



European Federation of Pharmaceutical
Industries and Associations

EFPIA Viewpoint: Health Technology Assessment (HTA) Application in Select Markets and Implications for Japan

“Putting the patient at the center of healthcare decisions”



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Contents

1. Introduction	4
2. What is Health Technology Assessment (HTA)?	5
3. Healthcare in Japan Today	6
4. Lessons from HTA Abroad	9
5. Impact of HTA on Cancer Treatment	12
6. EFPIA's Position on HTA in Japan	13
7. Executive Summary	16

Introduction

In 2012, the Ministry of Health, Labor and Welfare (MHLW) asked the advisory body, Chuikyo, to conduct a study on Cost-Effectiveness Analysis (CEA), an aspect of Health Technology Assessment (HTA), and to make recommendations regarding its introduction. Initially planned for launch in 2014, the greater than expected complexity of the task led to postponement of any introduction until April 2016.

Since 2012, a project team led by MHLW officials and a small group of health economists has focused its studies primarily on CEA and HTA methodologies, drawing from experiences in the UK and other countries. In June 2014, as part of specific measures for healthcare in the Japan Revitalization Strategy, the Cabinet requested the testing of CEA in the assessment for insurance coverage of innovative medical technologies. Subsequently, a pilot project was initiated involving five pharmaceutical and three medical device companies with the intention of identifying specific challenges that would result from the introduction of an HTA system.

The MHLW-led study has not yet solicited the views of a broad group of key stakeholders, such as patient advocates, clinicians, epidemiologists, health policy specialists, and the pharmaceutical industry. These stakeholders each have a unique perspective, knowledge and experience of dealing with HTA systems in other markets, which are critical to informing the discussion in Japan. The MHLW study has also not yet addressed Chuikyo's initial concerns regarding the purpose of introducing CEA and what benefits could reasonably be anticipated. Indeed, it is unclear where value will be added with respect to improved cost-effectiveness within the context of Japan's healthcare system and

National Health Insurance,¹ given that aspects of HTA are already embedded in the current pricing and reimbursement system.

Looking at the overseas experience, it is clear that the introduction of an inappropriate HTA system in Japan risks creating barriers to access and undoing the progress Japan has made in reducing its drug lag.

EFPIA Japan believes it is important that decision-makers collaborate in a transparent process with all stakeholders before finalizing a proposal regarding the trial introduction of Cost-Effectiveness Analysis (CEA) in April 2016. Specifically, EFPIA suggests the following five principles guide the evolution and discussion of HTA in Japan:

1. Involve all stakeholders in meaningful discussion (including patients, healthcare providers, and industry) at all stages of the process
2. Set priorities for the initial, trial introduction of HTA
3. Focus on achieving better health outcomes, not solely on costs
4. Ensure no negative impact on patient access or physician's freedom to prescribe
5. Reward innovation and minimize burden to both government and industry

¹ MHLW. 23 May 2012. Meeting Minutes. 1st meeting of Chuikyo HTA sub-committee. Retrieved from <http://www.mhlw.go.jp/stf/shingi/2r9852000002a7t6.html>

About EFPIA Japan

EFPIA Japan represents 25 R&D-based pharmaceutical companies operating in Japan. Our Mission is to contribute to healthcare and patients in Japan through the early introduction of innovative medicines and vaccines. To do this we encourage access to the most innovative therapies in the shortest possible time; support Japan in becoming a more dynamic and attractive place in which to invest; and aim to be seen as a trusted healthcare partner.

The combined sales of our member companies account for about one quarter of the pharmaceutical market in Japan, and EFPIA members account for around one-third of all new drugs approved in Japan. EFPIA member companies therefore deliver significant health benefits to Japanese patients and are an important part of the Japanese pharmaceutical industry.

What is Health Technology Assessment (HTA)?

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) defines Health Technology Assessment (HTA) as: “the process that uses evidence to evaluate the clinical efficacy, cost-effectiveness and broader impact of a health technology on patients and the health care system.”¹

Additionally, HTA International (HTAi) stresses that the assessment goes beyond clinical and economic aspects:²

HTA is a multidisciplinary field that addresses the clinical, economic, organizational, social, legal, and ethical impacts of a health technology, considering its specific healthcare context as well as available alternatives. The scope and methods of HTA may be adapted to the needs of a particular health system, but HTA processes and methods should be transparent, systematic, and rigorous.

HTA can take many forms, and be used to address such healthcare topics as:

- Drugs, biologics, devices, procedures
- Support systems, organizational, delivery and management systems (e.g., disease management programs, health care payment systems).

In contrast to this robust range of possible applications, CEA, which is only one of several approaches within HTA, employs a single outcome metric to compare costs and health effects across different interventions. Furthermore, it is important that HTA be used appropriately. For example, according to the European Network of HTA organizations (EUnetHTA), HTA is not a replacement for proper price setting methodologies.

The definition of HTA continues to evolve

The definition of HTA continues to evolve, as does its application and use. Across all markets where HTA is used, it is continually in a state of change: constantly adapting to incorporate new measures of value, reflect changing societal priorities, and address access challenges and patient needs. Although HTA is by nature contextual and takes different forms in different settings, HTA is in general becoming:

- **More comprehensive:** focusing on diseases and care pathways rather than individual technologies, and informing broader policy decisions beyond pricing and reimbursement.
- **More adaptive:** continuously collecting / assessing data and informing decisions across the life cycle.

- **More collaborative:** engaging a wider range of stakeholders.

Micro-HTA vs. Macro-HTA?

HTA is just one of many tools available to improve health system performance. As with any methodology, it has both strengths and limitations. It is critical that policymakers fully understand these strengths and limitations if they are to apply HTA appropriately. HTA can be applied at either or both of two levels: the “Micro-Level” and the “Macro-Level.” Micro-HTA analyzes data to assess the perceived value of a unique technology, e.g., pharmaceutical, device, or medical procedure, to foster or limit its utilization, or as an input to therapeutic guidelines. As Micro-HTA looks only at individual technologies, this alone will not likely result in their optimal use due to complexities and inefficiencies elsewhere in the healthcare system.

In contrast, Macro-HTA focuses on policy, infrastructure and organization, thus helping to guide or assess the policy-making process in such areas as: organizational structure, public health intervention programs, and the efficient allocation of resources.³ Given its more comprehensive approach, Macro-HTA is likely a better choice to support policy decisions that achieve better patient outcomes and more efficient healthcare systems.



¹ International Society for Pharmacoeconomics and Outcomes. (2014). Health care cost, quality, and outcomes: ISPOR book of terms.
² Health Technology Assessment International. 2015. Health Technology Assessment. Retrieved from <http://www.htai.org/htai/health-technology-assessment.html>

³ Towse, Adrian. 6 September 2014. Office of Health Economics. ISPOR 6th Asia-Pacific Conference. Broader approaches to HTA strengthening health systems to improve patient care: introduction of the concept of ‘Macro’ HTA.

The Context—Healthcare in Japan Today

Japan has one of the most successful national healthcare systems in the world

Foreign governments, nonprofit organizations, and other authorities have recognized the Japanese healthcare system repeatedly for delivering unparalleled access to medicines and high-quality healthcare. Japanese authorities have succeeded in developing a healthcare model that:

- Provides universal access without restriction based on residence, income or financial resources
- Provides high-quality treatments by properly trained medical specialists in private medical practice or employed by public or private medical institutions
- Controls healthcare expenditures through adequate and well-established mechanisms

Japan scores highly on health outcomes such as child mortality and longevity, and yet historically, Japan has had one of the lowest healthcare costs to GDP ratio of any major developed country. It is only in the past couple of years that Japan’s ratio has risen slightly above the OECD average, as a result of care for the aging population and slower economic growth—not as a result of pharmaceutical expenditure, which has grown only modestly.

In 2014, the OECD¹ and the World Bank² issued separate reports

¹ OECD. 5 November 2014. OECD Reviews of Health Care Quality: Japan. Retrieved from http://www.oecd.org/els/health-systems/ReviewofHealthCareQualityJAPAN_ExecutiveSummary.pdf
² Ikegami, Naoki (World Bank). 25 September 2014. Universal health coverage for inclusive and sustainable development: lessons from Japan. Retrieved from <http://documents.worldbank.org/curated/en/2014/09/20278271/universal-health-coverage-inclusive-sustainable-development-lessons-japan>

on the Japanese health care system, which showed that the current pricing system is a key part of its overall success.

“Japan is a country that achieves good health at relatively low cost. As well as long life expectancy, some indicators of healthcare are amongst the best in the world”—2014 OECD Report.

“Low cost is achieved through nationally binding prices based on a fee-schedule that is revised every other year”—2014 OECD Report.

Despite this praise, for the future betterment of Japanese healthcare, the OECD report also highlights key challenges the Japanese healthcare system will need to address in the coming years:

Weak Primary Care: Japan has an opportunity to improve many practices at the community physician level, adjusting infrastructure to better fit Japan’s changing demographics. This not only benefits patients, but will continue to improve Japan’s healthcare quality and efficiency.

Weak Information Structure: Japan faces some challenges due to an information structure that is underdeveloped and therefore under-utilizes quality outcomes—highlighting the need to improve infrastructure for evidence such as the Real World Evidence [that can be] used in HTA.

Health Spending in OECD Countries as Percent of GDP

Japan falls in line with OECD nations and performs better than many markets where HTA is used

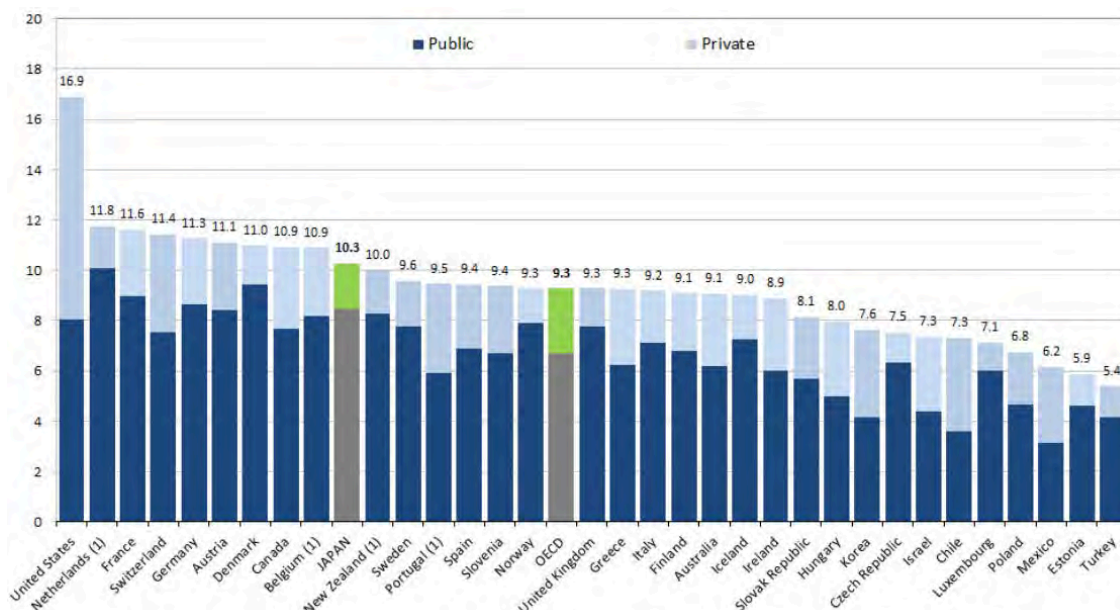


Figure 1. Expenditure on healthcare in Japan relative to other OECD countries. **Source:** Organization for Economic Cooperation and Development (OECD). (2014). *OECD Health Statistics 2014—How does Japan compare?* Retrieved from: <http://www.oecd.org/els/health-systems/Briefing-Note-JAPAN-2014.pdf>

Japan's reduction of its drug lag has been one of the great public policy successes of recent years

Over the past five years, the government of Japan has taken major steps towards the elimination of the “drug lag”—the period from first global launch to launch in Japan. This has been achieved partly by doubling the number of staff at the regulatory agency, the Pharmaceutical and Medical Devices Agency (PMDA), and streamlining approval processes. This has significantly reduced the time for the regulatory review of new drugs (Figure 2). Another significant factor has been the introduction in 2010 of the “innovation premium”, which largely protects patented products from price cuts. This has led to a sharp increase in the number of new drug development projects in Japan (Figure 3). Taken together, these policy changes amount to a significant improvement in the environment for innovation, and as a result many more innovative medicines are now available to Japanese patients. Notwithstanding the success in reducing the drug lag, Japan has not stopped there. The revision of the Pharmaceutical Affairs Law, the creation of the Japan Agency for Medical Research and Development (AMED¹) and the *Sakigake* registration package, all indicate a desire to further boost the pro-innovation environment in Japan.

The Japanese government also recognizes the strategic economic importance of the pharmaceutical industry. In February 2013, the Office of Health and Medical Strategy was moved under the

Improved PMDA Review Times
PMDA has nearly eliminated Japan's “drug lag”

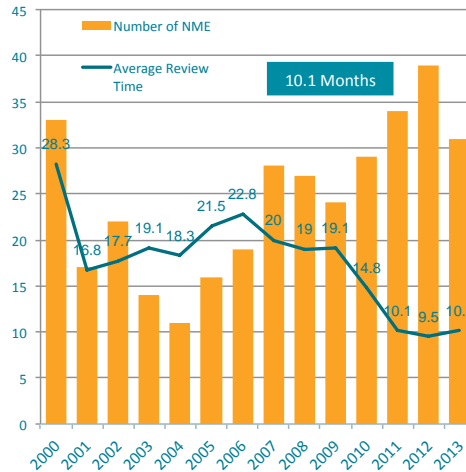


Figure 2. Source: 医薬産業政策研究所. 2014. 日本における新薬の臨床開発と認審査の実績 (No. 63, p. 21).

Increased EFPIA Member Company Drug R&D in Japan

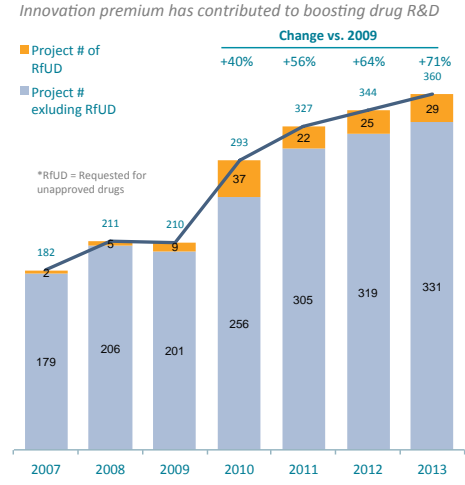


Figure 3. Source: Press release on R&D projects of 15 companies in Japan (n = 15). *RfUD = Requested for unapproved drugs.

direct control of the Chief Cabinet Secretary. Pharmaceuticals and medical devices have been identified as “globally promising industries” that will play a central role in the Abe administration’s economic revitalization and growth strategy.

Access in Japan

Broad, rapid and stable access to medicines is a hallmark of the Japanese healthcare system; patients and physicians have the treatment options they need. Based on EFPIA surveys of waiting times, Japan tops the list, with reimbursement usually following within 60 - 90 days of regulatory approval and immediately for indication extensions. If HTA is applied to these new, innovative products, it has the potential to delay or disrupt access, as it has done in many European markets. Chuijyo estimates that reassessment for CEA would add 3 to 6 months in Japan.²

¹ AMED: Established in April 2015 to pool the public funding to healthcare research from three ministries: MEXT, METI and MHLW.

² Professor Fukuda at Chuijyo meeting of May 27th, 2015.

Europe – Patients W.A.I.T. Indicator

Patients Waiting to Access Innovative Therapies

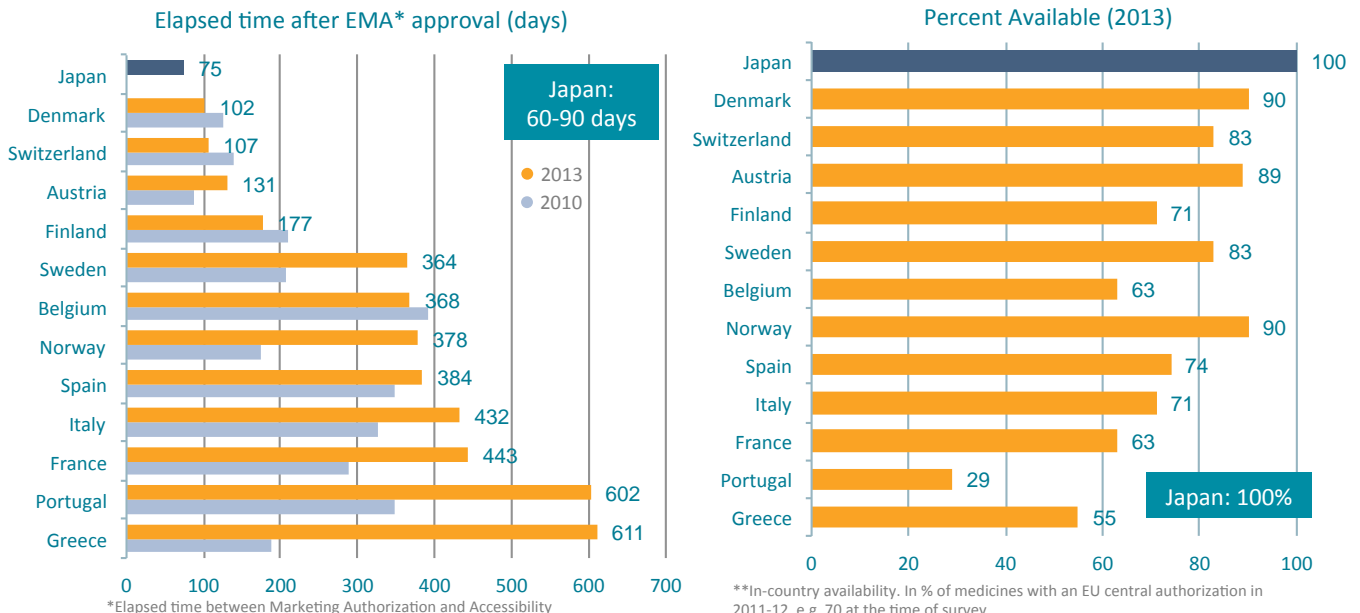


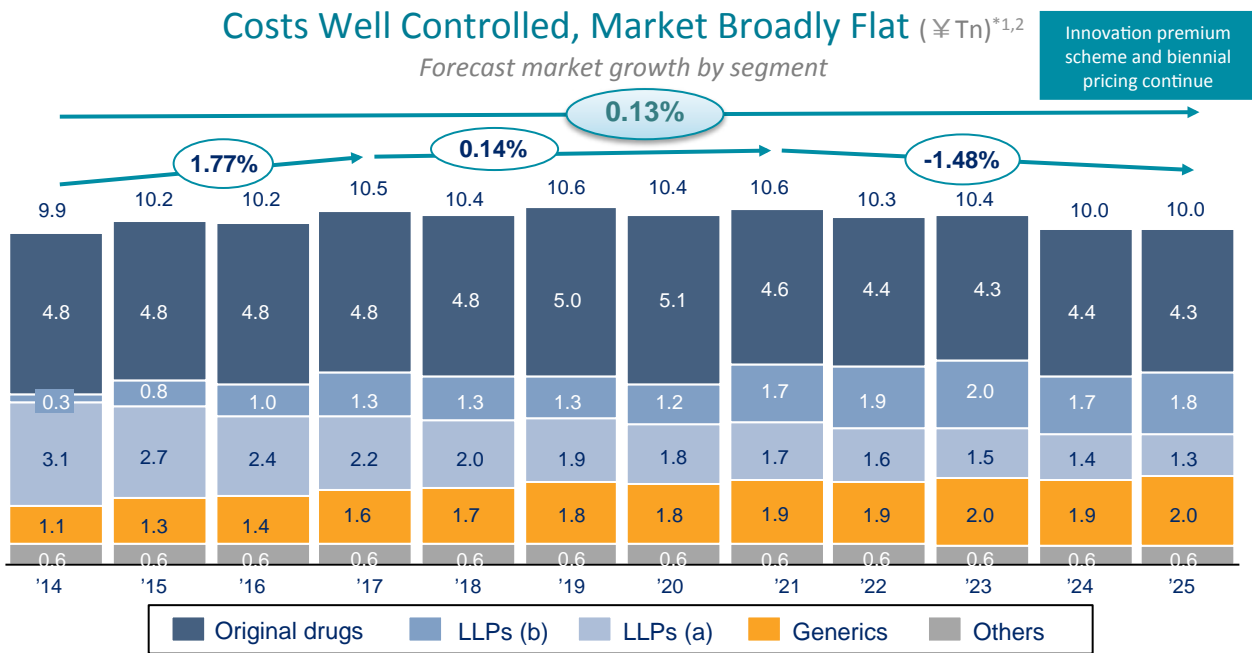
Figure 4. Source: EFPIA annual survey 2010 & 2013. NB: UK and Germany allow access immediately upon marketing authorization, but HTA hurdles—not within the scope of this W.A.I.T. analysis—apply and delay actual access. *EMA: European Medicines Agency.

Pharmaceutical Expenditure Not Driving Healthcare Spending Increases

While healthcare costs overall have increased in recent years, this has been driven mostly by aging and long hospital stays, which have a major impact on the public budget. Conversely, pharmaceutical expenditure in Japan is projected to remain stable over the next decade. A recent study completed by IMS in partnership with EFPIA Japan, modeled Japan's pharmaceutical

market through 2025. The study, recognizing pricing changes that took place in 2014, including scheduled loss of exclusivity after patent expiry and generic use incentives, shows slight market growth over the next 2 or 3 years, leveling off towards 2019 and receding as 2025 approaches.

In 2014, the pharmaceutical market grew by only 1.4% even including the consumption tax increase, and once the impact of the tax change is stripped out, the market actually shrank by 0.9%.



*1 LLPs (a) are long-listed products (LLPs) whose first generic alternative was launched before 2013. LLPs (b) are the other LLPs, whose first generic competitor is launched after 2013.
 *2 Sales are calculated assuming that the 5% consumption tax rate that existed on 1 January 2014 continues throughout the period. This is in order to look at the underlying growth in the market, stripping out the consumption tax effect.

Figure 5. Source: IMS Consulting Group.

Generic promotion providing significant cost savings

The governments' efforts to increase generic uptake in Japan have greatly boosted the generic market share over the past year, and projections based on current policies demonstrate an increased market share through 2025. The expense increase as a result of the innovation premium is more than offset by the increased market share of generics.

Improve the current system as it provides timely access and controls costs well

Japan has created a healthcare system that both controls costs and provides quick and broad access to patients. The efforts of the government to address the drug lag, promote innovation, and increase the generic market share have provided savings and also helped to create an environment conducive to innovation and research.

Therefore, it is very important that any policy decision, such as the introduction of HTA, is made with a full understanding of the impact it will have on the healthcare system. HTA has caused access delays in every market where it has been introduced—Japan should avoid undoing all the progress made in shortening the drug lag by implementing an inappropriate system.

Savings from Generic Promotion Greater than Cost of "Innovation Premium"

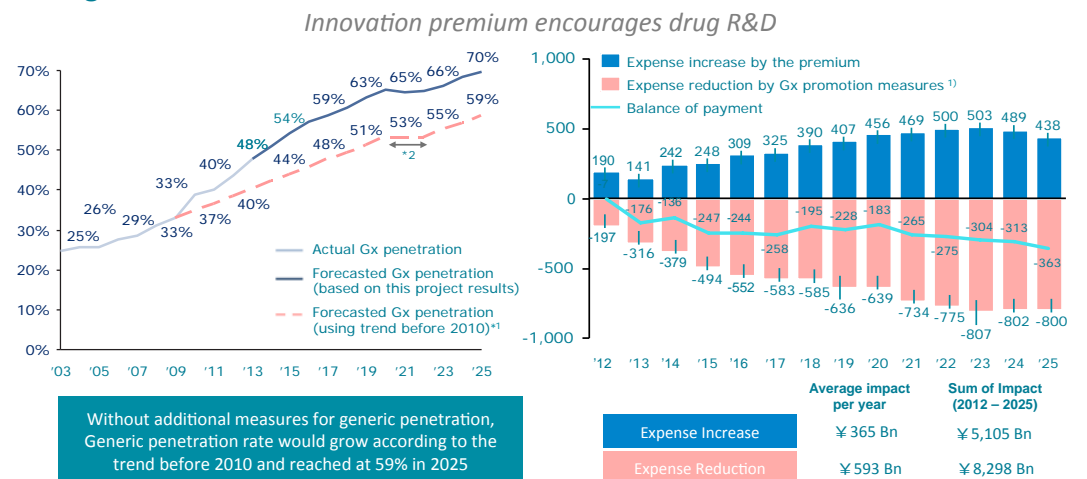


Figure 6. *1 We used Gx penetration trend from 2006 to 2009 *2 We assumed Gx penetration rate will not grow in 2021 and 2022, same as this project calculation result. Source: EFPIA Japan and IMS Joint Simulation Project.

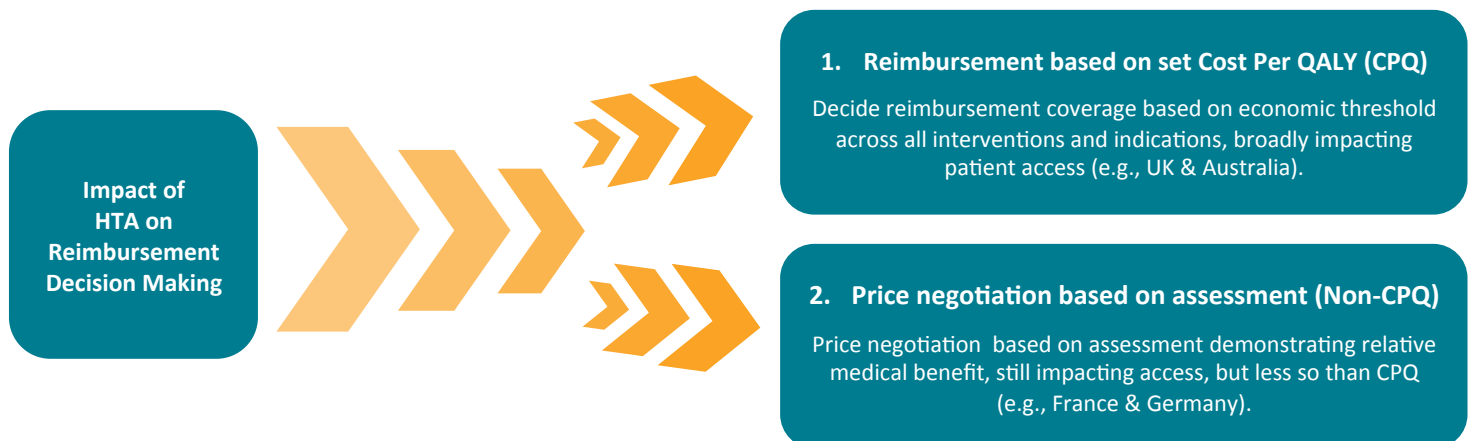
How HTA is Applied Around the World

Unlike Japan, where the price of new drugs and price revisions is set according to a detailed set of rules, some EU countries decide on reimbursement coverage and prices in consideration of Cost-Utility Analysis (CUA or cost per QALY, CPQ) or Cost-Effectiveness Analysis (CEA). The most visible consequences are additional delays and, frequently, the denial of access to many innovative products, an additional level of medical review after regulatory approval, and the creation of a large bureaucracy.

Since its introduction in countries like Australia (1993), Canada (1994) or the UK (1999), HTA has become different from its original intent, e.g., to solve regional differences in reimbursement in the UK and Canada. Recent trends point to HTA being used to support pricing decisions or to restrict access to innovative medicines deemed too expensive for public budgets. In the

closed environment of integrated payer-provider of the US managed care organizations, which track and analyze their own outcomes, HTA is used to support product selection and force their usage, at the expense of choice for prescribers.

Broadly, there are two main approaches to the application of HTA: [1] countries like the UK or Australia (with a centralized national health system) decide reimbursement coverage based on modeling and an economic, monetary threshold across all interventions and indications, while [2] countries like France and Germany (mix of private and public medical practice, similar to Japan) assess and rate the relative medical benefits (Relative Effectiveness Assessments, REA) as a basis for a negotiation of the price.



No country has found the ideal system

No country has found the ideal system and CEA itself has not prevented increases to healthcare costs as a result of aging. Currently, countries are reconsidering their HTA principles and methodologies with renewed emphasis on improving patient access, as there are great inequalities across European countries. One example is the creation of the Cancer Drug Fund in England in 2010.¹ In Scotland, after a review of the HTA process, patients are now specifically asked for their opinion when end-of-life or orphan drugs are rejected by the Scottish Medical Council (SMC), the HTA agency. Additionally, in France, a working group has

been set up in March 2015 to begin review of the current HTA system.

Generally, because all countries experience delays in access, the trend is for Coverage with Evidence Development (CED), a convergence of pharmacovigilance and real-life observation for economic assessment, and for adjustment of price and coverage over time.

¹ NHS England. 2015. The Cancer Drugs Fund. Retrieved from: <http://www.england.nhs.uk/ourwork/pe/cdf/>

HTA in the News

HTA often makes headlines, but not for the reasons it should. HTA agencies in the UK (NICE), Australia and Canada have been the target of numerous protests by patients and physicians where HTA was applied by governments to limit patients' access to new and innovative therapies. While HTA can provide

valuable information to policymakers, it is critical that patients and physicians are part of the decision-making process and that maintaining access continues to be a key government priority.

“Patients protest after kidney drugs rejected [by NICE]”

—The Guardian (England)¹

“NHS set for record £1.75bn surplus as patients protest over [access to] cancer drugs”

—The Telegraph (England)²

“Pancreatic cancer patients to pay \$15,000 or miss out”

“A drug company will stop supplying cut-price treatment for pancreatic cancer after the PBAC rejected a deal to list the medication for subsidy”

—Herald Sun (Australia)³

“Alzheimer’s drugs [access] court challenge”

“The first time a judicial review has been sought on a NICE decision”

—BBC News (England)⁴

1 Patients protest after kidney cancer drugs rejected. (2008 August 27). *The Guardian*. Retrieved from <http://www.theguardian.com/society/2008/aug/27/health.cancer>

2 Smith, R. NHS set for record £1.75bn surplus as patients protest over cancer drugs. (2008 August 27). *The Telegraph*. Retrieved from <http://www.telegraph.co.uk/news/health/2633064/NHS-set-for-record-1.75bn-surplus-as-patients-protest-over-cancer-drugs.html>







3 McArthur, G. Pancreatic cancer patients to pay \$15,000 or miss out. (2014 March 26). *Herald Sun*. Retrieved from <http://www.heraldsun.com.au/news/pancreatic-cancer-patients-to-pay-15000-or-miss-out/story-fni0fiyv-1226865659707>

4 Alzheimer’s drugs court challenge. (2007 June 25). *BBC News*. Retrieved from <http://news.bbc.co.uk/2/hi/health/6230530.stm>

Global Overview of HTA Systems

Where HTA has been introduced, it has taken on a number of forms. The chart below provides a brief overview of the HTA systems in five selected markets: France, Germany, UK, Sweden, and South Korea. Commonalities among all markets are a

negative impact on patient access, limited patient involvement, the creation of a large, expensive bureaucracy, and in some, a lack of transparency. This comparison highlights the need to develop a system contextualized for the Japanese market—addressing the specific needs of patients and the healthcare system.

							
		France	Germany	UK	Sweden	South Korea	Japan
Authority	Organization	HAS	G-BA/IQWiG [†]	NICE (+CHTE)	TLV	HIRA	N/A
	Staff Number	350	300/160 [†]	560	125	2,121	-
	Budget	54 M EUR 7.53 B Yen*	18 M EUR [†] 2.51 B Yen*	£60.8 M 11.64 B Yen*	155.74 M SEK 2.33 B Yen*	324 B KRW 36.25 B Yen*	-
Year of Introduction		2013 UPDATE	2011 AMNOG	1999	2002	2006	-
Impact on Access		Some Impact on Access France & Germany use HTA before price negotiations leading to limited direct impact on access. Still some examples of impact or limited access.		Significant Impact on Access Fixed Cost Per QALY (CPQ) threshold negatively impacts access. Long time to create requested evidence delays launch. Extensive value dossier requirements, and strict CPQ leads to very limited access.			Currently broad access is supported.
Initiation of HTA triggered by growing drug costs		✓	✓	✓	✓	✓	-
Products Chosen for Assessment		Medical Economic Evaluation (MEE) is undertaken for selected products based on healthcare priorities.	All new pharmaceuticals except those that are reference priced. <i>(*Hospital products outside scope of HTA).</i>	Selected products, priorities determined by an academic group through "Horizon Scanning."	All new pharmaceuticals <i>(*Hospital products outside scope of HTA).</i>		-
Decisions Mainly Driven By	CPQ	✗	✗	✓	✓	✓	-
	Non-CPQ (Clinical Effectiveness)	✓	✓	✗	✗	✗	-
Patient Input in HTA Process		Little/No Involvement Patients do not have a regular role in the evaluation process.	Some Involvement Limited input by patients (e.g., patient org. & societies).	Some Involvement Limited, but formally well-structured. <i>Scotland's SMC allows for significant patient involvement.</i>	Little/No Involvement Patients do not have a regular role in the evaluation process, nor a vote in the decision.		-
Transparency		The process of conducting MEE is clear, but lack of transparency of how MEE impacts pricing decisions.	Clear criteria and methodologies are communicated to stakeholders before an HTA is conducted. Subsequent price negotiation lacks transparency.	All guidance is to be published and the evidence on which decision was made is available to the company.	The process is very unpredictable and not transparent. Only a shorter summary of the final report is published.	Lack of transparency in HTA process and its impact on pricing.	Transparency and collaboration have been very limited. There has not been extensive dialogue with industry, patients, or other stakeholders.
Notes		MEEs undertaken for new drugs are reassessed after 5 years.	Product enters the market with free pricing until HTA is carried out. Process takes about 12 months until pricing. <i>*Methodology often applied so strictly that many assessments result in "no conclusion." *Lean dossier for orphan drugs</i>	The UK has introduced patient access schemes, such as Cancer Drug Fund, acknowledging the negative impact HTA has on access.	High costs to develop Health Economic models which take a significant amount of time. Societal aspects and costs, e.g., indirect costs are usually considered.	-	Japan has yet to identify how HTA/CEA adds value to Japan's pricing system and biennial pricing revisions.

*Based on June 2015 exchange rates.

Impact of HTA on Cancer Treatment

HTA can, and has, negatively impacted access within particular therapeutic areas—particularly oncology. Patients in countries that apply a strict cost-per QALY (CPQ) measure have restricted access to innovative medicines and lower overall cancer survival rates than patients from countries that are non-CPQ. In 2014, IMS published a study that looked at the impact of cost-per-QALY reimbursement criteria on access to cancer drugs.*

The study made the following primary findings:¹

- In the five CPQ countries examined (England, Scotland, Sweden, Canada, & Australia), patients have less access to new cancer drugs than patients in the five non-CPQ countries (U.S., France, Germany, Italy, & Spain).
- In these five CPQ countries, fewer new cancer drugs are reimbursed; reimbursement decisions take longer; and new cancer drugs have historically been adopted more slowly and, in the longer term, at lower rates.
- CPQ analyses are subject to many uncertainties and inconsistencies due to the nature of the variables used and their interpretation.

- Some data show lower rates of both cancer drug spending and cancer survival in countries using CPQ methodologies, particularly the U.K.
- CPQ countries do not necessarily spend less overall on cancer, but they may achieve less for patients.

*Nine Products Reviewed: Afinitor, Halaven (eribulin), Votrient (pazopanib), Jevtana (cabazitaxel), Zytiga (abiraterone acetate), Yervoy (ipilimumab), Zelboraf (vemurafinib), Azerra (ofatumumab), and Xgeva (denosumab).

Fewer new cancer drugs are reimbursed

While both CPQ and non-CPQ countries reimburse most non-cancer products, CPQ countries reimburse fewer cancer therapies resulting in limited access for their patients. Specifically, four of the five CPQ countries surveyed deny reimbursement of three of the nine cancer drugs reviewed—markedly worse than in non-CPQ countries.

In particular, recent reports from the NHS of the U.K., have found that overall survival rates of cancer patients in the U.K. are lagging 10 years behind the rest of Europe.^{2 3} While there are a number of factors that contribute to this disparity, including disease awareness and early diagnosis, uneven and low access has also been identified as a challenge patients face.

1 IMS Institute for Healthcare Informatics. December 2014. *Impact of cost-per-QALY reimbursement criteria on access to cancer drugs.*

2 NHS Choices. 5 December 2013. UK cancer survival rates below European average. Retrieved from <http://www.nhs.uk/news/2013/12December/Pages/UK-cancer-survival-rates-below-European-average.aspx>
 3 Foot, Harrison, Tony. June 2011. How to improve cancer survival: explaining England's relatively poor rates. The Kings Fund.

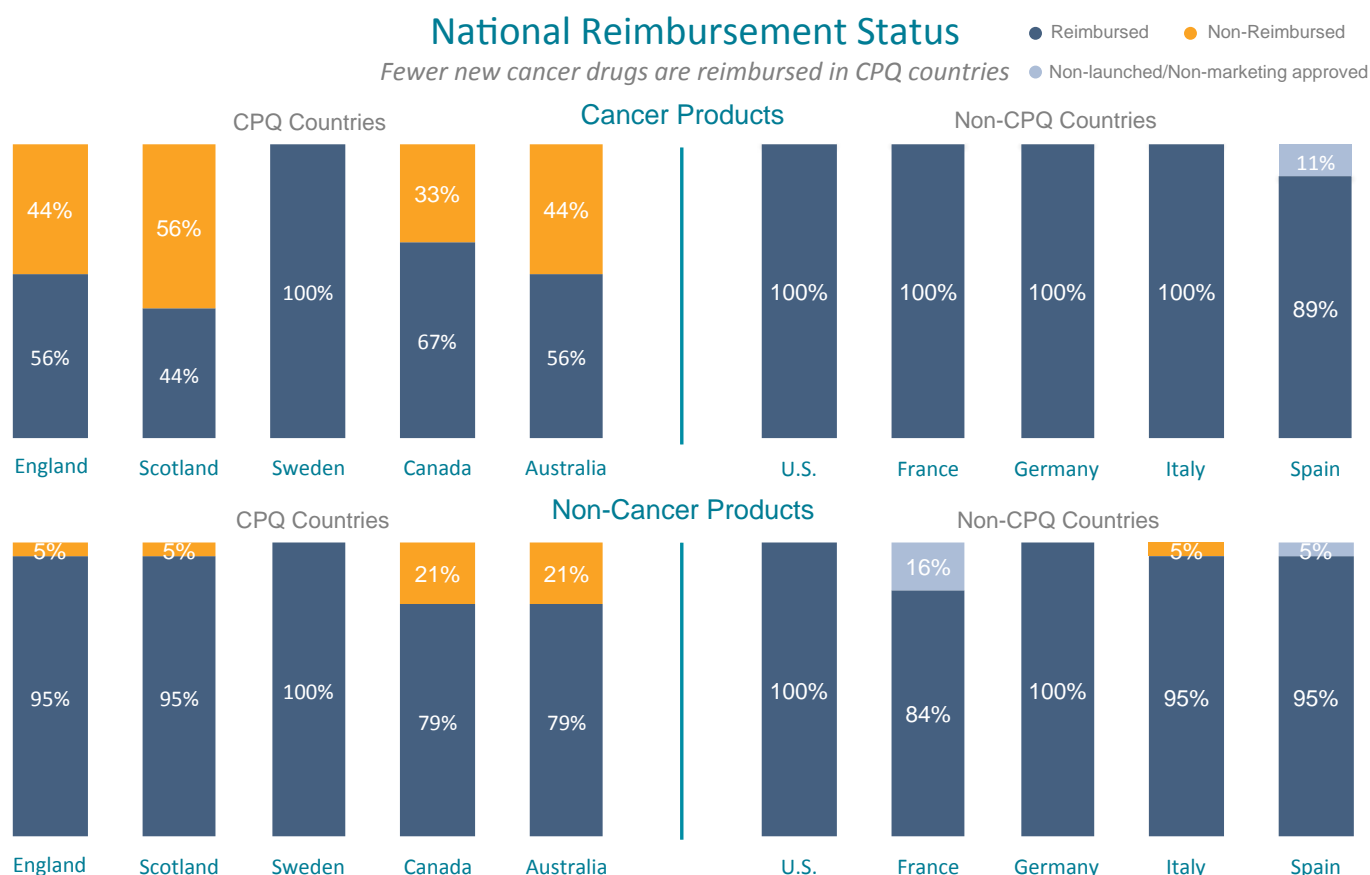


Figure 7. Source: IMS Institute for Healthcare Informatics. December 2014. *Impact of cost-per-QALY reimbursement criteria on access to cancer drugs.*

*In Sweden, reimbursement at the county level was considered, as national-level reimbursement decisions are not made for hospital drugs. Fig. 19 lists considerations for other markets. Sources: National Institute for Health and Care Excellence (NICE) (England), Scottish Medicines Consortium (SMC) (Scotland), The Dental and Pharmaceutical Benefits Agency (TLV) (Sweden), Reimbursement status listed for Ontario, British-Columbia and Alberta (Canada), Pharmaceutical Benefits Scheme (PBS) (Australia), Base des Médicaments et Informations Tarifaires, eVidal (France), Federal Joint Committee (GBA) (Germany), Italian Drug Agency (AIFA), paginesanitaria (Italy), BotPLUS (Spain)

EFPIA's Position on HTA in Japan

Japan's healthcare system delivers excellent outcomes and an outstanding level of access while simultaneously controlling costs. As such, EFPIA recommends that the first priority of MHLW should be the progressive adaptation and implementation of policy changes within Japan's current healthcare system, e.g., NHI pricing, technical fees, PMS and increasingly on prevention and care continuum through referrals, medical guidelines, integrated care, etc. EFPIA believes that placing a priority on further improvements to the current system is most likely to result in long-term cost containment together with continued broad access to innovative medical treatments in Japan.

Analysis across multiple markets where HTA has been applied to new drugs reveals that its inappropriate use has had a significant negative impact on access, particularly to cancer drugs, for patients and physicians. It is critical, therefore, that Japan not simply adopt methodologies developed for use within foreign healthcare systems that differ drastically from Japan's. EFPIA strongly recommends that in considering the possible adoption of HTA that MHLW harness the intellectual resources of health economists, industry, physicians, and patients to assist policy-makers in the task of identifying methodologies specifically tailored to Japan's unique needs. For example, assessing new

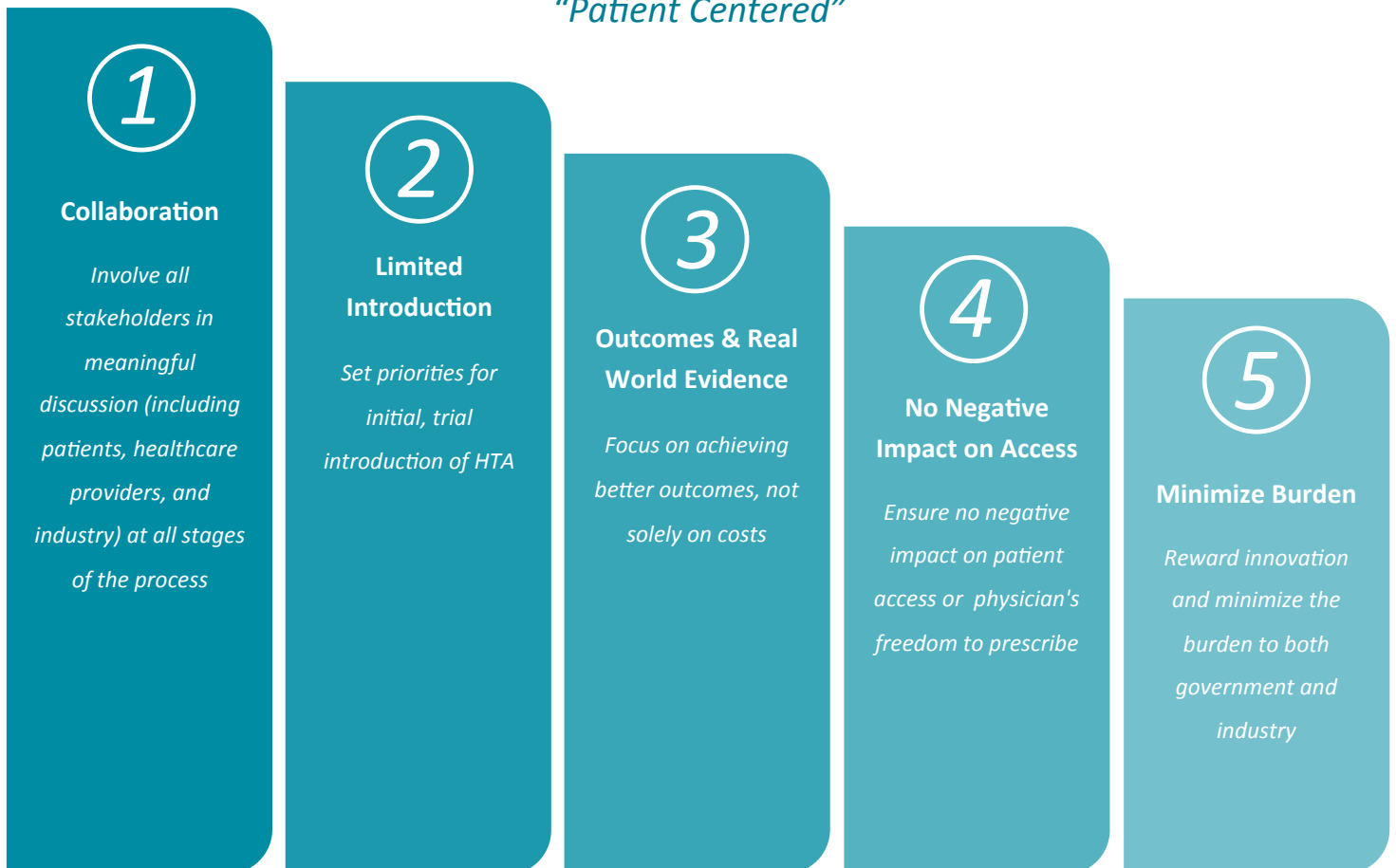
drugs always requires making assumptions and modeling outcomes due to the lack of real-life usage in the clinical setting. This often results in increased uncertainty and may adversely impact decision-making. As such, EFPIA recommends that any HTA system adopted by Japan be applied solely to marketed products at the time of re-examination or re-pricing as real-life drug usage and performance post-launch can be combined, as appropriate, with clinical data and modeling to provide a more comprehensive and accurate assessment of a therapy's actual clinical usage and value.

Experience in other countries demonstrates that HTA systems often impose significant burdens on industry and governments. MHLW must keep in mind that an excessively burdensome HTA system will negatively impact industry's ability to invest in R&D in Japan. EFPIA therefore recommends that prior to any decision to adopt HTA that MHLW establish a dialogue with industry and other stakeholders to assess data collection requirements, assessment measures, costs and other factors with the goal of developing pragmatic and creative solutions that minimize burden.

Specifically, EFPIA suggests the following five principles guide the discussion and evolution of HTA in Japan:

Five Principles to Guide HTA in Japan

"Patient Centered"



Five Principles to Guide HTA in Japan

1 Collaboration

Involve all stakeholders in meaningful discussion (including patients, healthcare providers, and industry) at all stages of the process

- EFPIA Japan believes that the understanding and involvement of patients in determining the impact of therapy on their health and quality of life is critical for sound policy-making. Involving patients can lead to more subjects involved, better data and better outcomes, and also give patients a better understanding of their own responsibility towards care, prevention and the use of scarce resources.¹
- As HTA can negatively impact access, healthcare providers and medical societies should be a key part of the discussion.
- Ensure transparency in the HTA process, including the selection criteria for reviewed products, the analysis methodology, and the use of the analysis in any pricing decisions.
- EFPIA Japan recommends that MHLW and Chuikyo involve the industry much more in the debate, given industry's extensive experience of HTA in other markets.

2 Limited Introduction

Set priorities for initial, trial introduction of HTA

- The effort and resources required by the introduction of HTA, even if limited to CEA, are considerable. The cost and time required to build capabilities and infrastructure should not be underestimated.
- Existing data collection systems, such as post-marketing surveillance and pharmacovigilance or disease registries, should be customized to generate real-life data sets during the life cycle of drugs.
- HTA is better suited to products already on the market, not at new products about to be launched for which no experience and only limited data are available.
- The application of HTA should remain flexible, recognizing therapeutic area differences and exempting specific classes (e.g., orphan drugs, oncology, unmet medical need, etc.)

¹ HTAi. (2015). HTA Resources for Involving Patients & Citizens. Retrieved from <http://www.htai.org/interest-sub-groups/patient-and-citizen-involvement/pcisg-resources/hta-resources.html>

- HTA could be used to assess the most effective treatment paths for a given disease, looking at all the treatments required and not only the medicines. In doing so, such a “Macro-HTA” approach could deliver better outcomes for patients.
- To improve outcomes, it makes more sense to combine results from randomized control trials (RCT) with other data sources and real world evidence (RWE), capturing how diseases are actually treated in real clinical practice, rather than limiting the analysis to the artificial environment of a regulatory clinical trial.

Outcomes & Real World Evidence

3

Focus on achieving better outcomes, not solely on costs

- Any decision to implement HTA on a trial basis in April 2016 must not reverse the great progress Japan has made in reducing the drug lag, shortening the regulatory review period for new drugs and new indications, and ensuring access to innovation.
- HTA should not restrict physician choice. Physicians should retain the authority to select the best therapy for their patients.

No Impact on Access

4

Ensure no negative impact on patient access or physician's freedom to prescribe

- Any trial introduction of HTA should impose the minimal burden necessary on both government and industry by avoiding unnecessary costs and creation of bureaucracy. These resources would be better spent on research and improving outcomes for patients.
- To continue to attract innovation, Japan needs to offer companies a predictable and attractive environment. To do this, flexibility will likely be required, together with a recognition of the challenges of data collection. Pragmatic and creative solutions may be necessary.
- The types of data required and the assessment measures used should be agreed through industry and government dialogue.

Minimize Burden

5

Reward innovation and minimize the burden to both government and industry

Further Considerations: *Use HTA to guide treatment and policy-making, not set prices or restrict access*

Rather than using HTA to determine pricing and reimbursement decisions for individual technologies, where Japan already has an effective NHI price system, resources could be spent

more meaningfully to address broader issues such as disease prevention, development of disease management programs, and healthcare delivery system planning. It is in these areas that the greatest opportunities for improvements lie, as suggested in the 2014 OECD and World Bank Reports on Healthcare in Japan (see page 6).

EFPIA Viewpoint: HTA Application in Select Markets and Implications for Japan

EFPIA member companies have significant experience in the application of HTA in European markets, and are familiar with the challenges that arise as a result of such systems.

Specifically, EFPIA suggests the following five principles guide the evolution and discussion of HTA in Japan:

1. Involve all stakeholders in meaningful discussion (including patients, healthcare providers, and industry) at all stages of the process
2. Set priorities for initial, trial introduction of HTA
3. Focus on achieving better outcomes, not solely on costs
4. Ensure no negative impact on patient access or physician's freedom to prescribe
5. Reward innovation and minimize the burden to both government and industry

HTA delays and may prevent access to innovative therapies

Japanese citizens have broad access to medicines, as new therapies progress relatively quickly from regulatory approval to reimbursement. Based on EFPIA surveys, Japan tops the list, with reimbursement usually following within 60-90 days of regulatory approval.

The decision to implement CEA on a trial basis in April 2016 must not reverse the progress made in reducing the drug lag.

Europe – Patients W.A.I.T. Indicator

Patients Waiting to Access Innovative Therapies

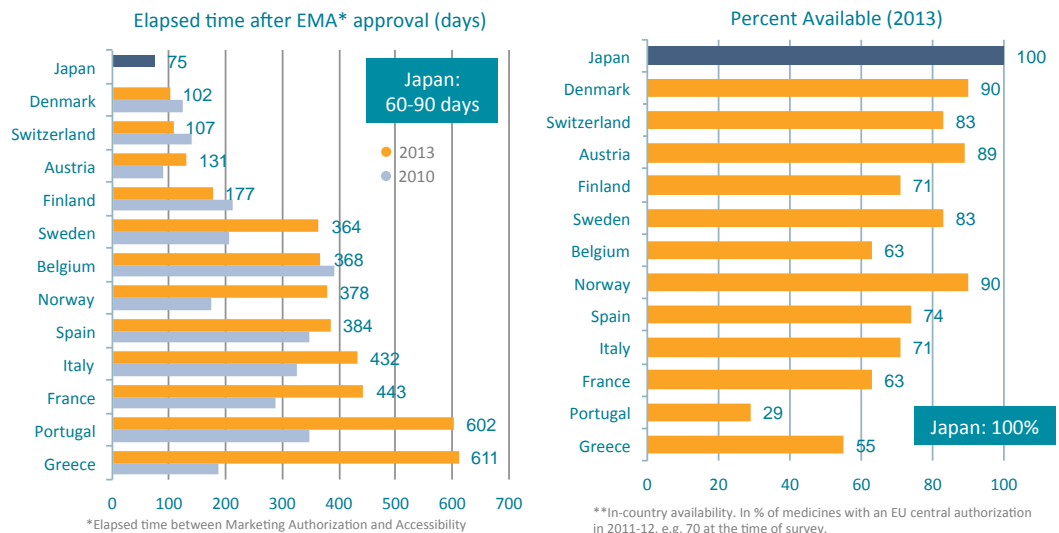


Figure 4. Source: EFPIA annual survey 2010 & 2013. NB: UK and Germany allow access immediately upon marketing authorization, but HTA hurdles—not within the scope of this W.A.I.T. analysis—apply and delay actual access. *EMA: European Medicines Agency.

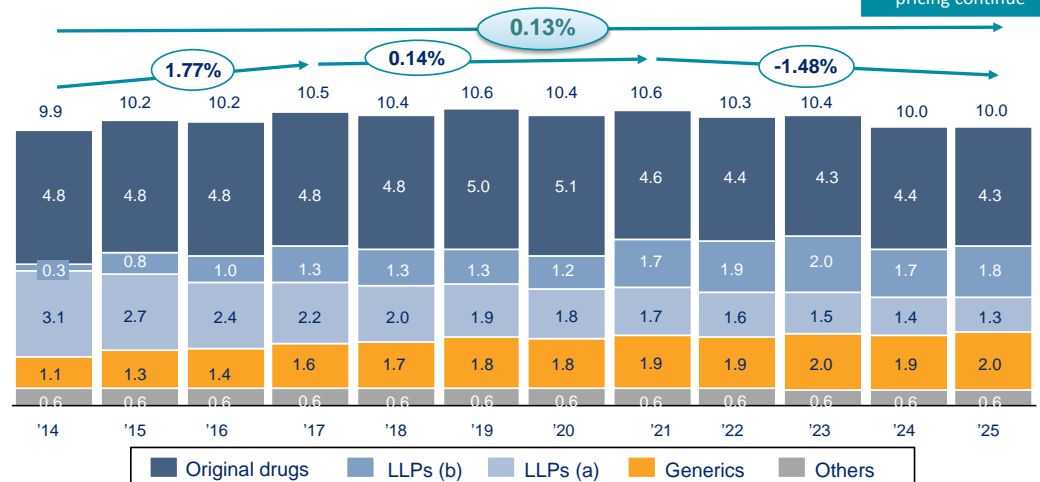
Costs of pharmaceuticals are already well-controlled by the current pricing scheme and generic use incentives

A recent IMS study (Fig. 5), which recognizes pricing changes that took place in 2014, including scheduled loss of exclusivity after patent expiry and generic use incentives, shows broadly flat pharmaceutical market growth over the next decade.

Costs Well Controlled, Market Broadly Flat (¥ Tn)^{*1,2}

Forecast market growth by segment

Innovation premium scheme and biennial pricing continue



*1 LLPs (a) are long-listed products (LLPs) whose first generic alternative was launched before 2013. LLPs (b) are the other LLPs, whose first generic competitor is launched after 2013.
 *2 Sales are calculated assuming that the 5% consumption tax rate that existed on 1 January 2014 continues throughout the period. This is in order to look at the underlying growth in the market, stripping out the consumption tax effect.

Figure 5. Source: IMS Consulting Group.