Update of Drug Pricing System in Japan

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Outline

1. Drug Price Standard system
2. The reform of drug price system in FY2016
3. Emergency measures for drug price
4. Health Technology Assessment

1. Drug Price Standard system

National Health Insurance Drug Price Standard

Items and prices of drugs usable in insurance-covered healthcare, specified by the Minister of Health, Labour and Welfare

(common for all medical insurance systems, including health insurance, National Health Insurance (NHI), and various mutual aid systems)

- Item list
  - A doctor or pharmacist operating under the health insurance program, in principle, must not use drugs other than “Drugs the Minister of Health, Labour and Welfare specifies”.
  - Items listed in the NHI Drug Price Standard are stipulated as “Drugs the Minister of Health, Labour and Welfare specifies”.

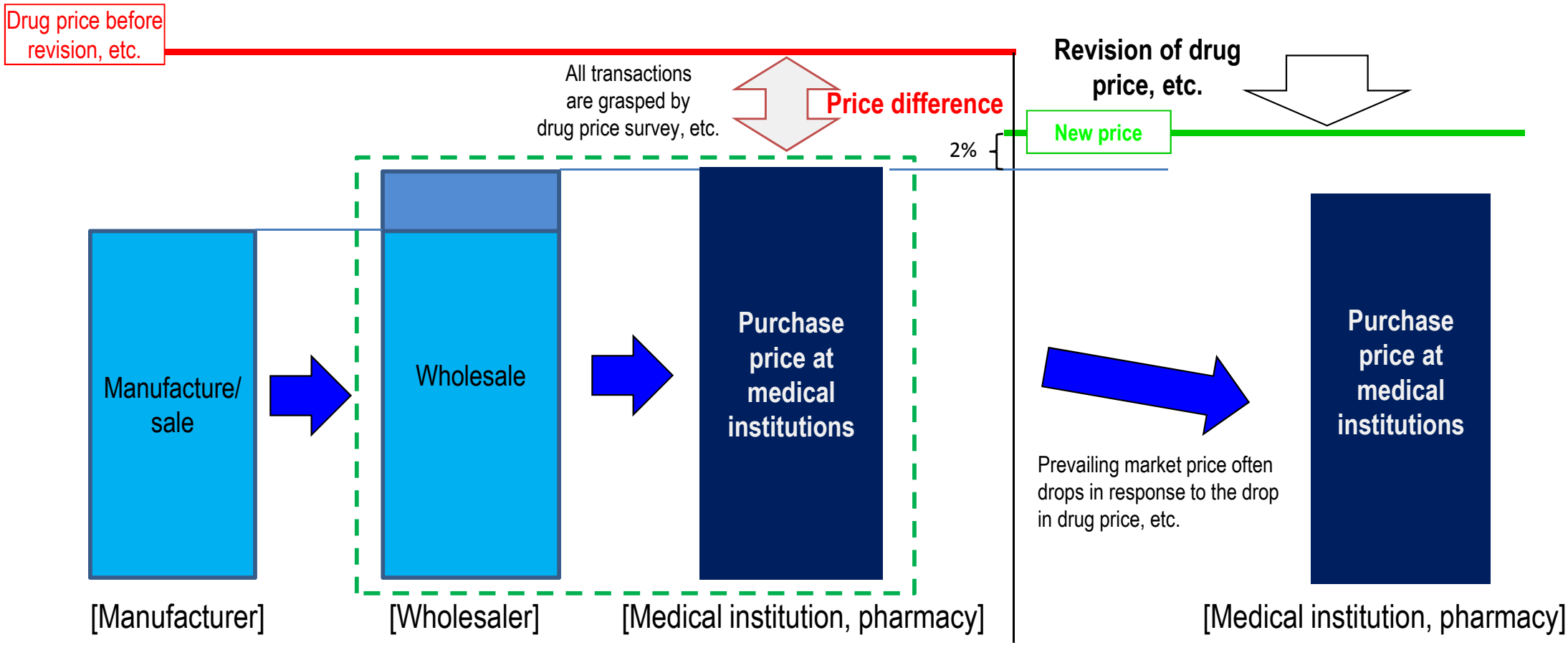
  = NHI Drug Price Standard specifies drugs usable in insurance-covered healthcare, and functions as an item list.

- Price table
  - When an authorized medical institution or pharmacy operating under the health insurance program makes insurance claims, the drug charge shall be calculated based on the price specified in the NHI Drug Price Standard.

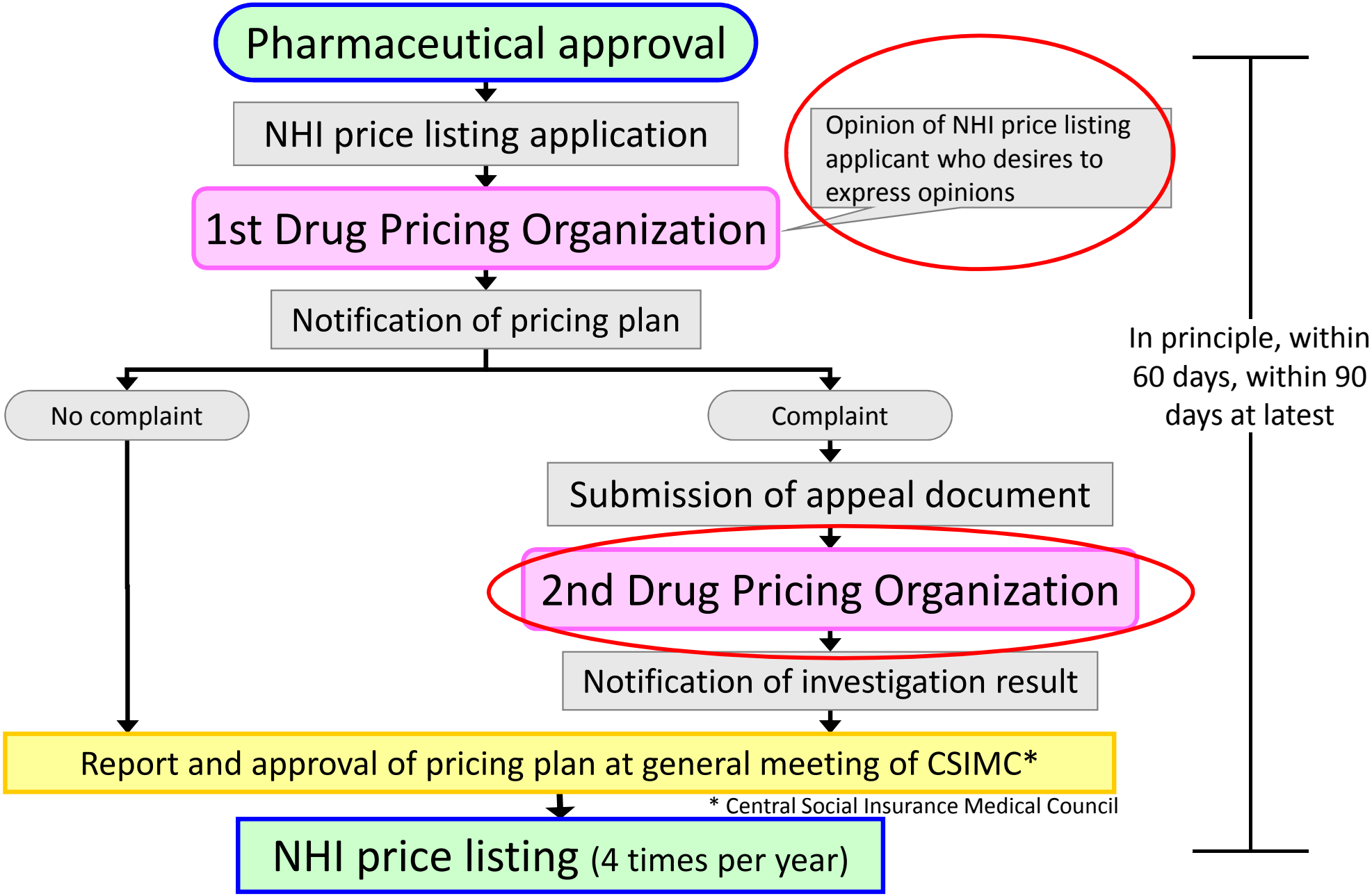
  = NHI Drug Price Standard specifies the claimable amount of drugs used in insurance-covered healthcare, and functions as a price table.

Revision of price of listed drugs

The actual purchase prices paid by medical institutions and pharmacies (prevailing market price) are surveyed (drug price survey) and the prices specified in the drug price standard are revised periodically based on the results of the survey.



New drugs price determination process



Price determination by comparable drugs

- When there are comparable drugs with similar efficacy, the daily drug price of the new drug is matched to the daily drug price of existing comparable drugs from the viewpoint of ensuring fair competition in the market. [Price determination by comparable drugs (I)]
  - A comparable drug shall be, in principle, a new drug within 10 years after NHI price listing and the drug price of generic drugs is not listed.

=

<Daily drug price matching>

¥50 × 3 = ¥X × 2

X = 75 yen

1 tablet = ¥50
3 tablets a day

1 tablet = ¥X
2 tablets a day

Comparable drugs refer to those similar in the following aspects.

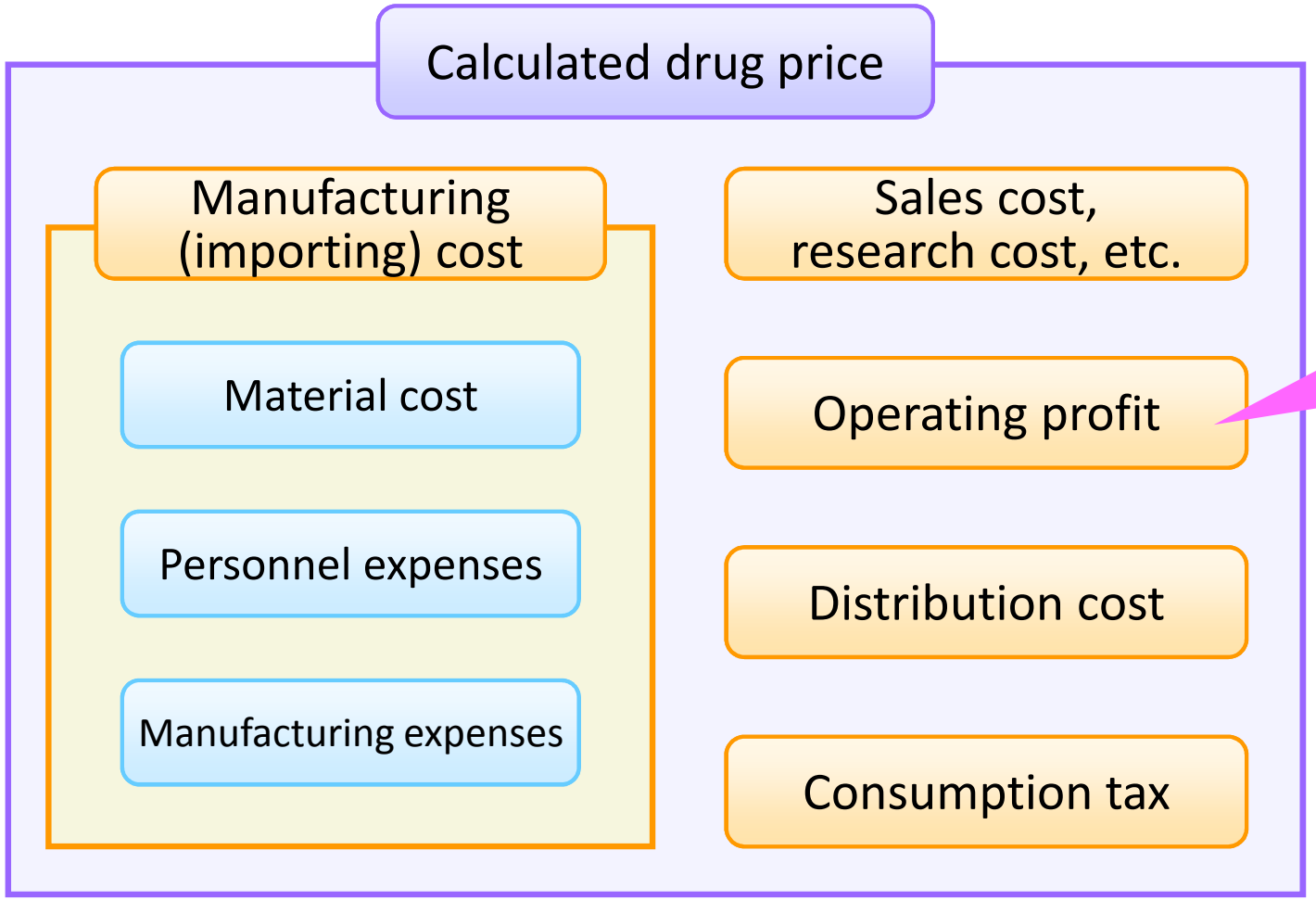
A Efficacy and effect
B Pharmacological action
C Composition and chemical structure
D Dosage form, division and use

- For the relevant new drug, when higher efficacy is identifiable compared to comparable drugs, a corrective premium is applied to the above amount. [Innovativeness premium, usefulness premium, marketability premium, child premium, and sakigake review designation scheme premium]

Innovativeness premium	70-120%	New action mechanism, high efficacy/safety, improvement of disease treatment method
Usefulness premium	5-60%	High efficacy/safety, improvement of disease treatment method
Marketability premium	5%, 10-20%	Orphan drug, etc.
Child premium	5-20%	Dosage and usage expressly includes those pertaining to children, etc.
sakigake review designation scheme premium	10-20%	Pharmaceutical approval was obtained in Japan ahead of other countries, etc.

Cost accounting system

Add up material cost, manufacturing expenses, etc., if there is no comparable drug



Operating profit varies drastically in the range from **–50% to +100%**, depending on the level of novelty, efficacy, or safety compared to the existing therapy.

In principle, in case of exceeding the average coefficient for the pharmaceutical industry, calculation is performed using a coefficient.

The drug price of the follow-on biologics (biosimilars)

- Case of follow-on products of biotechnology

  : **0.7 multiplication of the drug price of the original product**

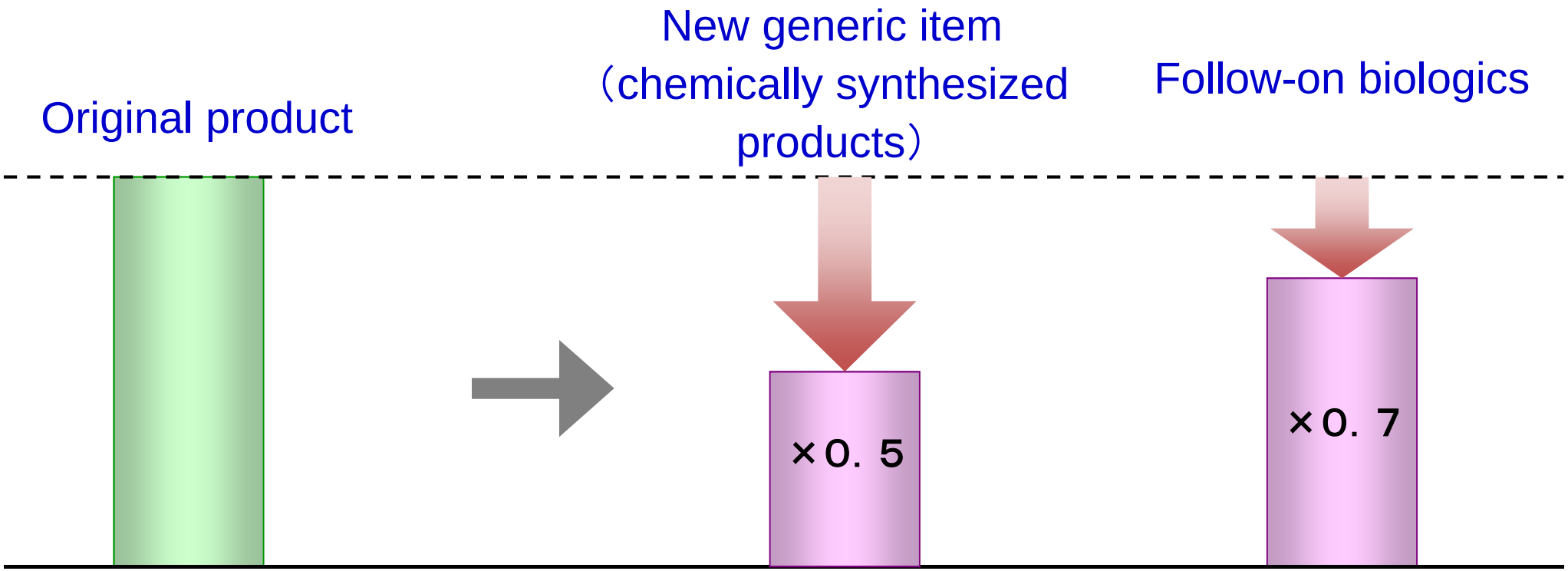
  ※If the medicine is more than 10 items, 0.6 multiplied

  ※Depending on the degree of clinical trial, up to 10% addition is allowed

- Case of chemically synthesized products

  : **0.5 multiplication of the drug price of the original product**

  ※If the medicine is more than 10 items, 0.4 multiplied



2. The reform of drug price system in FY2016

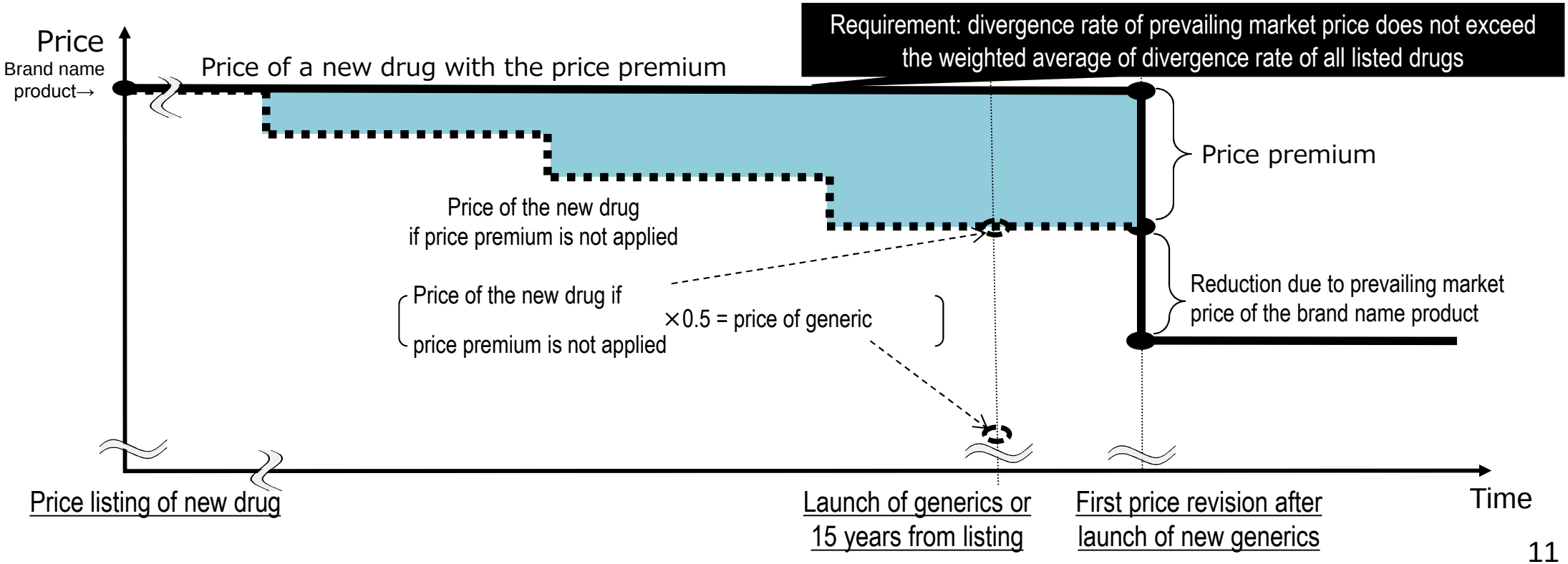
「Framework of the reform of drug price system in FY2016」

(approved in the general meeting of Central Social Insurance Medical Council on December 25,2015)

Continued trial implementation of price premium for promotion of new drug development and resolution of off-label use, etc.

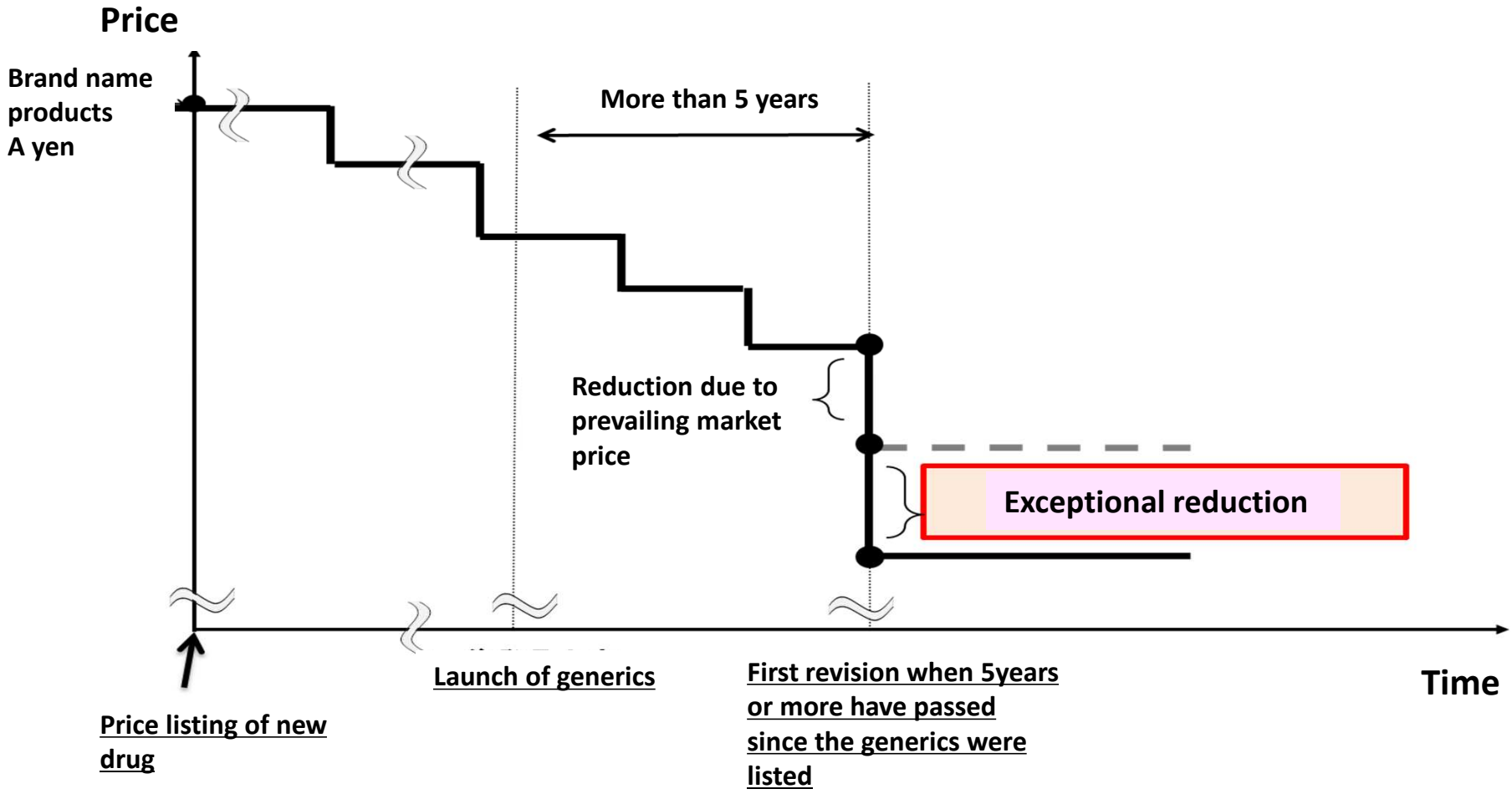
The trial implementation of the price premium shall be continued as innovation through the development of drugs that contributes to the growth strategy is promoted, and new requests for unapproved and off-label drugs are publicly invited.

After the reform of drug price system in FY2016, we will confirm how far the development of unapproved and off-label drugs is proceeding and evaluate concrete results of R&D of new medicine.We will also examine how the premium system should be in the future.



Revision of drug price that promotes replacement of drugs listed for a long time with generics

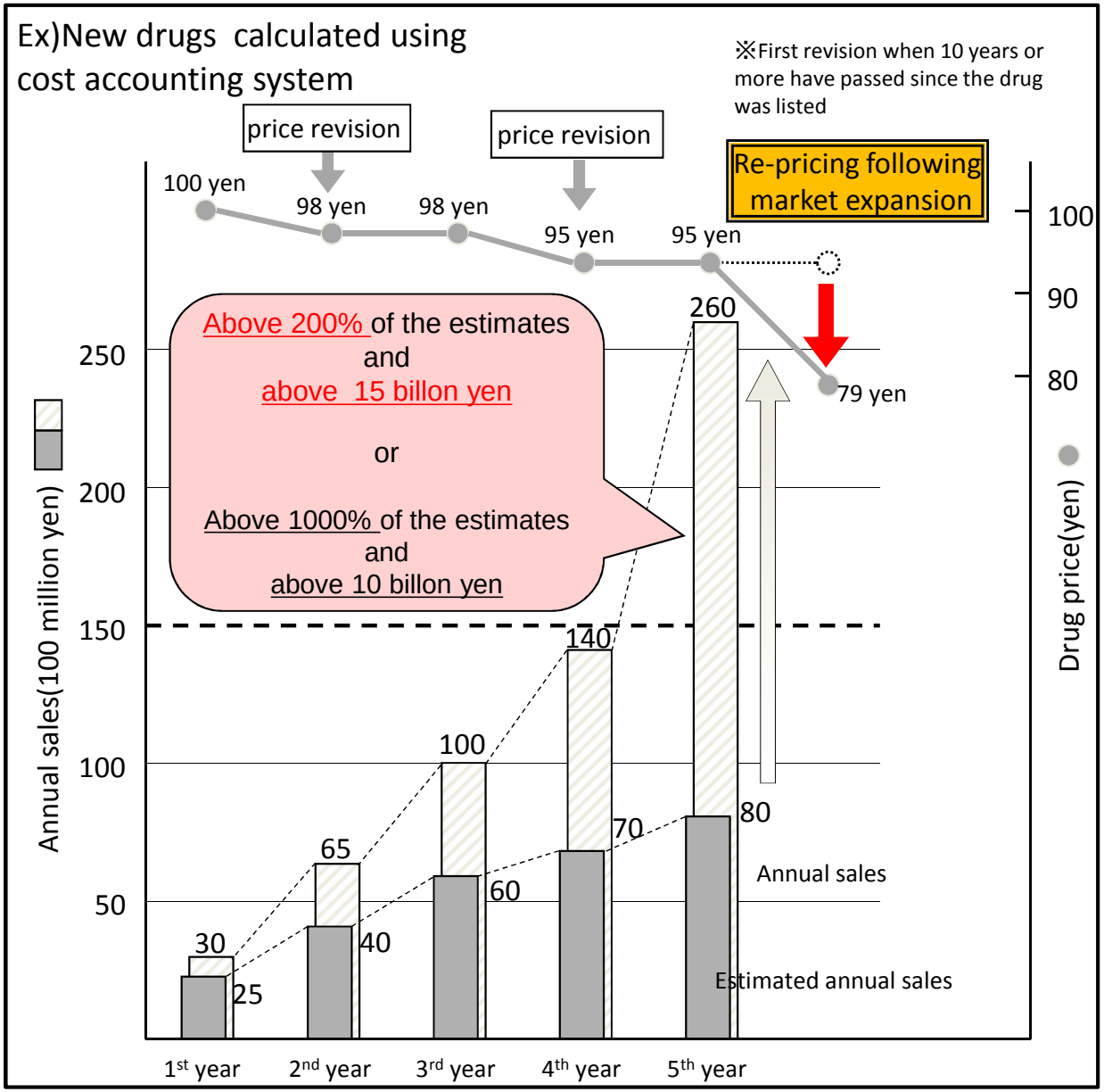
- "Exceptional reduction" shall be applied to individual brand name products that have not been appropriately replaced by generics even after 5 years of listing of these generics.
- The percentage of exceptional reduction is shown below.
  - Price reduction of brand name products with less than 30% of replacement rate by generics : 2.0%
  - Price reduction of brand name products with less than 50% of replacement rate by generics : 1.75%
  - Price reduction of brand name products with less than 70% of replacement rate by generics : 1.5%

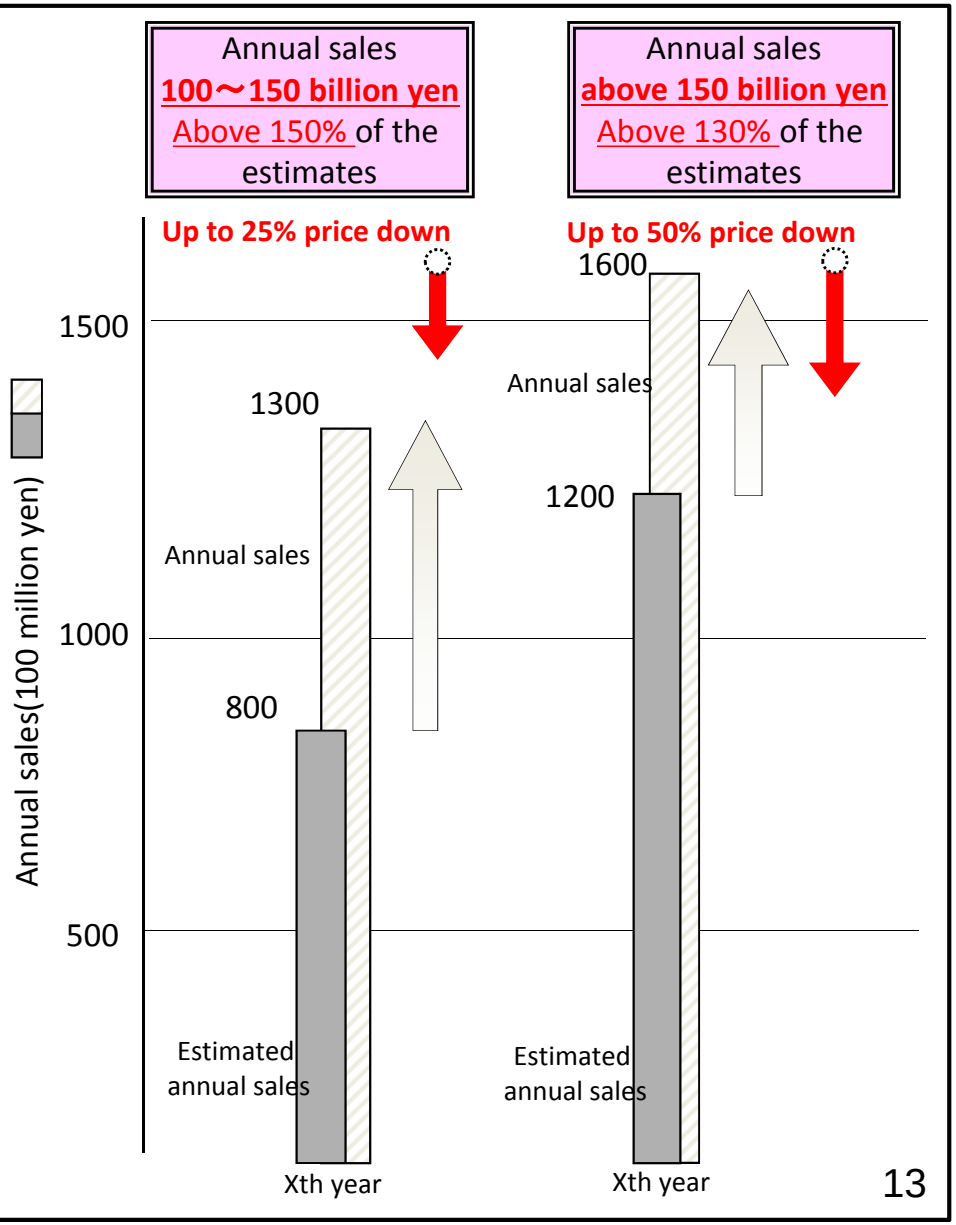


“Re-pricing following market expansion” for the drugs with huge annual sales

【Now（Previous）】
Price will be reduced when annual sales of a drug exceed its estimated figure to some extent.

【Revised】
The drugs with huge annual sales will be treated as an exception of the current rule.





「Framework of the reform of drug price system in FY2016」

(approved in the general meeting of Central Social Insurance Medical Council on December 25,2015)

Ⅱ Price revision of drugs already listed

3. Basic drugs

The system named "Basic drugs" is designed to prevent the drug from being minimum-priced or being subject to the rule of re-pricing unprofitable products.

As a trial implementation in the FY2016 drug pricing system reform,prices on those that meet all the requirements below will be fixed at that of a brand with biggest sales. The price will be maintained while they are authorized as basic drugs.

① 25 years or more passed after NHI price listing and each deviation rate of the market price to the drug price of a certain brand and drugs with same ingredient does not exceed the average deviation rate of all listed drugs.

② Having a multiplicity of uses ,for example, to be listed in general guidelines and widely used at medical institutions

③ drugs formerly subject to the rule of re-pricing unprofitable products

unti-pathogenic organism drugs and narcotic drugs forming the basis of health care for a long time

Profitable drugs are excluded from the basic drugs category. As for basic drugs,stable supply should be maintained while the prices are maintained.

Subject of basic drugs at the reform of drug price system in FY2016

The prices of basic drugs will be fixed at that of a brand with biggest sales and the price will be unchanged while they are authorized as basic drugs.

Subject：134 ingredients 439 items

Category	Number of ingredients (Number of items)	Example	Main efficacy
pathogenic organism	51（160）	AMOLIN FINE GRANULES EBUTOL Tablets Retrovir Capsules ARASENA-A for I.V. Infusion	various infections pulmonary tuberculosis etc HIV infection herpes simplex encephalitis etc
narcotic drugs	6（15）	MS Contin MORPHINE HYDROCHLORIDE INJECTION	pain relief of cancer with severe pain pain relief or sedation when suffering from severe pain etc
Unprofitable products	77（264）	HYDANTOL POWDER THYRADIN-S POWDER Endoxan PAM SOLDEM 3	epileptic fit congenital hypothyroidism multiple myeloma etc organophosphorus agent poisoning Rehydration when unable to intake orally etc

※ categorize as Unprofitable products when the drug can also be categorized into other categories

3. Emergency measures for drug price

Emergency price revision in the fiscal year 2016

General meeting-2,
Central Social Insurance
Medical Council
Nov. 16, 2016

1. Target items

[Criteria of the emergency revision of drug price in the fiscal year 2016]
(1) The drug price shall be revised for the following drugs:
  a. The drug listed in the NHI price list whose partial change of indications and dosage and administration was approved between October 2015 and March 2016
  b. The drug listed in the NHI price list whose company forecasted annual sales (drug price basis) in the fiscal year 2016 are more than 100 billion yen and the company forecasted annual sales are 10-fold or more of the forecasted annual sales at the time of NHI listing

○ Ministry of Health, Labour and Welfare extracted the drug which applies to the requirement in a. above and confirmed with the manufacturer if the relevant drug applies to the requirement in b. above. The manufacturer replied that the following products applied to the requirement b.

Product name	Manufacturer name
Opdivo intravenous infusion 20 mg Opdivo intravenous infusion 100 mg	ONO PHARMACEUTICAL CO., LTD

○ We suggest conducting the emergency price revision in the fiscal year 2016 for the relevant product.

2. Calculation

[Criteria of the emergency revision of drug price in the fiscal year 2016]
(2) Drug price will be revised to the price calculated by the formula designated in Annex 6-2 in the Criteria of drug pricing (approved by Central Social Insurance Medical Council on February 10, 2016). In the calculation, the company forecasted annual sales (drug price basis), etc. shall be used as annual sales.
α (corrected additional rate) shall not be applied.

○ Company forecasted annual sales of Opdivo intravenous infusion that apply to (1) were announced to be 126 billion yen in invoice price (shipped price) basis. In consideration of distribution cost, consumption tax, the rate of deviation as well as additional indications in the future, the total sales are estimated to be more than 150 billion yen (drug price basis) in the fiscal year 2016 (see next page 〈Reference〉).
On the contrary, if it is calculated according to (2), the drug price will be as follows:

Product name	Current drug price	Calculated drug price	Rate of change
Opdivo intravenous infusion 20 mg	150,200 yen	75,100 yen	-50%
Opdivo intravenous infusion 100 mg	729,849 yen	364,925 yen	-50%

Master reform plan for fundamental reform of the drug pricing scheme 1 (December 20, 2016)

1. Drastic Reform of the Drug Pricing System

(1) In order to enable responses to changes in circumstances after insurance listings and to enable a prompt response to the expansion of markets beyond a given size that accompany additional indications, etc., opportunities for new drug listings will be utilized to their maximum extent, and drug prices will be reviewed four times per year.

(2) In order to timely reflect the market price in drug pricing and suppress the burden placed on the Japanese people, drug price survey will be conducted annually and will cover all products, and drug prices will be revised based on the results.
To this end, in addition to the drug price survey currently being conducted biennially, a survey will be conducted for major businesses in the year in between, and drug prices for products with major price discrepancies (See Note) will be revised.
(Note) A conclusion will be reached on the specifics within the next year.

In addition, with regards to the drug price survey, the accuracy of the results of the survey and the survey methods, etc. will be verified, and based upon this, we will consider reviewing the drug price survey themselves, reaching a conclusion within the next year.

Master reform plan for fundamental reform of the drug pricing scheme 2 (December 20, 2016)

(3) In order to promote the creation of innovative new drugs, the pricing premium system for the promotion of new drug development and the resolution of off-label use will be given a drastic and zero-based review, and by fully implementing cost-effectiveness evaluations including raising the price of drugs with high cost-effectiveness, innovation will be evaluated by appropriately identifying the drugs that are truly effective, promoting investment in research and development.

In order to fully implement cost-effectiveness evaluations, in addition to basing it on expert knowledge, the method of implementation including organizations / systems from a third party perspective will also be considered, and a conclusion will be reached within the next year.

Master reform plan for fundamental reform of the drug pricing scheme 3 (December 20, 2016)

2. Future Initiatives in Conjunction with the Reform

(1) Thoroughly ensure the accuracy and transparency of the drug price calculation method. Specifically, while taking into consideration the high confidentiality of the information for the pharmaceutical companies, the clarification of the basis for drug price calculations and the enhanced transparency of the drug price calculation process will be considered, and a conclusion will be reached. In addition, particularly for highly priced drugs, improvements to methods for adjusting foreign prices will be considered, such as getting a more accurate grasp of foreign prices while taking into consideration differences in systems, and a conclusion will be reached.

(2) The business status of parties involved who will be impacted by the reform of the drug price system will be swiftly grasped, and based on the results, a response will be considered as needed, and a conclusion will be reached.

Master reform plan for fundamental reform of the drug pricing scheme 4 (December 20, 2016)

(3) With regards to Japan's pharmaceutical industry, in order to switch from a model that is dependent on long-listed products to an industrial structure with more extensive drug discovery capabilities, the enhancement of measures to support the research and development of innovative biopharmaceuticals and biosimilars will be considered, as well as the support of venture companies and promoting the competitiveness of generic drug companies in the market, and a conclusion will be reached.

(4) In order to ensure the stable distribution of pharmaceutical products, the efficiency of distribution will be increased while taking the business statuses into consideration, improvements in distribution will be promoted, and appropriate approaches to the profit structure will be made to accompany the market environment. In particular, in order to promote the appropriate formation of prices, effective measures for promoting single item unit price contracts and early settlement of terms will be considered, and a conclusion will be reached.

(5) For new medical technologies with established evaluations, measures for promptly providing them to the Japanese people will be considered based on cost-effectiveness, and a conclusion will be reached.

4. Health Technology Assessment

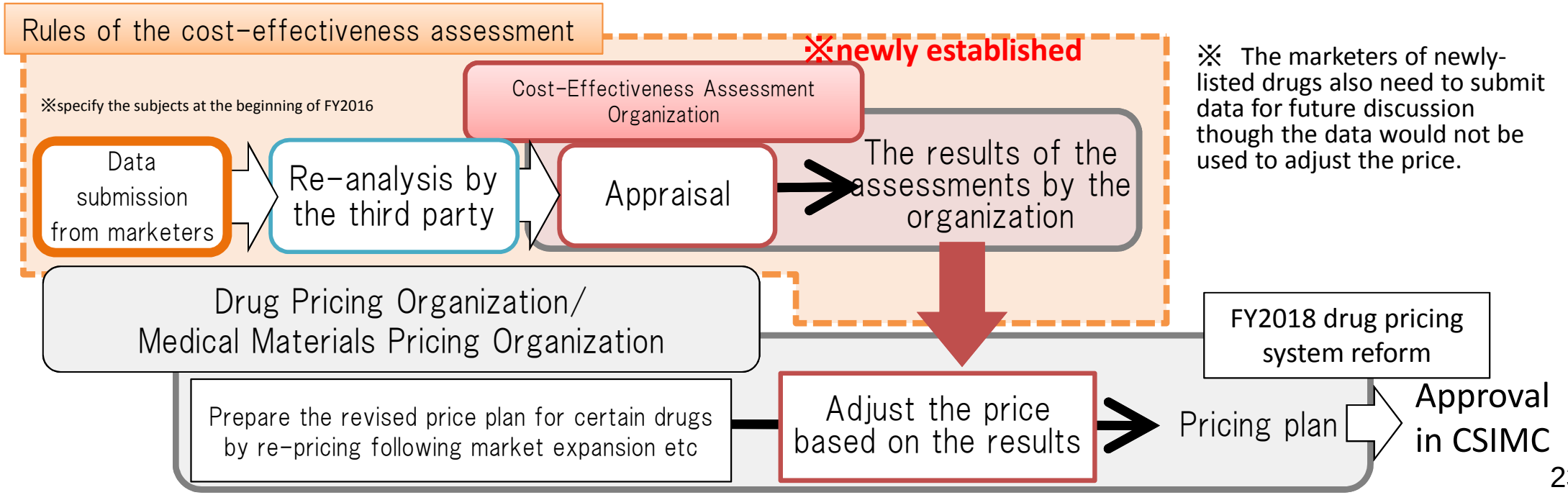
Trial implementation of the cost-effectiveness assessment

- We established "Special Committee on Cost-Effectiveness Assessment" as a branch of Central Social Insurance Medical Council ,out of concern for fiscal impact of growing expensive healthcare technologies. In the FY2016 drug pricing system reform, the cost-effectiveness assessment shall be introduced on a trial basis to evaluate medicine and medical instruments.

＜Discussion at Central Social Insurance Medical Council(CSIMC)＞

2012.5	Establishment of "Special Committee on Cost-Effectiveness Assessment" Discuss the relevant drugs,analytical method, and the use of the assessments etc,referring to overseas cases, on about once a month basis
2014.4～2015.11	Examine specific drugs and report the problems to the general meeting.Discuss each issue.
2015.12	Summarize how the cost-effectiveness assessment should be implemented on a trial basis.
2016.4	Trial implementation of the cost-effectiveness assessment

The flowchart of the trial implementation of the cost-effectiveness assessment (Outline)＞



※ The marketers of newly-listed drugs also need to submit data for future discussion though the data would not be used to adjust the price.

Summary of the selection criteria and Target Drugs/Medical Devises

<Selection criteria for already listed items>

[1] Exclusion criteria
- a) Designated rare intractable disease, hemophilia and HIV infections
- b) Request, etc., for the development based on the Review Committee on Unapproved Drugs, etc.

[2] Selection criteria

a) Drugs listed for fiscal years 2012 to 2015, whose price was determination by **similar efficacy comparison method**, meeting either of the following criteria.
- i) **The premium rate is the highest**.
- ii) **The expected peak sales is the highest** among drugs for which a premium of 10% or more was approved.

b) Drugs listed for fiscal years 2012 to 2015, whose price was determination by **cost calculation method**, meeting either of the following criteria.
- i) **The profit premium rate is the highest**.
- ii) **The expected peak sales is the highest** among the items for which a premium of 10% or more is approved.

* **Including pharmacological analogues** of the drugs selected based on these criteria.

(Also for newly listed items meeting the similar criteria , data submission is requested for future review, but not for price adjustments.)

	Drugs (7 items)	Medical Devises (5 items)
similar efficacy (functional category) comparison method	Sofosbuvir	Kawasumi Najuta Thoracic Stent Graft System
	Ledipasvir Acetonate/Sofosbuvir	Activa RC
	Ombitasvir Hydrate/ Paritaprevir Hydrate/Ritonavir	Vercise DBS System
	Daclatasvir Hydrochloride	
	Asunaprevir	
cost calculation method	Nivolumab	J-tec Autologous Cultured Cartilage
	Trastuzumab Emtansine	Sapien XT