The Evolution of HTA and Its Impact on Drug Prices in Japan

Content for this article was contributed by the EVERSANA Asia Pacific team.

Health Technology Assessment status in Japan

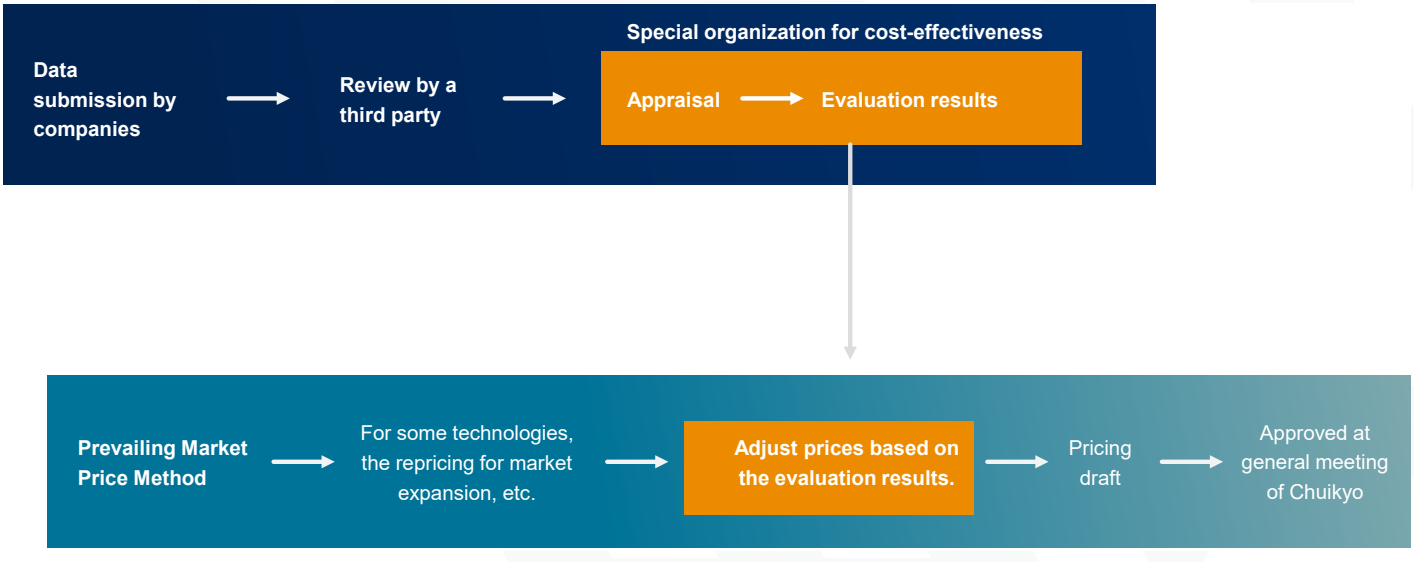
Health technology assessments (HTAs) are increasingly used worldwide to assess the clinical and economic impact of drug treatments and technologies, inform health policy, and guide drug pricing and reimbursement. In Japan, HTA occurs after the debut of a product and when companies enter the system, whereas in the UK HTA is scheduled to begin before the launch of the product. The purpose of using HTA in Japan is to adjust a portion of the price premium and complement current pricing rules. The reimbursement price to be applied nationally in Japan is determined by the Ministry of Health, Labor, and Welfare (MHLW) and approved by the Central Social Insurance Medical Council (Chiyo), with limited opportunity for input from manufacturers.

Following discussions, careful contemplation, and a three-year HTA pilot from 2016-2019 (Figure 1), the Japanese government launched a new version of its HTA system: cost-effectiveness assessment (CEA). As of April 2019, new and existing reimbursed medicines may be subject to a CEA. The results of these assessments may be used to adjust the National Health Insurance reimbursement price of a drug post-launch.

Drug Price and HTA Involvement

Japan's HTA is not applied either to set the initial listed price for a newly approved drug, or for deciding whether it should be reimbursed. CEA has been used to inform price adjustments of healthcare technologies. To implement full scale cost effectiveness evaluation, a new unit, the Center for Outcomes Research and Economic Evaluation for Health (CORE2-Health or C2H), was established in 2018 at the National Institute of Public Health in collaboration with the Chuikyo. HTA in Japan is used for price adjustments of financially impactful drugs. Those drugs are subject to CEA, which is expected to take ~18 months, and price adjustments depend on the CEA result. Japan HTA relies on ICER (incremental cost-effectiveness ratio) values. The system does not sufficiently adjust for factors such as disease burden and severity and societal impact. The price adjustment rate is based on ICER thresholds, as defined by the MHLW.

Figure 1: Process in pilot program



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The product selection criteria identify newly listed products with a peak sales forecast of over ¥10 billion (~US $92 million) or ¥5 billion to ¥10 billion annual sales and already listed products with ¥100 billion in peak sales or significantly high prices. The selection criteria outlined by MHLW are described in Table 1.

Table 1: Selection criteria in a cost-effectiveness evaluation

CLASSIFICATION	CATEGORY	SELECTION CRITERIA
Newly listed products* (meaning listed on health insurance after formal implementation)	**H1†**	Estimated peak annual sales are ¥10 billion or more
	H2†,‡	Estimated peak annual sales are between ¥5 billion and ¥10 billion
	H3	Products with notably high prices§ Products requiring reevaluation because robust new evidence with a major effect on evaluation has been discovered after completion of cost-effectiveness evaluation
Already listed products¶ (meaning listed before formal implementation)	**H4**	Products with annual sales of ¥100 billion or greater Products with notably high prices§ Products requiring reevaluation because robust new evidence with a major effect on evaluation has been discovered after the completion of cost-effectiveness evaluation
Similar products	**H5**	Products whose prices are calculated comparatively against those categorized in the H1 to H4 classifications

*Products with premiums in the similar efficacy (category) comparison method, or products with premiums or disclosure rates of 50% in the cost calculation method are prerequisite conditions for the targets of scope in the cost-effectiveness evaluation.
†Even if a product does not meet the selection criteria in terms of estimated peak sales at the time of listing, it will be sorted as falling into a particular classification if the annual market size exceeds the criteria due to market expansion. In this case, the product will be sorted into the H1 or H2 classifications according to their annual market size.
‡Products of H2 classification are initially chosen as candidate products for evaluation; they are subsequently selected as targets.
§Notably high price is not defined explicitly, but at least a product whose unit price is JPY a few million or higher is considered to meet this criterion.
¶Regardless of the pricing methods, products with annual sales of ¥100 billion or more owing to market expansion, or products with notably high unit prices, are selected as the scope of target in the cost-effectiveness evaluation, provided that the products have premiums ("H4 classification").

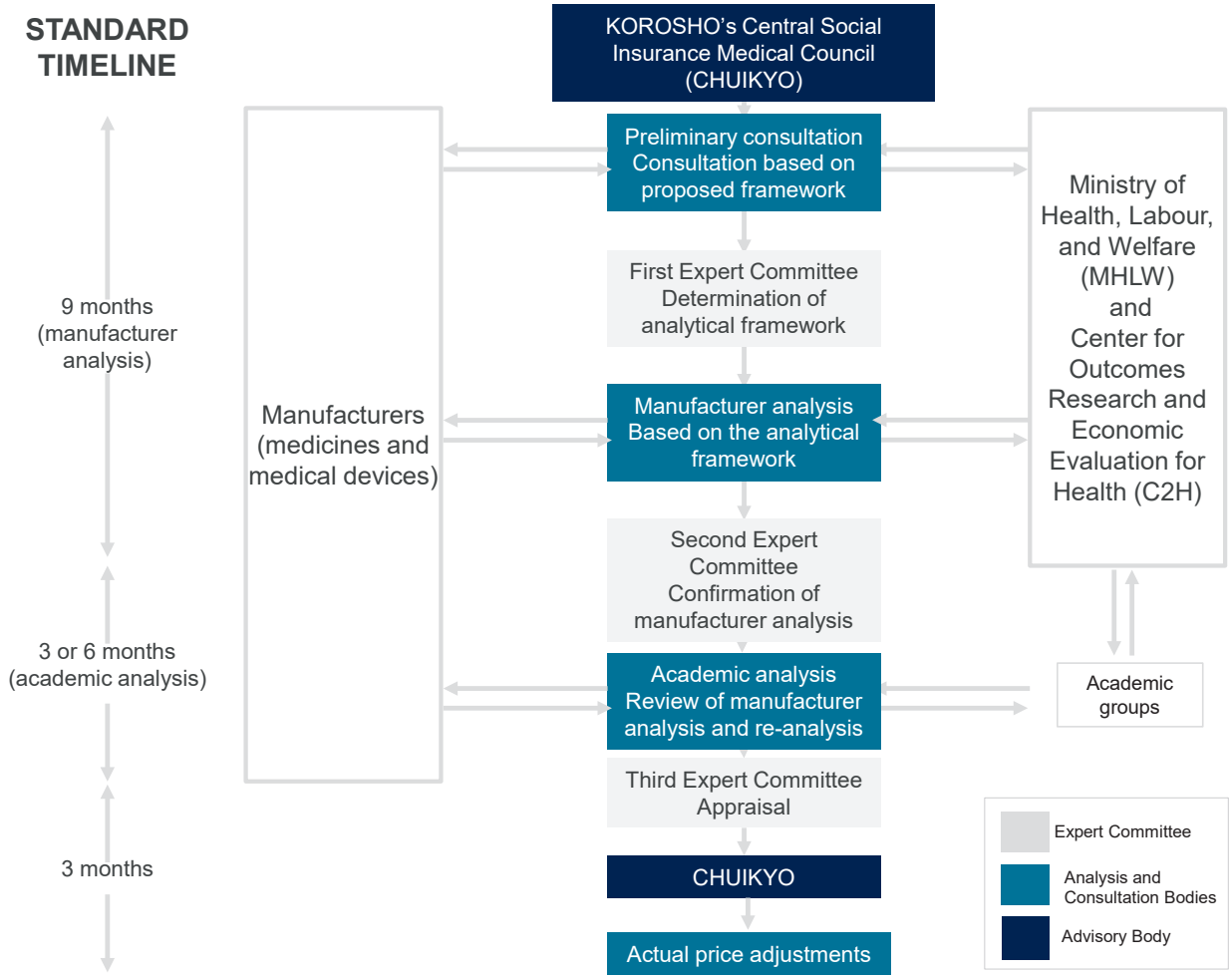
The MHLW outline also specified criteria for excluding products from the scope of CEAs:

- Products that receive high NHI prices due to a small number of patients
- Products that cannot be fully evaluated with the ICER (incremental cost-effectiveness ratio; costs per QALY gained) or QALY" (do " belong here?) such as cancer drugs.

Among the first group of products with small numbers of patients, state-designated intractable diseases, hemophilia, and HIV were defined as "rare diseases with no fully established treatment methods," and products "only used" for these diseases will be excluded from the coverage. Likewise, products "only used" for children (only products with pediatric approvals in Japan) will avoid CEAs.

However, products with high prices or high sale volumes (≥ ¥35 billion) could still be selected on a case-by-case basis by the Chuikyo. The cost-effectiveness evaluation process starts after the products are launched in the market. The results are reflected in the product prices after approximately 15–18 months **(Figure 2).**

Figure 2: Process for Japan's cost-effectiveness evaluation



Examples of Drug Pricing and HTA

As part of the HTA pilot program, seven drugs and six medical devices were selected for CEAs, and reported using an ICER. Kymriah and Trelegy were the first to have completed reviews under the current process and their downward adjustments were 4.3% and 0.5%, respectively as shown in **Figure 3.** From an external perspective, these cuts appear minor relative to the large cuts applied under other mechanisms. However, it is important to realize that under its current scope, Japan's HTA is designed primarily to modify awarded premiums, and the maximum adjustment is capped at 15%. Although actual pricing changes are small compared with other repricing measures, they serve as proofs of concept for a more expansive system in the future.

Figure 3: Kymriah and Trelegy Ellipta price adjustments

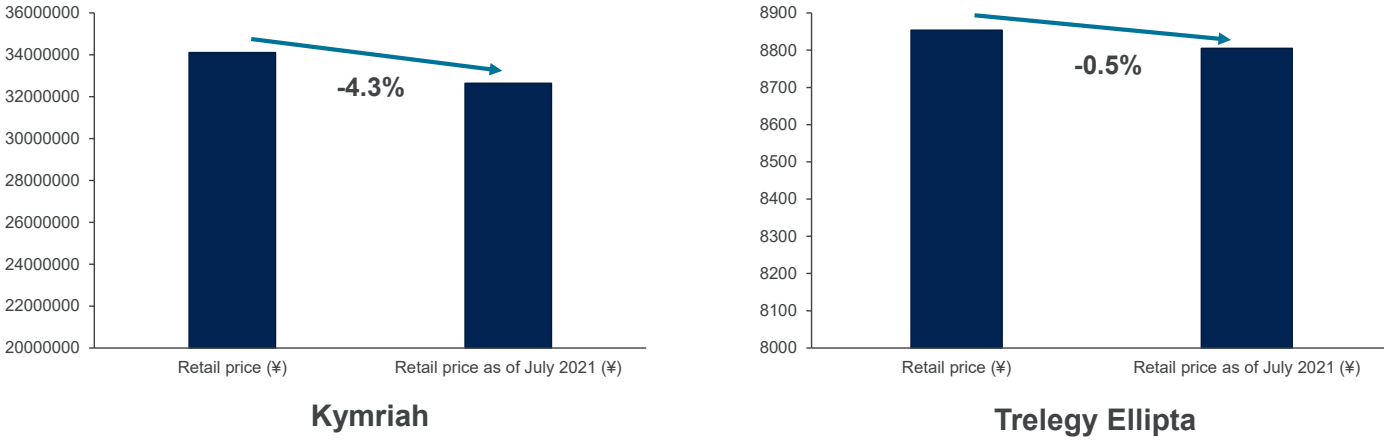
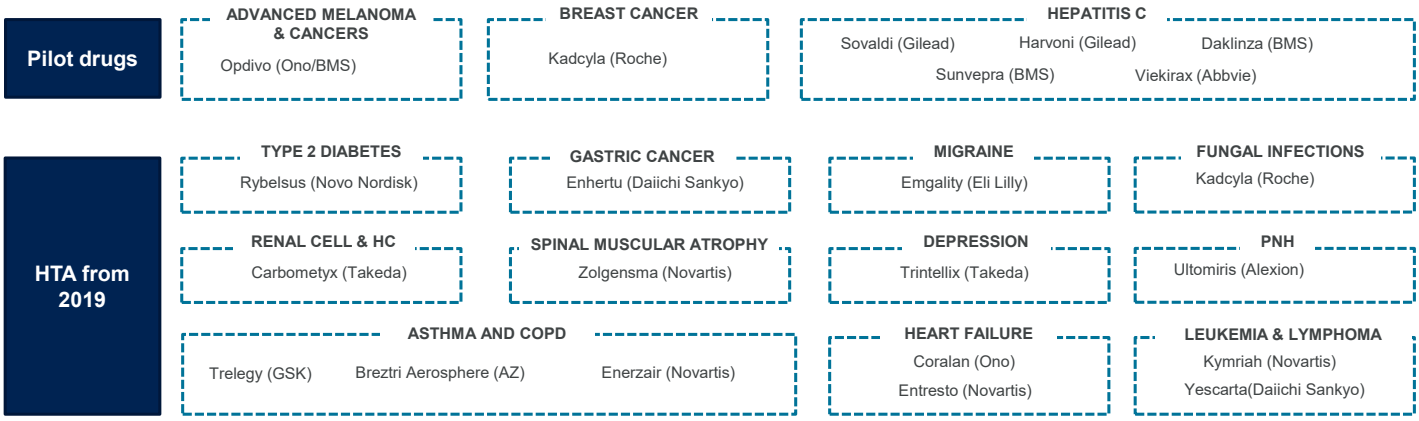


Figure 4 represents the drugs selected in the process of the pilot program for HTA in 2019. Japan's reimbursement policy panel on May 12, 2021, agreed to apply a 4.3% reduction for Alexion Pharmaceuticals' Ultomiris (ravulizumab) under the CEA system. The Chuikyo approved the health ministry's proposal to reduce Ultomiris's current NHI price of ¥730,894 to ¥699,570 per 300 mg/30 mL vial. On August 4, 2021, Takeda's antidepressant Trintellix (vortioxetine), received a 4.3% price reduction under the CEA system. The Chuikyo approved the health ministry's proposal to reduce Trintellix's current NHI price of ¥168.90 per 10 mg and ¥253.40 per 20 mg to ¥161.70 and ¥242.50, respectively.

Figure 4: Drugs selected for HTA review in Japan from 2019 onwards



Future Challenges

- HTA may be seen as an attempt to limit patient access to reduce government spending. Engaging all stakeholders will be essential for a successful implementation of HTA in Japan.
- The government will need to recruit and develop experts to conduct HTA assessment and review, as the present reliance on academia will no longer be sustainable as the HTA program expands.
- The pharmaceutical industry's concerns regarding the use of measures such as ICER and QALY will need to be addressed, and the rationale by which cost-effectiveness is applied in determining final pricing and reimbursement decisions will need to be clarified.
- Some unique features of the Japanese pricing and reimbursement system, such as the fixed-fee schedule, will make incorporating HTA into existing practices challenging for both government and manufacturers.
- Cooperation between the government and pharmaceutical manufacturers will be needed to reach pricing agreements.

EVERSANA's Participation in the HTA Process

- Pricing research approach uses our in-house price tool NAVLIN for analog analysis, understanding price trends, cost of therapy, and international reference pricing
- For a better understanding of market access dynamics, selection of appropriate comparators, and testing pricing range EVERSANA engages with ex-payers, KOLs, and ex-MHLW officials
- Evidence generation through targeted literature search and expertise in evidence synthesis (SLR and NMAs)
- We conduct economic analyses to justify cost-effectiveness at an established price

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