How to harmonize HTA and Value for innovation?

ISSUE PANELS – SESSION I
Monday, September 3, 2012, 11 AM~12 PM

How to harmonize HTA and Value for innovation?
(prepared by ISPOR Korea Chapter)

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- **Panelists:** Mi-Hai Park, PhD, Research fellow, Health Insurance Review and Assessment Service, Seoul, South Korea; Su-Kyoung Ko, PhD, Market Access Director, Pfizer Pharmaceuticals Korea Ltd., Seoul, South Korea; Eui Kyung Lee, PhD, Professor of Pharmaceutical Policy & Outcomes Research, School of Pharmacy, Sungkyunkwan University, Seoul, South Korea; Jeonghoon Ahn, PhD, MA, Senior Director, Office of Health Services Research, National Evidence-based Healthcare Collaborating Agency (NECA), Seoul, South Korea
How to harmonize HTA and Value for innovation?

• OVERVIEW:
  – Adopting pharmacoeconomics in drug pricing is a growing trend across the world. Pharmacoeconomics is an attractive tool as it standardizes the way to convert effectiveness into money, theoretically.
  – Some limitations, however, have been found out while enforcing it in real world. As drug pricing is a complex that includes not only scientific assessment but also political decisions, some problems have come up in adopting pharmacoeconomics as a fundamental principle when valuing a product.
  – The panel will consider the limitations of pharmacoeconomics in valuing a product and discuss how to supplement and improve it to value fairly.

How to harmonize HTA and Value for innovation?

• Dr. Park will explain current reimbursement decision-making process using HTA with the definition of rewardable innovation. Her presentation also includes the results of new drug assessment after the implementation of positive list system.
• Dr. Ko will discuss what kinds of issues have been found out in new product pricing based on cost-effectiveness from the eye of industry. She will also address the issue HTA cannot value drug fairly since HTA links price change by cost-containment measures with product value.
• Dr. Lee will discuss how to adjust pharmacoeconomics to value a new drug fairly. Flexible ICER threshold and premium based-on innovativeness could be one of options. Her presentation includes plenty of other countries case of innovation assessment and new drug pricing.
• Dr. Ahn will discuss the way to improve the situation by incorporating multi-dimensional social values. He will explain that process values and contents values should be considered for priority setting. Clinical effectiveness and cost-effectiveness aspect, which are main component of current HTA, are some of these values.
Each panelist will spend 10 minutes. Then a discussion including ‘Q&A’ session with floor will follow for 15 minutes.
Contents

I. Innovation

II. HTA

III. Current situation

IV. Future directions

I. Innovation
Innovative Technology: Definition

- No established definition of innovative technology
- CDR does not have a definition of innovative technology
- NICE
  ✓ No agreed-upon definition
  ✓ NHS Innovation Center: new-to-the-organization or new-to-the-NHS technology products resulting in a significant improvement in patient outcomes, experiences, safety and potentially cost effectiveness (Garner, S et al, 2010)

Innovative Technology: Definition

- **Radical innovations**, or “breakthroughs,” are moderately to highly effective treatments.
- **Substantial innovations** offer fair to modest improvements in health outcomes.
- **Incremental innovations** offer minor to moderate improvements.

(Morgan, S., R. et al., 2008)
Innovative Technology: Definition

- Valuable innovative medicines are both truly innovative and valuable.
- "Truly innovative" means that it offers additional clinical efficacy and/or effectiveness as compared to current care.
- Truly innovative medicines have a potential to lead to significant improvements in health outcomes.
  - They fill an unmet medical need, so they are called valuable.
- Valuable innovative medicine leads to net savings or induces a reasonable additional cost in an acceptable level to the additional health gain, it can be considered "value for money".

Rewardable innovation
II. HTA

- HTA: multidisciplinary field of policy analysis, studying the medical, economic, social, and ethical implication of development, diffusion, and use of health technology (INAHTA, [http://www.inahta.org/HTA/](http://www.inahta.org/HTA/)).

- The role of HTA in the process of pricing and reimbursement is becoming crucial.
  - The importance of cost-effectiveness analysis is critical in a society with substantial health expenditure.
  - Whether it is worthwhile to spend public money to cover the cost of the added therapeutic value.

- A health economic evaluation is defined as a comparative analysis of both the costs and the health effects of two or more alternative health interventions. (Drummond 2008)
Applied criteria for HTA-EU

- **Applied criteria for HTA in selected EU countries** *(Sorenson et al., 2008)*

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<th>Criteria</th>
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**Positive List System**

- **Positive list system**
  - Listing of drugs with higher therapeutic & economic value by using cost-effectiveness analysis
  - HTA as a tool to assess the willingness to pay for a new drug in societal perspective
  - Decision on social acceptance of economic burden of new drug

- **Economic evaluation**
  - Decision making tool for drug reimbursement in limited budget
  - Several limitations such as the reliability of evidence & uncertainties
HTA in Korea

- Reform the price and reimbursement system: Positive list system (2006. 12)

- Methodological development
  - Pharmaco-economic evaluation guideline (2006.11)
  - Submission guideline (2007.6)
  - Revision of pharmaco-economic guideline (2011.12)
  - Indirect comparison guideline (2011.12)

- Pre-submission Consulting Services (2009.2)

<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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<tbody>
<tr>
<td>consulting cases</td>
<td>32</td>
<td>60</td>
<td>52</td>
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</tbody>
</table>

HTA in Korea

- Public disclosure of the appraisal results

- Operate working group to facilitate communication and information exchange with industry

- Providing information and regular education for manufacturers
  - Annual weighted average price of individual ingredients
  - Claim data within the scope under the Act for protection of individual information of Public Organization

- Publish the articles on outcomes of the HTA
HTA in Korea

- Attending the ISPOR (International Society for Pharmaco-economics and Outcomes Research) conference to share the HTAs in Korea and to learn the new methodologies.
  - 2008 ISPOR: Characteristics of new pharmaceuticals having no alternatives
  - 2010 ISPOR: Assessment of pharmaco-economic evaluations submitted for reimbursement since Korean positive list system introduction
  - 2012 ISPOR: Factors influencing reimbursement price of new drugs after introduction of positive list system

In initial adoption of positive list system, HIRA developed methodological guidelines and tried to be transparent, now HTA is implemented in decision making.

Barriers to implementation of HTA

- Inadequate evidence of a clinically meaningful benefit to patients
- Studies are not available for many technologies.
- Data are not available at time of assessment.
- Methods need to be improved and standardized.
  - Particularly methods for assessment of relative effectiveness and cost-effectiveness

ISPOR conference 2010
III. Current situation

Listing procedure

KFDA (Korea Food & Drug Administration): Evaluation on the safety and efficacy (approval for marketing)

**New drug**
- Submission of application
  - manufacturer / importer

**HIRA (150 days)**
- Working review
  - HIRA staff
- Drug Benefit Coverage Assessment Committee (DBCAC)

**NHIC (60 days)**
- Price negotiation

**MOHW (60 days)**
- Drug Reimbursement Coordination Committee

**MOHW (30 days)**
- Health insurance policy review Committee

**Generic**

Sub-committees
- Economic evaluation
- Sub Committee
- Clinical advisory committee
- Healthcare review and assessment committee (HRAC)
- Serious illness review committee (SIRC)

**HIRA (150 days)**
- Drug Benefit Coverage Assessment Committee (DBCAC)

Factors considered
- Assessment report by DBCAC of HIRA
- Budget impact
- Price of the drug in foreign countries including OECD
- Patent status
- Domestic R&D expenditure

Negotiation fail / Non-essential drug
- MOHW (60 days)
- Drug Reimbursement Coordination Committee

Negotiation fail / Essential drug
- NHIC (60 days)
- Price negotiation

Reimbursement

Non-reimbursement (150 days)
Clinical Usefulness
- KFDA Approval material
- Textbook
- Clinical guideline
- Expert opinion

Improvement in therapeutic benefit
- Comparison with comparators
  - Cost-effectiveness (Utility) analysis
    - Cost–minimization analysis
      - Weighted average price comparable to the alternatives
  - Superior
  - Non-inferior

Essential drug
- No alternatives
- Life-threatening disease
- Orphan drug (rare disease)
- Overall survival improvement

Potential impacts on other aspects of public health, etc.
- Disease severity
- Social value (equity, etc.)

Reimbursement status in Other countries
- Budget impact

Reimbursement Determination

Evaluation of cost effectiveness

ICER (Incremental cost-effectiveness ratio)
- The ratio of the change in costs to incremental benefits of a therapeutic intervention or treatment comparing with the comparator
- Flexible ICER application taking account of severity of disease, burden of disease, impact on quality of life, innovativeness, etc.

\[
ICER = \frac{C_1 - C_0}{E_1 - E_0} = \frac{\Delta C}{\Delta E}
\]

Incremental cost saving
Quantified clinical usefulness as cost on safety, compliance, etc.

 Incremental effectiveness improvement
Quality of Life (QoL), safety aspect, clinical usefulness
New drug evaluation - considerations

Clinical usefulness: Substitutability, disease severity, therapeutic benefit, etc.
- Efficacy, safety, convenience and stability

Cost Effectiveness: Drug and administration cost, clinical effectiveness, result of HTA, etc.
- Disease severity, burden of illness, impact on QoL, innovation, etc.

Budget impact
- Patient number, expected volume, comparators (or alternative treatment), etc.
- Reimbursement status and price in foreign countries
- Potential impacts on other aspects of public health, etc.

Criteria for reimbursement

- Rule of rescue
  - No alternative treatments available
  - For life-threatening diseases
  - For rare disease with small number of patients
  - With proven clinical evidences such as life extension

- Exempt cost-effectiveness data
New drug assessment - Results

- Drug coverage assessment on new drug (2007-2011)

<table>
<thead>
<tr>
<th>Results</th>
<th>2007 (61.5%)</th>
<th>2008 (74.7%)</th>
<th>2009 (77.5%)</th>
<th>2010 (69.7%)</th>
<th>2011 (66.7%)</th>
<th>Total (71.5%)</th>
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<td>67</td>
<td>62</td>
<td>46</td>
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<td>22</td>
<td>18</td>
<td>20</td>
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<tr>
<td>Total</td>
<td>39</td>
<td>89</td>
<td>80</td>
<td>66</td>
<td>63</td>
<td>337</td>
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</table>

- Clinically improved drugs : total 115 cases
  - Efficacy 36.5%, safety 18.2%, convenience 60%
- Reasons of rejection
  - Obscure/unacceptable cost-effectiveness
  - Obscure clinical usefulness
  - Related with new health technology, etc

Evaluation of new drugs-example

- Accept clinical improvement in reduction of hypoglycemia and overweight of antidiabetic drug having new mechanism of action which showed non-inferiority to comparator
- Accept clinical improvement in reduction of weight significantly in obese diabetic patients while hypoglycemic effect is non-inferior to comparator
- Accept clinical improvement in reduction of adverse events such as tachycardia and wide therapeutic index because of longer half-life compared with comparator
IV. Future directions

Plan for evaluation of innovative drug

- **Drugs available cost-effectiveness study**
  - To be flexible in considering threshold of ICER depending on disease severity

- **Drugs not available cost-effectiveness study**
  - Patient access program
  - Drugs for rare diseases or severe diseases difficult to be proven their clinical benefit and cost-effectiveness
    - Risk-sharing for expected outcomes
    - Conditional reimbursement (conditions of clinical data)
    - Exempt cost-effectiveness data
Thank you for your attention!

Can ‘pharmacoeconomics’ value a product fairly?
Limitation of pharmacoeconomics in new drug pricing

Su-kyoung Ko, PhD
Market Access Director, Pfizer Korea
Contents

- Current situation of HTA on the pricing and reimbursement of new drugs
- The area to improve reimbursement decision making based on HTA
- How to harmonize HTA and reward for innovation?

*In this presentation, HTA means Clinical usefulness and Cost-effectiveness analysis. These have been evaluated by HIRA in Korea.*

Current situation of HTA on the pricing and reimbursement of new drugs
HTA on the pricing & reimbursement in Korea

**Process**
New product should pass the clinical usefulness assessment and economic analysis step by step.

**Methodology**
The reimbursement decision for a new drug depends on its clinical usefulness and cost-effectiveness.

\[
\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{C_T - C_C}{E_T - E_C}
\]

\[\text{Willingness to Pay (WTP)} = \text{ICER threshold}\]

\[\text{Effectiveness: Life years adjusted by Quality of Life (QoL)} = \text{QALY} \times \text{Extended life years}\]

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**Pricing & reimbursement of new drug is divided into two parts.**
1. HIRA* (HTA assessment) and 2. NHIC** (pricing negotiation)

- **HTA process (HIRA*, 5 to 8 months):**
  - Assess alternatives
  - Assess clinical usefulness
  - Clinical evidence, guideline, and etc.
  - Cost Effectiveness Analysis
  - Acceptable ICER Value
    - Yes
    - No
  - Cost Comparison
    - No
    - Accept WAP with Price Adjustment
    - Below WAP
    - Weight Average Price (WAP) of the treatment alternatives
  - Reimbursement
    - Essential Drug
    - No reimbursement
    - Life-threatening, rare disease and prolong life

- **Negotiation process (NHIC**, 2 to 1 months):**
  - Price Negotiations
    - Settlement
    - Break down
    - Non-reimbursement
  - Listing
Different views on the current HTA system

• 36 from 337 new drug application were evaluated cost-effective.

• 35% of the new drugs (118/337) were evaluated by cost-effectiveness analysis (include CMA) by HIRA
• 30.5% of clinically improved drugs (36/118) were evaluated as cost-effective.

**Policy maker**

“PE (HTA) can reward innovation based on clinical superiority”

“All new drugs are not necessarily means innovative drugs. If a drug is cost-effective, it should prove clinical superiority comparing existing comparator”

“If a drug is superior enough, it would get higher price even when comparator is much cheaper than the drugs.”

**Industry**

“Current HTA system cannot reward innovation properly and prohibit patient access to new drugs.”

“Most of new drugs is reimbursed by WAP or cost comparison because it is very difficult to prove superiority due to strict methodology of evaluation”

“If clinical usefulness is not turned to monetary value, it is evaluated as same as non-improvement, eventually”

‘Different point of views between policy maker and industry’,

This presentation is to find the area to improve of current HTA method and process, but it is not intended to undermine the accomplishments of HTA

Ref. 2012.6.8 HIRA presentation, in the explanatory session for industry (and modified through HIRA interview)
The area to improve of reimbursement decision making based on HTA

Area to improve in HTA system

- **Effectiveness**
  - Different view on the treatment alternatives
  - Handling uncertainty in clinical usefulness assessment
  - Difficulty to prove same efficacy

- **Cost (drug price)**
  - Price adjustment based on political decision

- **ICER threshold**
  - Controversies surrounding the only measurement for HTA: QALY

- **Assessment method**
  - Difficulty in assessing individualized treatment
  - Too much HTA driven decision-making
Area to improve in HTA system
Different view on the treatment alternatives

The current way of assessing alternatives limits proper valuation for innovative drugs: currently reimbursed drug in same therapeutic area dose not necessarily means comparable treatment choice.

Is it possible to value of Glivec® properly if it is compared to interferons (currently available treatment)?

Area to improve in HTA system
Handling uncertainty in clinical usefulness assessment

The clinical usefulness analysis relying on statistical significance, makes it difficult to assess the drugs for rare diseases with small subject numbers

Even with sufficient clinical significance, RCTs for rare diseases do NOT result in statistical significance
Area to improve in HTA system

Difficulty to prove same efficacy

Same efficacy means real same efficacy? = Same price or value?

3rd line therapy
(2nd line treatment failure patients group)

2nd line therapy
(1st line treatment failure patients group)

1st line therapy
(Initial treatment patient group)

Disease Severity INCREASE
&
Target population DECREASE

The numerically same efficacy rate on each therapy does not mean the real same efficacy because difference of target population. Under the current HTA system, 2nd or 1st line therapy is often evaluated as lower price than 1st line therapy since only BSC is available as comparators.

Area to improve in HTA system

Price adjustment based on political decision

Drug D is more cost-effective than drug C.

Drug C is more cost-effective than drug D.

Level of ACER have been changed without alteration of effectiveness level. It’s because of price reduction by political decision.
Area to improve in HTA system
Controversies surrounding the only measurement for HTA: QALY

Homogeneous measurement “QALY” for proving comparing clinical usefulness

- QALY: Mortality with morbidity in single numerical units, is involving trade-offs between quantity for quality of health.
- There are some arguments about the trade-off between Quantity and quality of health: Mortality and morbidity are totally different dimensions, and combining them into a single numerical unit is nonsense
- Valuing health gains in terms of QALYs means that life-years gained in full health counted as more valuable than life-years gained by those who are chronically ill or disabled.
- Consider how disability weighting, age-weighting and discounting influence the cost-effectiveness: with same intervention, Cost per LYG can be higher than Cost per QALY

Decision based on ICER per QALY cannot reflect the value of life extension sufficiently.


Area to improve in HTA system
Difficulty in assessing individualized treatment

Limitation of conventional treatment

- Patients can respond very differently to the same medication
- Differences in drug responses to differences in genes

Individualized treatment: Personalized medicine

- selection of patients likely to respond to treatment
- Avoidance of toxicity for unresponsive patients
- Money and time saving
- Fast development of personalized therapeutics

Effectiveness / Safety: increasing therapeutic effects and reducing side effects.
Cost: Higher price than conventional treatment → Uncertainty in proving its cost-effectiveness

Under the current HTA system, Can value for Personalized medicine/treatment be evaluated appropriately?

Ref. The Personalized Medicine Coalition (PMC), 2006
How to Harmonize HTA and reward for innovation?

Pursuing only efficiency can be dead end for HTA

[HTA will fail to gain traction with stakeholders so long as overall efficiency is viewed as its ultimate output.]

- The concept of comparing efficiency as a means to making coverage decisions for new interventions within a particular budget does not work because it does not address the trade-offs that are required

- If we want our HTAs to go beyond that without leaving our audiences behind, we will need to get into the much more difficult business of weighing the values our citizens place on different health benefits.

“We must back out of the dead end that is pursuing overall efficiency.”

Even by maximizing “health benefits acquired by limited resources”, it is another issue how the benefits are calculated → Must consider the various needs of the society
HTA should evolve in accordance with trend of drug development

State of the science and information have evolved to enable personalized medicine

- Growth in publications in the field of pharmacogenetics from 1967–2007
- "The right treatment for the right person at the right time" (The Case for Personalized Medicine, 2006)

Today

- Small molecules
- Broad indications
- Biologics
- SEBs
- Generic medicines

Tomorrow

- More Precision
- Personalized medicines
- More targeted patients: targeted therapy
- More niche

How can HTA evolve in accordance with this trend?


Decision making should be based on integrated value assessment

The listing decision of new drugs should be more integrated the aspects of the clinical usefulness, cost-effectiveness, budget impact, and social values rather than step by step process.

Current assessment of new drugs

Clinical usefulness → Cost-effectiveness → budget impact → Reimbursement

Barrier to get reimbursement

A collective assessment method considering social benefits

Clinical utility → Cost-effectiveness → budget impact → Social value → Reimbursement

Equity, Accessibility, Innovation
How to harmonize HTA and Value for innovation?

HTA should evolve to incorporate trend of evolving innovations, not only for currently proven clinical improvement or cheaper drugs

• Patient assess considering uncertainty, then price adjustment after assessment.
  ✓ If it is not possible to prove the clinical usefulness (uncertainty in future outcome, rare disease, etc), we can consider a mechanism to reimburse the drug without PE results rather than delaying the process. A PE analysis can be conducted after listing when the evidence is available.

• HTA which can value of personalized medicine and patient preference
  ✓ Introduce a mechanism to assess the increase of social benefits by individualized treatment options.
  ✓ Implement patient-based HTA; incorporate each patient’s unique perspective and preference

• Money of value or reward for innovation
  ✓ Introduce a way to reward innovation: Introduce a new assessment mechanism to replace PE analysis for highly innovative drugs (i.e. no alternatives)

Readings

- Eric Nord et al (2009), QALYs: Some Challenges
- Bjarne Robberstad (2005), QALYs vs DALYs vs Lys gained: what are the differences, and what difference do they make health care priority setting?
- J.Jaime Caro (2009), Editorial, Pursuing efficiency: A dead end for HTA?
- Lidia Becla, et al. (2011), Health Technology Assessment in the era of personalized health care
- John F.P. Bridges (2006), Lean Systems Approaches to Health Technology Assessment: A Patient-Focused Alternative to Cost Effectiveness Analysis
How to adjust pharmaco-economics to value a new drug fairly?

Eui-Kyung Lee, Professor
Pharmaceutical Policy and Outcomes Research
SungKyunKwan University
I. Flexible ICER threshold

< Limitations of QALY >

- QALY as one of the tools for health care resource allocation
  - The value is expressed on the basis of a collective of individuals’ utility.

- Assumptions in deriving QALY: Constant Proportional Tradeoff (CPT)
  - The tradeoff (between QoL and LYG) occurs proportionately without considering the duration of specific health status.
  - Implying that the patient is willing to trade a better of QoL with life expectancy, regardless of the patient’s remaining life years.

- But the assumption of constant proportional tradeoff(CPT) is reported to be not appropriate for terminally ill patients.
  - If the life expectancy <1 year, patients are highly unlikely to accept this.

(Boe Seung-jin et al, 2011)
**Decision making standards, based on the severity of disease**

- The controversy of an universal threshold value for different drugs & disease. (Kim, Yoon-hee et al, 2010)
  - The preferred option is what improves from severely ill health, not improvement from a better health state: An intervention which improves equity is preferred.
- NICE (U.K) : *End of life Treatments*
  - Assessment for treatments on extending life of terminal pts : Assume the same QoL of health state of the same age group for the extended life years
  - More weight should be given to QALYs occurred in the end stages of life for patients’ with terminal illness.
  - Additional weighting is considered to make the ICER of the treatment to be in the current threshold value.
- France: SMR reimbursement rate varies on the severity of disease
- Germany: efficiency frontier is derived based on different treatment groups

**Flexible ICER threshold**

- To apply flexible ICER threshold for the following drugs for the fair value
  - Drugs for severe disease
  - Drugs for small patient groups
    - Drugs for rare diseases
    - Targeted Therapy
  - Drugs for end stage of terminally ill patients
II. Premium Price based on Innovativeness

1. Problems with relative valuation

– Economic Evaluation is based on the comparison of incremental cost over incremental outcomes

– However, some problems with deciding “drug price” based on the incremental cost, and ICER.

  • One of the major factors to decide drug price is the relative value of new drug compared to the “old comparator”.

  • In this case one of the assumption is that the price of comparator is appropriate. Is that always true? It could be too high or too low in reality?

  • Price of drugs on the market is determined by many factors: value, policy, health care system etc

2. Foreign Cases: Innovation level and Pricing

• France: SMR (Clinical benefit level)

  – Reimbursement rate is based on SMR and the seriousness of disease (35%~65%)

• Reimbursement categories and rates by SMR

<table>
<thead>
<tr>
<th>Reimbursement category by clinical benefit (SMR)</th>
<th>Serious disease</th>
<th>Non-serious disease</th>
<th>Characteristic of category</th>
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<tbody>
<tr>
<td>Important (Major)</td>
<td>65%</td>
<td>35%</td>
<td>Normal rate determined by Minister of Health, UNCAM can modify it, 20 points</td>
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<tr>
<td>Moderate</td>
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<tr>
<td>Weak</td>
<td>35%</td>
<td>35%</td>
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<tr>
<td>Insufficient</td>
<td>Not listed</td>
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</table>

UNCAM=Union nationale des caisses d’assurance maladie (National Union of Health Insurance Funds)

[Source] PPRI 2008
France: ASMR & Price setting

<table>
<thead>
<tr>
<th>ASMR¹</th>
<th>Improvement of clinical benefit</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Major improvement (new therapeutic area, reduction of mortality)</td>
<td>Reference for comparable EU counties’ price² (fast track)</td>
</tr>
<tr>
<td>II</td>
<td>Significant improvement in efficacy and/or reduction of side-effects</td>
<td>Reference for comparable EU counties’ price² (fast track)</td>
</tr>
<tr>
<td>III</td>
<td>Modest improvement in efficacy and/or reduction of side-effects</td>
<td>Reference for comparable EU counties’ price or negotiation³</td>
</tr>
<tr>
<td>IV</td>
<td>Minor improvement</td>
<td>Price negotiation⁴ Reference for comparators’ price</td>
</tr>
<tr>
<td>V</td>
<td>No improvement</td>
<td>Price negotiation⁴ Below comparators’ price</td>
</tr>
</tbody>
</table>

¹ ASMR I, II is regarded as highly innovative. In the case of domestic-developed new drugs with no foreign references, the manufacturers set the price and negotiate.
² The price of highly innovative pharmaceuticals (level of improvement of clinical benefit, ASMR) levels I to III should not be lower than the cheaper price observed in comparable European countries (Germany, Spain, Italy, UK).
³ If the total budget does not exceed 40mn€/year, it may be omitted negotiations of the ASMR III products
⁴ Rarely refers to the foreign price

Germany

- Medical and therapeutic value
  - In the past, innovation was determined by patent position, but nowadays only drugs with **therapeutic benefit** can be evaluated as innovative by G-BA.
  - Innovation of new drug can be classified as 3 levels

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curability</td>
<td>Major additional benefit</td>
<td>Important additional benefit</td>
</tr>
<tr>
<td>Freedom from symptoms</td>
<td>Long-term freedom from severe symptoms</td>
<td>Alleviation of the disease that is noticeable for the patients</td>
</tr>
<tr>
<td>Extension of duration of life</td>
<td>Significant extension</td>
<td>Moderate extension</td>
</tr>
<tr>
<td>Side effects(SE)</td>
<td>Extensive avoidance of serious SE</td>
<td>Relevant avoidance of serious SE or significant avoidance of other SE</td>
</tr>
</tbody>
</table>

**Highly Innovative**

**Slightly Innovative**
### PMPRB categorization and pricing

<table>
<thead>
<tr>
<th>Category</th>
<th>Measure of Innovation</th>
<th>Maximum price ceiling</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category 1</strong></td>
<td>• First medicine for a particular illness or a particular indication.</td>
<td>• Median International price</td>
</tr>
<tr>
<td>Breakthrough</td>
<td></td>
<td>:France, Germany, Italy, Sweden, Swiss, UK, US</td>
</tr>
<tr>
<td>Improvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Category 2</strong></td>
<td>• Substantial therapeutic improvement</td>
<td>• Higher of either</td>
</tr>
<tr>
<td>Substantial</td>
<td></td>
<td>(i) Median International price</td>
</tr>
<tr>
<td>Improvement</td>
<td></td>
<td>(ii) Highest non-excessive price of TCC comparators.</td>
</tr>
<tr>
<td><strong>Category 3</strong></td>
<td>• Moderate therapeutic improvement</td>
<td>• Midpoint of</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>(i) Median International price and</td>
</tr>
<tr>
<td>Improvement</td>
<td></td>
<td>(ii) Highest non-excessive price of TCC comparators.</td>
</tr>
<tr>
<td><strong>Category 4</strong></td>
<td>• Slight or no therapeutic improvement, and is not considered a breakthrough or</td>
<td>• Highest non-excessive price of TCC comparators.</td>
</tr>
<tr>
<td>Little or no</td>
<td>substantial or moderate improvement</td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td></td>
<td>• If no comparators,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>then price ceiling will be the lower of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(i) Lowest non-excessive price and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) Median international price</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If not possible to conduct TCC test, then median international price.</td>
</tr>
</tbody>
</table>

TCC = Therapeutic Class Comparison
PMPRB = Patented Medicine Price Review Board

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### Degree of Innovation for New Drugs

(1) **1st step: Availability of alternative treatments**

a) Drugs for orphan diseases or for patients who have absolute contraindications to existing therapies
b) Drugs for patients who resistant or non-responsive to first-line therapies already available
c) Although existing of the recognized treatment, the case of the new treatment such as the following:
   c1) Drugs with a better efficacy, safety or pharmacokinetic profile
   c2) Pharmacological innovations: drugs with a novel mode of action
   c3) Technological innovations: new molecular entities

(2) **2nd step: Relevance of the therapeutic effect**

a) Major benefit: improved efficacy
b) Partial benefit: improved but minor benefit
c) Minor or temporary benefit

(3) **3rd step: Degree of therapeutic innovation**

a) Important, b) Moderate, c) Mild
Italy

Figure 1: Calculating the Degree of Innovation for New Drugs

Step 1: Availability of Alternative Therapies + Step 2: Relevance of Therapy - Step 3: Degree of Innovation

- No alternative
- Alternative, but Intolerance/Non-response
- Alternative

Source: Silvia Chiroli, Amgen

Japan

New Drug

1. Comparable drug available
   - 1. Premium pricing
     - Innovation premium 70~120%
     - Usefulness premium (I) 35~60%
     - Usefulness premium (II) 5~30%
     - Marketability premium (I) 10~20%
     - Marketability premium (II) 5%
     - Pediatrics premium 5~20%
   - 2. Average foreign price adjustments
     * Reduced if 1.5 times or higher
     * Increased if 0.75 times or lower
   - 3. Cost Accounting System
     - Manufacturing (import) cost
     - Selling expense, administrative expense
     - Operating profit
     - Distribution cost
     - Consumption tax, etc.

2. Comparable drug not available
   - 2. Average foreign price adjustments
     * Reduced if 1.5 times or higher
     * Increased if 0.75 times or lower

3. Inter-specification adjustments

* As for highly useful kit product, 5% premium is added to the price calculated as the price of 3, shown above plus the raw material cost of the characteristic part of the kit product.
3. Suggestions for Premium Price based on Innovativeness

(1) Systematic approach to categorize the level of clinical usefulness

- Clinical usefulness level: 3~5 levels (High/Intermediate/Low)
- Explicit criteria to assess clinical usefulness
  - Disease severity
  - The interchangeability with alternatives (existing drugs)
  - Therapeutic effect
  - Treatment objective: Cure vs. Disease modification vs. Prevention
- To organize an assessment committee and enhance expert consultations
  - I.e. Commission de Transparence (CT) in France, IQWiG in Germany, Comitato Scientifico e Tecnico (CST) in Italy
- Government-initiated research or support to provide infrastructure for comparative effectiveness assessment.

3. Suggestions

(2) Innovation assessment & new drug pricing

- To incorporate the level of clinical usefulness as one of the important factors for reimbursement decision & price negotiation
- It will be valuable at the following cases:
  - If alternatives are available,
    - Clinically superior, but the price of comparator is not appropriate
  - If alternatives are not available (Placebo-controlled trials, etc):
    - Exemption from cost-effectiveness assessment, then premium based on level of clinical usefulness in addition to WAP in other countries.
    - Criteria is needed for ‘no alternatives are available’
  - reflect absolute value, in addition to relative value based on the comparator price
Social Values and Health Priority Setting

Jeonghoon Ahn, PhD
National-Evidence based Healthcare Collaborating Agency(NECA), Korea
The Values

**Process Values**
- Transparency
- Accountability
- Participation

**Content Values**
- Clinical effectiveness
- Cost effectiveness
- Justice/equity
- Solidarity
- Autonomy

Sarah Clark and Albert Weale (2012), JHOM 26(3), 293-316.

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Progress Values

<table>
<thead>
<tr>
<th>Values</th>
<th>Context</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transparency</td>
<td>Decision making in healthcare priority is inevitably controversial, since it means privileging some needs over others. Making decisions based on explicit pre-set criteria and as transparent as possible can avoid unnecessary controversies.</td>
</tr>
<tr>
<td>Accountability</td>
<td>Being accountable in health priority setting means having the obligation to answer questions regarding decisions about which interventions are prioritized and providing public justification for the decisions.</td>
</tr>
<tr>
<td>Participation</td>
<td>Healthcare priority setting decisions are fundamentally value judgments – and value judgments will inevitably vary between individuals and groups within society. As such, it has been suggested, the decision making process is more likely to be legitimate if it enables different interests to contribute via participation (Saltman and Figueras, 1997).</td>
</tr>
</tbody>
</table>
### Content Values

<table>
<thead>
<tr>
<th>Values</th>
<th>Context</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical effectiveness</td>
<td>The value of clinical effectiveness is a fundamental one in priority setting decisions, given that it is clearly undesirable to waste limited resources on procedures that are ineffective or, worse still, that may actually do harm. The positive aim of the principle, then, is to ensure that health benefits are achieved.</td>
</tr>
<tr>
<td>Cost effectiveness</td>
<td>The aim of the principle of cost effectiveness is to ensure that the most health benefits are obtained from the available resources. Cost-effectiveness seeks to establish whether differences in costs between alternative interventions can be justified in terms of the health benefits they respectively produce.</td>
</tr>
<tr>
<td>Justice / Equity</td>
<td>The term ‘justice’ is often used by political theorists and philosophers for the value that economists call ‘equity’. The difference in terminology is confusing because ‘equity’ is also used in jurisprudence to refer to the principle that like cases should be treated as like. In what follows we refer to ‘justice’ but start from the principle that like cases should be treated as like.</td>
</tr>
<tr>
<td>Solidarity</td>
<td>Solidarity can take different forms: it can take a contractual form, such as membership of a welfare state or of a basic health care package, where it is primarily expressed through a willingness to share the financial risks of ill-health, or a more generalized humanitarian form which is expressed in decisions which give priority to those who are worst-off in health terms (Hoedemaekers and Dekkers, 2003).</td>
</tr>
<tr>
<td>Autonomy</td>
<td>The concept of autonomy has a varied set of meanings (see Feinberg, 1986) but it is often used to refer to the ability of individuals to be self-directing and to make decisions for themselves about important matters. The notion of autonomy goes hand in hand with that of responsibility: if one is to be self-directing and make important choices, those choices will be one’s own and thus also one’s own responsibility.</td>
</tr>
</tbody>
</table>
Process values: Transparency

How might we define transparency?

- Everyone knows who makes decisions
- Everyone knows who makes decisions and by what processes
- Everyone knows who makes decisions, by what processes and for what reasons

Process Values: Accountability

To whom is accountability owed?....

And accountability for what?

- Patients
- Health professionals
- Priority Setters
- Clinical effectiveness
  - Value judgements
- Meeting basic entitlements
- Clinical effectiveness
  - Value judgements
- Financial Expenditure
  - Cost effectiveness
- Taxpayers
- Insurance payers
Process Values: Participation

**Who might participate?**
Patients, health professionals, experts, taxpayers, insurance payers, citizens....

**Why value participation?**
- If people have their say, then they can’t complain at the result
- Decisions are more legitimate if different interests can contribute
- It improves the quality of decisions
- Those whose money is being spent should have a say in what it’s used for

Content Values: Clinical Effectiveness

**How to define clinical effectiveness?**
- Any interventions showing some evidence of benefits
- Only intervention that definitely provides benefits
- Only intervention that definitely provides benefits to patients is better than available alternatives

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Page 78
Content Values: Cost-Effectiveness

**How important is cost-effectiveness, relative to other values?**

- It’s just **one factor amongst many** and should not have privileged status
- It’s **one of the most important factors** but not always decisive – however it might be unusual for other values to over-rule it
- It’s **of primary and decisive importance**

Content Values: Justice/Equity

**What might justice/equity require in priority setting?**

- All patients with the **same condition should be treated the same**
- Some patients should be **positively prioritised** because of their status – eg. vulnerable populations, the young, the poor, people with dependents
- Some patients should be **negatively prioritised** because they are responsible for their condition
Content Values: Solidarity

What might solidarity require?

- All have access to ‘comprehensive care’, however defined
- All have access to a ‘basic package’, however defined
- Entirely private arrangements

Content Values: Autonomy

How important is autonomy?

- Autonomy as personal preference and personal responsibility
- We should give low priority to individual preferences, and individual responsibility should not condition access to treatment.
- People should be able to exercise some preferences over some care
- People are responsible for spending their own money and for their own lifestyle choices
END OF DOCUMENT