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Topics: Recent topics in public health in Japan 2019

＜ Review ＞

Application of economic evaluation of pharmaceuticals and medical devices in Japan

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Abstract

In Japan, annual medical expenditure reached 40 trillion yen in 2013 and it continues to increase under public health insurance scheme. One of the reason of increasing medical expenditure is population aging. However, another big reason is increasing technologies in health care, such as advanced medical devices and new pharmaceuticals. Insurance coverage and reimbursement prices are discussed and determined by the Ministry of Health, Labour, and Welfare. The Ministry has to consult with Central Social Insurance Medical Council (Chuikyo). Chuikyo has own rules for pricing pharmaceuticals and medical devices.

From fiscal year 2012, discussions on economic evaluation began within a subcommittee of the Chuikyo, Several issues were discussed in the subcommittee, such as target products to be evaluated, methods for evaluation, use of evaluation results. Based on the discussion in the subcommittee, in 2016, a pilot program of cost-effectiveness evaluation started for 7 pharmaceuticals and 6 medical devices. In the evaluation process, manufacturers of selected products were asked to submit cost effectiveness analysis, according to the guideline for cost effectiveness analysis. Then, submitted data were reviewed and re-analysed, if necessary, by expert groups. The results were discussed in the expert committee of cost effectiveness to make final decision. Based on the results, prices of some products were adjusted.

From 2019, economic evaluation of pharmaceuticals and medical devices will be fully implemented in order to provide efficient health care. To make the new evaluation system meaningful , "Center for Outcomes Research and Economic Evaluation for Health (CORE2-Health)" was established in the National Institute of Public Health to provide good evidence on cost effectiveness.

keywords: cost effectiveness, health technology assessment, pharmaceutical, medical device, Central Social Insurance Medical Council, reimbursement price, Japan

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I. Background

In Japan, annual medical expenditure reached 40 trillion yen in 2013 and it continues to increase. One of the reason of increasing medical expenditure is population aging because per capita medical expenditure for the elderly is much higher than the expenditure for younger generation. However, another big reason is increasing technologies in health care, such as advanced medical devices and new pharmaceuticals. Innovative technologies are continuously developed and introduced. Some of those technologies cost a lot to health care finance. It is important to balance technology advancement and cost for sustainable health care delivery.

Economic evaluation of health care technologies may be one of the solutions for efficient use of health care budget. It is often described as a part of health technology assessment (HTA)[1]. In some countries, such as England, Canada, and Australia, economic evaluation of pharmaceuticals and medical devices are used to determine coverage by the publicly

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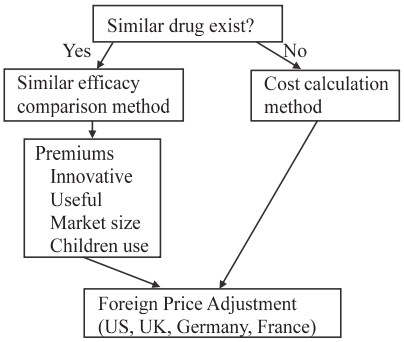

Figure 1 Process of New Drug Pricing before 2018

funded health care system. Even in Asia, Korea and Thailand already started such an approach. In Japan, since 1992 when new medicines are added to the reimbursement list for public health insurance, economic evaluation data can be submitted to the Ministry of Health, Labour and Welfare (MHLW). However, there is a lack of clear rules regarding how to use the submitted data. In fact, even if economic data are submitted, many pharmaceutical companies do not believe that such data are reflected in the pricing of their products.

In Japan, insurance coverage and reimbursement prices are discussed and determined by the MHLW. The Ministry has to consult with Central Social Insurance Medical Council (Chuikyo) before those decisions are made. Chuikyo has own rules for pricing pharmaceuticals and medical devices.

Reimbursement prices of new drugs are determined using two methods: "the similar efficacy comparison method" and "the cost calculation method" (Figure 1). The similar efficacy comparison method is applied when similar drugs have been already listed in terms of efficacy and pharmacological properties. The daily price of the new drug is set at the same as that of the comparator. If a new drug is evaluated as an innovative one, the MHLW adds a premium which can range between 5% and 120% of the comparator's daily price.

The degree of innovation is judged by the following four points: (a) new action mechanism, (b) higher efficacy or safety, (c) improvement of treatment for target disease, and (d) beneficial drug formulation. The percentage of the premium depends on the degree of innovation. If one of the four criteria is met, then the new drug may obtain a 5%–30% premium. The premium of a new drug featuring two of (a)–(c) is 35%–60%, and that of a drug with all of (a)–(c) is 70%–120%. In addition, if a new drug has a small market size or pediatric labeling, then an additional premium may be applied.

If there is no appropriate comparator, then the cost calculation method is used. The cost is calculated by summing the costs of manufacturing, research and development(R&D), administration, marketing, and profit. R&D, administration, marketing, and profit rate are set according to the average rate of pharmaceutical industry. However, for a new innovative (or not innovative) drug, the profit rate might be adjusted from −50% to 200% of the standard profit rate based upon the degree of innovation, safety, and efficacy compared with existing therapy.

The price, using either of these methods, may be revised by comparison with the average list price from four countries: US, UK, France, and Germany. If the calculated price is more than 1.25 times, or less than 0.75 times, the average price abroad, this price is raised or lowered.

From fiscal year 2012, discussions on economic evaluation began within a subcommittee of the Chuikyo, i.e., the "Special Committee on Cost-Effectiveness," which consists of 16 individuals (6 representatives of healthcare payers, 6 healthcare professionals, and 4 third parties), in addition to 4 industries and 3 health economists as non-voting members. Several issues were discussed in the subcommittee, such as target products to be evaluated, methods for evaluation, use of evaluation results. Based on the discussion of the subcommittee, the government announced in the "Basic Policy on Economic and Fiscal Management and Reform 2015" that "it will consider the cost-effectiveness of insurance coverage of medicine and medical devices as a way to cope with the sophistication of healthcare" and "the government will introduce such cost-effectiveness analysis on a trial basis for the FY2016 revision of remunerations" [2]. In 2016, a pilot program of cost-effectiveness evaluation started[3].

II. A pilot program of cost effectiveness evaluation at Chuikyo

At the beginning of the pilot program of cost effectiveness evaluation of pharmaceuticals and medical devices, two important basics were agreed in Chuikyo in 2016. One was the target poducts. The subcommittee considered whether it should evaluate new products which would be approved after FY2016 or existing products which were already in the market. In Japan, almost all prescription drugs are covered by health insurance scheme within 60 days (90 days maximum) after approval. And, all the drugs have their reimbursement prices determined at Chuikyo. If we would conduct cost effectiveness anslysis after approval, it would cause the delay of insurance coverage. The delay of insurance coverage of drugs compared to US or European countries had been a big issue, which was called "drug lag". The government and the Pharmaceuticals and Medical Device Agency (PMDA) have struggled to overcome the issue. If a new step of cost effectiveness analysis might cause the ad-

ditional delay, it would not be acceptable. In order to avoid such an additional delay, Chuikyo decided to pick up existing products to be evaluated in the pilot program. The other issue was how to use the results of cost effectiveness analyses. In many countries those results are used to determine whether the new technology should be covered by publicly funded scheme. However, this approach might cause to limit access to those new technologies from patients. In order to avoid this problem, Chuikyo decided to use the economic evaluation results to adjust reimbursement prices of pharmaceuticals and medical devices. In such a manner, patients do not lose their access to those technologies.

III. Target products

The evaluation does not target all drugs and medical devices. Target products are determined by Chuikyo, and the selection criteria were established based upon the degree of innovation (premium rate) and market size. Target products were chosen among the products, for which reimbursement decisions were made between FY 2012 and FY 2015. Four categories were set as target criteria: drugs and medical devices (1) with the highest premium rate, priced by the similar efficacy (category) comparison method; (2) with ≥10% premium and highest sales (or highest price, in case of medical devices), priced by the similar efficacy (category) comparison method; (3) with highest premium rate, priced by the cost calculation method; and (4) with ≥10% premium and highest sales (price), priced by the cost calculation method, excluding rare intractable diseases. In addition, the pilot program also targets drugs which were similar to the selected drugs in terms of pharmacological effect, as well as devices belonging to the same reimbursement category.

By this rule, 13 products (7 drugs and 6 medical devices) were selected by Chuikyo. Drugs for anti-hepatitis C and PD-L1 antibody, which receive much attention in the press, were included as target products.

IV. Evaluation process

The manufacturers of the target products were requested to submit economic evaluation data by the end of FY 2016. Once this was completed, academic groups, including experts on clinical epidemiology and health economics, independently reviewed the data in early FY 2017 (Figure 2). Because Japan had no official HTA agency, such as NICE in the UK. the National Institute of Public Health (NIPH) coordinated this review process. The reviewed data were finally sent to another subcommittee under Chuikyo, the "expert committee of cost-effectiveness", which was established in FY2016.

To establish standard methodology for submission, our research team, funded by MHLW, was asked to develop a methodological guideline for cost-effectiveness evaluation by the subcommittee for the pilot program (Figure 3)[4]. Manufacturers had to carry out the analysis stipulated by the guideline. In the guideline, it was mentioned that the analyses should be done from public healthcare payer's perspective, which only include direct medical costs under public health insurance scheme. It was also mentioned that quality-adjusted life year (QALY) should be used as a basic outcome unit.

The expert committee had a role to perform "appraisal" of the data including a social and ethical perspective, while the special committee was in charge of designing a system for cost-effectiveness evaluation. This appraisal allowed the

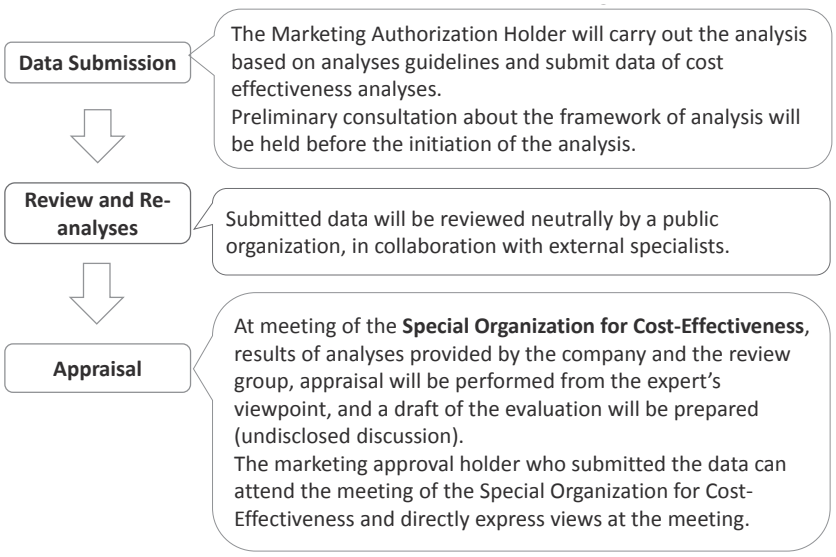

Figure 2 Process of Cost Effectiveness Evaluation of Pharmaceuticals and Medical Devices in the Pilot Program

1 Objectives
2 Perspective of analysis
3 Target population
4 Comparator(s)
5 Additional benefit in effectiveness/safety
6 Methods of analysis
7 Time horizon
8 Choice of outcome
9 Sources of clinical data
10 Calculation of costs
11 Long-term care costs and productivity loss
12 Discounting
13 Modeling
14 Uncertainty
15 Reporting/publication

Developed by the research group funded by MHLW.

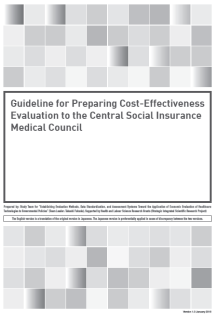

Figure 3 Guidelines for Cost Effectiveness Analysis

expert committee to judge whether an evaluated healthcare technology was cost-effective or not. This committee was closely protected, including the names of members or schedules, like drug pricing organization. The results of the evaluation were reflected in reimbursement prices in the next revision, FY 2018.

The cost per QALY threshold in the pilot program was set to be 5 million yen per QALY (Figure 4-A). However, price of the products were not reduced to meet the threshold. If the result showed ICER was below 5 million yen per QALY, the price was not adjusted. If the ICER was 10 million yen or more per QALY, the price was adjusted at maximum reduction rate. The maximum rate was the 90% of the premium. If the ICER was between 5 and 10 million yen per QALY, the price was adjusted with linear relationship. Because the economic evaluation results were used to complement existing pricing rules and target products were chosen among the products which had 10% premium or more, maximum reduction rate was set as 90% of the premium.

In addition to the price reduction scheme, Chuikyo adopted a new idea to increase price of the products under several conditions. The conditions were that economic evaluation result showed the target product dominated the old therapy, which meant the new product improved the outcome with lower cost, and that maximum increase rate was 10% of overall price. Such price increasing scheme was not seen in other countries. In Japan, price of pharmaceuticals and medical devices are determined at Chuikyo based on the pricing rules. So manufacturers are not able to decide prices even when they are patented. The new scheme was to encourage to produce such cost effective technologies.

V. Price adjustment and issues

In March 2018, based on the cost effectiveness results, prices of the two of the target products, nivolumab and trastuzumab emtansine were reduced, though actual reduction rate were not disclosed. On the other hand, the price of Kawasumi Najuta Thoracic Stent Graft System was increased.

However, 7 products out of 13 in the pilot program, analysis results submitted by manufacturers and reanalysis group were markedly different, even though both analyses followed the guideline. Major reasons for the discrepan-

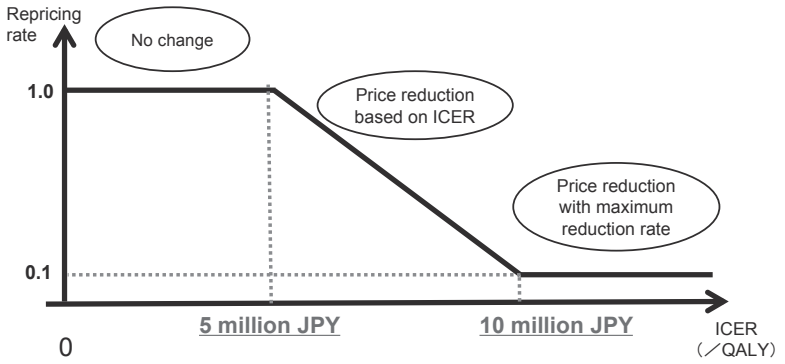

Figure 4-A Determination of repricing rate in the pilot program

cy were; difference of the scope (eg. target population, comparator), difference in the selection of data used in the analyses (eg. data sources, definition of the target patients group). Because it was a pilot program, the subcommittee decided to verify the reasons of the discrepancy in order to consider a more rational analysis. For this purpose, analyses as a verification were performed in 2018.

VI. Modification of the pilot program toward full-scale implementation

The government announced in its "Basic Policy on Economic and Fiscal Management and Reform 2018" that "the government will continue to review specific contents when it comes to the full-scale implementation of cost-effectiveness evaluations, and will come to a conclusion in FY 2018"[5]. Based on this announcement and experiences of the pilot program, the cost effectiveness evaluation subcommittee under Chuikyo intensively discussed several issues, such as target products, evaluation process, and use of evaluation results.

Finally , the plan for the full-scale implementation was proposed in the subcommittee on January 23, 2019[6].

Several modification were made to the pilot program. Target products will mainly be new pharmaceuticals and medical devices which will be approved after full-scale implementation, which have premiums in the initial price setting, and estimated peak annual sales beyond a certain level. In order to avoid the delay of reimbursement, drugs and devices will be priced under current pricing rules first, and when the evaluation is done, the price will be adjusted.

The number of target products are somewhat uncertain. In Japan, lack of experts in this field is one of the issues. So the number of evaluation will depend on the availability of resources.

Expected time frame is that 9 months after selection of target products will be preparation time for manufacturer submission, including pre-analyses consultations. Submitted analyses will be reviewed, and re-analysed if necessary, in 3 to 6 months. Appraisal and final decision making for re-pricing will take 3 months. So it is expected to go through the whole process in 15 to 18 months after insurance coverage.

Re-pricing scheme will be also modified from the pilot program. It was proposed that price reduction rate would be two steps instead of linear relationship between 5 to 10 million yen per QALY, because uncertainty for estimating ICER should be considered (Figure 4-B). In the linear relationship implied no allowance of uncertainty of ICER. The same reduction rate will be applied when ICER is between 5 to 7.5 million yen per QALY, and so will be when ICER is between 7.5 to 10 million yen per QALY. This scheme seems more reasonable if we consider methodological limitation about uncertainty.

In order to increase the number of evaluation, importance of educational program to perform more analyses was also pointed out in the proposal.

The plan for full-scale implementation will be discussed and determined by the end of March, 2019, and the new system is expected to start in April, 2019.

Under the limited budget for health care in Japan, efficient use of health care resources are required. Economic evaluation is becoming more and more important. In order to perform economic evaluation and its application to policy making, the National Institute of Public Health established a new unit, "Center for Outcomes Research and Economic Evaluation for Health (CORE2-Health)" in April, 2018. The center is willing to act as leading agency in Health Technology Assessment (HTA) in Japan.

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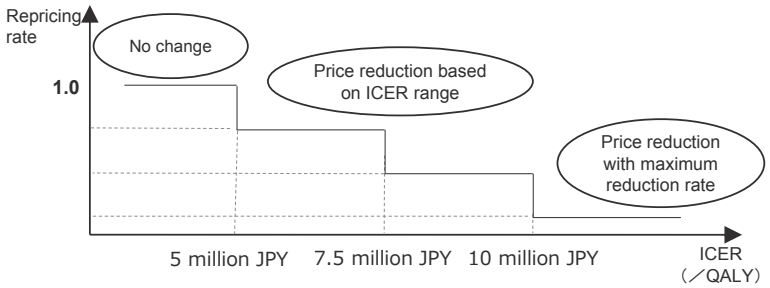

Figure 4-B Determination of pepricing rate in the full-scale implementation

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Application of economic evaluation of pharmaceuticals and medical devices in Japan

日本における医薬品・医療機器の経済評価の応用

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抄録

日本では，公的医療保険制度で賄われる国民医療費が2013年に40兆円を超え，年々増加している．医療費が増加する理由の一つは人口の高齢化だが，他の要因として，新規の医薬品や医療機器の導入という技術進歩によるものが考えられる．保険収載の判断や償還価格の設定は，厚生労働省が中央社会保険医療協議会（中医協）に諮問し，医薬品や医療機器の価格設定のルールに基づいて決定される．

2012年に経済評価の応用に関する議論が中医協の新たな部会で開始された．ここでは評価対象とする技術，評価方法，評価結果の活用方法などについて議論されてきた．この議論に基づいて，2016年には７つの医薬品と６つの医療機器を対象として費用対効果評価の試行的導入が開始された．評価プロセスでは，まず当該品目の製造企業が分析ガイドラインに基づいて費用効果分析のデータを提出し，これを専門家グループがレビューし，必要に応じて再分析した．これらの結果は費用対効果評価専門組織で議論され最終的な結果が決められた．この結果に基づき，いくつかの品目については価格調整された．

2019年からは，効率的な医療提供を促進するために，医薬品・医療機器の費用対効果評価が制度として導入される見込みである．このようなしくみを意義のあるものにするために，費用対効果に関するエビデンスを提供する組織として，国立保健医療科学院に保健医療経済評価研究センターが設置された．

キーワード：費用対効果，医療技術評価，医薬品，医療機器，中央社会保険医療協議会，償還価格，日本