PEER REVIEWED

Pricing Pharmaceuticals in Japan

Development and pricing strategies to maximise the opportunity in a mature market

Introduction: 2018; A Year of Seismic Shift in the Japanese Market

The year 2018 was epic for the Japanese pharmaceutical industry, largely because of the fundamental National Health Insurance (NHI) pricing reforms implemented in April. The repercussions of this change in policy is yet to be fully felt as of the beginning of 2019; however, some of the cautionary signs are already seen, for example some domestic companies exited the market last year because of the unattractive prospects. This was unprecedented, particularly for a full-fledged domestic pharma company such as POLA Pharma or Fujifilm RI Pharma, and it is difficult to imagine that these two will be the only ones and more moves are expected in the coming months.

IQVIA Institute predicts that the compounded annual growth rate of the pharmaceutical spending in Japan, which was at a healthy 2% in the last five years, will drop to somewhere between Δ3% to 0% from 2018 to 2022[1]. Japan is the only market in IQVIA's "Developed Country" category expected to show either negative or zero growth in this timeframe. Nevertheless, the same report forecasts that Japan will still be the third largest pharmaceutical market in 2022, with its spending between 85 and 89 billion US dollars. Another report by EFPIA also describes that the Japanese share of the new medicines sales will remain at 7.1%[2]. This suggests that the Japanese market will continue to be open to innovative pharmaceutical products. Various initiatives are taken by the Japanese authorities to encourage innovation within the country, mostly in the form of appraisals reflected in the price of the pharmaceutical product submitted for approval and NHI listing[3]. Given on the one hand this remaining appreciation to innovation, and on the other the expectedly sluggish growth of the market, leaders of pharmaceutical and biotech companies could face difficulty in making decisions on approaching this market in the Far East.

In order to understand the key success factors of a given technology and how the Japanese market appreciates it, it is critical to have the right knowledge about how the value of a drug product will be determined and will be reflected in its price, and how the applicant company can maximise its price potential. In this series of articles, I would like to review the principles of pricing and market access (PMA) in Japan. In this first article, I would like to provide an overview of the Japanese PMA system from the vanishing point of the global pharmaceutical markets. In the future articles, I will discuss the methodology and the underlying concepts (including the political intentions) of how the price of the drugs is determined and may change over time. This will be followed by the discussion about the patient access system in Japan. This may have some implications to the local development strategy of a given pharmaceutical product and the ongoing debate about the implementation of health technology assessment in the PMA process. We will also cover the recent NHI pricing reform and its significance to the industry as a whole.

Japan as a "Therapeutic Referencing" Market

PMA conditions and structures greatly vary within the global markets and across regions within countries[4]; each of them has uniquely evolved over time. One of the approaches to deal with this vast diversity is to typify the systems by using relatively simplified criteria. Schoonveld proposed the following "archetypes" of the payers in order to segment them[5].

From Table 1 we can see that Japan roughly belongs to the "Therapeutic Referencing" segment because the justification of the valuation of the drugs are largely based on comparison to the values of other available drugs, with adjustments based on the interpretations of the relative therapeutic benefit against the comparator. While this approach is applied in many of the developed markets, there is a wide range of divergence in the way it is implemented. The following are the key characteristics of the Japanese drug valuation system compared to the other "Therapeutic Referencing" markets:

- Reimbursement of any prescription drug is effectively granted upon approval. Reimbursement levels are predetermined and uniform across indications and generally across any patient population. This means that the valuation of the drugs are predominantly reflected in the initial price at approval.
- Japan's patient access to new medicines is the best among the developed countries. The median time for approval for a new pharmaceutical product in 2015 was only 311 days in Japan, compared with 422 days in

Payer segment	Description	Example of countries
Health Economics Driven	Cost-effectiveness drives price or reimbursement approval	UK, Canada, Australia, South Korea
Therapeutic Referencing	Price or reimbursement based on demonstrated value over comparator (health economics can play a secondary role)	Germany, France, Spain, Italy, Japan
Competitive Insurance-based	Free market environment with competing private insurance	United States
Emerging Cash	Primarily cash-paying patients	Russia, China, India

Table 1. Payer archetypes based on Schoonveld's classification

Europe and 333 days in the US[6]. This is because of the automatic reimbursement in the NHI system which covers the entire population, strict supply obligations, and the great effort to close the "drug lag" by the Pharmaceuticals and Medical Devices Agency (PMDA)[7].

- As of 2019, there are no predetermined cost containment measures which are designed to influence the prescription decision of expensive new drugs, effectively. Cost containment measures such as diagnostic procedure combination (DPC), which is an inpatient prospective payment system similar to diagnostics-related group, puts most of the expensive new drugs out of the basket to allow those drugs to be reimbursed separately.
- Instead of placing a pre-designed utilisation control scheme, the pricing authorities may cut the NHI price of the pharmaceutical products at a discretional timing and to an arbitrary level when sales have reached a significant level.
- Japan is the only country in the global market that calculates the official list price of a drug product based on its cost structure. If there is no comparator product available in the domestic market, the applicant company can submit the information regarding the various costs. The authorities will determine the price of the drug by stacking the costs and even allowing a certain level of profit margin.
- If there is a comparator product available in the Japanese market, prices of new drugs will reference the comparator. Officially, drug price reference only looks for the internal market and if the price gap is large against the average of the three European major markets (i.e. Germany, France and the UK), adjustments will be made.
- Also to keep in mind is that Japanese drug prices are highly influenced by the prices of the same product in the major European markets. Therefore, European price assumptions, but not US prices, have an important implication in the pricing strategy in Japan.
- Other than markups on top of the benchmark comparator price, Japanese pricing authorities do not explicitly evaluate the intrinsic value of a drug. Unlike the other Western countries, neither cost-effectiveness analyses nor budget impact analyses are incorporated fully in the valuation process, yet. However, a "trial implementation" is on its way.

Key Characteristics of the Market

1. Rapid Pricing Decisions

One of the key differences of the Japanese PMA compared to other market authorities is the short lead time for pricing and reimbursement decisions after approval. In Japan, it will typically only take 60 to 90 days to have the NHI price of any new drug that joins the list. For example, compare that to EMA, which approved 47 drugs for 77 solid tumour indications and the median times from the EMA approval to the HTA decision was 188, 209, 384, and 405 days in France, Germany, Scotland, and England, respectively[3]. Together with the universal coverage and the diminishing "drug lag", this continues to offer a great commercial opportunity to the pharmaceutical industry.

2. Powerful Physician Authority

Another important aspect is the greater authority given to the individual physicians to choose the medical intervention they offer to their patients. Physicians in Japan have the freedom to prescribe any drug with little limitations. This means that the utilisation of any given drug is difficult to control at a national level. Optimal Clinical Use Guidelines has been recently implemented by the MLHW together with the academic community to try to limit the usage of a newly approved drug to the most appropriate patients. This may become an important role in controlling the level of consumption for expensive new drugs.

Such great authority given to physicians not only inhibits utilisation control but also does not allow indirect

	Japan	France	Germany	US (Private sector)
Direct Price Control	• Initial price: internal referencing or cost calculation ±premium • Price dynamics: price cuts based on the levels of discount and size of the product sales	• Internal price referencing based on benefits over the comparator (ASMR ratings) • Price dynamics will be subject to various negotiations (e.g. price-volume)	• Innovative, value-adding drugs will negotiate the price with sickness funds, while those without added value will be referenced to comparators	•Pharmaceutical companies are basically free to set the prices of their own products •Based on the continued negotiations with insurers or MCOs, prices tend to increase, especially for innovative drugs
Indirect Price Control	• Reimbursement levels are designed as a fixed percentage of the NHI price • DPC is a cost capping system widely adopted in hospitals; however, new drugs tend to be excluded from the basket	• Reimbursement levels vary, depending on the level of medical benefits •Rebates are subject to contract negotiations •Hospital drugs are covered by a DRG-like system (T2A), with exceptional product with a different control	• Therapeutic class "price referencing" will apply for a group of products in the same WTO-ATC category, which will effectively work as a reimbursement limit •Inpatient drug use is under a DRG reimbursement rate system.	• Formulary negotiations between healthcare plans/PBMs and pharmaceutical companies will influence the pricing decisions
Utilisation Control	• Optimal Clinical Use Guidelines are implemented recently	• Utilisation controls are subject to contract negotiations	• Prescribing budget and spending guidelines powerfully control the physicians' prescription behaviour	• Payers are increasingly using utilisation management measures, e.g. step therapy, prior authorisations or appeals processes

Table 2. Comparison of cost control mechanisms among major 'Therapeutic Referencing' countries and the US private sector

pricing or reimbursement control, to effectively work as a cost containment measure in Japan. Under the NHI system, almost all of the approved prescription pharmaceuticals are reimbursed at the same percentage against the designated NHI price. Insurers do not have the freedom to alter this percentage. Therefore, insurers in Japan are basically incapacitated and the power balance is largely in favour of the physician.

From an industrial perspective, these conditions make Japan an extremely attractive market. The company trying to introduce a product to the Japanese market will basically only have to care about the NHI price of the drug. In other words, development strategies for new drugs in Japan are still quite simple. The most important feature in the target product profile is the clinical benefit of the product. The key to success in Japan is physician preference in prescription decision-making, while in the rest of the developed countries you will also have to understand the payer perspective.

3. Lack of Opportunity to Negotiate

As described in Table 2, while the drug prices in France, Germany and the US are determined and evolve through a continued negotiation process, the window of opportunity to negotiate prices with the Japanese authorities is extremely limited. There are only two formal meetings within the 60 (or 90) day initial pricing process. There is no official hearing from the industry side even when the NHI prices will be significantly cut. The authorities will almost unilaterally determine the prices and in a sense, companies will have to consider drug prices as a given. However, there are some recent cases that the applicant refused the granted NHI price and delayed the launch of the product, which effectively extended the negotiation process. Istodax from Celgene and Taltz from Eli Lilly are among those products.

We will discuss the pricing process in detail in the following articles.

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