National Health Insurance (NHI) pricing formula in Japan

Improvement in methodology of pricing for new drugs and orphan drugs

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Today's Topics

- Pharmaceutical industry of Japan
- Central Social Insurance Medical Council (CSIMC)
- Premium to promote the development of new drugs and eliminate off-label use
- NHI drug pricing formula for new drugs
- Recent cases
- Conclusion

Summary of pharmaceutical industry in Japan

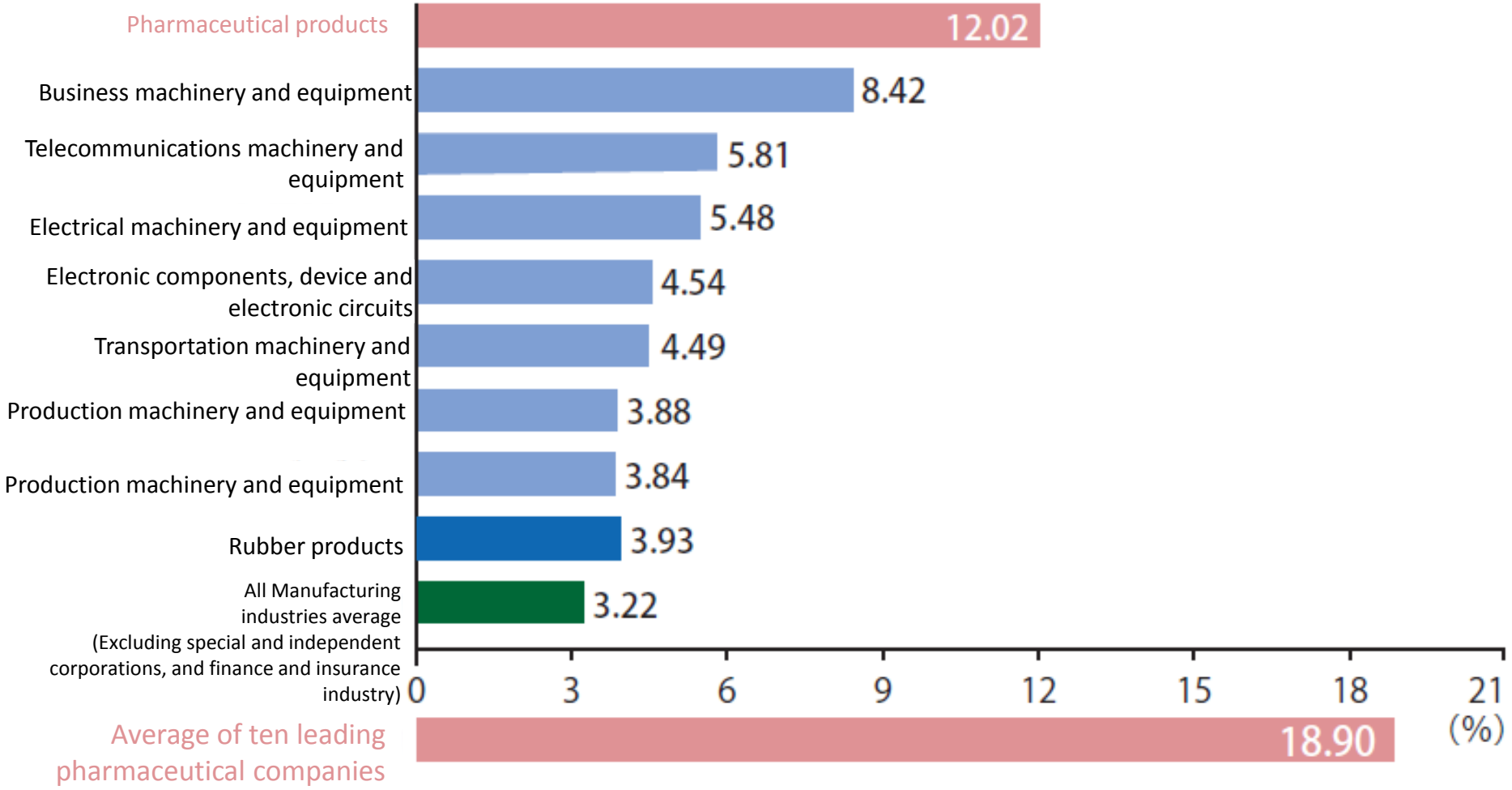
- **Number of pharmaceutical companies (2012 fiscal year)[*1] :** 349
  - Japan Pharmaceutical Manufacturers Association (JPMA) member companies (Research and development-oriented companies) : 72[*4]
- **Number of employees (2012 fiscal year) [*1]:** 167,514
  - Vs total employees[*2]: 0.27%
- **Drug production revenue (2012 fiscal year)[*3]:** 6.9767 trillion yen
  - Production revenue versus GDP ratio: 1.48%
  - Prescription drugs value: 6.263 trillion yen (89.8%)

*1: 2012 fiscal year Pharmaceutical and medical device industry Survey (Ministry of Health, Labor and Welfare) *2: 2012 fiscal year Labor force survey (Ministry of Internal Affairs and Communications) *3: 2012 Statistics of Production by Pharmaceutical Industry (Ministry of Health, Labor and Welfare) *4: As on April 1, 2014

Source: Transform the contribution of the drug industry and drugs

Research and development investment of top key industries

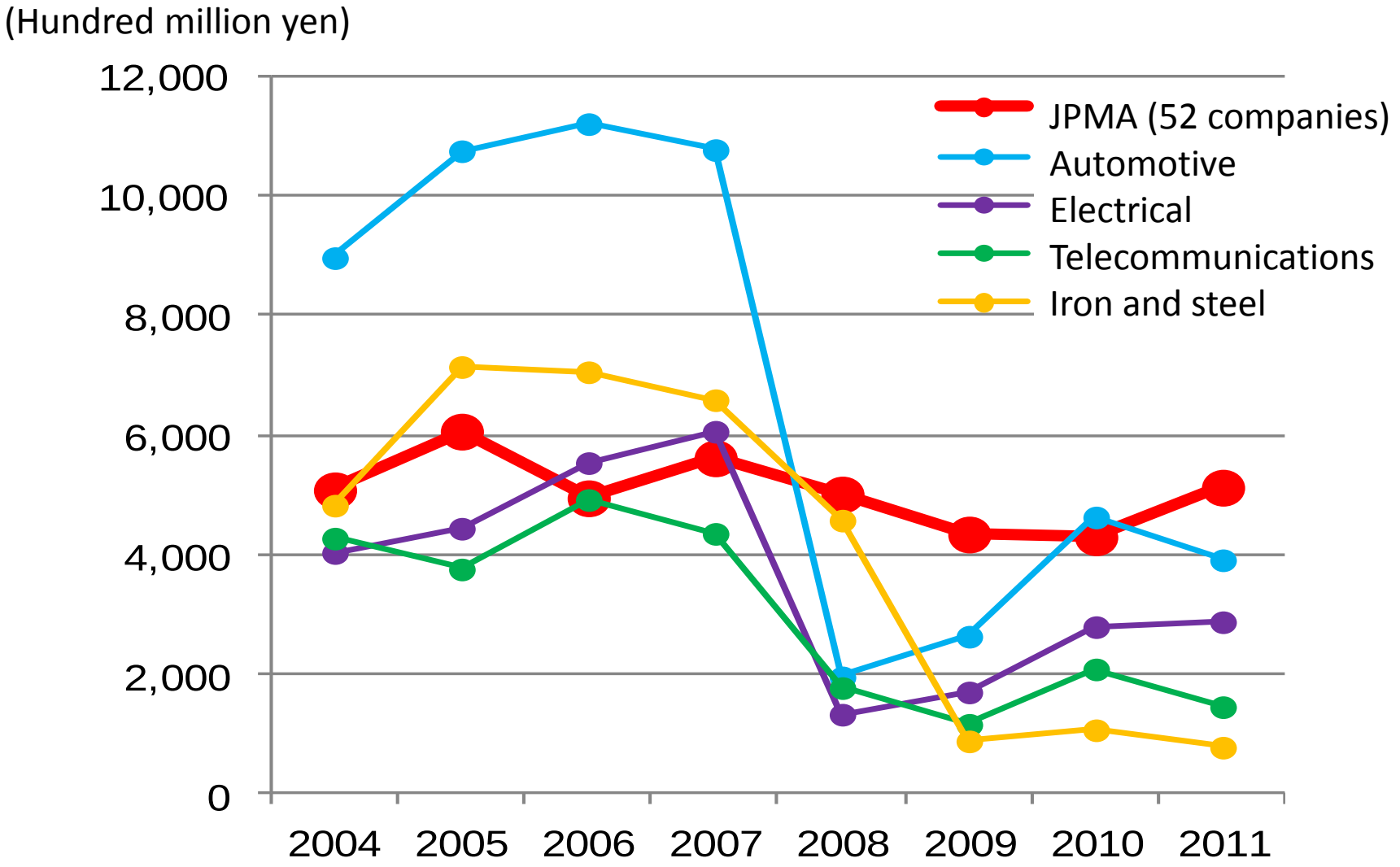
Ratio of Sales to Research and Development Expenses (2010)



Source: Japan Pharmaceutical Manufacturers Association DATA BOOK 2012, JPMA

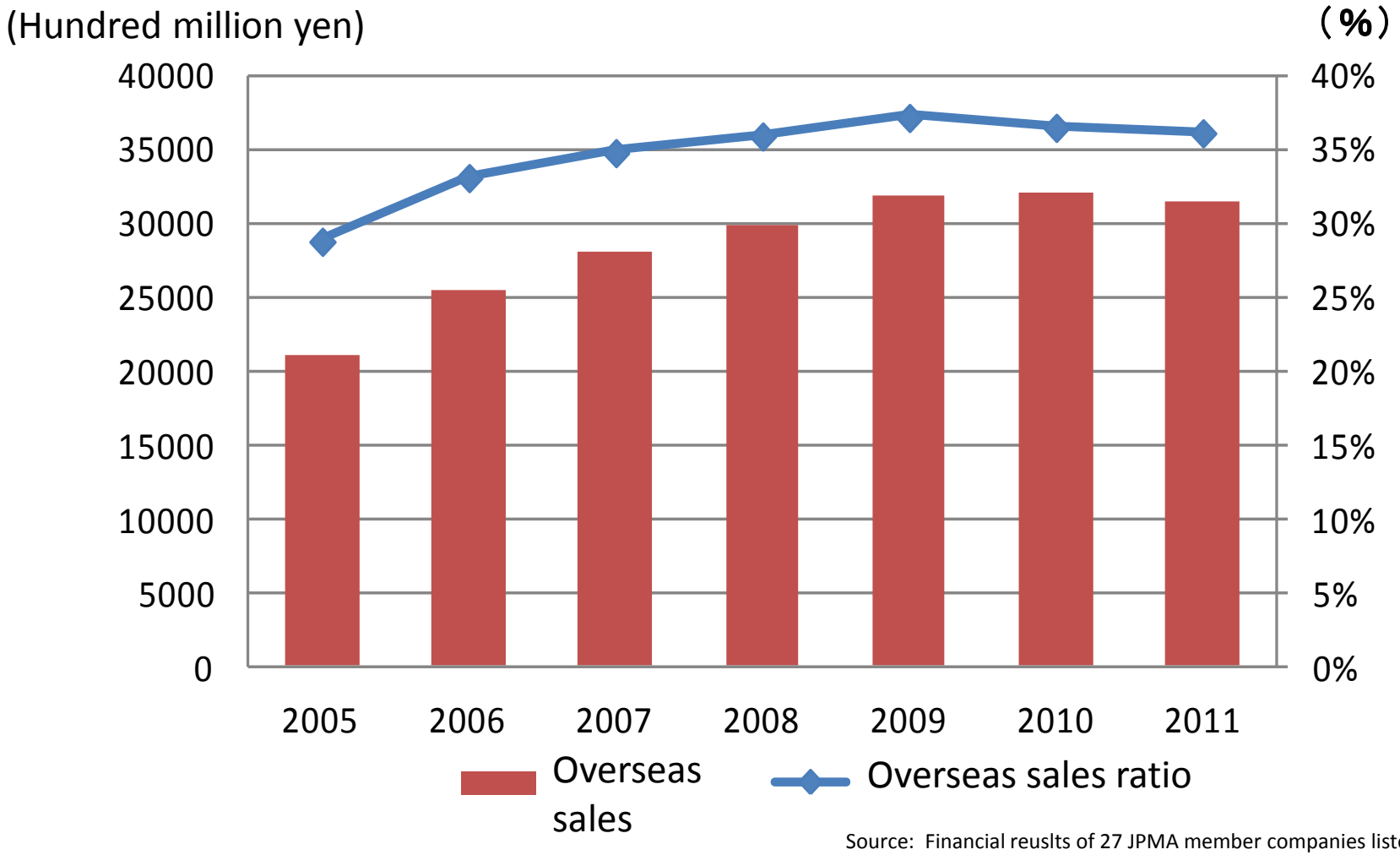
Stable high level tax bearing capacity

Transition of domestic tax payments of principal manufacturing industry



Source: Pharmaceutical industry vision 2013 Data Book Ministry of Health, Labor and Welfare Transformation

Overseas sales and transition of overseas ratio for Japanese companies



Source: Financial reuslts of 27 JPMA member companies listed on the Tokyo Stock Exchange (TSE)
Prepared by: Office of Pharmaceutical Industry Research, Japan Pharmaceutical Manufacturers Association

Innovative new drugs from Japan contributing to the world's health

[Blockbuster products from Japan]

Position 2012	Position 2011	Product name	Company name	Drug efficacy	Sales (mil. $) 2,012	Sales (mil. $) 2011	Expansion rate
1	4	*Humira*	Abbott / Eisai	Rheumatoid arthritis treatment	9,611	8,216	17.0%
2	3	*Remicade*	J&J / Merck /Tanabe	Rheumatoid arthritis treatment	9,117	8,969	1.7%
3	6	*Enbrel*	Amgen / Pfizer	Rheumatoid arthritis treatment	8,512	7,877	8.1%
4	5	Seretide / Advair	GSK	Anti-asthma drugs	8,023	8,148	-1.5%
6	7	Crestor	Shionogi / AZ	Hypolipidemic agent	6,722	7,043	-4.6%
7	14	*Lantus*	Sanofi	Diabetes treatment drug	6,379	5,451	17.0%
10	15	Abilify	Otsuka / BMS	Schizophrenia treatment drug	5,433	5,102	6.5%
27	21	Blopress / Atacand	Takeda / AZ	Hypertension treatment drug	3,271	3,228	1.3%
30	31	Olmesartan	Daiichi Sankyo	Hypertension treatment drug	3,144	3,037	3.5%
41	43	Luprin / Lupron	Takeda / Abbott	Anti-cancer agents	2,250	2,327	-3.3%
42	34	Aciphex / Pariet	Eisai / J&J	Anti-ulcer agents	2,218	2,711	-18.2%
43	22	Actos	Takeda	Diabetes treatment drug	2,112	4,162	-49.3%
48	48	Prograf	Astellas	Immunosuppressive agent	1,917	1,991	-3.7%
61	37	Aricept	Eisai	Alzheimer's treatment drug	1,546	2,534	-39.0%
69	63	Takepron / Prevacid	Takeda	Anti-ulcer agents	1,440	1,512	-4.8%
80	94	Vesicare	Astellas	Hyperactive bladder drug	1,302	1,180	10.3%
100	102	MohrusTape / Pap	Hisamitsu	Anti-inflammatory agent	1,067	1,064	0.3%

New drugs from Japan

Source: "International Drug Information" (April 8, 2013 issue)

Central Social Insurance Medical Council (hereinafter referred to as CSIMC)

The price of new drugs is discussed and determined in a place open to the public called CSIMC.

CSIMC general meeting (January 22, 2014)

CSIMC members list (As on August 27th, 2014)

1. Payment side committee members

矢内　邦夫（全国健康保険協会東京支部長）
白川　修二（健康保険組合連合会専務理事）
花井　圭子（日本労働組合総連合会
総合政策局長）
花井　十伍（日本労働組合総連合会「患者本位の医療を確立する連絡会」委員）
石山　惠司（日本経済団体連合会社会保障委員会医療改革部会部会長代理）
田中　伸一（全日本海員組合副組合長）
榊原　純夫（愛知県半田市長）

2. Medical side committee members

鈴木　邦彦（日本医師会常任理事）
中川　俊男（日本医師会副会長）
松本　純一（日本医師会常任理事）
万代　恭嗣（日本病院会常任理事）
長瀬　輝誼（日本精神科病院協会副会長）
堀　憲郎（日本歯科医師会常務理事）
安部　好弘（日本薬剤師会常務理事）

3. Public interest members

印南　一路（慶應義塾大学総合政策学部教授）
田辺　国昭（東京大学大学院法学政治学研究科教授）
西村　万里子（明治学院大学法学部教授）
野口　靖子（早稲田大学政治経済学術院教授）
松原　由美（明治安田生活福祉研究所主席研究員）
森田　朗　（国立社会保障・人口問題研究所所長）

4. Expert advisors

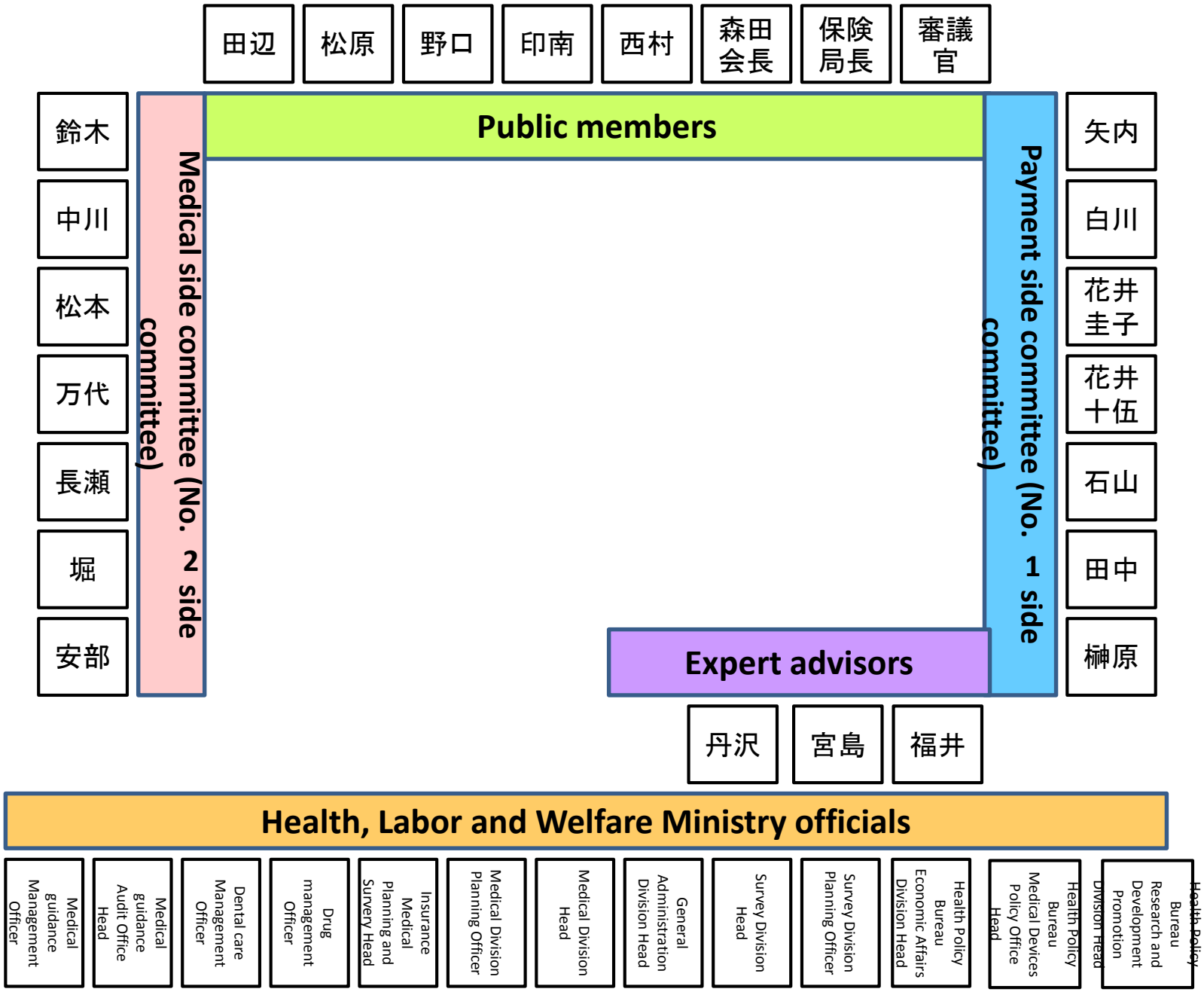
藤原　忠彦（長野県川上村長）
福井　トシ子（日本看護協会常任理事）
宮島　善文（日本臨床衛生検査技師会会長）
丹沢　秀樹（千葉大学医学部附属病院歯科・顎・口腔外科教授）

Drug pricing expert committee Expert advisors

加茂谷　佳明（塩野義製薬株式会社常務執行役員）
土屋　裕（エーザイ株式会社代表執行役副社長）
吉村　恭彰（株式会社アステム代表取締役社長）

昌子　久仁子（テルモ株式会社取締役上席執行役員）
田村　誠（アボットジャパン株式会社ガバメントアフェアーズバイスプレジデント）
十河　功二（株式会社イノメディックス統括営業本部本部長代理）

CSMIC General Assembly committee seating chart (As on October 8, 2014)



CSIMC organization chart

Central Social Insurance Medical Council

- Established regulations
  Social Medical Insurance Medical Council Act Article 1
  National Government Organization Act Article 8
- Affairs under the jurisdiction
  Matters concerning medical treatment fees・Matters concerning "Rules for Health Insurance-covered Medical Facilities and Medical Practitioners"・Matters concerning applicability of insurance for new drugs or medical devices, submit own proposals in addition to deliberating and reporting in response to the consultation of the Minister of Health, Labor and Welfare Ministry.

Report [Expert committee]

Report [Sub-committee]

Report

Insurance treatment materials expert committee

- Established regulations
  Rules of Article 14, Central Social Insurance Medical Council
- Affairs under the jurisdiction
  Study and deliberation of technical matters on insurance treatment materials reforms, etc.

Drug pricing expert committee

- Established regulations
  Rules of Article 14, Central Social Insurance Medical Council
- Affairs under the jurisdiction
  Study and deliberation of technical matters on drug pricing reforms, etc.

Medical treatment fees basic issues subcommittee

- Established regulations
  Rules of Article 15, Central Social Insurance Medical Council
- Affairs under the jurisdiction
  The views on the basic issues are coordinated beforehand out of the affairs under the jurisdiction of the Central Social Insurance Medical Council.

Study implementation sub-committee

- Established regulations
  Rules of Article 15, Central Social Insurance Medical Council
- Affairs under the jurisdiction
  The views on the Medical Economic Survey are coordinated beforehand.

[Verification subcommittee]

Reimbursement result verification subcommittee

- Established regulations
  Rules of Article 14, Central Social Insurance Medical Council
- Affairs under the jurisdiction
  Verify the results of the medical treatment fees and link to the discussions of medical treatment fees revision.

Report

[Insurance treatment materials expert organization]

- Established regulations
  Central Social Insurance Medical Council
- Affairs under the jurisdiction
  In the process of insurance coverage of special insurance treatment materials, participation in the selection of similar functions and certification of usefulness performed by the Ministry of Health, Labor and Welfare, and hearing, etc. from manufacturers, etc. who are dissatisfied with the draft decision prepared by the Ministry of Health, Labor and Welfare

[Drug Pricing] Organization]

- Established regulations
  Central Social Insurance Medical Council
- Affairs under the jurisdiction
  In the process of drug pricing, participation in the selection of similar drugs and certification of usefulness performed by the Ministry of Health, Labor and Welfare, and hearing, etc. from manufacturers, etc. who are dissatisfied with the calculation proposal prepared by the Ministry of Health, Labor and Welfare

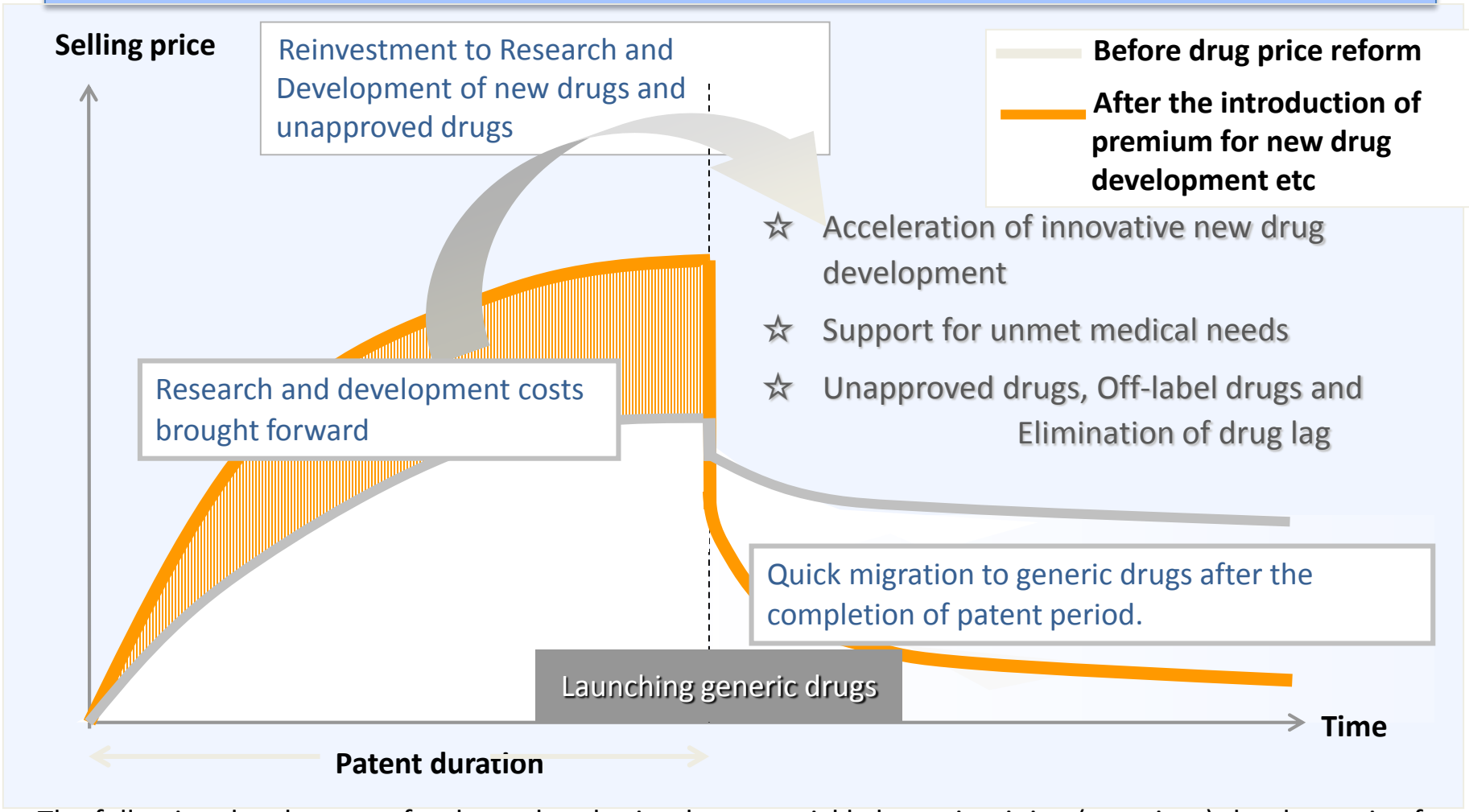
[Advanced medical treatment technology expert meeting]

- Established regulations
  Central Social Insurance Medical Council
- Affairs under the jurisdiction
  Study of the advanced medical treatment provided by facilities with specially approved medical treatment insurance

[Reimbursement result verification subcommittee]

- Established regulations
  Central Social Insurance Medical Council
- Affairs under the jurisdiction
  Surveys and studies etc on the technology issues for the review of medical treatment fees system etc

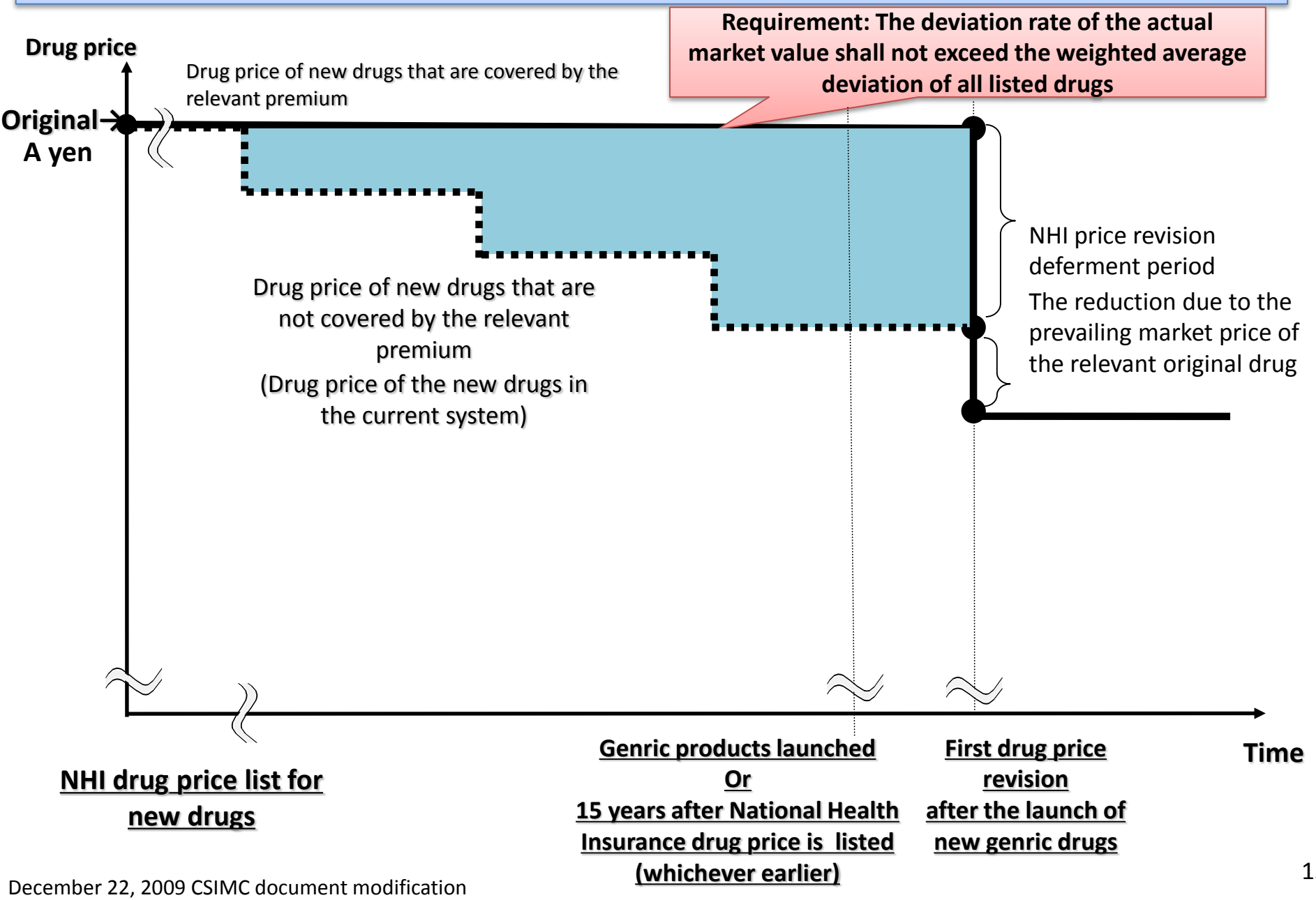
Concept of “premium to promote the development of new drugs and eliminate of off-label use”



The following development funds can be obtained more quickly by maintaining (premium) the drug price for new drugs during the patent period.

As a result, the development of new drugs and unapproved drugs is promoted and the needs of patients and medical professionals can be met quickly.

Example for drug pricing of new drugs covered by premium to promote the development of new drugs and eliminate off-label use



December 22, 2009 CSIMC document modification

Current state of Japan's pharmaceutical market

Number of articles and market share based on the classification of drug price standard list items.

		Number of items	Quantity Share	Amount Share
Original drug	Generic drug not available	2,074	18.2%	49.3%
	Generic drug available	1,562	31.2%	31.7%
Generic drug		8,038	27.6%	11.1%
Other items		3,629	23.0%	8.0%

(Note) ・Only number of items is as of April 2014
・Volume and revenue shares are based on the quantity and drug price at the time of survey in September 2013
・"Other items" are drugs (Blood products) which have been approved before 1967 and cannot be separated into original drugs and generic drugs
・Share total need not be necessarily 100.0 since it is rounded off to 2 decimal places

Source : Ministry of Health, Labor and Welfare Japan

National Health Insurance (NHI) pricing formula for new drugs

New pharmaceutical products

With similar drugs

① Similar efficacy comparison method (I)

① Correction premium

innovation premium 70 - 120%
Usefulness premium (I) 35 - 60%
Usefulness premium (II) 5 - 30%
Marketability premium (I) 10 - 20%
Marketability premium (I) 5%
Children premium 5 - 20%
Pioneering premium 10%

④ Foreign average price adjustment

- Reduction adjustment if 1.25 is exceeded
- Reduction adjustment if 0.75 is exceeded

⑤ Adjustment between regulations

② Similar drug efficacy comparison method (II)

(New drug with little novelty)

In comparison with the drug prices of similar drugs of the past few years Lowest price

Ahead of overseas, First in Japan
acquisition of the regulatory approval
etc

Reference US, UK, Germany and France prices

④ Foreign average price adjustment

- Reduction adjustment if 1.25 is exceeded

⑤ Adjustment between regulations

Without similar drugs

③ Cost accounting method

Manufacturing (importing) cost
Selling expenses and general administrative expenses
Operating income
Marketing cost
Consumption taxes etc

Current rate 16.9%
A variation is created within the range-50 - +100%

④ Foreign average price adjustment

- Reduction adjustment if 1.25 is exceeded
- Reduction adjustment if 0.75 is exceeded

⑤ Adjustment between regulations

(Note) Premium (5%) by adding the raw material cost of the kit characteristic parts after ⑤ of the above for highly useful kit products

① Similar drug efficacy comparison method (I)

~ Basic rules ~

- If similar drugs are available with same effectiveness, from the point of ensuring a fair competition in the market, the daily drug price is matched to the daily drug price of existing similar drugs. [Similar drug efficacy comparison method (I)]
  - As a rule, new drugs that are within 10 years after NHI drug price listing for which generic drugs have not been listed are used as the comparison drugs.

1 tablet = 50 yen
Daily 3 tablets

=

1 tablet = X yen
Daily 2 tablets

<Daily drug price matching>

50 yen X3 tablets = X yen X 2 tablets

X = 75 yen

Similar drugs refers to those drugs which have similarities when viewed from the following matters.

a Efficacy and effectiveness
b Pharmacological actions
c Composition and chemical structural formula
d Dosage form, dosage form classification, and dosage form and usage

- A premium correction is done to the above amount if high usefulness is observed for the relevant new drug after comparison with the similar drug.

[Innovation premium, Usefulness premium, Marketability premium, Children premium and Pioneering premium]

Innovation premium	70 - 120%	New action mechanism, high efficacy and safety, and improvement of disease treatment method
Usefulness premium	5 - 30%	High efficacy and safety, and improvement of disease treatment method
Marketability premium	5%, 10 - 20%	Orphan drug etc.
Children premium	5 - 20%	Matters pertaining to children have been explicitly included in the dosage and administration etc
Pioneering premium	10%	Obtained regulatory approval in Japan ahead of overseas

① Correction premium for similar drug efficacy comparison premium (I)

~ Basic rules ~

Innovation premium (70 - 120%)

Newly listed drugs meeting all of the following requirements
a Must have new action mechanism that is clinically useful.
b Must objectively show high usefulness and stability when compared to similar drugs.
c Improvement of the treatment methods for the disease or injury covered by the relevant newly listed drug must be shown objectively with the relevant newly listed drug.

Usefulness premium (I) (35 - 60%)

Newly listed drug satisfying two conditions out of the three conditions for innovation premium

Usefulness premium (II) (5 - 30%)

Newly listed drugs meeting any one of the following requirements
a Must have new action mechanism that is clinically useful.
b Must objectively show high usefulness and stability when compared to similar drugs.
c Improvement of the treatment methods for the disease or injury covered by the relevant newly listed drug must be shown objectively by the relevant newly listed drug.
d It must be objectively shown to have high medical usefulness compared to similar drugs by the improvement in the formulation.

Pioneering premium (10%)

Newly listed drugs meeting all of the following requirements
a Must have a different new mechanism of action compared to existing drugs that have been approved in either a foreign country (limited to United States, United Kingdom, Germany and France) or in Japan.
b. Drug which has obtained regulatory approval in Japan ahead of overseas.
c It must not be a drug that is expected to be distributed only in Japan and must have been confirmed overseas by either development status (including developmental planning) and clinical trial notification.
d The drug must have received innovation premium or usefulness premium (I).

+

Marketability premium (I) (10 - 20%)

Newly listed drugs meeting all of the following requirements
a It is a drug that can be used for rare disease based on the regulations of the Pharmaceutical Affairs Law, and the efficacy and effectiveness for the disease or injury covered must be the principal efficacy and effectiveness of the relevant newly listed drug.
b The comparison drug of the listed drug must not have been subject to the marketability premium (I).

Marketability premium (II) (5%)

Newly listed drugs meeting all of the following requirements
a The principal efficacy and effectiveness of the relevant newly listed product must correspond to the drug efficacy that is stipulated separately.
b The comparison drug of the listed drug must not have been subject to the marketability premium (I) or marketability premium (II).

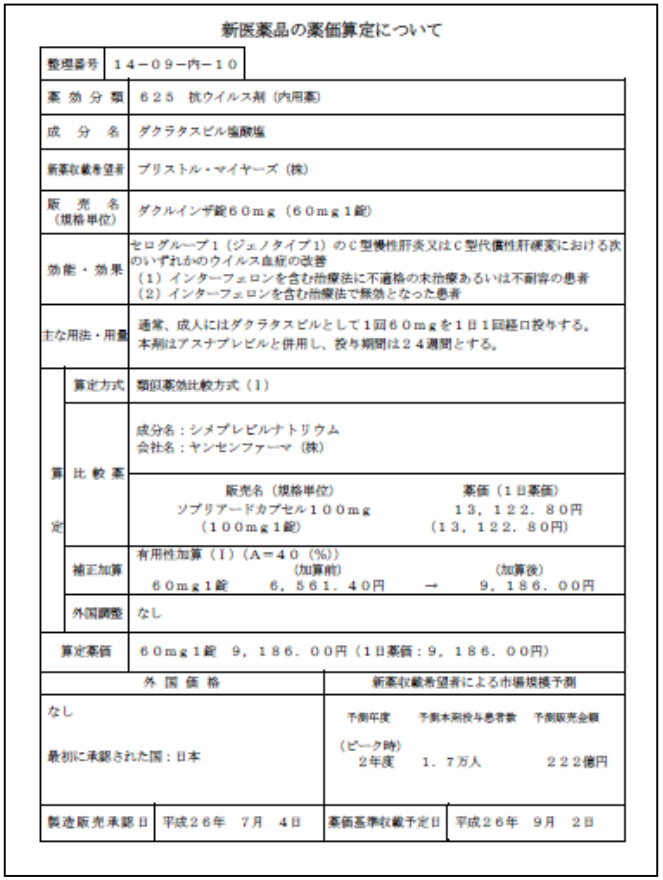
Children premium (5 - 20%)

Newly listed drugs meeting all of the following requirements. However, this is excluded if clinical trials for pediatric efficacy have not been implemented in Japan.
a The principal efficacy and effectiveness or the relevant efficacy and effectiveness of the relevant newly listed product must explicitly include the usage and dosage of children (including young children, infants, newborns and low birth weight infants).
b The comparison drug of the listed drug must not have been subject to children premium.
(Note) If marketability premium (II) is also applicable, children premium is given priority.

Specific case A

Item: Daklinza 60mg
Constituent name: Daclatasvir Hydrochloride
Efficacy and Effectiveness: Chronic hepatitis C and compensated cirrhosis
Dosage and Administration : Generally, for adults 60mg of Daclatasvir is administered orally at one time once a day. The administration duration of this drug along with Asunaprevir is 24 weeks.

(From the documents of CSIMC August 27, 2014)



新医薬品の薬価算定について

整理番号	１４－０９－内－１０
薬効分類	６２５　抗ウイルス剤（内用薬）
成分名	ダクラタスビル塩酸塩
新薬収載希望者	ブリストル・マイヤーズ（株）
販売名（規格単位）	ダクルインザ錠６０ｍｇ（６０ｍｇ１錠）
効能・効果	セログループ１（ジェノタイプ１）のＣ型慢性肝炎又はＣ型代償性肝硬変における次のいずれかのウイルス血症の改善 （１）インターフェロンを含む治療法に不適格の未治療あるいは不耐容の患者 （２）インターフェロンを含む治療法で無効となった患者
主な用法・用量	通常、成人にはダクラタスビルとして１回６０ｍｇを１日１回経口投与する。 本剤はアスナプレビルと併用し、投与期間は２４週間とする。
算定 算定方式	類似薬効比較方式（Ｉ）
算定 比較薬	成分名：シメプレビルナトリウム 会社名：ヤンセンファーマ（株）
算定 比較薬	販売名（規格単位）：ソブリアードカプセル１００ｍｇ（１００ｍｇ１錠） 薬価（１日薬価）：１３，１２２．８０円（１３，１２２．８０円）
算定 補正加算	有用性加算（Ｉ）（Ａ＝４０（％）） ６０ｍｇ１錠　（加算前）６，５６１．４０円　→　（加算後）９，１８６．００円
算定 外国調整	なし
算定薬価	６０ｍｇ１錠　９，１８６．００円（１日薬価：９，１８６．００円）

外国価格	新薬収載希望者による市場規模予測
なし 最初に承認された国：日本	予測年度：（ピーク時）２年度 予測本剤投与患者数：１．７万人 予測販売金額：２２２億円
製造販売承認日：平成２６年　７月　４日	薬価基準収載予定日：平成２６年　９月　２日

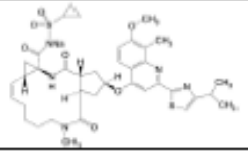
薬価算定組織における検討結果のまとめ

算定方式	類似薬効比較方式（Ｉ）	第一回算定組織	平成２６年　８月　１日

		新薬	最類似薬
最類似薬との特性	成分名	ダクラタスビル塩酸塩	シメプレビルナトリウム
	イ．効能・効果	セログループ１（ジェノタイプ１）のＣ型慢性肝炎又はＣ型代償性肝硬変における次のいずれかのウイルス血症の改善 （１）インターフェロンを含む治療法に不適格の未治療あるいは不耐容の患者 （２）インターフェロンを含む治療法で無効となった患者	セログループ１（ジェノタイプⅠ（１ａ）又はⅠ（１ｂ））のＣ型慢性肝炎における次のいずれかのウイルス血症の改善 （１）血中HCV RNA量が高値の未治療患者 （２）インターフェロンを含む治療法で無効又は再燃となった患者
	ロ．薬理作用	HCV NS5A 複製複合体阻害作用	HCV NS3-4A プロテアーゼ選択的阻害作用
	ハ．組成及び化学構造		
	ニ．投与形態 剤形 用法	内用 錠剤 １日１回２４週間経口投与	内用 カプセル剤 １日１回１２週間経口投与
補正加算	薬理性加算（７０～１２０％）	該当しない	
		該当する（Ａ＝４０（％））	
	有用性加算（Ⅰ）（３５～６０％）	本剤は、HCVウイルス増殖を直接抑制する新規の臨床上有用な作用機序を有すると認められる。 また、本剤は標準治療であるインターフェロン治療に不適格未治療/不耐容患者に対して有効性を示したこと、経口投与のみによる治療を可能とし、インターフェロン療法で一部の患者に必要とされている投与初期の入院等も必要ではないこと等から、治療方法の改善が客観的に示されていると認められる。 しかしながら、現在の標準治療である3剤併用療法を前治療とした患者でのデータはないこと、肝機能障害への対応が必要となることを踏まえ、Ａ＝４０％とした。	
	有用性加算（Ⅱ）（５～３０％）	該当しない	
	市場性加算（Ⅰ）（１０～２０％）	該当しない	
	市場性加算（Ⅱ）（５％）	該当しない	
	小児加算（５～２０％）	該当しない	
	先駆導入加算（１０％）	該当しない	
当初算定案に対する新薬収載希望者の不服意見の要点			
上記不服意見に対する見解		第二回算定組織	平成　年　月　日

Specific case A

薬価算定組織における検討結果のまとめ

算定方式	類似薬効比較方式（Ⅰ）	第一回算定組織	平成２６年　８月　１日
最類似薬選定の妥当性		新薬	最類似薬
	成分名	ダクラタスビル塩酸塩	シメプレビルナトリウム
	イ．効能・効果	セログループ１（ジェノタイプ１）のC型慢性肝炎又はC型代償性肝硬変における次のいずれかのウイルス血症の改善 （１）インターフェロンを含む治療法に不適格の未治療あるいは不耐容の患者 （２）インターフェロンを含む治療法で無効となった患者	セログループ１（ジェノタイプⅠ（１ａ）又はⅡ（１ｂ））のC型慢性肝炎における次のいずれかのウイルス血症の改善 （１）血中HCV RNA量が高値の未治療患者 （２）インターフェロンを含む治療法で無効又は再燃となった患者
	ロ．薬理作用	HCV NS5A 複製複合体阻害作用	HCV NS3-4A プロテアーゼ選択的阻害作用
	ハ．組成及び化学構造		
	ニ．投与形態 剤形 用法	内用 錠剤 １日１回２４週間経口投与	左に同じ カプセル剤 １日１回１２週間経口投与
補正加算	画期性加算（７０～１２０％）	該当しない	
		該当する（Ａ＝４０（％））	
	有用性加算（Ⅰ）（３５～６０％）	本剤は、HCVウイルス増殖を直接抑制する新規の臨床上有用な作用機序を有すると認められる。 また、本剤は標準治療であるインターフェロン治療に不適格未治療/不耐容患者に対して有効性を示したこと、経口投与のみによる治療を可能とし、インターフェロン療法で一部の患者に必要とされている投与初期の入院等も必要ではないこと等から、治療方法の改善が客観的に示されていると認められる。 しかしながら、現在の標準治療である3剤併用療法を前治療とした患者でのデータはないこと、肝機能障害への対応が必要となることを踏まえ、Ａ＝４０％とした。	
	有用性加算（Ⅱ）（５～３０％）	該当しない	
	市場性加算（Ⅰ）（１０～２０％）	該当しない	
	市場性加算（Ⅱ）（５％）	該当しない	
	小児加算（５～２０％）	該当しない	
	先駆導入加算（１０％）	該当しない	
当初算定案に対する新薬収載希望者の不服意見の要点			
上記不服意見に対する見解		第二回算定組織	平成　年　月　日

Pricing method: Similar drug efficacy comparison method (I)
Calculated drug price: 60mg 9,186.00 yen

Correction premium: Usefulness premium (I)　40%

<Basis>

This drug has been recognized to have a new action mechanism which is clinically useful in directly inhibiting the proliferation of HCV virus.

In addition, this drug has shown usefulness for patients who were disqualified, untreated or intolerant to Interferon therapy which is the standard treatment, and this drug makes treatment possible with oral administration alone and does not require hospitalization as required by some of the patients during the initial administration period with Interferon therapy and therefore it is considered that objective improvement of treatment method has been shown

(Omitted)

↓

<Quantitative evaluation>

Usefulness premium (I)

(5p + 3p) X 5% = 40%

(From the documents of CSIMC April 27, 2014)

② Similar drug efficacy comparison method (II)

~ Special rules ~

- For new drugs with little novelty, lowest price is used after comparison with the drug prices of similar drugs of the past few years.

[Similar drug efficacy comparison method (II)]

- For new drugs with little novelty: Those satisfying all the following conditions
  - Excluded from correction premium
  - Three or more similar drugs with same pharmacological action must exist
  - More than three years must have passed since the NHI drug price listing of a similar drug with the oldest pharmacological action

- The lower amount of ① or ② is used as a rule

① Cheapest daily drug price of the similar drug which has been listed in the past 6 years

② Average price of daily drug price of the similar drug which has been listed in the past 10 years

-If this exceeds -③ Premium amount (Drug price of the most similar drug) based on similar efficacy comparison method (I),

Further,

④ Cheapest daily drug price of the similar drug which has been listed in the past 10 years

⑤ Average price of daily drug price of the similar drug which has been listed in the past 15 years is calculated, and the lowest amount of ③ - ⑤ is considered.

③ NHI drug pricing formula for new drugs

~ Special rules ~

- If there are no similar drugs, cost of the raw materials and manufacturing are added. [Cost accounting method]

(Example)

①	Raw material cost	(Active ingredients, additives, containers and boxes)
②	Labor cost	(= 4,137 <Note 1> X Working hours)
③	Manufacturing cost	(= ② X 3. 599 <Note 2>)
④	**Product manufacturing (importing) cost**	
⑤	Selling expenses・research expenses	(= (④ + ⑤ + ⑥) X 0. 462 <Note 2>)
⑥	Operating income	(= (④ + ⑤ + ⑥) X 0. 169 <Note 2>)
⑦	Marketing cost	(= (④ + ⑤ +⑥ + ⑦) X 0. 068 <Note 3>)
⑧	Consumption tax	(8%)

Total: Calculated drug price

Strike a better balance for operating margin (current 16.9%) in the range -50 - +100% depending on the degree of innovativeness, usefulness and safety when compared with existing treatment

<Note 1> Labor cost unit price: "Monthly Labor Survey" (Ministry of Health, Labor and Welfare) Average from 2010 to 2012
<Note 1> Labor expense ratio, selling expenses and general administrative expenses ratio, and operating margin:
"Handbook of financial data of industries" (Japan Development Bank) 2010 - 2012 average
<Note 3> "Marketing cost ratio: Survey of the Prescription Pharmaceuticals Industry of Japan" Economic Affairs Division, Health Policy Bureau, Ministry of Health, Labor and Welfare) 2010 - 2012 average
As a rule the underlined values uses the average coefficient of pharmaceutical manufacturing industry (The most recent average value that can be obtained at the end of the previous fiscal year)

Specific case B

Brand Name: Opdivo drip injection 20mg/100mg
Constituent name: Nivolumab (Genetical recombination)
Efficacy and effectiveness: Malignant melanoma for which resection is not possible
Calculation method: Cost accounting method Premium results: operating margin 60%
(From the documents of CSIMC August 27, 2014)

新医薬品の薬価算定について

整理番号	１４－０９－注－５		
薬効分類	４２９　その他の腫瘍用薬（注射薬）		
成分名	ニボルマブ（遺伝子組換え）		
新薬収載希望者	小野薬品工業（株）		
販売名（規格単位）	オプジーボ点滴静注２０ｍｇ（２０ｍｇ２ｍＬ１瓶） オプジーボ点滴静注１００ｍｇ（１００ｍｇ１０ｍＬ１瓶）		
効能・効果	根治切除不能な悪性黒色腫		
主な用法・用量	通常、成人にはニボルマブ（遺伝子組換え）として、１回２ｍｇ／ｋｇ（体重）を３週間間隔で点滴静注する。		
算定	算定方式	原価計算方式	
	原価計算 製品総原価	９４，６２０円	４５９，７７８円
	原価計算 営業利益	３４，９９７円（流通経費を除く価格の27.0%）	１７０，０５５円（流通経費を除く価格の27.0%）
	原価計算 流通経費	９，４５７円（消費税を除く価格の６．５%） 出典：「医薬品産業実態調査報告書」（薬生労働省医政局経済課）	４５，９５３円（消費税を除く価格の６．５%） 出典：「医薬品産業実態調査報告書」（薬生労働省医政局経済課）
	消費税	１１，１２６円	５４，０６３円
	外国調整	なし	なし
算定薬価		２０ｍｇ２ｍＬ１瓶 １５０，２００円	１００ｍｇ１０ｍＬ１瓶 ７２９，８４９円

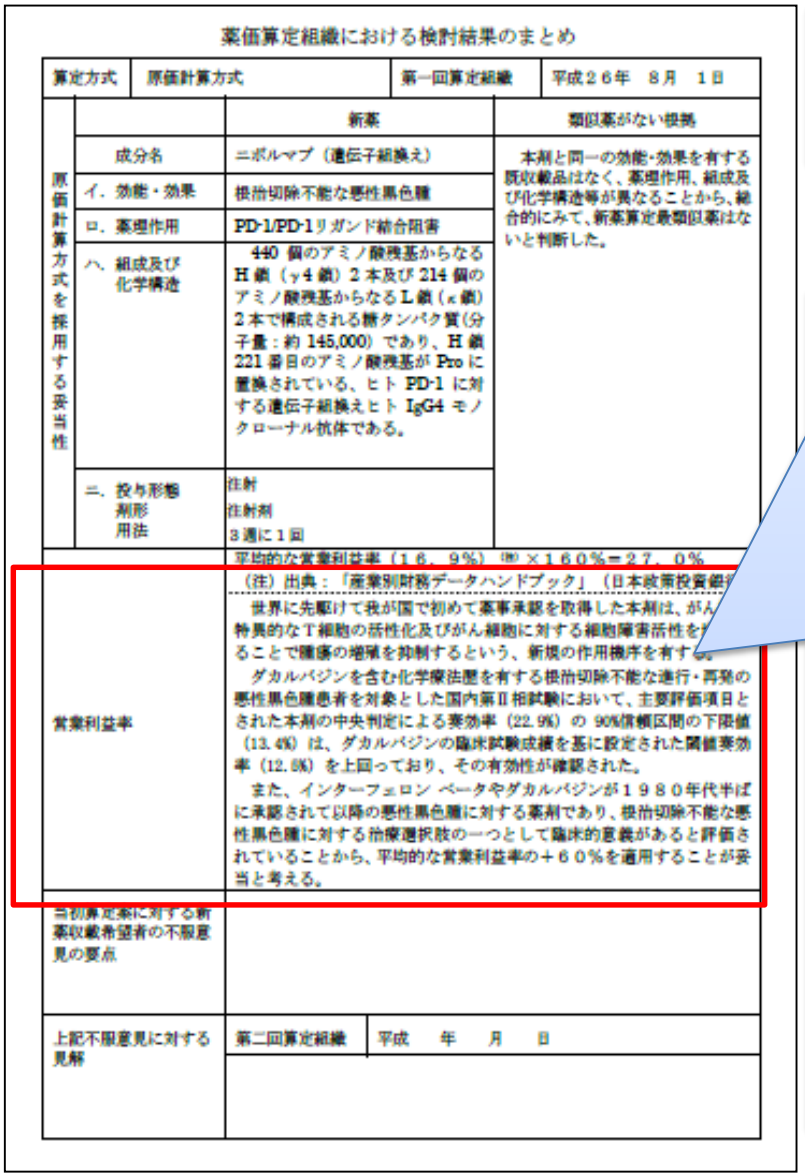
外国価格	新薬収載希望者による市場規模予測
なし 最初に承認された国（年月）： 日本（２０１４年７月）	予測年度　予測本剤投与患者数　予測販売金額 （ピーク時） ２年度　４７０人　３１億円

製造販売承認日	平成２６年　７月４日	薬価基準収載予定日	平成２６年　９月　２日

薬価算定組織における検討結果のまとめ

算定方式	原価計算方式	第一回算定組織	平成２６年　８月　１日
原価計算方式を採用する妥当性		新薬	類似薬がない根拠
	成分名	ニボルマブ（遺伝子組換え）	本剤と同一の効能・効果を有する既収載品はなく、薬理作用、組成及び化学構造等が異なることから、総合的にみて、新薬算定最類似薬はないと判断した。
	イ．効能・効果	根治切除不能な悪性黒色腫	
	ロ．薬理作用	PD-1/PD-1リガンド結合阻害	
	ハ．組成及び化学構造	440 個のアミノ酸残基からなるH 鎖（γ4 鎖）2 本及び 214 個のアミノ酸残基からなるL 鎖（κ 鎖）2 本で構成される糖タンパク質（分子量：約 145,000）であり、H 鎖 221 番目のアミノ酸残基が Pro に置換されている、ヒト PD-1 に対する遺伝子組換えヒト IgG4 モノクローナル抗体である。	
	ニ．投与形態 剤形 用法	注射 注射剤 ３週に１回	
営業利益率		平均的な営業利益率（１６．９%）[注]×１６０%＝２７．０% （注）出典：「産業別財務データハンドブック」（日本政策投資銀行） 世界に先駆けて我が国で初めて薬事承認を取得した本剤は、がん抗原特異的なT 細胞の活性化及びがん細胞に対する細胞障害活性を増強することで腫瘍の増殖を抑制するという、新規の作用機序を有する。 ダカルバジンを含む化学療法歴を有する根治切除不能な進行・再発の悪性黒色腫患者を対象とした国内第II 相試験において、主要評価項目とされた本剤の中央判定による奏効率（22.9%）の 90%信頼区間の下限値（13.4%）は、ダカルバジンの臨床試験成績を基に設定された閾値奏効率（12.8%）を上回っており、その有効性が確認された。 また、インターフェロン ベータやダカルバジンが１９８０年代半ばに承認されて以降の悪性黒色腫に対する薬剤であり、根治切除不能な悪性黒色腫に対する治療選択肢の一つとして臨床的意義があると評価されていることから、平均的な営業利益率の＋６０%を適用することが妥当と考える。	
当初算定案に対する新薬収載希望者の不服意見の要点			
上記不服意見に対する見解		第二回算定組織	平成　年　月　日

Specific case B



薬価算定組織における検討結果のまとめ

算定方式	原価計算方式	第一回算定組織	平成２６年　８月　１日
原価計算方式を採用する妥当性		新薬	類似薬がない根拠
	成分名	ニボルマブ（遺伝子組換え）	本剤と同一の効能・効果を有する既収載品はなく、薬理作用、組成及び化学構造等が異なることから、総合的にみて、新薬算定最類似薬はないと判断した。
	イ．効能・効果	根治切除不能な悪性黒色腫	
	ロ．薬理作用	PD-1/PD-1リガンド結合阻害	
	ハ．組成及び化学構造	440 個のアミノ酸残基からなるH鎖（γ4鎖）2本及び214個のアミノ酸残基からなるL鎖（κ鎖）2本で構成される糖タンパク質（分子量：約 145,000）であり、H鎖221番目のアミノ酸残基がProに置換されている、ヒトPD-1に対する遺伝子組換えヒトIgG4モノクローナル抗体である。	
	ニ．投与形態・剤形・用法	注射 注射剤 ３週に１回	
営業利益率		平均的な営業利益率（１６．９％）㈱×１６０％＝２７．０％ （注）出典：「産業別財務データハンドブック」（日本政策投資銀行 世界に先駆けて我が国で初めて薬事承認を取得した本剤は、がん特異的なT細胞の活性化及びがん細胞に対する細胞障害活性を…ることで腫瘍の増殖を抑制するという、新規の作用機序を有す… ダカルバジンを含む化学療法歴を有する根治切除不能な進行・再発の悪性黒色腫患者を対象とした国内第Ⅱ相試験において、主要評価項目とされた本剤の中央判定による奏効率（22.9%）の90%信頼区間の下限値（13.4%）は、ダカルバジンの臨床試験成績を基に設定された閾値奏効率（12.5%）を上回っており、その有効性が確認された。 また、インターフェロン ベータやダカルバジンが１９８０年代半ばに承認されて以降の悪性黒色腫に対する薬剤であり、根治切除不能な悪性黒色腫に対する治療選択肢の一つとして臨床的意義があると評価されていることから、平均的な営業利益率の＋６０％を適用することが妥当と考える。	
当初算定案に対する新薬収載希望者の不服意見の要点			
上記不服意見に対する見解		第二回算定組織	平成　年　月　日

Pricing method: Cost accounting method
Calculated drug price: 20mg 150,200 yen
100mg 729,849 yen (Adult 50kg: 34,755 yen)

Operating margin:
Average operating margin (16.9%) X 160% = 27.0%

<Basis>
This drug has **obtained regulatory approval in Japan ahead of the world**, **and has a new action mechanism with which it inhibits the proliferation of tumors by increasing the activation of cancer antigen-specific T cell and cytotoxic activity against cancer cells.**

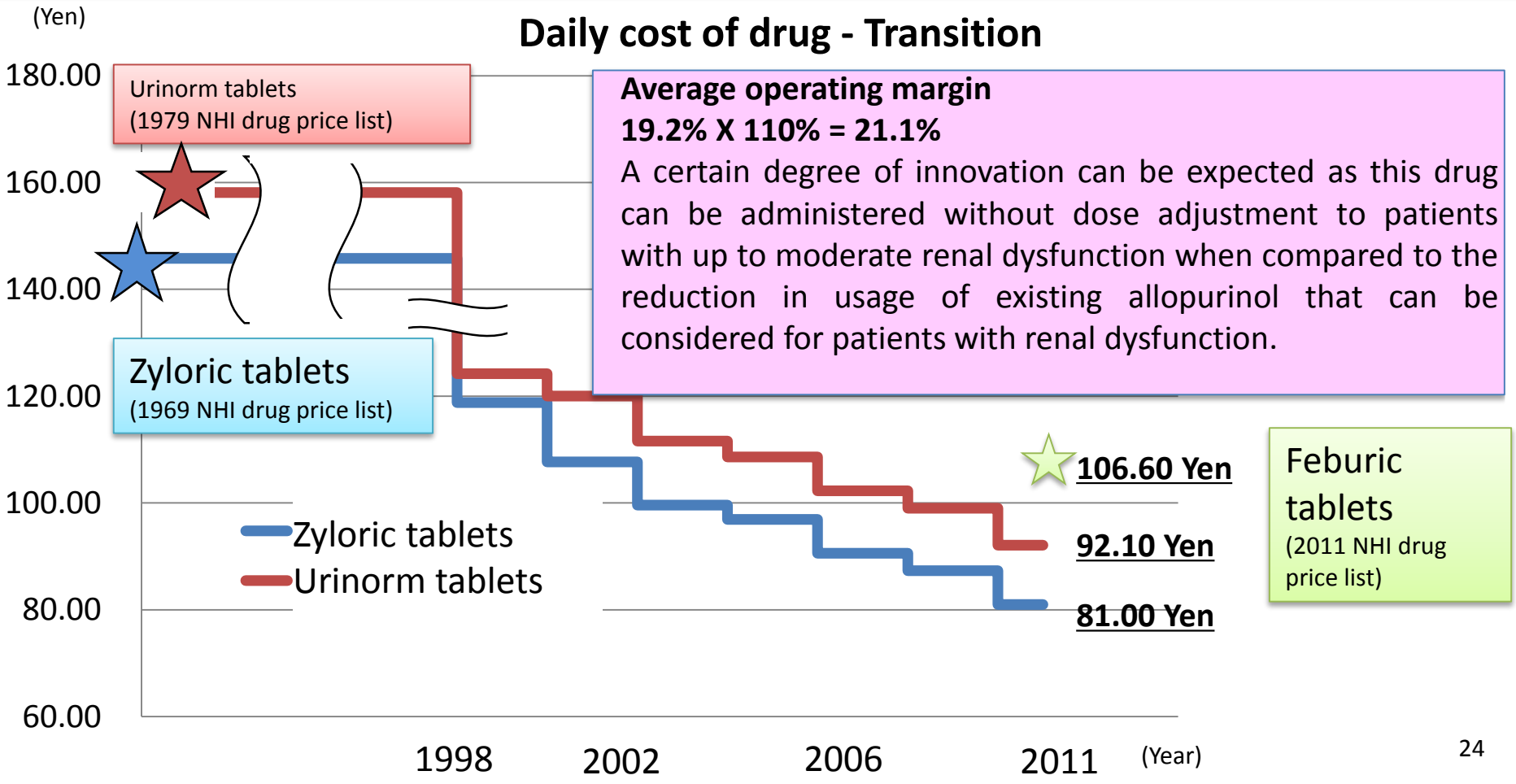
In the Japan Phase II trials, patients with advanced or recurrent malignant melanoma that cannot be subject to radical resection and with chemotherapy history which included Dacarbazine were covered, lower limit (13.4%) of the 90% confidence interval of the response rate (22.9%) for this drug based on the central review considered as the primary endpoint was above the threshold response rate (12.5%) which was set based on the clinical trial results of Dacarbazine, **and the usefulness was confirmed.**
In addition, it is considered reasonable to apply the +60% of the average operating margin since Interferon beta and Dacarbazine after approval in the mid 80 's have been evaluated to be clinically significant as a treatment option for malignant melanoma.

(From the documents of CSIMC August 27th 2014)

Specific case C

■ **Feburic tablets (Febuxostat)** **Efficacy and Effectiveness: Gout, hyperuricemia**

In this zone, no new drugs have been developed for almost 30 to 40 years following the listing of Allopurinol and Benzbromarone. This is a case in which the rule of "As a rule, new drugs that are within 10 years after NHI drug price listing for which generic drugs have not been listed are used as the comparison drugs" was applied and calculation has been done using the cost accounting format.

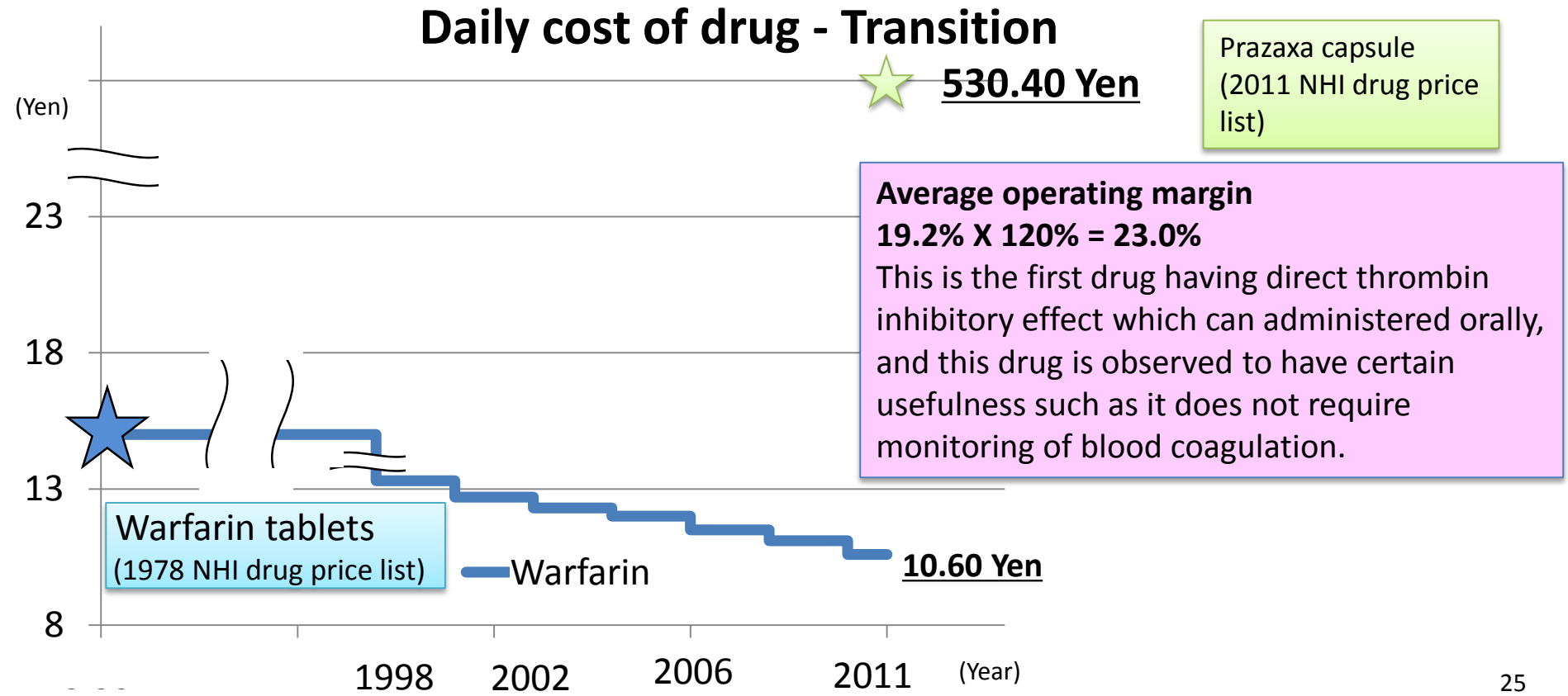


Specific case D

■ **Prazaxa capsules (Dabigatran etexilate methanesulfonate)**

Efficacy and Effectiveness: Inhibits the onset of thrombosis

In this zone, no new drugs have been developed for almost 30 years following the listing of the similar drug Warfarin potassium. This is a case in which the rule of "As a rule, new drugs that are within 10 years after NHI drug price listing for which generic drugs have not been listed are used as the comparison drugs" was applied and calculation has been done using the cost accounting format.



Conclusion

National Health Insurance (NHI) new drug pricing - Background

- Research and development type enterprises are present in Japan, the country is also boosting the development of Japanese companies from the point of view of industrial development
- The new drug development premium was proposed by the industry for the first time and it was introduced
- The drug prices for new drugs is calculated within the balance of the entire drug price system
- In principle, new drug prices are calculated matching to the prevailing market price (matched to the daily drug price)
- On the other hand, new drugs not in the long development zone are calculated without referring to the drug price of old pharmaceutical products
- Attempted to make the premium of usefulness system and adjustment premium of operating margin transparent