Factors Associated With Positive Cost-Effectiveness Judgments in HIRA Drug Reimbursement Decisions : An 8-Year Retrospective Review

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INTRODUCTION

Since 2007, South Korea has implemented pharmacoeconomic evaluation as part of its positive listing system to selectively reimburse new drugs that demonstrate superior clinical and economic value compared with existing therapies. This framework provides an evidentiary basis for determining whether new drugs represent value that is acceptable for public reimbursement. In principle, drugs that show improved clinical outcomes relative to standard treatments are subject to pharmacoeconomic evaluation, and the results are summarized using the Incremental Cost-Effectiveness Ratio (ICER)

In reimbursement decision-making, the Health Insurance Review & Assessment Service (HIRA), Korea's national HTA agency, applies several reimbursement assessment criteria, including clinical usefulness, cost-effectiveness, budget impact, reimbursement status in reference countries, and conditions to be fulfilled by the manufacturer (e.g., Risk-Sharing Agreements). Rather than applying a fixed ICER threshold, HIRA evaluates cost-effectiveness flexibly, taking into account disease severity, societal disease burden, quality-of-life impact, and the degree of therapeutic innovation, as stipulated in the relevant regulatory guidelines.

This study analyzed reimbursement cases from the most recent eight years (2017–2024) to examine how these appraisal factors influence the level of accepted ICERs. **The objective is to identify the key factors associated with positive cost-effectiveness judgments and to assess whether actual evaluation practices align with the intended objectives of the pricing and reimbursement system.**

OBJECTIVE

- **Primary Objective:** T-test
  - Differences in ICER according to Appraisal Factors
- **Secondary Objective:** Multiple Regression Analysis
  - Correlation between Appraisal Factors and ICER

METHOD

Inclusion and exclusion criteria

- New drugs that underwent pharmacoeconomic evaluation and received positive reimbursement decisions from the Pharmaceutical Benefit Coverage Assessment Committee between 2017 and 2024. In principle, drugs were classified by active ingredient; however, when a single ingredient was evaluated for multiple indications resulting in separate ICERs, each indication was treated as a distinct analysis case.
- Case that passed committee review but was ultimately not reimbursed due to failure in final price negotiation was excluded from analysis. ICER cases below KRW 10 million/QALY (n = 1) were considered outliers due to their limited sensitivity to appraisal factors and were excluded.
- ICER values were recorded as reviewed and determined by the Committee, and in cases with a risk-sharing agreement (RSA), the accepted ICER reflected the actual reimbursed price under RSA terms.
- As a result, a total of 42 cases (41 unique ingredients) were selected for evaluation.

Table 1. Independent variables for T-test

Assessment criteria	Independent variables
Clinical usefulness	Availability of alternatives (Yes=1, No =0)
	Disease severity : Life-threatening disease (Yes=1, No =0)
Budget impact	Number of target patient population - Based on 200/1,000 (≥=1, <=0)
	Absolute budget impact : Based on KRW 10B, 50B (≥=1, <=0)
Listing in Reference Countries	Based on 3 countries (≥=1, <=0)
Risk-Sharing Agreements[2]	Eligible for RSA (Eligible=1, Not Eligible=0)

Data extractions and analyses

1. **Variable Specification**
   - **Dependent variable**: ICER (Incremental Cost-Effectiveness Ratio)
   - **Control variables:** Year of committee appraisal (2017–2024), reimbursement status (reference: reimbursed), economic evaluation type (cost-effectiveness analysis, cost-utility analysis).
   - **Independent variables:** T-test [Table 1], Multiple regression analysis [Table 2]

2. **Statistical Analysis**
   - Microsoft Excel (2021)
   - Level of statistical significance was set at 5%.

Table 2. Independent variables for Multiple regression analysis

Assessment criteria	Representative variable	Multicollinearity variable[1)]
Clinical usefulness	Disease severity	Availability of alternatives
Budget impact	Number of target patient population (based on 200[2)])	Absolute budget impact
Reference countries' reimbursement status (in at least 3[2)])		-
Risk-Sharing Agreements		-

1) Multiple regression analysis is a statistical technique that can identify the independent effect of a specific variable after controlling for the influence of other variables when multiple independent variables simultaneously affect a dependent variable. When all appraisal factors are included as independent variables, a high degree of correlation among variables can cause a "multicollinearity problem." To address this, highly correlated variables were merged into representative variables (single composite indicators) and used in the regression analysis

2) The criteria of 200 target patients and reference countries' reimbursement status (in at least three reference countries) reflect meaningful thresholds conventionally used in reimbursement appropriateness assessments. A target patient number of 200 distinguishes rare or small patient populations, whereas a reimbursement status in three reference countries is a requirement for waiving pharmacoeconomic data submission.

RESULTS

- **Primary Results - T-test : Differences in ICER according to Appraisal Factors**

- (Clinical Usefulness)

- For availability of alternatives, ICER was slightly higher when alternative drug was not available, but the difference was not statistically significant (p > 0.05).
- Regarding disease severity, drugs indicated for life-threatening conditions showed a mean ICER of approximately KRW 42M per QALY, which is KRW 12.5M higher than for non-life-threatening diseases.

- (Budget Impact)

- A trend toward higher mean ICERs was observed in drugs for small patient populations, but the difference was not statistically significant; Absolute budget impact did not significantly affect mean ICER.

- (Risk-Sharing Agreement)

- Drugs subject to risk-sharing agreements demonstrated a significantly higher mean ICER compared to those without such arrangements.

- (Reference countries' Reimbursement Status)

- The number of reference countries with reimbursement did not significantly affect mean ICER, though the majority of evaluated drugs (all but two) were reimbursed in three or more countries.

Table 3. T-test result - Differences in Mean ICER by Appraisal factors

Assessment criteria		Group	No. of Drugs	Mean ICER (KRW/QALY)	T-test Significance
Availability of alternatives		Yes	38	35,768,138	n.s
		No	4	37,240,467	
Disease severity: Life-threatening disease		Yes	21	42,242,788	*
		No	21	29,573,932	
Target patient population	Based on 200	≥200	33	35,201,668	n.s
		<200	9	38,499,565	
	Based on 1,000	≥1,000	22	33,152,268	n.s
		<1,000	20	38,940,061	
Absolute budget impact (KRW)	Based on 10 billion	≥10B	23	37,439,185	n.s
		<10B	19	34,055,255	
	Based on 50 billion	≥50B	7	41,265,143	n.s
		<50B	35	34,837,003	
RSA		Eligible	26	40,519,602	*
		Not Eligible	16	28,415,091	
Listing in Reference Countries		≥3	40	36,190,416	n.s
		<3	2	30,267,247	

*p<0.05: significant; n.s, not significant

1USD = 1,426 KRW (NOV, 2025)

- **Secondary Results - Multiple Regression Analysis : Correlation between Appraisal Factors and ICER**

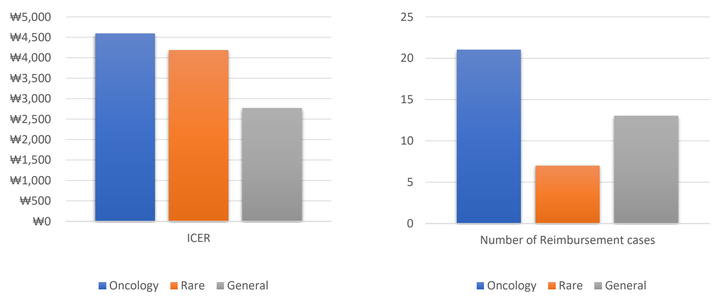
- (Model Fit)

- Multiple correlation coefficient (R) : 0.70
- Adjusted R-squared : 0.49

- (Analytical Results)

- The presence of life-threatening disease and inclusion in a risk-sharing agreement were each significantly associated with higher ICER values .
- Based on baseline ICER of approximately 31.4M per QALY, the ICER increased by approximately 7.48M per QALY, for drugs indicated for life threatening diseases, and by approximately 10.76M per QALY for drugs subjected to RSA

- **General Characteristics of Data**



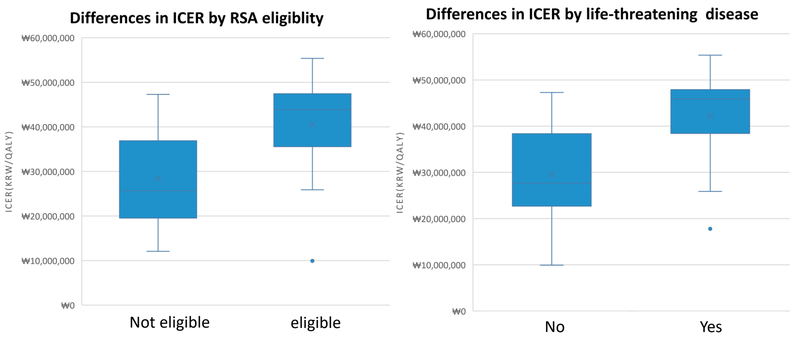
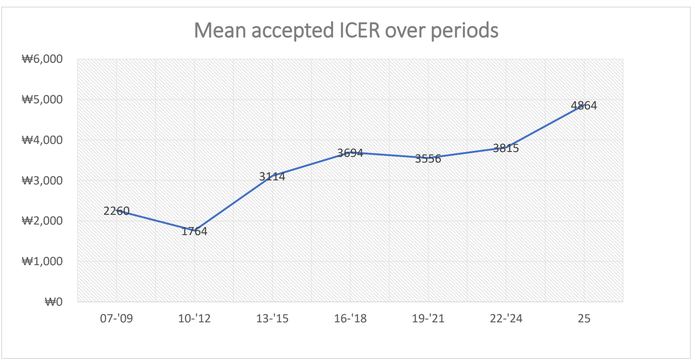


Table 4. Results of Multiple Regression Analysis

Variables		Coefficient	Significance
Y intercept		31400528.04	-
Clinical usefulness	Life-threatening disease (Yes)	7,481,105	*
Budget impact	Number of target patient population (≥ 200)	- 6,634,205	n.s
Reimbursement status in reference countries (≥ 3)		1,914,475	n.s
RSA (Eligible)		10,761,013	*

*p<0.05: significant; n.s, not significant

1USD = 1,426 KRW (NOV, 2025)



DISCUSSION & CONCLUSIONS

This study aimed to analyze whether reimbursement assessment criteria influenced the acceptability threshold of ICER for new drugs listed for reimbursement over the past eight years (2017–2024), and to examine if assessment factors specified by HIRA regulations are reflected in actual reimbursement decision-making, with analysis conducted using t-test and multiple regression statistical methods.

Results from t-test and multiple regression revealed that drugs for life-threatening diseases and drugs subject to risk-sharing agreements had significantly higher ICERs ($p<0.05$). This suggests that clinical severity may act as an adjustment factor for the cost-effectiveness threshold during reimbursement decision processes. Additionally, the observation of higher ICERs for drugs subject to risk-sharing agreements indicates that, even under greater uncertainty about therapeutic effects, relatively higher cost-effectiveness may be permitted due to the presence of financial risk dispersal mechanisms.

Ultimately, this study demonstrates that economic evaluation does not rely on a single linear decision rule, but rather reimbursement decisions result from a contextual process considering disease characteristics, clinical value, and budget management tools in a comprehensive manner.

Nevertheless, limitations include the relatively small sample size for rare and special disease groups, requiring caution in interpreting results. As this analysis only addressed newly listed drugs and official evaluation criteria, there may exist additional value elements influencing new drugs that were not captured in this study.

Therefore, in addition to currently considered evaluation criteria, continuous exploration and discussion are needed regarding elements that reflect the clinical, social, and patient-centered values of drugs.

REFERENCES

1. 「Detailed Evaluation Criteria for New Drugs Subject to Negotiation」, 1.1.1. Selection criteria for alternative drugs for drug cost comparison, Drugs (including treatment methods) currently used for the relevant indication; drugs included within the same treatment scope as the indication according to approval and reimbursement standards (for anticancer drugs, includes announced regimens when applicable); drugs indicated in formularies, textbooks, clinical guidelines, or clinical research articles are selected.
2. 「Detailed Evaluation Criteria for New Drugs Subject to Negotiation」, 1.8. Determination of eligibility for risk sharing, In any of the following cases: (ex, When an anticancer or orphan drug is used for a serious disease threatening survival, for which alternative or equivalent drugs or treatments do not exist.)
3. Kennedy, P. (2008). A Guide to Econometrics (6th ed.). Malden, MA: Blackwell Publishing.

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