers Squibb, have successfully listed products at favorable price points at the provincial level, while others, such as Pfizer and Merck, have succeeded in listing products at the national level. Companies that take a clear, focused and data-driven approach to access have demonstrated success in this market.

To create a successful access strategy for products in China, companies can consider 5 courses of action:

1) Build a greater understanding of each decision maker's economics and incentives

To build innovative access solutions, companies must better understand the economics facing each decision maker in the system. Understanding the critical trade-off decisions made by national and provincial governments and hospitals will enable more effective negotiation and more targeted value stories when discussing reimbursement.

2) Draft innovative value stories

Traditional value measures like QALY, DALY and ICER are not widely utilized in China. However, companies offering effective value stories that leverage available data to show how a therapy adds value to the overall health care system are experiencing dramatic success in the market. Finding the right way to express therapeutic value in China can create engaging dialogues with access stakeholders and drive greater success with reimbursement and price points.

3) Focus on patient groups with the highest unmet need

Receiving access in China requires a clear understanding of which patient segments gain the greatest benefit from treatment. Companies must precisely define their ideal patient population for both reimbursement and prescription decisions to help administrators and physicians more easily understand the real-life value of a therapy, giving greater likelihood of reimbursement.

4) Consider a regional instead of a national approach

Provinces have substantial authority over reimbursement, tendering and, now, regulatory approval. Therapies such as Baraclude have had considerable success pursuing targeted reimbursement at the provincial level before attempting to gain greater reimbursement coverage. Working to develop a targeted, sequenced approach to access in China can create positive momentum for market access and set favorable reference price points for products.

5) Actively participate in pilot programs and other partnerships

The myriad of partnerships in recent years highlight the range of opportunities that can be capitalized on by joining forces. Companies will need to participate fast, though, as availability of potential partners remains limited and first-mover advantages can have long-lasting competitive impacts.

Building a successful access program is an exciting and unique challenge. Despite current barriers, recent changes create hope for more positive momentum as the government looks to achieve its aim of providing universal health care to the population. Capitalizing on these opportunities is possible through continued focus, experimentation and tenacity.

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