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9. Market Access in Japan

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9.1 Market Background

In 1961, Japan was the first country to implement universal healthcare coverage in Asia.

Japan has also been consistently ranked as one of the nations with the longest life expectancy. In 2016, with an average expectancy of 85 years, a male life expectancy of 81.7 and a female life expectancy of 88.5 Japan had the second highest life expectancy at birth in the world. Similarly, infant mortality rate is one of the lowest in the world, recorded at 2.1 deaths per 1,000 live births in 2014. Other health data also indicated another positive aspect of the Japanese healthcare. It has a very low obese prevalence among the OECD Countries. An example is that in 2015, only 3.7% of the total adult population (aged 15 or above) was considered obese.

All in all, the aforementioned key health indicators reflect the quality of healthcare in Japan, which is ranked as one of the best in the world. The affluence of the country, built with several decades of strong economic development, provided the basis of a better health for its population. On the other hand, this achievement is now being tested by a diminishing replacement rate of the population, as well as a growing elderly population.

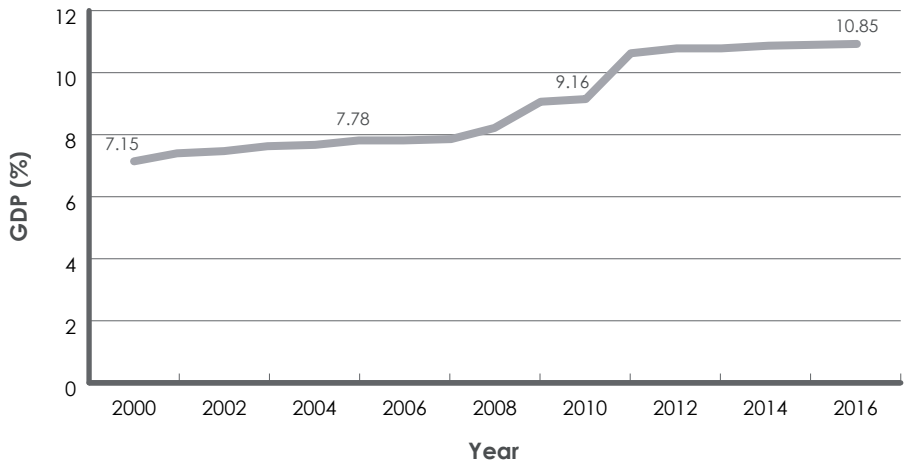

Figure 1. Japan healthcare spending % GDP 2000-2016 [OECD Health Statistics]

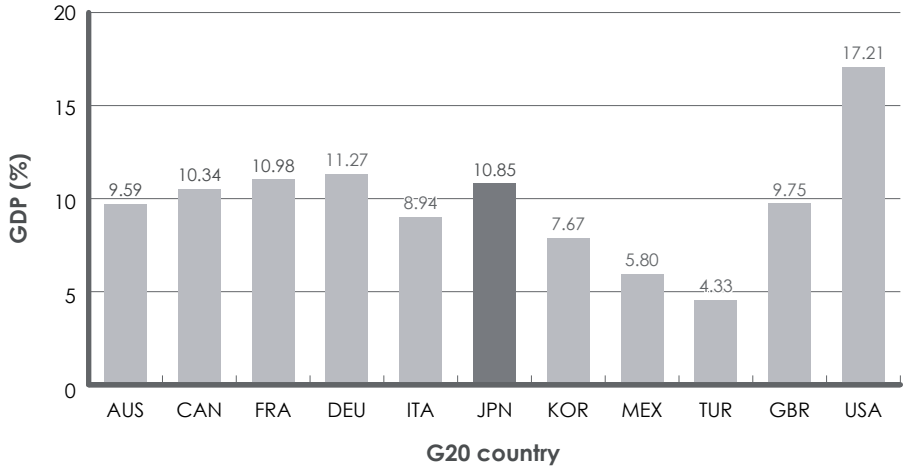

Figure 2. G20 Countries healthcare spending in 2016 [OECD Health Statistics]

	Healthcare spending 2015 (% GDP)	
	Public	Private
France	79	21
Germany	84	16
Italy	75	25
U. K.	80	20
Japan	84	16
South Korea	56	44

Table 1. Healthcare spending by public and private sectors 2015 [OECD Health Statistics]

Effectively, it requires the allocation of a hefty amount of public resources. The Japanese government increased its healthcare spending from 7.15% of GDP in 2000 to 10.89% of GDP in 2015, i. e. USD 343.5 billion to USD 527.3 billion (Figure 1). Figure 2 and Table 1 show healthcare spending in some G20 Countries.

9.2 General Outlook of Healthcare System and Health Policies

The present status of the healthcare system in Japan is closely tied to two factors; the economic situation and the demographics of the population. Japan has entered into a chronic economic stagnation since the 1990s. Its fiscal deficit, which is projected to be

JPY 11.3 trillion (USD 103 billion), or 1.9% of GDP for the fiscal year 2018, has become a perpetual cause for concern for its fiscal policy. While the country is diving into a deeper deficit, healthcare spending is surging in another direction; from USD 1,501 per capita in 1996 to USD 4,519 per capita in 2016. This three-fold increase of healthcare spending is mostly borne by the government, which is always the major payer for healthcare services in Japan. The public sector is responsible for 84% of the payment for the total healthcare expenditure in 2016, which was almost at the same level in 1996, which was 80.1%. Nevertheless, due to a declining birth rate, a decrease in the working population and a sluggish economic recovery, all these factors contribute to a diminishing base for social contributions. This is in contrast with the healthcare budget, which is continuously driven up by an aging population who demands more medical attention. All these factors form the cradle of needs for the search of an effective solution to relieve the financial pressure on the healthcare system.

As the Japanese Ministry Health Labour & Welfare (MHLW) pointed out, the change in the demographic structure is having a huge effect on the resources of the society. The latest set of statistics indicated that in 2016 27.3% of the total population was aged 65 or over (Figure 3). The proportion of this age group in the population has increased by 10% in the past 16 years, from 17.36% in 2000. According to a forecast, the ageing trend among the population will continue. The 65+ age group will increase to 31.8% of total population by 2030, and to 40.5% by 2055. If nothing changes in the healthcare structure, in next two decades the spending on healthcare for the elderly will dramatically increase. It is worrisome that this financial burden is definitely going to be worse and that the next generation might have to bear the financial burden.

The country also faces an unusual but significant challenge in formulating major policy changes to its healthcare system. In a 10-year period between 2007 and 2017, the Prime Minister changed seven times. Given the game of Merry-Go-Round the Prime Ministers are engaged in, the government, unsurprisingly, only managed to implement mainly piecemeal reforms in the long-established universal healthcare system.

The history of the current Japanese healthcare system started in 1961, when its population was required to participate in either an employee health insurance program or in the local/regional-based health insurance program. The latter became known as the National Health Insurance scheme, NHI. Effectively, from then Japan started to have a mandatory social health insurance for every employed subject. A national pension system was also set up, specifically for people employed in large corporations. This pension scheme was then extended to people working in small companies and the self-employed, as well as the unemployed between 20 and 60 years. In 1973, a legislation was passed under the Welfare Law specifically for the elderly, so that this segment of the population could have free access to the healthcare service. A comprehensive universal health coverage was thus fully implemented.

At present, there are two main categories of health insurance schemes in Japan (Table 2). The first falls under the category called Company Health Insurance (*Shakai Hoken*) and it covers all the full-time employees in companies that employ more than 500 people. This insurance scheme also covers civil servants, school teachers, as well as all their family

members. Their insurance plans are managed by the Japan Health Insurance Association (JHIA), Mutual Aid Association and Association/Union Administered Health Insurance (previously called the Government Managed Health Insurance, GMHI).

The second main category is the National Health Insurance (*KokuminKenko Hoken* – Citizen Health Insurance), which is for those who are self-employed, and for people employed in small companies, part-time or contract workers, as well as those who are working in the fishery and agriculture industries, the unemployed and the elderly. NHI is responsible for managing the health insurance plans for these groups of people.

The health insurance system is financially supported by the contributions from employees and employers, which amount to the equivalent of 48.7% of the total medical ex-

Health Insurance System	Employee based health insurance			Seamen's Insurance	Mutual aid association		
Insurance target	General employees		The insured under Article 3-2 of the Health Insurance Aids		National public employee	Local public employee, etc.	Private school teachers/ staff
Insurer	JHIA	Health Insurance Society	JHIA		Mutual aid associations		Corporation
Insurance plan	1	1,409	1	1	20	64	1
Number of subscribers (1,000 persons)	36,392	29,131	19	125	8,836		

Health Insurance System	National Health Insurance (NHI)			Medical care system aged 75+
Insurance target	Farmers, self-employed, etc.		Retired person (under Employee health insurance)	
Insurer	Municipalities	NHI associations	Municipalities	Union for medical care aged 75+
Insurance plan	1,716	164	1,716	47
Number of subscribers (1,000 persons)	35,937			15,767

Table 2. The health insurance system structure. Modified from [MHLW – Annual Health, Labour and Welfare Report 2016]

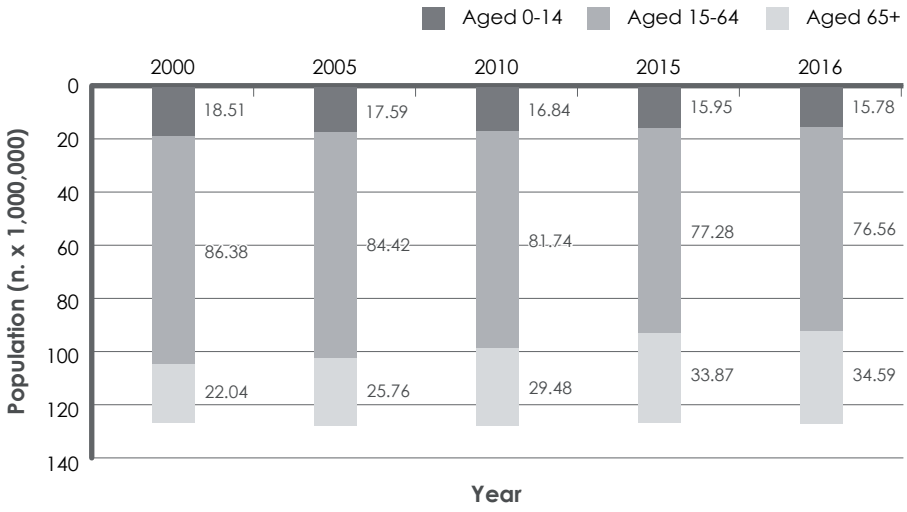

Figure 3. Japan population by age group 2000-2016. Modified from [MHLW – Statistics and Other Data]

penditure in the fiscal year of 2014. In the same year, the government subsidies to low-income and unemployed people and the elderly amounted to the equivalent of 38.8% of the total medical expenditure. Thus, patients' out-of-pocket contributions account for a relatively small portion of the total medical spending. For example, in the same year (2014), it was only the equivalent of 11.7% of the total medical expenditure (Figure 3).

Therefore, the basic principle of the Japanese healthcare services is to ensure that all people have an equal access to medical services and facilities, and are entitled to a nearly uniform benefits package, covering almost all drugs and treatments, except experimental methods. People do not need to choose their insurance scheme, because it is determined by their employment type. This health insurance system has not undergone any major structural changes for the past 50 years. Also, because of this reason, people are well aware of the benefits they are entitled to, and also accustomed to access the medical service at low cost, without many limitations.

Unfortunately, the slow economic growth in the past 20 years accentuated the deficiencies of the system. In effect, it is a system lacking a rigorous system of checks and controls on its services. It is because of this lack of checks and controls that some problems aggravated over time, such as over-prescriptions and the abuse of in-patient services. Japan is known for setting the record of the longest average hospital stays, at 17.2 days, versus the OECD Countries average of 8.1 days in 2013.

The healthcare model that Japan adopted is basically fee-for-service reimbursement, with the patient responsible for 30% of the medical costs, and their insured scheme paying for the remaining 70%. The patients' proportion will decrease to 20% when they reach

70 years of age, and again to a further 10% when they reach 75. Within this co-payment system, the ceiling of the annual treatment cost for the patient is set at a maximum of JPY 600,000 (USD 5,417). The patient's payment ceiling will change to JPY 310,000 (USD 2,827) in 2020. For certain types of special treatments, such as those that require long-term medical care, patients could also leverage other supplementary health insurance programs to relieve their financial burden.

One important consideration within the existing healthcare system has always been waiting to be addressed. It's the current inefficient referral system for treatment. In 2014, 67.4% of the 8,493 hospitals in Japan were run privately, as were 83% of the 100,461 clinics. These private healthcare institutions are very independent, with little information sharing or co-operation between them. In the absence of a central information gathering system, the structure does not promote a condition whereby the optimal allocation of healthcare resources could be achieved. Only in 2015, a medical information network – called Information Communication and Network (ICN) – was implemented by the Japan Medical Associations (JMA).

Since the healthcare demand has risen, due to an increasing number of elderly patients, it becomes evident that, to maintain its quality, the system must have a robust and continuous source of funding. Yet, the Japanese healthcare system does not draw its financial resources from various revenues, but is increasingly relying on the government's budget more than before. An interesting comparison would that with South Korea, where the healthcare system is additionally supported by the taxes on tobacco consumption; and with China, which is additionally supported by the revenues from a national lottery.

So, the increasingly significant drawback in the current system is due to the fact that the financial contributions drawn from the employees' health insurance premium are not directly proportional to the growth. The sluggish economic situation resulted in a shrinking workforce. The problem is then further exacerbated by the fact that a significant proportion of the young people under the National Health Insurance (*KokuminKenko Hoken*) tends to skip their contribution, since most of them are working part-time or as contract workers. This group of people is most likely to have lower income and less job security *per se*. To contribute to the healthcare insurance scheme run by the National Health Insurance, they actually have to pay a higher premium than those who are employed full-time and are with the Company Health Insurance scheme (*Shakai Hoken*).

Since in recent years the Japanese business is dealing with an increasingly fast-changing environment, many companies are no-longer keeping up with the culture of providing life-long employment. Instead, they hire on contract terms. This lead to an increasing number of part-time and contract workers: hence the growing risk of these young people opting not to contribute to their insurance plans; and that, in turn, becomes another causal factor for the diminishing healthcare financial resources.

Without a structural reform of the healthcare system and an improved economic situation, which would generate more revenue for the treasury, the government is struggling to keep up with the brisk pace of healthcare spending. The government tried to control healthcare spending by increasingly tightening the cost control on all pharmaceutical products, including patent protected and non-protected drugs. There is a regular bienni-

al drug price review since 1992. The result of this review has been a median 4-7% reduction in the NHI reimbursement price to both hospital and pharmacies in the last decade.

However, it was only in 2016, when it became once again more stable, that the government could attempt a more comprehensive revision of the healthcare system. It examined the price revision on medical services, the promotion of community-care services, and the review on how to price marketed pharmaceutical products.

In late 2016, the Japanese Central Social Insurance Medical Council (*Chuikyo*) announced a long list of price revision for hospital fees and pharmacies, that they will charge the patients with, under the public health insurance schemes. A surcharge of USD 46 (JYP 5,000) will also be imposed on patients going to a hospital for a consultation without a doctor's referral. The aim is to encourage community based care, by increasing the financial incentive for doctors to treat patients at home rather than at the hospital. By far the most significant policy implemented to reduce the healthcare burden was to renegotiate the prices paid for drugs and to introduce policies to promote the consumption of generics. The updated generic drugs pricing policy involves a reduction in the price from 60% to 50% of the originator product, and a review on the biennial calculation of the drug price. There will be a further discussion on this topic later on in this chapter.

Among all these measures, what caused a lot of concerns among the pharmaceutical industry is the increasing frequency and magnitude of the drug price review. The drug price for the in-line product could be reviewed yearly as of 2018. For the block-buster products, the annual drug sales exceeding a threshold of USD 1.37 billion (JYP 150 billion) might face a cut of up to 50% on their price tag. Ono Pharmaceutical has already been forced to cut down 50% on the price of Opdivo (for cancer treatment) in 2017, and Gilead Pharmaceutical has also reduced 30% of the price of their Hepatitis C treatments in 2016.

Though the immediate effect of limiting the growth of healthcare spending is evident, feedbacks from the pharmaceutical industry are mixed. Some would say that it should discourage pharmaceutical companies to launch a new innovative product in Japan. Against all the odds, the thought of cost containment is likely to remain paramount for the Japanese administrators.

9.3 Structure of Decision Making and Pathways of Market Access

"Medical fee" in Japan refers to all the costs involving medical services, and that includes consultation, diagnosis, treatment and surgery, as well as the cost of medicines, etc. The "medical fee schedule" is in effect a price list containing the official pricing; and reimbursement is the same for the whole country. The formulation and price level of the medical fee is strictly regulated by Ministry of Health, Labor and Welfare (MHLW – *Koseirodosho*), based on the recommendations of the Central Social Insurance Medical Council (*Chuikyo*).

The Medical Council provides the price setting principle, and the price and conditions of the medical fees. They discuss the principle of medical policy and formulate the principles of price revisions on medical fees. The Medical Council has a total 20 nominated members, including seven representatives from payers – i.e. employee-based health insurance scheme and community-based health insurance scheme – seven representatives from healthcare professionals, mainly physicians and pharmacists, and six representatives from the academic world (Figure 4). The overall healthcare budget is determined by the National Diet (*Kokkai*), which is the equivalent of the Parliament.

In principle, once a pharmaceutical product is approved by the Pharmaceutical and Medical Devices Agency (PMDA), it is then included in the NHI reimbursement list for consideration.

In 2011, the government rectified a notorious problem called 'drug lag'. Previously, new therapies would take up to 660 days, or 22 months, to be launched. Patients' access to a new therapy was seriously delayed. To address the issue of 'drug lag', PMDA increased the number of staff from 520 in 2011 to 750 in 2014, and simplified the new drug application process. For new drug applications, the timeline after changes became an average of 60 days, and a maximum of 90 days for them to be approved for reimbursement. At present, it is quicker to introduce a new therapy or new treatment in the Japanese market, than in Europe, where the average is 180 days.

The current guideline on the drug pricing system is based on the announcement of 'Drug Pricing Standard' Notification no. 0210-(1) and no. 0210-(2) made in 2016 by the Economic Affairs Division at Health Policy Bureau, a subsidiary of the Ministry of Health, Labor and Welfare. This included an updated guideline for a regular drug price review process that started in 1992. It was originally developed to narrow the gap between the reimbursed price and the market price of pharmaceutical products sold to hospitals, clinics

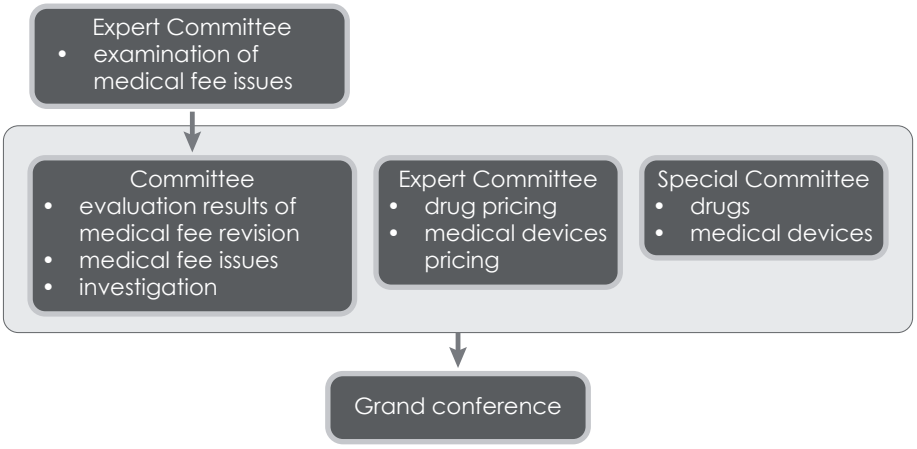

Figure 4. Structure of Central Social Insurance Medical Council (*Chuikyo*) and its committees

and pharmacies. This NHI price review is biennial. Prior to each review, an official survey of market prices was carried out in the fall of the previous year, and the results of this survey constituted a reference for determining any changes in the drug price.

The acceptable gap between the reimbursed price and the market price, known as *yakassa*, has been set at 2% since 2000. If discounts on the product exceed this amount, then the product would be subject to price cuts during the price review. The last price review was carried out in 2016, with reference to the survey conducted in 2015, and that was before the pilot study on cost-effectiveness was conducted, in the same year. It is estimated that only about 22% of the drugs on the market were not affected by those particular discount-based price-cuts.

The Medical Council also provides guidelines on new drug pricing, and they also have the option of adding a price premium for what they consider innovative therapies.

The basic rule for re-pricing the launched products is to calculate the weighted average price of the drug class and then add the consumption tax (8% VAT). The price adjustment for the last few years was 2% (called the R-zone, a price adjustment range). Both the market price and sales volume in hospitals and pharmacies were considered for the calculation of the weighted average price. Table 3 shows the drug price review on long-listed pharmaceutical products in the years 1992-2016.

Year	Year of survey conducted for reference	R-Zone (Price adjustment range %)	Average price cut (%)
1992	June 1991	15	-8.1
1994	June 1993	13	-6.6
1996	June 1995	11	-6.8
1997	September 1996	10 (8% for long-listed products)	-3.0
1998	September 1997	5 (8% for long-listed products)	-9.7
2000	September 1999	Range adjusted 2	-7.0
2002	September 2001	Range adjusted 2	-6.3
2004	September 2003	Range adjusted 2	-4.2
2006	September 2005	Range adjusted 2	-6.7
2008	September 2007	Range adjusted 2	-5.2
2010	September 2009	Range adjusted 2	-6.3
2012	September 2011	Range adjusted 2	-6.3
2014	September 2013	Range adjusted 2	n. a
2016	September 2015	Range adjusted 2	n. a.

Table 3. Drug price review on long-listed pharmaceutical products for the years 1992-2016 [IMS Market Prognosis 2012; JPMA, 2017]

Special Price Adjustment in the 2016 Drug Price Review

The special price adjustment in the fiscal year 2016 was specifically targeted on drugs that have been on the reimbursement list for a long time. If these products have a generics version launched at least five years before, but the generic penetration remains less than 70% (previously set at 60% in the 2014 drug price review), an additional price revision is triggered (Table 4). This latest guideline has increased the pressure on reducing the price for those drugs that have been on the reimbursement list for a long time, but are able to remain in the market with low generic penetrations.

Another feature newly added to the 2016 price review was to impose an additional price cut when the product is achieving very high annual drug sales. This policy change was made with special reference to those drugs with sales substantially greater than the predicted ones. The special price adjustment in price review, initiated in 1996, was made to monitor those products that have exceeded their predicted sales, and the products with added indications after the original listing for the NHI reimbursement. The level of sales foreseen is very important, since it is used to determine the price of the drug during the negotiation for reimbursement (Table 5 and Table 6).

Drug Price Review 2014		Drug Price Review 2016	
Generic penetration (%)	Price reduction (%)	Generic penetration (%)	Price reduction (%)
< 20	-2.0	< 30	-2.0
20-40	-1.75	30-50	-1.75
40-60	-1.5	50-70	-1.5

Table 4. Special price adjustment for long-listed products with low generic penetration in 2016 [2016 HIRA International Symposium]

Drug Price Review 2014		Drug Price Review 2016	
Level of predicted sales	Price reduction (%)		Price reduction (%)
≥ 2-times of predicted annual sales and/or annual sales > JPY 15 billion (USD136.6 million)	-17	≥ 1.5-times of predicted annual sales and/ or annual sales > JPY 100-150 billion (USD 910 million-1.37 billion)	Maximum reduction 25
≥ 10-times of predicted annual sales and/or annual sales > JPY 10 billion (USD 91 million)	-17	≥ 1.3-times of predicted annual sales and/ or annual sales > JPY 150 billion (USD 1.37 billion)	Maximum reduction 50

Table 5. Recalculation the price of drugs with very high annual sales in Drug Price Review 2014 and 2016 [2016 HIRA International Symposium]

	Product	Market Authorization Holder	Predicted sales	Price before reduction	Price after reduction
Method 1	Avastin	CHUGAI Pharmaceutical	• JPY 30. 1 billion • (USD 274.6 million) • 18,000 patients	JYP 180,000 (USD 1,648)	JYP 160,000 (USD 1,465)
	Plavix	Sanofi	• JPY 53. 4 billion • (USD 488.8 million) • 670,000 patients	JYP 280 (USD 2.56)	JYP 200 (USD 1.83)
Method 2	Sovaldi	Gilead Sciences	• JYP 98. 7 billion • (USD 903.4 million) • 19,000 patients	JYP 62,000 (USD 567.5)	JYP 42,000 (USD 384.4)

Table 6. Examples of price reduction on drugs with very high annual sales in 2016 [2016 HIRA International Symposium]

Note.

Method 1: ≥ 1.5-times of predicted annual sales and/or annual sales > JPY 100-150 billion (> USD 910 million-1.37 billion)

Method 2: ≥ 1.3-times of predicted annual sales and/ or annual sales > JPY 150 billion (> USD 1.37 billion)

Previously, if there was a large discrepancy between the predicted sales and the actual ones, these companies would be asked to cut their product prices during the following drug price revision. In the new pricing system introduced in 2016, an *ad hoc* drug price reduction will be put into effect immediately, rather than waiting until the next regular biennial drug price review.

However, it is interesting to point out that the drug price review 2016 was not introduced solely for the purpose of cost containment. On the contrary, a premium up to a maximum of 5.41% of the drug price could be added for product considered innovative. This specifically referred to products that had been on the NHI listing for less than 15 years, and without a generic version available on the market. In addition, these products will not be subject to price adjustment. This was specifically aimed to support innovative products and to eliminate the issue of off-label use.

Cost-effectiveness Assessment in the 2016 Drug Price Review

In April 2016, in the same year as the drug price review, a pilot project of cost-effectiveness assessment for pharmaceutical products and medical devices was introduced. The pilot was significant for the country because it had been the first review of this nature for drug pricing in at least 50 years, and was only possible for a relatively long period of three years of political stability.

This reform started with a pilot scheme of 13 products, of which 7 were pharmaceutical products and 6 medical devices. Treatments for hemophilia, HIV and rare intractable diseases were excluded from this cost-effectiveness assessment, as with new products that were rejected for reimbursement. The re-pricing of these products should be completed by end of the fiscal year 2017. However, as the fiscal year in Japan actually starts in April, it means that the actual implementation will be in April of the following year, 2018. Given that the Japanese business practice is known for its opaque nature, the scheme proposed could be considered as a relatively bold move for the future development of the access to the pharmaceutical market in the country.

The aim of this trial of cost-effectiveness analysis was to use the results for the re-pricing of drugs and devices in the NHI list at the end of the fiscal year 2017. This re-pricing will be done after applying all the pricing rules of the 2016 biennial drug price review. This exercise might help MHLW to show that the final updated price is reasonable and should be acceptable, since it is based on a form of economic analysis. As yet, details of how to integrate the results of the cost-effectiveness assessment in price revision are not yet specified, but a discussion on the topic is planned in the next drug price review in the fiscal year 2018.

Based on the selection criteria developed by the Special Committee set up under the Central Social Insurance Medical Council – *Chuikyo* in 2012 on cost-effectiveness, both new drugs and medical devices listed between 2012 and 2015 could be chosen in the pilot project. The selection was that of the products that had received the approval for reimbursement with the highest rate of premium, with a sales record which also had reached the highest level of predicted peak sales. These were then compared with products which had received a 10% premium approval on their price.

The companies, once their drugs were selected for the pilot project, were requested to submit data on their degree of cost-effectiveness, as well as their projection regarding the highest level of sales. In the same application, they also have the option of asking for an additional premium that is ≥10% of the government reimbursement price. It is interesting to note that while MHLW believed that it was very important to have the assessment result as reference materials, the Special Committee did not take them into consideration in their calculation of the official pricing.

Looking from the historical perspective, pharmaceutical companies in Japan could submit economic evaluation data in their application for listing as early as 1992. However, in the absence of clear guidelines on precisely what types of information or data were required, and also to what extent the information would influence the decision on the level of price and reimbursement, out of 256 applications for reimbursement between 2006 and 2011, only eight were new drugs that had submitted economic evaluation data for review.

Then, it was only twenty years later, in 2012, that a committee on cost-effectiveness assessment was formally set up under the Medical Council (*Chuikyo*). It became the Special Committee on Cost-Effectiveness. It drew its members from health insurance, healthcare providers, pharmaceutical industry, public sector and experts in health economic assessment. The function of this committee was to take cost-effectiveness as an important

reference in the decision making process for price and reimbursement. Yet, the committee took four years to arrive at the common ground of using Quality-Adjusted Life Years (QALY) as the basic measurement outcome. But they have not yet agreed on how to translate QALY into financial units. On the other hand, the committee said to be willing to accept to consider other types of outcome measurement in their assessment, if they were considered by NHI to be appropriate to the related disease area and medical technology.

Strictly speaking, Japan could be considered as a pioneer in Asia in the use of economic assessment in the reimbursement process for drugs and medical devices, although Australia was the first country to conduct mandatory economic appraisal in the reimbursement process in 1993. Yet after 25 years, the related policy in Japan still has a lot of rooms for improvement in the use of the economic perspective in pricing and reimbursement.

The one significant progress that needs to be acknowledged is the confirmation on the selection criteria of products eligible in the pilot project (Table 7). This pilot project started in 2016, and is expected to be completed by 2017. Despite a delay of two years from the original schedule, it remains the first formal step for the government to apply an economic assessment in the pricing and reimbursement process.

At present, Japan does not have the equivalent of a formal HTA agency to support the assessment, such as NICE in the UK or IQWIG in Germany. In the pilot project, the coordination with pharmaceutical companies and the academic representative is done through the National Institute of Public Health (NIPH). The economic assessment data covered a period of two years from the fiscal year 2016 to 2017. After the initial data submission, NIPH will then send the data to the academic group, composed of clinical epidemiologists and health economists, for approval. The data were again sent to a sub-committee under the Special Committee on Cost Effectiveness, called Expert Committee of

For the listed drugs whose reimbursement decision were made in fiscal years 2012 2015	
Products using similar efficacy comparison method	• Received the highest premium rate, or • ≥10% premium and the highest sales (or price)
Products using cost calculation method	• Received the highest premium rate, or • ≥10% premium and the highest sales (or price)
For the new drugs whose reimbursement listing was done after October 2016	
Products using similar efficacy comparison method	• Predicted highest sales JYP 50 billion (USD 45.5 million) for drugs • Predicted highest sales JYP 5 billion (USD 4.5 million) for medical devices
Products using cost calculation method	• Predicted highest sales JYP 10 billion (USD 9.1 million) for drugs • Predicted highest sales JYP 1 billion (USD 0.9 million) for medical devices

Table 7. Selection criteria for products participating in the pilot projects [Shiroiwa, 2017]

	Pharmaceutical products		Medical devices
	Generic name	Brand name	
Similar efficacy comparison method	Sofosbuvir	Sovaldi	KawasumiNajuta Thoracic Stent Graft System
	Combination of LedipasvirAcetonate/ Sofosbuvir	Harvoni	Activa RC
	Combination of Ombitasvir Hydrate/Paritaprevir Hydrate/Ritonavir	Viekirax	Vercise DBS System
	Daclatasvir Hydrochloride	Daklinza	Brio Dual 8 neurostimulator
	Asunaprevir	Sunvepra	
Cost calculation method	Nivolumab	Opdivo	J-tec Autologous Cultured Cartilage (JACC)
	Trastuzumab/Emtansine	Kadcyla	Sapien XT

Table 8. Pharmaceutical products and medical devices selected for the cost-effectiveness assessment in the pilot project [Takashi, 2014]

cost effectiveness for review and assessment. Members of this Expert Committee remained anonymous to the public, and they decided whether they considered the medical technology in application cost-effective. After the review, there will be a close-meeting between the Special Committee on Cost-Effectiveness and the company, as the Market Authorization holder, with a draft of the written result for assessment. The final decision on price and reimbursement rests with the Medical Council (*Chuikyo*). Table 8 reports the pharmaceutical products and medical devices selected for the cost-effectiveness assessment in the pilot project.

"Basic Drug" in the 2016 Drug Price Review

The pilot study of price adjustment based on a cost-effectiveness assessment was one of the measures for an *ad hoc* price cut in Japan. From the biennial drug price review between 2008 and 2012, there were a total of three instances of special adjustments of drug price and an average price cut of 4-6 % on long-listed products. So far, the rules for these drug pricing remained blurred and diffused. While the objective of the Japanese government is to control the rising expenditure on pharmaceutical products, it remained equally important that an excessive discounting would not affect or discourage the launch of innovative therapies, since the cost control measure should also not hamper the development of the pharmaceutical industry. For that reason, to counter the pressure to lower

Box 1. Definition of "basic drug" [JPMA, 2017]

1. The drug has an established position in the clinical settings and has been clearly shown to be widely used in clinical practice.
2. The basic drug may have similar products with same ingredients and dosage form; it is required that at least one product has been listed on NHI reimbursement for 25 years or longer.
3. The basic drug may have similar products with same ingredients and dosage form; the average price differences between the NHI reimbursement price and the current market price of these similar products (including basic drug) cannot exceed that of all the listed reimbursement products.

the prices, there was also an upward special price adjustment for innovative therapies which would put on a price premium protection as of 2011.

On top of all these various considerations, another pricing measure on basic drugs was announced in 2015 to ensure a stable supply of essential drugs (Box 1). It was the 'Comprehensive Strategy to Strengthen the Pharmaceutical Industry', which was published by the Ministry of Health, Labor and Welfare. It stated that "if a drug has been listed in the drug price list for a long period of time, and has successfully undergone a drug price revisions, but its supply is difficult to discontinue due to the demand in the clinical prac-

Category	Number of ingredients (products)	Products (example)	Indications
Pathogenic organism	51 (169)	• Amolin fine granules • Ebutol tablets • Retrovir capusles • Arasena-AIV drip	• Various infectious diseases • Pulmonary tuberculosis • HIV infection • Herpes simplex • Encephalitis, etc.
Narcotics	6 (15)	• MS Contin tablets • Morphine hydrochloride injection	• Pain relief for various cancers • Pain relief/sedation for severe pain
Unprofitable	77 (264)	• Phenytoin powder • Thyradin powder • Endoxan bulk powder (oral use) • Pam IV injection • Soldem 3 transfusion	• Convulsive seizure • Congenital hypothyroidism • Multiple myeloma • Organophosphate poisoning • Hydration when oral intake is impossible

Table 9. Examples of "basic drug" in the drug pricing system reform of fiscal year 2016 [2016 HIRA International Symposium]

tice, it is necessary to ensure its continuous and stable supply to the market". The aim was to ensure that even the minimum NHI reimbursement price set in the price recalculation would still generate enough financial incentive for the company. From the 2016 drug price review there was a total of 134 active ingredients and 439 products falling into this category (Table 9).

Pricing Rules for New Drugs

There are two methods used for assessing the pricing of new drugs. The first method is comparing similar products. This is feasible when a reasonable comparator therapy can be identified. Basically, the requirement is that the comparator is a branded drug launched within 10 years, without any generic present on the NHI reimbursement list. This comparison method is designed for pricing a new product based on the cost per day of the comparator therapy. For the new product two different ways of comparison can be chosen within this method; i) with an innovative product or ii) with a me-too product which refers to a product with little novelty. The differences between these two comparison methods are on the following price adjustment. New products priced using the second way of comparison, me-too products, will not be awarded a price premium. On the other hand, the products will have to adjust their price downwards if their price is set at 1.25 times or higher than the average foreign market price, which refers to the average market price in the US, Germany, France and the UK.

The second method is cost calculation when no comparator is identified. It measures the level of profit for the product. This method takes into account the cost of raw materials, labor cost, manufacturing expenses, manufacturing cost, marketing, as well as R&D cost, distribution cost, consumption tax and operating profit. The calculation of operat-

	Premium applied	Characteristics
Innovative Premium	70-120%	• New mechanism of action • High efficacy or safety • Significant improvement in treatment
Value Premium	5-60%	• High efficacy or safety • Significant improvement in treatment
Marketability Premium	5% or 10-20%	• Orphan drugs, etc.
Pediatrics Premium	5-20%	• Pediatric indication • Dosage • Administration, etc.
SAKIGAKE Premium	10-20%	• The new listing drug designated as a reference model for promoting local R&D in Japan (SAKIGAKE designation)

Table 10. Premium applied on new innovative drug in the drug pricing system reform of fiscal year 2016 [2016 HIRA International Symposium]

ing profit is obtained from a combined figure with a ratio on marketing cost and administration cost, as well as a ratio on expenses and labor cost. The derived figure on operating profit will be multiplied by a coefficient factor based on the average figure collected from the pharmaceutical industry in the last 3 years. Depending on the novelty, safety and efficacy of the new drug, the figure of the target for its operating profit could be revised upwards by up to 100%, or revised downwards by as much as 50%. The unit cost of labor is referenced to the average figure from the monthly labor survey in Japan, conducted by MHLW. The cost of distribution is in reference to the average figure released

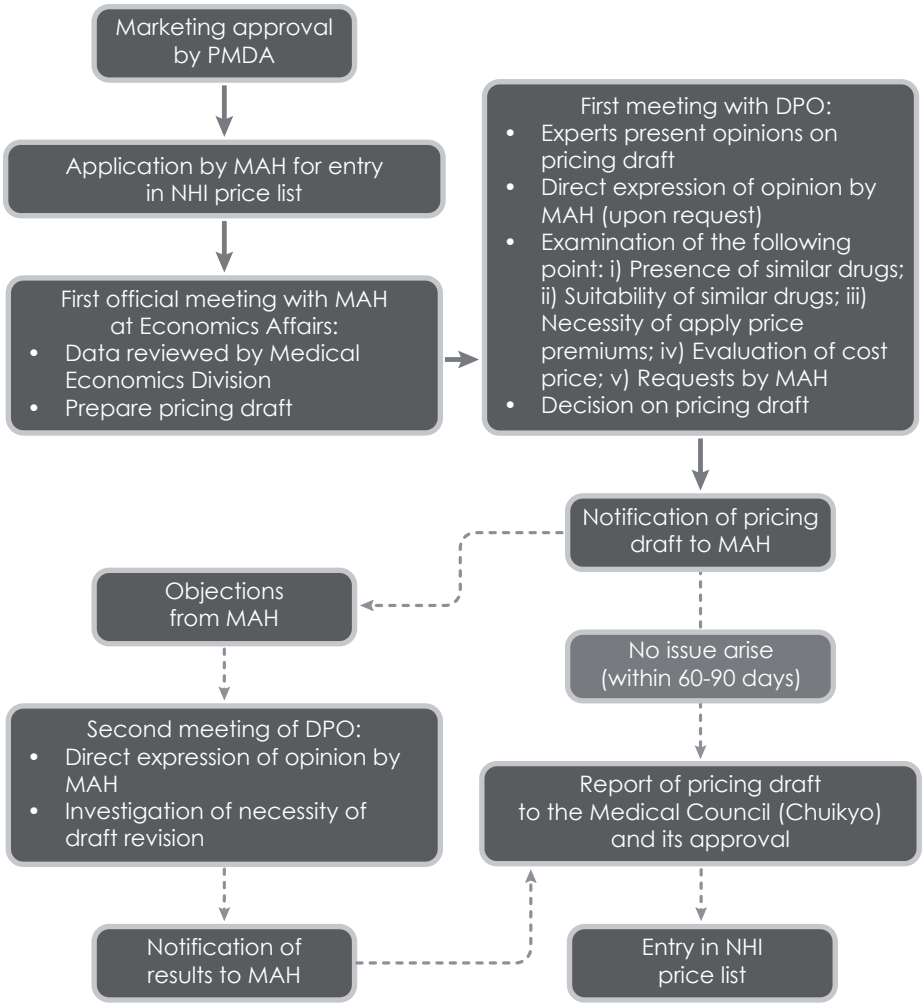

Figure 5. New drug price setting process. Modified from [JPMA, 2017]

on 'Current Report of Pharmaceutical Industry', carried out by MHLW. For the 2016 drug price review, these reference figures were derived from the average of the years 2012 to 2014.

If a new product is rated as innovative, a premium rate can be added, regardless the method used in new drug pricing. This is an incentive program started in 2010 to encourage the development of innovative drugs. Since the regular price review eroded the drug price, this premium pricing system provides a buffer for subsequent price cuts on the new drug (Table 10).

At this point, the new drug receives a temporary price. In the next step, this temporary price will be compared with the new product average market price listed in several foreign Countries. There are four Countries chosen for this adjustment process: the US, Germany, France and the UK. The temporary price may need to be adjusted if it meets one of the following conditions: i) if the temporary price is 1.25 (or more) times the average foreign price, the price of the new drug will be adjusted downwards; ii) if the temporary price is 0.75 (or more) times the average foreign price, the price of the new drug will be adjusted upwards. Figure 5 reports the new drug price setting process.

Pricing Rules for Generics

The Japanese government believes that one of the effective solutions to cut down the spending on pharmaceutical products is promoting the use of generics. In 2007, the Japanese government set a prescription goal on national generics equal to 30% by volume by 2012. In 2016, the government adjusted the target of generic prescription to 70% by the middle of 2017. This target was again revised to 80% or more by the end of 2020. Though the government encourages the prescription of generics, their penetration is expected to be still low by international standard. For example, the use of generics in Germany and the UK are both around 70%. In 2015, according to the IMS sales data, the generics volume share was 33.5% of the total of the dispensed pharmaceutical products. Based on the research findings from MHLW, the generics share is 56.2%. The calculation of generic penetration only looks at off-patent originator medicine as the denominator.

As of 2008, new generics drugs have the opportunity to enter the NHI reimbursement list twice a year. In addition, pharmacies also receive financial incentives from the government to dispense generics. The 2016 drug price review changed the minimum generics dispensing quota. Financial incentives will be given when the pharmacy uses over 65%of generics per prescription. If the physicians do not want to use generics, they are now required to specifically note that down next to the medicine, on the prescription. If not specified, it is possible to substitute the product with its generic at the dispensary. But the most impactful measure on the promotion of the use of generics remains the direct price control. In the past, the reimbursement price on generics was 70% of the originator's price for the first generic drug. In 2016, a reduction in starting prices for new generics takes it down to 50% of the current price of the original drug, and might go down to 40% if 10 or more similar products are listed simultaneously.

9.4 Challenges

Examining the "Basic Policy on Economic and Fiscal Management and Reform 2017", if one were to predict the possible future development of the drug price system, Japan is likely to continue the direction of cost-effectiveness based on drug use, and it will encourage the development of innovative therapies. Fiscal deficits are unlikely to deter the government to shy away from the principle of universal healthcare coverage. Rather, the pressure on reducing the budget is likely to continue, and to concentrate on 'me-too' products and products that have been on the reimbursement list for a long time. It has been announced that the biennial Drug Price Review will now be changed to an annual one as of 2018. Considering these changes, it seems that only the highly rated innovative products could successfully apply to add a premium on their price. In order to successfully contain the acceleration of price increase, an evidence-based drug pricing system is likely to be the solution for the government in assessing the 'innovativeness' and 'usefulness' of the new medical technologies. If the details of a review system could be finalized by the end of the fiscal year 2017, then perhaps there will be a realistic chance of successfully introducing Health Technology Assessment (HTA).

The real question regards the extent to which the updated policies could so far accommodate two key objectives: a 'sustainable universal healthcare system' and the 'promotion of innovation'. If the government does succeed with the present pilot study, then it might be even able to relieve the growing financial burden on healthcare spending, while maintaining the remarkable quality of the people's health.

So far, to stimulate once again the economic growth in the country, the current government has strongly focused on the 'Japan Revitalization Strategy'. The core essence of a part of this strategy is to encourage the industry to invest more back in the country. Pharmaceutical companies are an important sector of the industry, especially with their research and product development. On the other hand, the government also faces the dilemma of reducing the spending on pharmaceutical products. So there is a very delicate balance of the economic interest. With the latest updates and pilot schemes of the drug pricing system, the pharmaceutical industry might not find Japan such a profitable market. An example is the government strategy on the promotion of biosimilars.

The pathway for the access of biosimilar into the country market was introduced in 2009, and it was mostly aligned with the guideline of the European Medicine Agency (EMA). The price of biosimilars is set as 70% of the reference product. On top of that, biosimilars can add a 10% premium to their price, based on the level of investment in clinical development. With the premium, the maximum price of a biosimilar could therefore be 77% of the reference product. All biosimilar products are priced the same, regardless of the sequence they enter the market in, and are not subject to price erosion depending on their date of market entry.

Currently, biosimilars could enter the NHI list either in May or in November. The May application should be approved by January, and the November application should be approved by July of the following year. Once the product is included in the reimbursement

list, it could gain access quickly to hospitals or the retail market, and be available for prescriptions almost right away. Patients can have a 70% reimbursement of the treatment cost when using biosimilar product. Furthermore, a financial incentive is offered to hospitals if they meet the minimal biosimilar dispensing quota, which is 22% of their total dispensations. The market access of biosimilars is quite clear and straightforward in this sense.

Table 11 reports the list of biosimilars launched in Japan in the years 2009-2017 . By April 2017, a total of 11 biosimilar products from 5 different biologics were launched in Japan. This is less than the products launched in West-Europe Countries. Even though Japan offered a favorable price and premium, the biosimilar penetration is limited. In Germany, in the period between 2007 and 2017, 18 biosimilar products were launched, using a free-pricing system. The price of biosimilars can retain 75% of the reference product in the market, with an additional 25-30% on rebate contract.

In Japan, not all listed biosimilar could actually reach their ceiling price of 70% of their reference product. In addition, it is rare to see a premium added to a pricing for biosimilars. Out of the 11 biosimilar products listed, so far there is only one product which can receive the 10% price premium: it is the biosimilar of epoetin alfa, by Kissei Pharmaceutical/JCR.

Biosimilars are also in the program of biennial drug price review with other products on the reimbursement list. Biosimilar products have undergone an average of 2% price cut during the last few re-pricing review. Since the biennial drug price review will switch

Biosimilar	Marketer	Reference product	Approval Date
Somatropin BS SC Sandoz	Sandoz/Nipro	Genotropin (somatropin)	September 2009
Epoetin Alfa BS Syringe JCR	Nippon Kayaku	Espo (epoetin alfa)	May 2010
Filgrastim BS Syringe NK	Nippon Kayaku	Gran (filgrastim)	May 2013
Filgrastim BS Syringe Mochida	Mochida	Gran (filgrastim)	May 2013
Filgrastim BS Syringe F	Fuji Pharma	Gran (filgrastim)	May 2013
Filgrastim BS Syringe Teva	Teva	Gran (filgrastim)	May 2013
Filgrastim BS Syringe Sandoz	Sandoz/ Sawai	Gran (filgrastim)	November 2014
Infliximab BS IV Infusion CTH	Celltrion	Remicade (infliximab)	November 2014
Infliximab BS IV Infusion NK	Nippon Kayaku	Remicade (infliximab)	November 2014
Insulin Glargine BS Cartiridge Lilly	Eli Lilly	Lantus (insulin glargine)	August 2015
Insulin Glargine BS Injection Kit (FFP)	Fujifilm Pharma Co.	Lantus (insulin glargine)	July 2016

Table 11. List of the biosimilars launched in Japan in 2009-2017

to yearly from 2018, this might even encourage physicians and patients not to switch to biosimilars, or even generics. The relatively low co-payment amount for the originator or reference product will certainly be a factor affecting the use of biosimilar. This implies that there is a hidden challenge to market access in Japan.

Health Technology Assessments help policy-makers and the pharmaceutical industry to make a scientific calculation of a drug's value and price. But several elements are required to make the assessment meaningful and impactful.

Firstly, an accurate and transparent framework for the cost-effectiveness analysis in the drug pricing system is fundamental. After four years of discussion, the Special Committee on Cost Effectiveness only arrived at an alignment of using QALY as the base unit to measure the performance of medical technology, but it has not yet reached a consensus on the cost of QALY. There is always the question of whether it should be at a fixed cost, or if it should be kept flexible with the assessment criteria. Until the completion of the pilot project, at the end of the fiscal year 2017, the extent of the economic evaluation of the pilot study on the impending drug pricing system cannot be known.

Another concern about the market access environment in Japan is the fact that the decision-making process generally takes a long time. Take, for example, the decision of introducing HTA in pricing and reimbursement. It would have taken a total of 4 years, from the establishment of the first special committee in 2012, to finalizing the details of the policy on HTA in 2018 – if, that is, it could finally take place by the end of fiscal year 2017. It will not be a surprise if the Japanese government fails to conclude the assessment in a timely manner during the introduction of the HTA.

With the attempt of introducing the health technology assessment, Japan has not yet designated a formal institution to manage the policy. At present, the National Institute of Public Health is responsible for coordinating the pharmaceutical companies with the Special Committee on Cost-Effectiveness, which was set up in 2012. Members of the Special Committee could be on a three 2-consecutive-year term, or a maximum service term of 6 years. The service duration of the committee members is especially interesting, because the time expiration of their maximum term also almost coincides with the completion of the very first pilot project on cost-effectiveness assessment for re-pricing. Whether these members could transfer their learning, derived from the pilot project, to policy formulation before they finish their term of service, it remains an interesting question. A successful continuity of the HTA development in the drug pricing system will only be feasible when the knowledge can be transferred and integrated.

Apart from the issue of continuity, the market also faces another challenge in the absence of local HTA experts and experienced executives to support the assessment process. It is believed that many members of the Special Committee on Cost Effectiveness had very little knowledge on HTA when they joined the committee itself. Experience in the industry, useful to help carry out the assessment, was also limited. The collection of patients and clinical data for economic assessment is an important preparation step in the implementation of an economic analysis, but it takes time.

If one takes the HTA development in South Korea as a reference, the latter encountered a bottleneck in 2006, when the government started to implement HTA within the

Section	Content
Perspective	'Public healthcare payer's perspective' is considered standard. Other perspectives could be applied, if necessary
Target population (patient group)	Patients who meet the indication of the medical technology at the time of the analysis
Comparator	Medical Technology, reimbursed by public health insurance (NHI), widely used in clinical practice and expected to be used to a larger extent.
Additional benefit	The additional benefit in terms of effectiveness, safety, and/or other attributes of the medical technology should have a systematic review
Method of analysis	Cost-effectiveness analysis (CEA); Cost-utility analysis (CUA) should also be used
Subgroup analysis	Applicable if it is necessary
Time period	The length of time should be sufficient to evaluate the value of medical technology
Outcome	Quality-Adjusted Life Year (QALY) as the base unit of the outcome
Methods to calculate the QoL score	Preference-based instruments with scoring algorithms developed in Japan
Mapping	Yes
Clinical data (source of information)	Systematic review
Indirect comparison	Yes (if a comparator does not exist)
Cost calculation	All costs paid by public insurers (NHI, central and local governments), patients, productivity loss (applicable, depends on the perspective)
Cost (source of information)	Medical fee schedule and NHI drug price list
Estimation of productivity loss	Human capital method
Discount rate	2% (sensitivity analysis 0-4%)
Modeling	Yes
Sensitivity analysis	Deterministic and probabilistic sensitivity analysis
Reporting	Standard format is set; Result of the analysis should be open to public access

Table 12. Summary of the Guideline for Economic Evaluation of Drugs and Medical Devices in Japan [Shiroiwa, 2017]

price and reimbursement process. The lack of experience and the volume of applications overwhelmed the system. Consequently, it took two years to resolve the problems associated with the processing of the applications with the new system. The same problem is likely to occur when Japan starts to formally introduce HTA in 2018.

Moving to a new approach concerning reimbursement, the industry will also need to adapt and prepare itself for the new data requirement, including epidemiological data and cost data in the assessment of new medicines. In this case, an agreement between the government and the industry on the methodology used in the analysis is critical. The first draft on the guideline of Economic Evaluation of Drugs and Medical Device was officially approved by the Medical Council in February 2016 (Table 12). This guideline contains 15 sections, and it has an overview of how the economic assessment should be made. Perhaps this will provide the common platform for a fruitful dialogue between the industry and the government to successfully adopt the new approach.

9.5 Look-out for Near Future

Japan is the third biggest economy in the world, but its slow growth is unlikely to improve, at least in the next 3 years. The government announced that the primary budget deficit will increase to JPY 8.3 trillion (USD 83 billion) for the fiscal year 2020. This government budget deficit projection will be a substantial increase from the previous projection of JPY 5.5 trillion (USD 50 billion), announced in 2016. It means that the government continues to expect that the growth of tax revenue will be slower than expected. Due to its huge unpopularity, the plan to increase consumption tax from the current 8% to 10% has been delayed to 2019. The government spending will certainly outpace revenue in the next few years.

Under the budget pressure, the government should be very cautious in allocating its resources, and that includes the healthcare services sector. The overall objective seems that to prioritize the healthcare benefits for the elderly and the children. This is reflected in the proposed 'Comprehensive Reform of Social Security and Tax', which has been submitted to the National Parliament (DIET) for approval in 2018. The resources will be in the form of creating home care/long-term care within the community. The current administration has also promised to increase the benefit coverage and pension for low-income people and part-time workers. Should these policies be executed, the government would need additional financial resources.

So far, there is no indication that the government will increase the patients' co-payment or add new healthcare funding. Health-technology assessment is the major attempt by the government to justify the price of new medical technologies. Otherwise, it is expected that further cost-containment measures applied to pharmaceutical products will be the way for the government to solve the issue of the increase in healthcare spending.

In fact, the frequency and magnitude of the special price adjustment have increased in the last few years. New pricing rules were announced and implemented at short no-

tice. These changes are becoming too frequent and are affecting long-term planning for the industry. Changes always work better if they are applied progressively, rather than sporadically.

If the government truly believes the principle of universal health coverage and maintenance of low co-payment, for its long-term success, then a review and overhaul of the whole system would be far more effective than any fragmentary change.

The use of cost-effectiveness assessments could be an improved method to support pricing decisions. Since the Medical Council (*Chuikyo*) plans to transfer the lessons learned from the pilot project to the actual implementation of HTA in 2018, the market access pathway will change. However, in order for the new system to be effectively run, it is certainly desirable to have collaborations and good communications between the payers, the new HTA organization, the patients and the pharmaceutical industry. It is not unusual to encounter practical problems in moving from one system to another – and some of them have already been mentioned before, such as incomplete local epidemiological data, insufficient number or knowledge on the part of HTA experts to assist the analysis, pharmaceutical companies which also need to train their own market access executives, potential delay for patients in accessing the new technologies, etc. It is important for the government to prepare the mitigation plan and keep the industry informed. This will allow the industry to implement a timely management of the issues and prepare itself for the launch plan. Patients could then benefit from the medical technology, with the resources provided by the government. It is but a common goal for both the government and the pharmaceutical industry to work for the interest of the patients. However, there is one last consideration that is vital for the government, in order to achieve a reasonable drug price at an efficient cost-benefit: the system must be backed up by a good data infrastructure, and an efficient data sharing system. Only then it could generate the evidence needed to facilitate an accurate value assessment.

Lastly – and this is especially relevant to this country – Japan desperately needs the continuation of a stable political climate. At last the Prime Minister office has been held for a few years, after a long period of frequent changes: now it would be detrimental to all parties concerned if such office were to frequently rotate once again.

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