European Federation of Pharmaceutical Industries and Associations

Cost-Effectiveness Analysis (CEA) in Japan: Basic Understanding and Implications for Japan

"Putting the patients at the center of healthcare

EFPIA
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Full scale implementation of Cost-Effectiveness Analysis in 2019

Cost-effectiveness analysis (CEA) is a mechanism to calculate the appropriate price for pharmaceuticals after reimbursement decision has been made. Japan's "Central Social Insurance Medical Council (Chuikyo)", an advisory body of the Ministry of Health, Labor and Welfare (MHLW) is deliberating CEA with a view to full scale introduction in FY2019. The council commenced the debate on CEA in 2011 and introduced a pilot program from 2016 on selected products[1]. The trial included novel therapies such as Opdivo, an anticancer drug, where the discoverers were awarded the Nobel Prize in Physiology or Medicine in 2018. A decision on the implementation of CEA is expected in FY2018.

What is Health Technology Assessment?

Health technology assessment (HTA) is a scientific tool used for making policy decisions[2]. The International Society for the Promotion of Health Technology Assessment (HTAi) defines HTA as a multidisciplinary field that addresses the clinical, economic, organizational, social, legal, and ethical impacts of a health technology whilst considering its specific healthcare context as well as available alternatives.

There is need for a transparent, systematic, and rigorous CEA processes and methods used to evaluate the value of new and conventional pharmaceuticals and medical equipment.

For example, suppose a new breakthrough anticancer agent B becomes available in cancer therapy for which anticancer agent A was conventionally used.

When the anticancer agent is switched from A to B, CEA is evaluated from a combination of a cost and effect perspective. Cost refers to the difference existing from medical expenses and the effect refers to the time patients live more healthily with an improved quality of life (QoL). An incremental cost effectiveness ratio (ICER), an assessment index, is calculated to compare differences for each increment if/when A is switched to B for increase in cost and effect.

ICERs uses the unit quality-adjusted life year (QALY) - survival year x quality of life (QoL) - to demonstrate spuriously the pharmaceutical value in the form of "XXXyen/QALY" on how much it costs additionally to achieve at full health for a year using the drug.

Challenges in Cost-Effectiveness Analysis

Demonstrating the value pharmaceuticals provide is not as simple as displaying mechanically ICER or mathematical formulas. For example, to judge that CEA is not good for costs in cancer treatment exceeding XXXyen the input from citizens about "what medical care should be" is essential.

Moreover, CEA for drugs a difficult problem exists on how to solve uncertainties such as range for ICER and drugs selected for comparison.

The ICER is used to measure the effect of the drug and varies greatly depending on the difference in targeted patient group, evaluation method for efficacy. When there are multiple studies for reference to decide ICER it is difficult to set it to one[3].

The adjustment of premium rate by ICER for drug pricing is being considered for the current debating system. A standard threshold such as 5million yen/QALY is currently set to adjust the premium rate. A 5million yen/QALY was set as the threshold amount based on prior research investigating the amount for willingness to pay by people on "How much can an individual will pay for health in 1 year?" On the other hand, health economists believe price setting is difficult in a price set of 4-6million yen/QALY for ICER range[4].

Results from CEA will change by comparators with respect to drugs selected for comparison. However, within CEA guidelines the drug's comparators or its method for evaluation has not been decided[3]. Even at the trial program problems related to this are cited as issues pending decision.

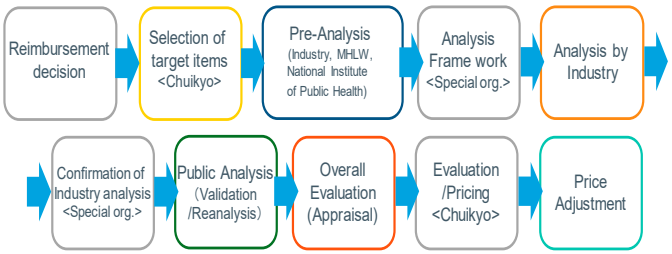
Within the current CEA process (Fig 1.) stakeholder participation is limited and contrary to other countries there is no direct involvement of patients. Systems for CEA such as in the UK the structure is set to reflect opinions of patient groups and to improve patient access to pharmaceuticals by giving patients an opportunity to express their opinion.

Furthermore, the debate in Japan for full scale implementation has a negative influence on "evaluation for innovation"[5]. Innovation of new pharmaceutical such as in UK is also subject to evaluation for social and ethical considerations that cannot be assessed by ICERs alone.

Overlap of Pricing and Reimbursement System

In Japan there has been already a standard drug pricing system which will overlap with the system for CEA. For example, during new drug pricing, a rule (similar efficacy comparison method) in the price system states to add the premium to the evaluation for efficacy etc. compared to similar existing drugs. This is said to be a drug pricing method based on a concept like HTA. At the same time, with full scale implementation under debate, a system of CEA based on such rules for the purpose to adjust the drug price afterwards will result in an "overlap of HTA".

Figure 1: Flow of CEA for full scale implemenation[6]



1. Isao K 2016 HTA Workbook Application in clinical, policy, and business application
2. Mie A 2013 Global overview and challenges in Health Technology Assessment (HTA) JPMA News Letter No.153
3. Takeru S 2013 A commentary on "Guideline for economic evaluation of healthcare technologies in Japan" Vol.62 No.6 p590-598
4. Chuikyo 11th Assembly (2018Nov7) https://www.mhlw.go.jp/stf/shingi2/0000211220_00002.html
5. Chuikyo Assembly (2017Aug9) https://www.mhlw.go.jp/stf/shingi2/0000174273.html
6. Chuikyo 12th Assembly (2018Nov21) https://www.mhlw.go.jp/stf/shingi2/0000211220_00003.html

Global Overview of HTA Systems

Japan is still in its early days in HTA and much can be adopted from countries with full implementation whereby various challenges have been met. Whilst transparency of the system is still low in some countries, common issues such as adverse effects on patient access and restricted patient participation in HTA exists in each country. (Fig 2).

Countries such as UK focusing on health economics assessment have experienced restricted patient access due to reimbursement decision of a new pharmaceuticals being made based on HTA; causing a societal problem[2]. An example has been the delay in the introduction of a new breast cancer drug in UK[7].

In principle, all pharmaceuticals authorized for marketing in Japan are subject to reimbursement in accordance with the public health insurance system for the whole nation. Currently the Chuikyo is debating on the full implementation of CEA and has confirmed that it will not be used for reimbursement decision[8].

Learning from other countries it is recommended Japan to incorporate a system which includes unrestricted patient access, patient participation in policy decision processes from all stakeholders, and a detailed and evidence-defined transparent system for CEA. It is vital to design a system capable of evaluating the total value of pharmaceuticals and not excessively dependent entirely on ICER whilst maintaining the balance between patient needs and national health insurance system.

Figure 2: Global overview of HTA

		France	Germany	UK	Sweden	South Korea
Authority	Organization	HAS	G-BA/IQWiG	NICE (+CHTE)	TLV	HIRA
	Staff Number	400	120/160	613	125	20
	Budget	51M Euro 6.53B Yen	40M Euro (G-BA) 5.14B Yen (G-BA)	54.7M Pound 7.69B Yen	155.74M Krona 1.95B Yen	1.3B Won 128M Yen
Year of Introduction		2013	2011	1999	2002	2006
Impact on Access		Slight	Slight (Evaluation method is unclear with emergence of companies that do not sell new drugs)	Moderate (Due to price reduction of pharmaceuticals by CEA companies put off sales and reimbursement use with limited patient access)	Moderate (Patient access is restricted due to massive and rigorous paperwork for HTA which are complicated for companies to prepare)	Severe (Delay in review and process due to use in reimbursement and price setting. Insufficient economic valuation hinders business development incentives)
Products Chosen for Assessment		Pharmaceutical products with large financing	Nearly all new pharmaceuticals (Hospital products outside scope)	Pharmaceuticals selected by the government (both new and existing drugs)	All new pharmaceuticals and existing drugs are selected individually	All new pharmaceuticals
Patient Participation in HTA Process		None	Little involvement	Little involvement (Process of expressing opinions of patients and patients' families specified by the guidelines)	Little involvement	None
Transparency		Average (Committee on transparency with meetings held every two weeks)	Low (Problems in CEA and intermediate evaluation process are not published with final report released late)	High (Annotations on all intermediate results and evaluations are released for each process)	Low (The entire process is not been published and a short summary is released at the end of the process)	Very low (Inadequate and uncertain economic evaluation)

7. The Telegraph (2016) https://www.telegraph.co.uk/news/2016/11/03/joy-as-first-breast-cancer-drug-approved-for-widespread-use-in-t/
8. Chuikyo Council 41st Assembly (2017June28) https://www.mhlw.go.jp/stf/shingi2/0000169311.html

EFPIA Viewpoint – Four Principles of CEA

The European Federation of Pharmaceutical Industries and Associations (EFPIA) has significant experience in the application of HTA in European markets. EFPIA suggests the following four principles for CEA system in Japan.

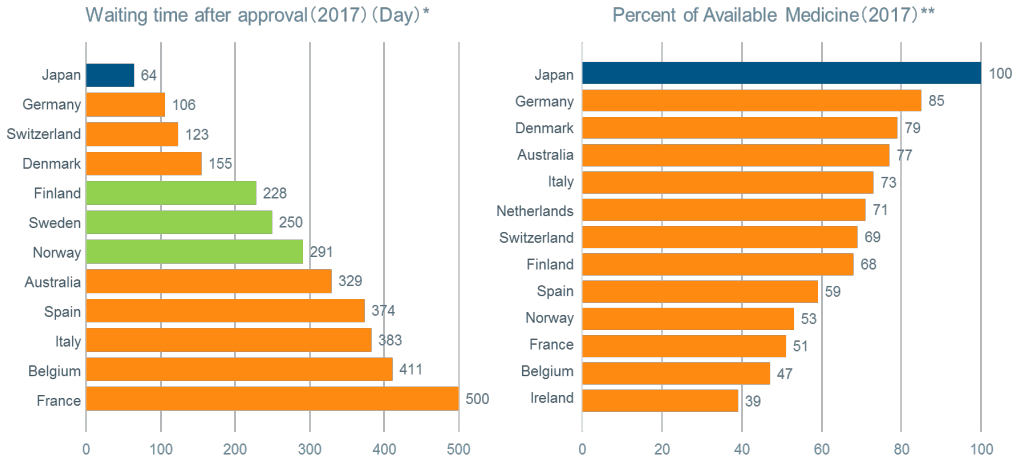
1. Should not be used to reimbursement determination in order to protect patients' access
2. CEA should be used as a complementary tool for the system of drug pricing and reimbursement
3. Evaluate ethical and social value of pharmaceuticals from a long-term perspective
4. Involve all stakeholders in comprehensive evaluation to secure transparency

Drug lag exacerbates patient access

A major cause of drug lag – a delay in making drugs available for patient access in a country – is drugs approved in other countries but not permitted for Japan. The problem has started to resolve in recent years. From an EFPIA survey, it is evident that Japan has the shortest time for patients to access treatments after marketing authorization (Fig. 3).
However, a CEA system used to decide drug pricing and reimbursement will again give rise to drug lag in future.

Figure 3: Europe & Japan – Patients W.A.I.T. Indicator

Patients Waiting to Access Innovative Drugs



Source: EFPIA Market Access Delays Analysis (2018)

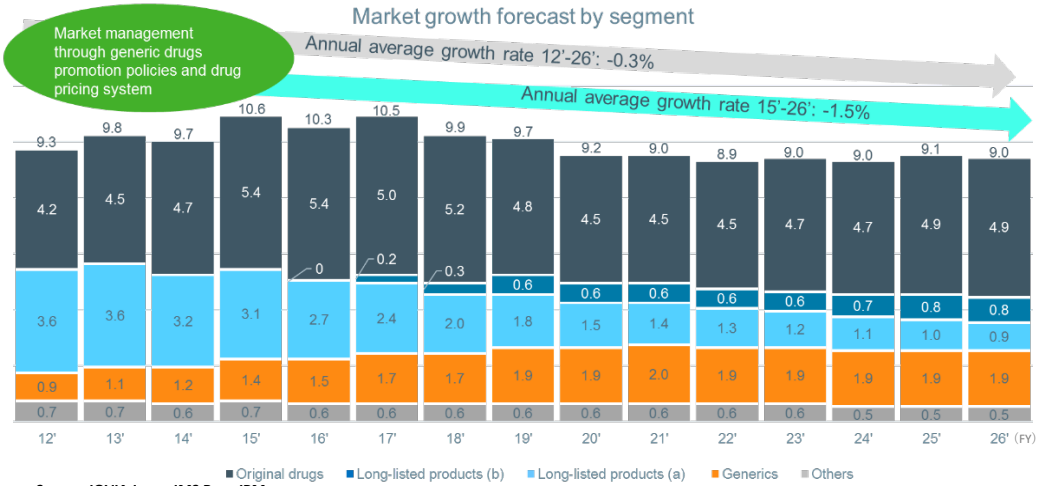
* Some products are not covered by the general reimbursement scheme and so the zero-delay is artificially declining the average.
In France, some innovative products without competitors can be made available prior to market authorisation under the system of Temporary Authorisations. As there are not taken into account in analysis, the average for France is higher than in reality.
The average time between marketing authorisation and patient access, measured by the number of days elapsing from the date of EU marketing authorisation (or effective marketing authorisation in non-European Economic Area countries) to the day of completion of post-marketing authorisaion administrative processes.
Fundamentally the "waiting time" in Japan is 60 days and as only the timing of coverage by reimbursement for price revision is 90 days, the weighted average of these values are used in this analysis.

**The rate of availability, measured by the number of medicines available to patients. For most countries, this is the point at which product gains access to the reimbursement list.

Adequate management of drug expenses

Drug costs in Japan are managed adequately by promotion policies of inexpensive generic drugs due to patent expiration and current effective pricing system. A recent study by EFPIA and IQVIA revealed that costs are managed appropriately (Fig 4). Furthermore, growth in the pharmaceutical market is projected as unchanged until 2026 and no sharp cost increase is forecasted.

Figure4: Adequate management of drug expenses and the annual average growth rate is forecasted to be -1.5% (1T yen unit) *1,2



Source: IQVIA Japan IMS Base JPM

*1: In Fig. 4, Long-listed products (LLPs) are products whose first generic alternative was launched. LLPs (a) products were launched before 2016; LLPs (b) are the other LLPs, launched/scheduled to be launched after 2017.

*2: Assumption of requirements such as continuing price maintenance premium, achievement of 80% generic drugs, and annual price revision of products with large divergence rate for long-listed and generic products.