Analysis of new drug reimbursement decision in South Korea: over a decade of experience

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Objective

Conflicting opinions by different stakeholders on listing rate and time to patient access

To analyze the rate of listing and time to patient access based on publicly disclosed reports for reimbursement decisions during the period over a decade in Korea

Ref) http://www.slideshare.net
Methods

New drug reimbursement and pricing decision process

HIRA: Health Insurance Review and Assessment Service
ICER: Incremental cost-effectiveness ratio
PE: Pharmacoeconomics evaluation
NHIS: National Health Insurance Service
A7: Seven advanced reference countries (US, UK, Italy, German, Japan, Swiss and France)

* Depends on the type of risk sharing, pharmacoeconomics evaluation is needed. Four types of risk sharing are as following: Refund, Conditional treatment continuation, Expenditure cap, Utilization cap
Methods
Variables and statistical analysis

All new drugs during the period under positive listing system from July 2007 to March 2018
• Using disclosed evaluation results by HIRA

Drug category and HIRA review process
• Three drug types: Oncology, orphan and the others
• HIRA review pathway: Before / after introduction of new pathways

Listing rate and time to patient access
• Time to patient access: Time to event analysis (Kaplan-Meier plot)
  ✓ Event: National Health Insurance listing
  ✓ Censored data: Calculated the date from MFDS approval to the last DREC

HIRA: Health Insurance Review and Assessment Service; MFDS: Ministry of Food and Drug Safety
DREC: Drug Reimbursement Evaluation Committee
### Characteristics of submitted drugs by listing status

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Total (N=360)</th>
<th>Listed drugs (n=298)</th>
<th>Non-listed drugs (n=62)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology drugs</td>
<td>59 (16.4)</td>
<td>49 (16.4)</td>
<td>10 (16.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Orphan drugs</td>
<td>52 (14.4)</td>
<td>37 (12.4)</td>
<td>15 (24.2)</td>
<td>0.027</td>
</tr>
<tr>
<td>Non-oncology &amp; non-orphan drugs</td>
<td>249 (69.2)</td>
<td>212 (71.1)</td>
<td>37 (59.7)</td>
<td>0.096</td>
</tr>
<tr>
<td><strong>HIRA review pathway</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Essential drugs</td>
<td>9 (2.5)</td>
<td>9 (3.0)</td>
<td>0</td>
<td>0.368</td>
</tr>
<tr>
<td>Acceptable cost-effectiveness</td>
<td>286 (79.4)</td>
<td>269 (90.3)</td>
<td>17 (27.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CEA/ClIA</td>
<td>57</td>
<td>56</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CMA or below WAP</td>
<td>229</td>
<td>213</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>PE exemption</td>
<td>16 (4.4)</td>
<td>15 (5.0)</td>
<td>1 (1.6)</td>
<td>0.325</td>
</tr>
<tr>
<td>Risk sharing agreement</td>
<td>18 (5.0)</td>
<td>18 (6.0)</td>
<td>0</td>
<td>0.052</td>
</tr>
<tr>
<td><strong>Etc</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessed under changed regulation</td>
<td>111 (30.8)</td>
<td>104 (34.9)</td>
<td>7 (11.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Domestic company</td>
<td>147 (40.8)</td>
<td>115 (38.6)</td>
<td>32 (51.6)</td>
<td>0.065</td>
</tr>
<tr>
<td>A7 listing status (≥3 countries)</td>
<td>188 (52.2)</td>
<td>160 (53.7)</td>
<td>28 (45.2)</td>
<td>0.264</td>
</tr>
</tbody>
</table>

*P*-value was calculated by Fisher’s exact test.

HIRA: Health Insurance Review and Assessment Service
CEA: Cost-effectiveness analysis; CUA: Cost-utility analysis; CMA: Cost-minimization analysis; WAP: Weighted Average Price
PE: Pharmacoeconomics evaluation; A7: Seven advanced reference countries (US, UK, Italy, German, Japan, Swiss and France)

* Regulation change in January 2014: risk-sharing agreement, exemption of pharmacoeconomics analysis and price negotiation.

### Listing rates by drug types in comparison of before and after the introduction of new review pathways

**Time effect is significant...**

At 2 years from MFDS, the listing rate of oncology or orphan is around only 50%
**Time to patient access from MFDS approval to listing (1)**

- The median time taken for listing for total 360 drugs: 16.2 months (95% CI: 14.1-18.3)

* Mean time is two fold higher than median

**The time to patient access from MFDS approval to listing (2)**

- After the introduction of new pathway, the median time is 10.9 months (95% CI: 10.2-11.7)
  - The main driver is an exemption of price negotiation with WAP pathway

* Mean time is two fold higher than median
Limitations

Used the MFDS approval date, not submission to HIRA as the initiation of application

Analyzed only disclosed information by HIRA
- Sensitive information is censored such as submission price, weighted average price of alternatives and price of comparators for cost-effectiveness analysis
- Only final submission data is included in HIRA’s reports

MFDS: Ministry of Food and Drug Safety
HIRA: Health Insurance Review and Assessment Service
Meaningful improvement in patient access by Government’s initiative

Substantial improvement on listing rate owing to RSA and PE exemption, especially for oncology drugs

- All drug: Before 77.9% vs. After: 93.7%
- Oncology drugs: Before 77.1% vs. After: 91.7%
- Examples
  - ERBITUX (cetuximab) via RSA and CAPRELSA (vandetanib) via PE exemption

Shortened the time to patient access for WAP pathway through exemption from price negotiation

- WAP with price negotiation exempted: 10.9 months (95% CI: 8.7-13.1)

Even improvement...
Patients who have severe or intractable disease go through a hard time for > 2 years without optimal treatment

Unmet needs in orphan drugs’ coverage

Indistinct impact of new pathways on a coverage for orphan drugs

- Listing rate at status quo in spite of introduction of the new pathways (71.1% vs. 71.4%)
- Not much advantage in pricing and reimbursement decision for orphan disease compared to rare disease treatment

Some orphan drugs were rejected despite of the long review period

- Time to patient access
  - Average 44.5 months (95% CI: 29.8-59.2) vs. Median 23.7 months (95% CI: 8.6-38.7)
- Example
  - XOLAIR (omalizumab): orphan drug for severe allergic asthma, with the longest period (11 years) remaining non-reimbursement owing to uncertainty in cost-effectiveness
Limitations of PharmacoEconomics (PE) approach

PE is the only pathway to get a premium to alternatives but...

- Most specialty drugs used new pathway, not conventional PE approach
- Only 57 (16%) of total drugs were accepted through CUA or CEA

Longer review period and a rocky road

- Time to patient access with PE: 28.9 months (95% CI: 22.8-35.1)
- RSA requires cost-effectiveness data to decide the net price
  - Time to patient access with RSA: 29.1 months (95% CI: 25.5-32.7)
  - Time to patient access with PE exemption: 18.7 months (95% CI: 11.9-25.4)

Proposals from industry

Expand NHI coverage to other disease area

- NHI coverage was weighted towards oncology
- Urgency for non-life threatening but rare or intractable disease

Give flexibility in PE assessment

- Focus on drugs’ value, not only speed
  - Most drugs listed through CMA or below WAP (same or less compared with alternatives)
- Time to consider from various angles: discount rate, selection of comparator, utility, flexibility of acceptable ICER and etc.

Broaden adoption of new pathway (RSA and PE exemption)

- Showed clear advantage in pricing and timeline
- Need a relaxation in the eligibility scope: only oncology or rare disease treatment, no alternative and life-threatening
- Create additional new pathway (e.g., listing accompanied with post-assessment)
Thank you

Any questions?

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