

Full Scale Introduction of Cost-Effectiveness Evaluations in Japan

Overview (2/20/2019)

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[Translated by Center for Outcomes Research and Economic Evaluation for Health (C2H), National Institute of Public Health (NIPH)]

Disclaimer: The English version is a translation of the original version in Japanese. The Japanese version is preferentially applied in cases of discrepancy between the two versions.

History on the discussion of cost-effectiveness evaluations

- The Central Social Insurance Medical Council (CSIMC) set up a Special Committee on Cost-Effectiveness Evaluation in May 2012. Based on the experience gained with the trial implementation from FY 2016, the CSIMC continues to consider applying new cost-effectiveness evaluation methods to the Japanese public healthcare system.

Around 2010=	Discussions at the CSIMC on the implementation of cost-effectiveness evaluations
<u>May 2012</u>	<u>Special Committee on Cost-Effectiveness Evaluation established under the CSIMC</u>
November 2013	Interim report published by the CSIMC
June 2015	In the “Basic Policies on Economic and Fiscal Management and Reform 2015,” it was decided that cost-effectiveness evaluation would be implemented on a trial basis at the 2016 Revision of Medical Fees.
<u>April 2016~</u>	<u>Trial implementation of cost-effectiveness evaluations</u>
June 2018	In the “Basic Policies on Economic and Fiscal Management and Reform 2018,” it was decided that the full-scale implementation of cost-effectiveness evaluations continues to be considered, and a conclusion should be reached within FY 2018.

Discussed issues on cost-effectiveness evaluation at CSIMC

- The following issues have been discussed by the Special Committee on Cost-Effectiveness Evaluation (and joint committee meetings) based on experiences from the trial implementation, scientific reports by health economists, and opinions from industry.

Date	Main issues discussed
2018 June 13	Cost per QALY reference values (threshold) for price adjustments
August 22	Appraisal
October 17	Methods of utilizing results of cost-effectiveness evaluations, selection of target products, handling of rare diseases, methods of price adjustments
November 7	Methods of price adjustments
November 21	Selection of target products, process of analysis, methods of price adjustments
December 5	Academic analysis for reviewing manufacturers' submissions, members of Expert Committee of Cost-Effectiveness Evaluations, methodological guidelines for cost-effectiveness analysis, methods of price adjustments
December 19	Interviews with industry
2019 January 23	Draft report on full-scale implementation of cost-effectiveness evaluations
February 7	Interviews with industry
February 20	Final approval of full-scale implementation by CSIMC general assembly

(*) August 22nd was the meeting of the Special Committee on Cost-Effectiveness Evaluation. Other dates were joint committee meetings with the Special Committee on Cost-Effectiveness Evaluation, Drug Pricing, and Medical Device Pricing.

Main governmental policies on cost-effectiveness evaluations

Basic Policies on Economic and Fiscal Management and Reform 2015 (Cabinet Approval June 30, 2015)

In response to advances in healthcare, aim to promptly ensure full-scale implementation of the cost-effectiveness evaluation when determining reimbursement for pharmaceutical products and medical devices, after the trial implementation at the FY 2016 Revision of Medical Fees

Regarding the Fundamental Reform of the Drug Pricing System Essential Features (December 20, 2017) (Excerpt)

For cost-effectiveness evaluations, a system should be adopted where the cost-effectiveness of pharmaceutical products/medical devices with a large market size is analyzed, and then drug/medical device prices are revised based on the results.

Working towards this, price adjustments of the targeted 13 products should be made effective in April 2018 based on the results of the trial evaluation. Technical issues that were revealed in the trial implementation will be summarized.

At the same time, the full-scale implementation should continue to be considered, reaching a conclusion within FY 2018.

Basic Policies on Economic and Fiscal Management and Reform 2018 (Cabinet Approval June 15, 2018) (Excerpt)

Based on the "Basic Policies for Fundamental Reform of the Drug Pricing System," in addition to alleviating the public burden and enhancing the quality of healthcare, convert the structure of the pharmaceutical industry into a structure with a high degree of drug discovery capabilities. (Omission) The full-scale implementation should continue to be considered, reaching a conclusion within FY 2018. (Omission)

For decision of reimbursement for new medicines and medical technologies, economic evaluations such as a cost-effectiveness evaluation and financial impact should be considered, including the utilization of services covered and non-covered by insurance. Surveys, research, and considerations on health technology assessments should be promoted. To achieve the goal, promotion of personnel development, Japanese data accumulation, and analyses of the data should be required.

List of Issues on Cost-Effectiveness Evaluations

- (1) Utilization of the results of cost-effectiveness evaluations
- (2) Selection criteria for target products
 - [1] Selection criteria for products targeted for cost-effectiveness evaluations
 - [2] Timing for selecting target products and procedures for disclosure
 - [3] Exclusion criteria (rare, pediatric, and severe diseases)
- (3) Analytical Process
 - [1] Consultations prior to analysis (preliminary consultation)
 - [2] Consultations during manufacturers' analysis
 - [3] Role and members of the Special Committee of Cost-Effectiveness Evaluations
 - [4] Academic analysis for reviewing and re-analyzing manufacturers' submission
 - [5] Time schedule of the evaluation process
 - [6] Methodological guidelines for cost-effectiveness analysis
 - [7] Cases lacking enough data for analysis
- (4) Appraisal
 - [1] Verification of analysis from a scientific perspective
 - [2] Special consideration (rare, pediatric, and severe diseases)
 - [3] Reporting and disclosing results of evaluations
- (5) Price adjustments
 - [1] Targets of price adjustment by cost-effectiveness evaluation
 - [2] Method of adjusting prices according to ICER
 - [3] Setting cost per QALY reference values (threshold)
 - [4] Method of adjusting prices for products requiring special consideration
 - [5] Rate of price adjustments
 - [6] Products evaluated as "dominant" or having a low ICER value.
 - [7] Timelines and procedures for price adjustments
- (6) Building greater capacity for cost-effectiveness evaluations

(1) Utilization of the results of cost-effectiveness evaluations

- The results of cost-effectiveness evaluations should not be used to determine reimbursement conditions, but should be used to adjust prices after listing the medicine and medical devices.
- Based on the results of full-scale implementation going forward, methods of utilization will continue to be discussed after improving the capacity of cost-effectiveness evaluations.

(2) [1] Selection criteria for products targeted for cost-effectiveness evaluations

- Considering the influence on public health insurance finances, innovative medicines and medical devices with a large financial impact should be the main target of cost-effectiveness evaluations.
- The criteria shall be as follows, considering the limited capacity of the cost-effectiveness evaluation.

	Classification	Similar Efficacy Comparison Method (Similar Function Classification)	Cost Calculation Method	Selection Criteria
(i) Newly-Listed Products: after full-scale implementation*1	H1	Products with a premium ^(*2)	Products with a premium ^(*2) , or a disclosure rate of under 50%	<ul style="list-style-type: none"> • Peak sales (estimate): JPY 10 billion or more
	H2			<ul style="list-style-type: none"> • Peak sales (estimate): JPY 5 billion or more, less than JPY 10 billion
	H3			<ul style="list-style-type: none"> • Products identified by the CSIMC General Assembly, such as products with a prominently high price^(*3)
(ii) Previously-listed Products: before full-scale implementation	H4	Products with a premium ^(*2)		<ul style="list-style-type: none"> • Products with sales of JPY 100 billion or more • Products identified by the CSIMC General Assembly, such as products with a prominently high price^(*3)
Similar products	H5	Products similar to those in the H1-H4 Classification		<ul style="list-style-type: none"> • Medicine for which the price is calculated in comparison with target products^(*4) • Medical devices for which price is calculated in comparison with target products^(*4), and that are categorized in the same functional classification

(*1) Even if product does not meet the selection criteria in terms of the peak sales (estimate) at the time of listing, it will be selected if its annual market size exceeds JPY 5 billion due to the expansion of the market size. In this case, it will be positioned as an H1 or H2 classification according to its annual market size.

(*2) Products for which either an innovativeness premium, utility premium, or improvement premium (/\) (medical devices) was calculated will be targeted

(*3) Products determined by the CSIMC General Assembly, such as products with a prominently high unit price, products for which new findings were discovered after the completion of the evaluation that would have a major impact on the evaluation, and other products for which a re-evaluation was required.

(*4) Products targeted for cost-effectiveness evaluations in the H1-H4 classification

(2) [2] Timing for selecting target products and procedures for disclosure

- Promptly select products to be targeted for cost-effectiveness evaluations.
- In order to ensure that evaluations advance smoothly, stagger the timing of selections rather than selecting many products simultaneously.
- With regards to newly-listed products (H1 to H3 classifications) and similar products (H5 classification), the Expert Committee on Drug/Medical Device Pricing will create a proposal as to whether they will meet the criteria, and the CSIMC General Assembly will make the final approval.
- With regards to previously-listed products (H4 classification), upon listening to the opinions of the Expert Committee on Drug/Medical Device Pricing, the MHLW will create a proposal as to whether they will meet the criteria, the CSIMC General Assembly will make the final approval.

Timing for selecting products and disclosure

Classification	Timing of Product Selection	Disclosure	Handling After Selection
H1	Four times per year (selected upon listing)		After selection, promptly begin cost-effectiveness evaluation analyses.
H2	Four times per year (Select as "candidate products for evaluation" upon listing)	Disclose at the CSIMC General Assembly at the time of selection.	Position as "candidate products for evaluation." Based on the selection status of the H1, H3, and H4 classifications, select (2 times per year) medicines and medical devices in order from products with the highest peak sales (estimate), considering the annual upper limit for the number of products that can be evaluated, and begin analyses.
H3	Four times per year (selected upon listing)		After selection, promptly begin cost-effectiveness evaluation.
H4	Four times per year (Selection using new listings as an opportunity)		After selection, promptly begin cost-effectiveness evaluation.
H5	Four times per year (selected upon listing)		Do not conduct a cost-effectiveness evaluation, but adjust prices according to the representative products.

(2) [3] Exclusion criteria (rare, pediatric, and severe diseases) (Part 1)

(i) Principals

- If the results of cost-effectiveness evaluations are used to determine reimbursement, patient access may become a major issue. But if price adjustments are made after listing, it will be less of a concern.
- Meanwhile, even if the results are used only for price adjustments, it may be a disincentive for R&D. Restricted access cannot be denied for the following products. For these products, a special consideration will be needed.
 - [1] Products for which the unit price (drug/medical device price) is high because they have a small number of patients.
 - [2] Products for which the value cannot be fully assessed by ICER (QALY).
- To ensure the transparency of the system, specific criteria are required for determining what kinds of the products need special consideration.

(ii) Excluded products

- The following products will be excluded from target for cost-effectiveness evaluations.
 - Products having at least one indication for rare diseases (i.e., designated intractable diseases, hemophilia, and HIV infections) for which there are insufficient treatments;
 - Products having at least one indication for children (i.e., pediatric dosage and administration is approved in Japan)
- If the products has a large market size (JPY 35 billion or more) or has a prominently high unit price, it may be targeted for a cost-effectiveness evaluation upon the decision of the CSIMC General Assembly. (Even if the product falls under the above)

(2) [3] Exclusion criteria (rare, pediatric, and severe diseases) (Part 2)

Products special consideration is required

Products	[1] Products for which the unit price (drug/medical device price) is high because they have a small number of patients		[2] Products for which the value cannot be fully assessed by ICER (QALY)
Target product	<ul style="list-style-type: none"> • Products <u>only</u> used for rare diseases^(*1) with insufficient treatment • Products <u>only</u> used for children^(*2) 	<ul style="list-style-type: none"> • If some of the indications include rare diseases^(*1) with insufficient treatment and pediatric diseases^(*2) 	<ul style="list-style-type: none"> • Anti-cancer drugs^(*3)
Special consideration	The products are excluded from targets of cost-effectiveness evaluations ^(*4)	They will be targets for evaluation, but will be given special consideration in the appraisal process and price adjustments ^(*5)	

(*1) Designated intractable diseases, hemophilia, and HIV infections.

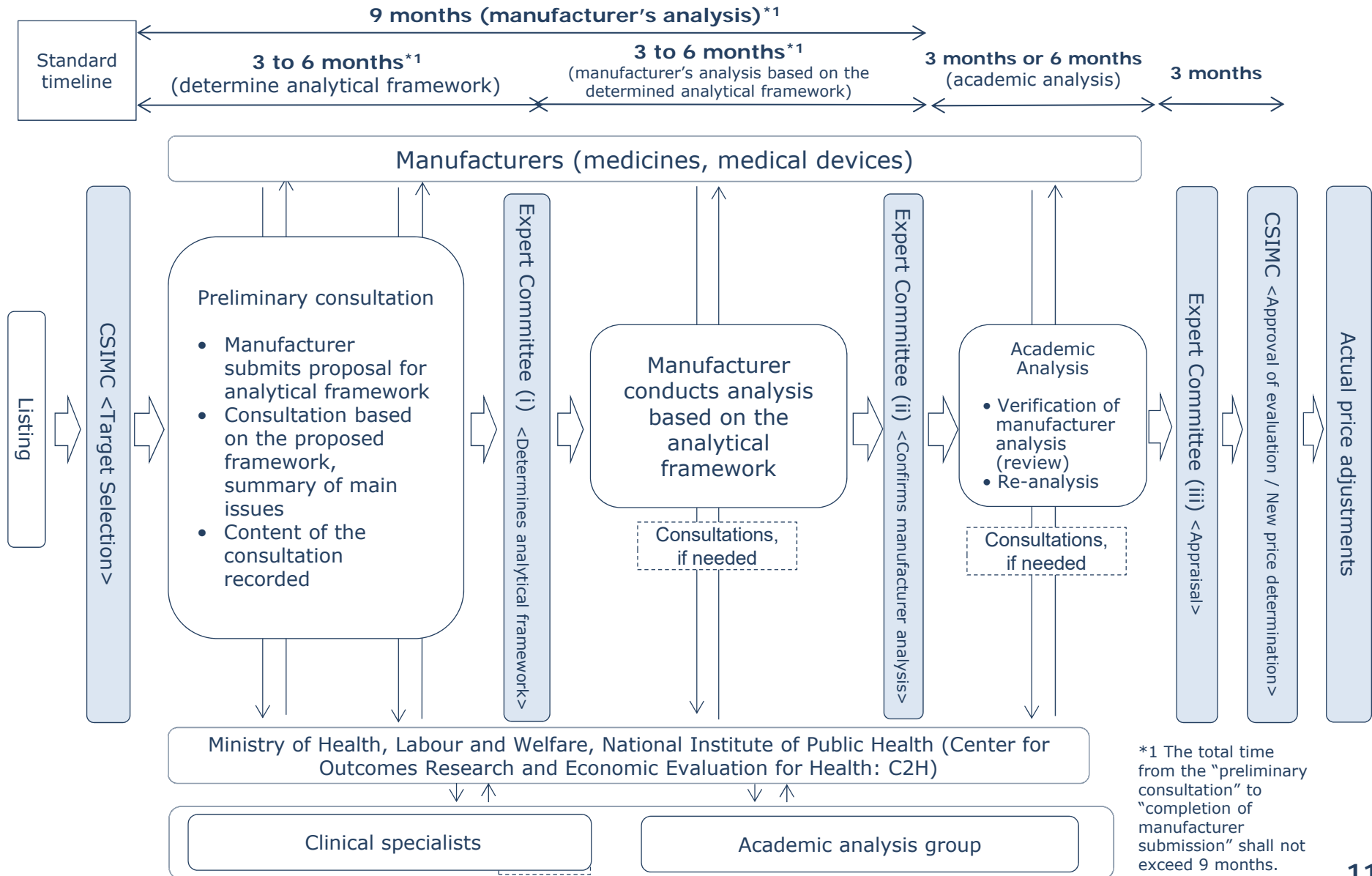
(*2) Pediatric dosage and administration is approved in Japan.

(*3) Special consideration is required if cancer is one of the approved indications.

(*4) However, if the products has a large market size (JPY 35 billion or more) or has a high unit price, it may be targeted for a cost-effectiveness evaluation upon the decision of the CSIMC General Assembly.

(*5) Analyses including “public long-term care costs and productivity loss” can be also submitted only if they were conducted based on findings in Japan. Although they will not be used for price adjustments, the submitted results of analyses will be disclosed, and used for accumulating experiences.

(3) [1]-[5] Process for cost-effectiveness evaluations



(3) [1] Preliminary consultations and [2] Consultations during analysis

- With regards to preliminary consultations/consultations during analysis, the manufacturer and the academic analysis group shall not be in direct contact. Instead, the National Institute of Public Health (NIPH) C2H will discuss with the manufacturer inquiring of the academic analysis group.
- In principle, the analytical framework will be determined wherever possible in the preliminary consultations, and analysis has to be conducted based on this framework. However, mutual inquiries can be made when conducting the (manufacturer and academic) analysis.
- The content of consultations will be as follows:
 - (i) Preliminary consultation
 - Analytical framework such as comparator, target population, pivotal studies of the target product
 - Summary of main issues when conducting the (manufacturer and academic) analysis.
 - (ii) Consultations during analysis
 - New findings discovered during analysis (limited to scientific issues)
- The content of consultations will be recorded for the report to the expert committee.

(3) [3] Role and members of the Expert Committee on Cost-Effectiveness Evaluations (Part 1)

- Discussions from the standpoint of healthcare providers and insurers will be conducted at the CSIMC General Assembly. The expert committee will conduct technical discussions from a academic perspective.
- To ensure the neutrality and scientific validity of cost-effectiveness evaluations, the expert committee will be involved at the following three stages:
 - (A) Confirmation of the contents of preliminary consultation, determining analytical framework
 - (B) Confirmation of the manufacturer analysis (whether the analysis was conducted based on the decided analytical framework)
 - (C) Appraisal based on the results of both the manufacturer and academic analysis
- The expert committee will not be disclosed as they will discuss using confidential information.
- Manufacturers can directly state their opinions to the expert committee and conduct the necessary discussion.
- Manufacturers who are dissatisfied with the final draft of evaluation results can submit a written complaint and state their opinions at the expert committee.

Different roles between the CSIMC general assembly, special committee, and expert committee

	CSIMC General Assembly	Special Committee on Cost-Effectiveness Evaluation	Expert Committee on Cost-Effectiveness Evaluations
Role	<ul style="list-style-type: none"> • Approve the rules of cost-effectiveness evaluations • Approve target products, determine price adjustments 	<ul style="list-style-type: none"> • Discuss the rules of cost-effectiveness evaluations 	<ul style="list-style-type: none"> • Discuss the contents of preliminary consultation and determine analytical framework • Discuss manufacturer analysis • Appraisal
Meeting	Public	Public	Private
Members	<ul style="list-style-type: none"> • 7 members from the payer • 7 members from the healthcare provider • 6 members from the public interest • 10 expert members 	<ul style="list-style-type: none"> • 6 members from the payer • 6 members from the healthcare provider • 4 members from the public interest • 4 expert members • 2 academics 	<ul style="list-style-type: none"> • Health economist • Clinical specialist • Biostatistician/Epidemiologist • Bioethicist

(3) [3] Role and members of the expert committee on cost-effectiveness evaluations (Part 2)

- Because the expert committee will evaluate the results of the analysis from a technical perspective, they will consist of expert-health economists, clinicians, biostatisticians, and bioethicists.
- Conflicts of interest with manufacturers and competitors will be confirmed.

Members of the Experts Committee on Cost-Effectiveness Evaluations and their roles

Committee Members		Roles
Main Committee Members	• Health economist	• Verifies contents of the cost-effectiveness analysis from the standpoint of health economics
	• Clinical specialist	• An individual with a broad range of knowledge comprehensively confirms the validity of the analysis
	• Biostatistician/Epidemiologist	• Considers the scientific validity of the systematic review
	• Bioethicist	• Conducts considerations from an ethical perspective in appraisal
Specialists in each area	• Clinical specialists in each area	• Clinical specialists from each area participate according to the products to confirm the validity of the analysis

Comparison with the other Expert Committees on Drug and Medical Device Pricing

	Expert Committee on Cost-Effectiveness Evaluations	Expert Committee on Drug Pricing (Drug Pricing Organization: DPO)	Expert Committee on Medical Device Pricing
Main Committee Members	<ul style="list-style-type: none"> • Health economists 4 • Clinical specialists 2 • Biostatisticians/Epidemiologists 2 • Bioethicist 1 	<ul style="list-style-type: none"> • Physicians 7 • Dentists 1 • Pharmacists 2 • Health economists 1 	<ul style="list-style-type: none"> • Physicians 12 • Dentists 2 • Health economists 1
Specialists in each area	Designate clinical specialists in each area (around 30)	<ul style="list-style-type: none"> • Physicians 27 • Dentists 1 • Pharmacists 10 • Health economists 4 	<ul style="list-style-type: none"> • Physicians 22 • Dentists 1 • Pharmacists 5 • Health economists 3

(3) [4] Academic analysis

(i) Academic analysis

- Review the submitted manufacturer analysis.
- If the academic analysis group judges that a revision of the analysis is necessary from the standpoint of scientific validity, an independent academic analysis (re-analysis) will be conducted.

(ii) Implementing academic analyses

- The National Institute of Public Health (C2H) will lead the academic analysis. Multiple academic analysis groups will be established, and they will conduct the academic analyses. The National Institute of Public Health (C2H) will coordinate them and evaluate the results of the academic analyses.
- The selected academic institutions will be disclosed.
- The National Institute of Public Health (C2H) will designate which academic analysis group will handle each product, taking into consideration conflicts of interest and their capacity.

(iii) Conflicts of interest

- The products that each of the academic analysis groups are in charge of will not be disclosed until the evaluations are complete. Contact between manufacturer-and academic analysis groups will be prohibited.
- As they will be handling confidential manufacturer information, the academic analysis groups will be required to protect confidentiality.
- Inquiries to manufacturers will be conducted through the National Institute of Public Health (C2H), if needed.

(3) [5] Time schedule of the evaluation process and [6] Methodological guidelines

Standard time schedule

- In order to proceed cost-effectiveness evaluations without delay, set a standard time schedule for each evaluation process.
 - Manufacturer analysis Approximately 9 months
 - (Breakdown) • Preliminary consultation Approximately 3 to 6 months
(until analytical framework has been determined)
 - Manufacturer analysis based on the framework Approximately 3 to 6 months
(the total period should not exceed approximately 9 months)
 - Academic analysis Approximately 3 months (approximately 6 months if a re-analysis is conducted)
 - Appraisal and new price determination Approximately 3 months
- The progress of the each evaluation shall be reported periodically to the CSIMC General Assembly.
- There may be a case that manufacturers, such as small manufacturers that do not have enough capacity, cannot finish the analysis by the deadline. If the standard period is exceeded, report the reason to the CSIMC General Assembly.

Methodological guidelines

- The cost-effectiveness analysis has to be conducted according to the analytical guidelines.
- The interpretations of the analytical guidelines for each product will be discussed in the preliminary consultation, if needed.
- It will also be reviewed as needed after the full-scale implementation.

(3) [7] Cases lacking enough data for analysis

- For products determined to be “impossible to analyze” due to lack of data, upon deliberation by the expert committee, the evaluation process may be interrupted by final approval of the CSIMC General Assembly.
- If the evaluation process is interrupted, the CSIMC General Assembly can ask the manufacturer to accumulate the necessary data by a predetermined deadline. If the data cannot be acquired, the CSIMC General Assembly will conduct price adjustments similar-to products with the poorest cost-effectiveness, based on deliberations by the expert committee.
- If sales of the product are suspended during analysis or if the originally planned market is reduced considerably, the CSIMC General Assembly may discontinue the evaluation process upon deliberation by the expert committee.
- Although the manufacturer may insist that analysis is impossible, the academic analysis group and expert committee will analyze the product. In these cases, the expert committee will determine the draft of price adjustments using the results of the academic analysis only.
- Upon accumulating cases where the evaluation process was interrupted or discontinued, these will be used to consider revision of the current evaluation system.

(4) [1] Verification from a scientific perspective and [3] Disclosure of evaluation

- If it is difficult to determine the ICER as a single value, the analysis results can be submitted as an ICER with a range. For example, there are multiple data suitable for analysis.
- If the product has multiple target populations, the ICER is to be calculated for each population. In this case, the entire new price will be determined by the weighted averages of each adjusted price based on the ICER for each population.
- Promptly disclose the adjusted new price and the ICER as a range.
- In addition, the scientific issues including ICER values will be disclosed in a report in order to deepen scientific discussions and enhance the quality of future analyses.

The case of Drug X, indicated for Disease A and Disease B

			Percentage of population	Adjustment rate
Population A	ICER= JPY 3 million	→ No adjustment	0.8	0% x 0.8
Population B	ICER = JPY 6 million	→ Price adjustment 30% ^(*1)	0.2	+
				30% x 0.2
				= 6% (entire adjustment rate)

Reference value (JPY 5 million)

(*1) See slide 22 for details.

(4) [2] Special consideration (rare, pediatric, and severe diseases)

(i) Principals (Reprint of slide 9)

- If the results of cost-effectiveness evaluations are used to determine reimbursement, patient access may become a major issue. But if price adjustments are made after listing, patient access will be less of a concern.
- Meanwhile, even if the results are used only for price adjustments, it may be a disincentive for R&D. Restricted access cannot be denied for the following products. For these products, a special consideration will be needed.
 - [1] Products for which the unit price (drug/medical device price) is high because they have a small number of patients.
 - [2] Products for which the value cannot be fully assessed by ICER (QALY)
- To ensure the transparency of the system, specific criteria are required for determining what kinds of the products need special consideration.

(ii) Products to be given special consideration in the appraisal process

- The following products will be targeted for cost-effectiveness evaluations, but will be given special consideration in the appraisal process and price adjustments.
 - Products having at least one indication for rare diseases (i.e., designated intractable diseases, hemophilia, and HIV infections) for which there are insufficient treatments;
 - Products having at least one indication for children (i.e., pediatric dosage and administration is approved in Japan)
 - Anti-cancer drugs (if cancer is one of the approved indications and analysis is conducted for population with cancer).
- Analyses including “public long-term care costs and productivity loss” can be also submitted only if they were conducted based on findings in Japan. Although they will not be used for price adjustments, the submitted results of analyses will be disclosed, and used for accumulating experiences.

(5) [1] Target of price adjustments

- Target of the price adjustments will be as follows to be harmonized with the existing drug and medical device pricing system.
 - (i) Similar Efficacy Comparison Method (Similar Functional Classification Comparison Method)
 - Part of premium will be targeted by price adjustments.
 - (ii) Cost Calculation Method
 - Products with a disclosure level under 50%
 - For medicines, part of both the operating profit and the premium will be targeted by price adjustments. For medical devices, part of both the operating profit and its correction will be done ([1] and [2] in the figure).
 - Products with a disclosure of 50% or higher
 - For medicines, part of premium will be targeted by price adjustments. For medical devices, the corrected portion of the operating profit margin will be done ([3] in the figure).

Target of price adjustments in the cost calculation method (medicines) (*1)

[1] [Products with a low disclosure rate and premium]: Premium + operating profit

Total product cost (low disclosure rate)	Operating profit	Premium (*2)
Distribution cost		
Consumption tax		
<div style="text-align: right; margin-right: 50px;">} Target of price adjustments </div>		

[2] [Products with a low disclosure rate and no premium]: Operating profit

Total product cost (low disclosure rate)	Operating profit
Distribution cost	
Consumption tax	
<div style="text-align: right; margin-right: 50px;">} Target of price adjustments </div>	

[3] [Products with a high disclosure rate and premium]: Premium

Total product cost (high disclosure rate)	Operating profit	Premium
Distribution cost		
Consumption tax		
<div style="text-align: right; margin-right: 50px;">} Target of price adjustments </div>		

[4] [products with a high disclosure rate and no premium]: Not targeted

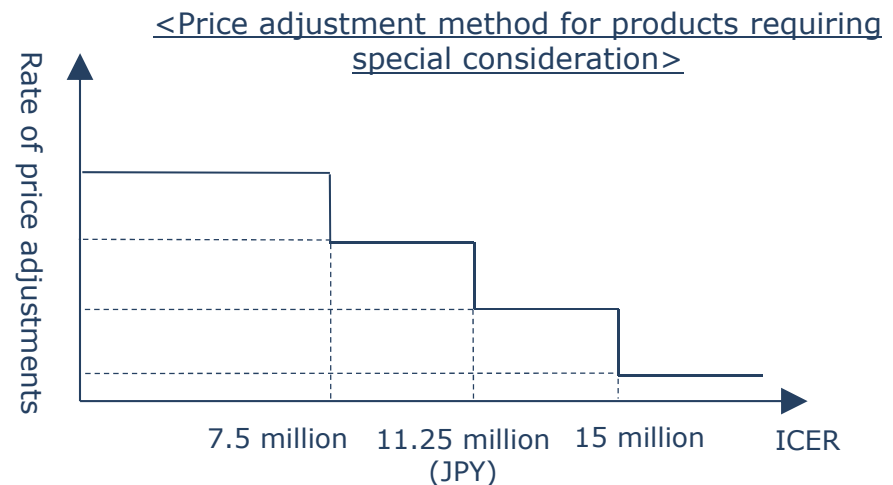
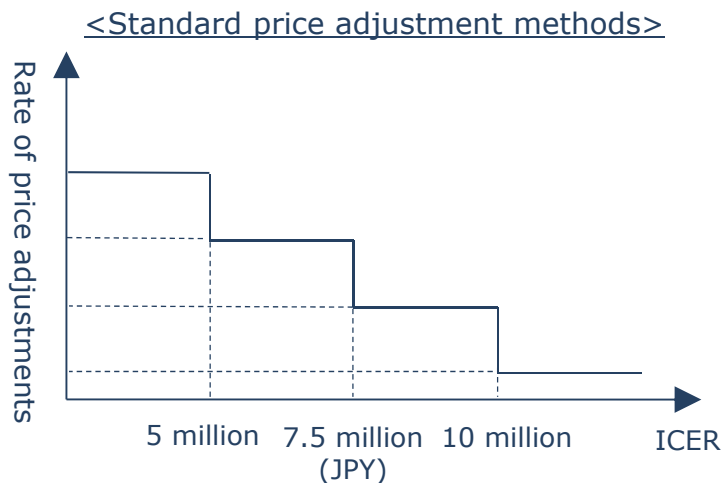
Total product cost (high disclosure rate)	Operating profit
Distribution expenses	
Consumption tax	

(*1) Products with a low disclosure rate and premiums will receive price adjustments for both the premium and operating profit, based on the cost-effectiveness evaluations.

(*2) For medical devices, equivalent to the corrected portion of the operating profit margin.

(5) [2]-[4] Method of price adjustments according to ICER, setting reference values (threshold), and price adjustments for products requiring special consideration

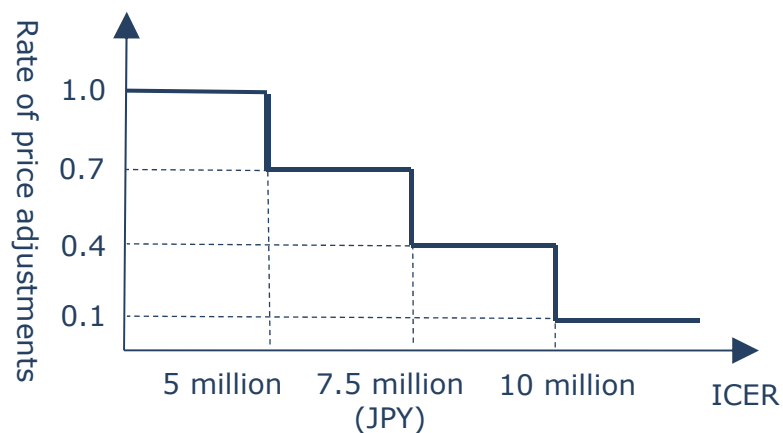
- The price adjustment rate will be determined in a stepwise manner.
- JPY 7.5 million/QALY, which is in between existing reference values (threshold) [JPY 5 million/QALY and JPY 10 million/QALY] will be newly used for price adjustments.
- The reference values for products requiring special consideration in the appraisal process shall be JPY 7.5 million/QALY, JPY 11.25 million/QALY, and JPY 15 million/QALY based on the relationship between GDP per capita and reference values in other countries.
- For products that include rare and pediatric diseases and cancer as a part of their indications, these high reference values will be used only for the population with the diseases.
- If the range of ICER straddles the reference value, the expert committee will determine a more scientifically valid adjustment rate(*).



(5) [5] Rate of price adjustments (Part 1)

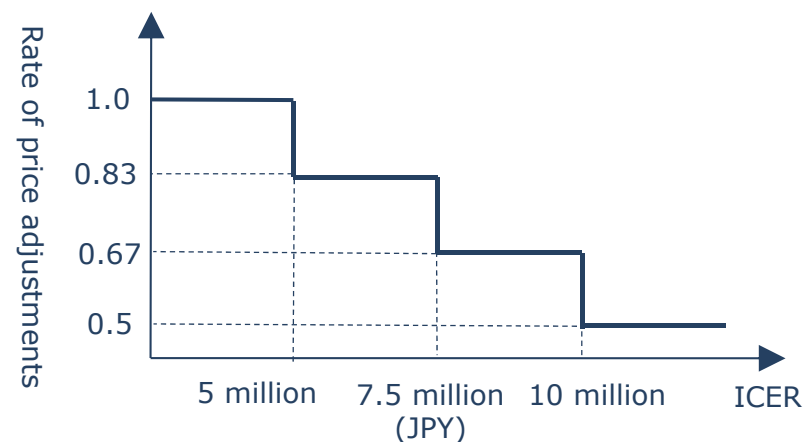
- With the Similar Efficacy Comparison Method (Similar Functional Classification Comparison Method), price adjustments will be conducted for the targeted part (e.g., utility premiums) as shown in Figure 1.
- With the Cost Calculation Method, different rates of price adjustment will be used respectively for premium (medicines) or the corrected portion of the operating profit margin (medical devices) (Figure 1) and operating profit margin (Figure 2).

Figure 1: Rate of Price Adjustments for Premium



Premium after price adjustment
 = Premium prior to price adjustment ×
 Rate of price adjustment

Figure 2: Rate of Price Adjustments for Operating Profit



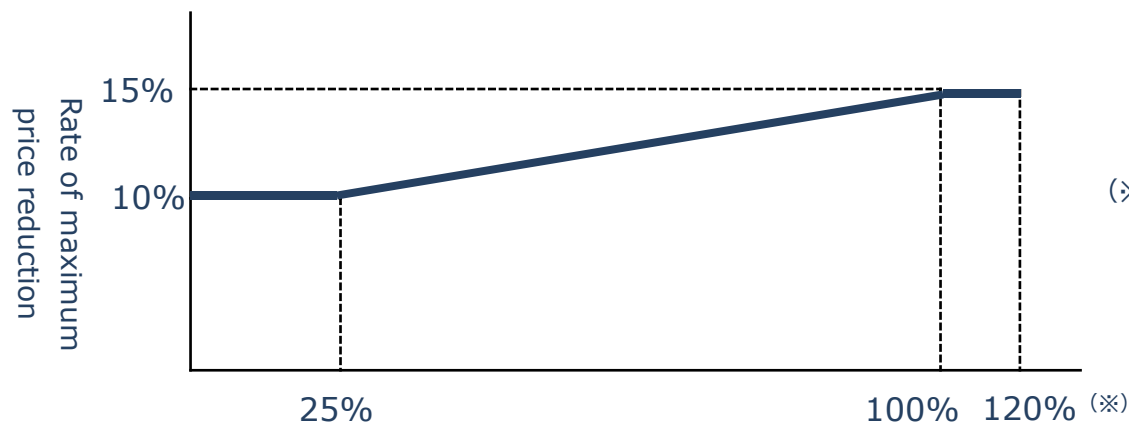
Operating profit margin after price adjustment
 = Operating profit margin prior to price adjustment ×
 Rate of price adjustment

(5) [5] Rate of price adjustments (Part 2)

- To ensure the stable supply of medicines required by patients, the maximum price reduction is determined as follows:
 - (i) Products with ≤ 25% premium (※)
 - The rate of maximum price reduction is 10% of the entire drug and medical device price prior to adjustment
 - (ii) Products with 25% < premium ≤ 100% (※)
 - The rate of maximum price reduction is percentage of the drug and medical device price prior to adjustment, determined by the following equation.

$$\text{rate of maximum price reduction} = (10 + [\text{premium rate} (\%) (\text{※}) - 25] / 15) \%$$
 - (iii) Products with > 100% premium (※)
 - The rate of maximum price reduction is 15% of the drug and medical device price prior to adjustment
- The new price shall not fall below the price corresponding to an ICER of JPY 5 million/QALY (for anti-cancer drugs, JPY 7.5 million/QALY).

Relation between the premium rate and maximum price reduction rate



(※) In the case of medicines for which the price is set by the cost-calculation method, use the premium rate before multiplying by the adjustment rate depending on disclosure level.

(5) [6] Products evaluated as “dominant” or having a low ICER value

- For products that are superior in cost-effectiveness, the prices will be raised if certain conditions are satisfied.
 - (i) Effectiveness improves (or is equivalent to) with lower costs than comparator (“Dominant”)
 - (ii) ICER is JPY 2 million/QALY or less.

Conditions for raising prices and rate of increase

	(i) Dominant	(ii) Under ICER JPY 2 million/QALY
Condition [1] • Clinical studies indicate that the product is superior (or equivalent) in effectiveness to the comparator.	○	○(*1) (Other conditions ^(*2) to be stipulated)
Condition [2] • The product is innovative, rather than just improved. For example, a completely different product, a different basic structure, or different action mechanism from comparator.	○	○
Rate of price adjustment ^(*3)	+50% ^(*4) (Not to exceed 10% of the entire price)	+25% ^(*5) (Not to exceed 5% of the entire price)

(*1) For products with an ICER under JPY 2 million/QALY, clinical studies indicate that the product is superior (or equivalent) in effectiveness to the comparator.

(*2) Conditions stipulated simultaneously (clinical research needs to satisfy all of the following conditions)

(1) Accepted as an original paper by an academic journal given an impact factor (five-year average) of over 15.0 by Clarivate Analytics “InCites Journal Citation Reports” at the time of its acceptance or publication (this excludes review journals and young journals founded within the last 10 years).

(2) The clinical study that satisfies (1) need to show statistical superiority to the comparator in the cost-effectiveness evaluation in Asian populations, including Japanese.

(*3) Excluding operating profit.

(*4) The amount of price increase shall not exceed less than 1/2 of cost reduction per patient.

(*5) The amount of price increase shall not exceed the price corresponding to an ICER of JPY ICER 2 million/QALY.

(5) [7] Timelines and procedures of price adjustments and (6) Building greater capacity

Timelines of price adjustments

- Conduct price adjustments based on the results of cost-effectiveness evaluations at the time of listings (4 times per year) for new medicines and new medical devices.
- The results of the evaluation and new price after adjustment will be reported to the CSIMC General Assembly to acquire final approval.
- Taking stocks into consideration (bought at the price prior to adjustment), a certain period will be secured from the time of determining the new price to the time of the actual price adjustment.

Building greater capacity

- Undertake capacity building by increasing the number of experts on cost-effectiveness evaluations.
- Specifically, to increase experts to contribute to the academic analysis, consider newly establishing an educational program. Concurrently enhance the systems at the Ministry of Health, Labour and Welfare and the National Institute of Public Health (C2H).

(7) Future Investigations on Cost-effectiveness Evaluations

The Central Social Insurance Medical Council (CSIMC) established a committee for cost-effectiveness evaluations in May 2012 and promoted investigations on the most desirable application of cost-effectiveness evaluation in Japan.

In order to compile this outline, issues were organized by the special committee for cost-effectiveness evaluations and the joint committee. They are based on previous discussion at the CSIMC, results of trial introduction, inputs from academics, and opinions from relevant industries.

From this April, the new system will be initiated based on this outline, accumulating experiences on the cost-effectiveness evaluation and substantiating the evaluation system.

Furthermore, investigations will be performed on the expansion of the selection criteria, analysis processes, appraisal, price adjustment, and desirable utilization of the results at listing in order to make it a more efficient and highly transparent system. Such investigations will continue by taking into account of performing appropriate pricing, the effects on the medical insurance system finances, and the necessity to ensure transparency of pricing, with reference to efforts in other countries.

In addition, investigations will be performed on factors and items that should be specially taken into account in the appraisal and price adjustment, based on analysis submitted from companies and rules in other countries.