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ORIGINAL RESEARCH

An Industry Survey on Unmet Needs in South Korea's New Drug Listing System

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Abstract

Introduction Since introducing the positive listing system in 2007, the South Korean government has undergone multiple changes in its drug listing system. As there is a lack of studies that evaluate the system from an industry perspective, this paper examined South Korea's new drug listing system from the suppliers' perspective.

Methods We surveyed members of the three main pharmaceutical industry associations online. The survey (a 5-point Likert scale) covered their satisfactory levels, demands, and updates on the current new drug listing system, especially pharmacoeconomic evaluation, pharmacoeconomic evaluation exemption, and risk-sharing agreement.

Results A total of 56 respondents participated in the survey. The self-reported satisfaction level for value recognition of new drugs was 1.6 (±0.7) points (5 points = very satisfied). The most highly demanded reforms for PE, RSA, and PEE were incremental cost-effectiveness ratio threshold (92.9%), reimbursement scope expansion (91.1%), and eligible disease (83.9%). Lastly, they also claimed that the indication-based pricing system must be introduced (83.9%).

Conclusions Pricing and reimbursement policies need to improve in such a way that would enable better access to new drugs while still facilitating their development. Given the nature of the current system, some innovative rare disease treatments and anticancer drugs remain unreimbursed, resulting in low satisfaction levels across the pharmaceutical industry. Hence, pathways to speed up the reimbursement assessment process and expand the range of reimbursable diseases are required. Pharmaceutical companies are also important stakeholders, like in the case of clinicians and patients, and their opinions should also be considered in the process of pricing and reimbursement policy reforms.

Keywords Drug listing system · Pricing and reimbursement · Risk-sharing agreement · Pharmaceutical industry · National health insurance · Indication-based pricing system

Introduction

With the biotech industry on the rise, the availability of new drugs that address patients' unmet needs is now higher than ever. However, the prices of such innovative drugs are very high, to the point where accessing these drugs is impractical unless reimbursed by health insurance [1, 2]. Furthermore, from the perspective of pharmaceutical companies, revenues gained from these new drugs are crucial to the research and development (R&D) of additional, innovative drugs [3, 4]. Hence, facilitating their access via reimbursement is critical, not only for the patients but also for pharmaceutical companies' R&D. However, both the government payer and the relevant authorities alike are inclined toward prudence, in terms of making decisions related to reimbursement, because of their significant impact on budgets [5, 6]. Countries that make decisions based on cost-effectiveness, such as South Korea, the United Kingdom, and Australia, have been known to limit reimbursement for drugs whose clinical efficacy and cost-effectiveness are proven. Hence, complementary systems, such as risk-sharing agreement (RSA) and flexible incremental cost-effectiveness ratio (ICER), and threshold in pharmacoeconomic evaluation (PE) have been implemented in these countries to improve accessibility [7–9].

In 2007, South Korea initiated the positive list system (PLS), which uses cost-effectiveness and the clinical efficacy of drugs as important factors for pricing and reimbursement

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(P&R) [9–11]. While the PLS may seem practical, in that only cost-effective drugs are listed, it may prolong review time; furthermore, it tends to deter access to anticancer drugs and rare disease drugs that have difficulty proving their cost-effectiveness [9, 12]. To overcome these limitations, complementary policies have been enacted in South Korea. For instance, RSA and PE exemption (PEE) may be applied to anticancer and rare disease drugs if certain conditions are met. Such policies have been proven to increase the rate of reimbursement significantly and to decrease the review time of new drugs [9]. In particular, RSA is considered to have improved access to new drugs while having also limited the impact on the national health insurance budget [13, 14].

A survey intended both to evaluate the current P&R system and to identify areas requiring improvement has been conducted on the stakeholders by Health Insurance Review & Assessment service (HIRA) [15–17]. Notably, however, no survey has yet been conducted to assess the overall achievements and issues of the various P&R policies and requests for reform from the pharmaceutical industry perspective. Hence, there is a strong need to identify the unmet needs resulting from the current system, from the perspective of the suppliers and developers of new drugs, to address the issue of patient access more effectively. Additionally, political decision-making and social agreements (for example, social consensus among the patients, the government, the medical service providers and the national public, on whether to focus the expenditure of the national health insurance budget on life-threatening disease therapies or chronic disease management) should also take into account these industry perspectives to achieve workable solutions.

The listing of innovative drugs in South Korea by global multi-national pharmaceutical companies affect P&R decisions in other countries as well [18–20]. This is more so because the South Korean P&R review results are referenced by pricing authorities in other countries that have similar P&R systems. On this point, this study aims to survey the assessment of Korea's new drug P&R system, and to do so from the perspective of pharmaceutical companies. Based on this industry point of view, problems with the current policies will be assessed. Finally, suggestions for improving access to new drugs and development in the pharmaceutical industry will be made.

South Korea's P&R System

Ever since introducing the PLS in South Korea, cost-effectiveness evaluation has become an essential review item for new drug listings. Regarding drugs that have proven their superiority in clinical efficacy to alternatives, premium pricing may be possible through PE evaluation. Drugs with non-inferior clinical efficacy in comparison to their alternatives may be listed at a price either at or below the weighted average price (based on national claim data) of alternative products. For anticancer and rare disease drugs, RSA and PEE pathways may be available upon meeting the relevant eligibility criteria. Additionally, if the strict standard of the Essential Drug pathway is met, then listing may be viable without PE evaluation—and at the highest possible price among the various P&R pathways. The net price under the RSA pathway is determined based on PE evaluation; the visible price is based on the adjusted average price in the A7 countries (US, UK, Swiss, German, Italy, France, and Japan). As for the PEE pathway, the actual price is determined based on the lowest adjusted price among the A7 countries. The adjusted average price in the A7 countries serve as the maximum for all new drug prices, and the final reimbursement price is determined based on negotiation with the NHIS which references the A7 prices [9–11].

Regarding the listing process, once the drug listing evaluation application is submitted to HIRA, the applicable reimbursement scope is then determined either by the Central Review Committee (CRC) for non-anticancer drugs or by the Cancer Disease Review Committee (CDRC) for anticancer drugs. Thereafter, PE pathway review drugs are assessed by the Pharmacoeconomic Evaluation Committee (PEC) and RSA pathway drugs are evaluated by the Risk-Sharing Agreement Committee (RSAC). Next, the determination of reimburseability is made by the Drug Reimbursement Evaluation Committee (DREC). Lastly, the final drug reimbursement price and volume are determined by negotiating with the National Health Insurance Service (NHIS) [9–11, 21, 22].

Reimbursement scope expansion for general drugs is determined through budget impact analysis (if the expansion's budget impact is KRW 10 billion or more, then NHIS negotiation is also required), and RSA pathway drugs must prove cost-effectiveness regarding the expanded scope [10]. The expansion of the reimbursement scope for PEE pathway drugs is tenable if the expanded scope meets the PEE pathway criteria; if such criteria is not met, then expansion can be made possible by proving cost-effectiveness [23]. Because South Korea only has a single price per product, if the drug price is reduced due to reimbursement scope expansion, then this reduced price will also apply to the previously listed indications.

Methods

For a term of 2 weeks (from March 30, 2022, to April 11, 2022), P&R experts of the companies affiliated with 3 pharmaceutical associations (Korean Research-based Pharmaceutical Industry Association [KRPIA], Korea

Pharmaceutical and Bio-Pharma Manufacturers Association [KPBMA], and Korea Biomedicine Industry Association [KoBIA]) were surveyed using Google forms. The main survey questions are as follows.

1) How satisfactory is the current new drug listing system (patient access, budget management, and value assessment of new drugs)?
2) Is there a need for improvement in the P&R pathway for the new drugs?
3) Which P&R review process (CRC, CDRC, PEC, RSAC, DREC and NHIS) for cancer drugs and non-cancer drugs that has the strongest need for reform? Please list in the order of priority.
4) Is there a need for implementing P&R policies that have not yet been implemented in South Korea?

Answers were based on a 5-point Likert scale, and descriptive statistics were used. The mean and standard deviation were identified for continuous variables, while frequency and percentage were identified for categorical variables. Student's *t*-test for continuous data and Fisher's exact test for categorical data (significant level 0.05, two-sided test) were conducted to explore statistical differences among participant characteristics.

Results

Participant Characteristics

Among the 68 survey recipients, a total of 56 recipients responded to the survey (response rate: 82.4%). Fifteen (26.8%) experts had fewer than 5 years of experience, while 17 (30.3%) had 5–10 years of experience, and 24 (42.9%) had 10 years or more. Twenty-seven (48.2%) experts had fewer than 5 cases of listing experience after the initiation of the PLS, 15 (26.8%) had 5 to 9, and 14 (25.0%) had 10 or more. Nineteen (33.9%) experts were affiliated with Korean pharmaceutical companies; 37 (66.1%) were affiliated with multi-national companies. Fourteen (25.0%) were affiliated with companies whose sales totaled less than KRW 100 billion, while 28 (50.0%) were affiliated with companies whose sales were between KRW 100 billion and KRW 500 billion. Fourteen (25.0%) experts work at companies with sales of over KRW 500 billion, as of 2021 (Table 1).

Satisfaction with the New Drug Listing System

The satisfaction level for the new drug listing system (on a scale of 5) was as follows. Patient accessibility: mean 2.3 (SD: 0.9); financial balance: mean 2.6 (SD: 1.0); value assessment of new drugs: mean 1.6 (SD: 0.7). New drug value assessments were evaluated as being the least satisfactory (Fig. 1). No statistically significant differences between participants affiliated with Korean companies and those affiliated with multi-national companies were observed in all 3 aspects (Student's *t*-test, $p = 0.519$, 0.116, and 0.934).

Needs for Improving the New Drug Listing System

As for RSA improvement, 87.5% replied that it is necessary. This number was higher than that of the other P&R pathways, that is, PE (83.9%) and PEE (80.4%). No statistically significant differences were observed between participants affiliated with Korean companies and those affiliated with

Table 1. Characteristics of survey participants ($N = 56$).

Variables	n (%)
P&R experience	
< 5 years	15 (26.8)
5 ~ 10 years	17 (30.3)
≥ 10 years	24 (42.9)
New drug listing experience after the introduction of PLS (number of products)	
< 5 products	27 (48.2)
5 ~ 10 products	15 (26.8)
≥ 10 products	14 (25.0)
Company type	
Domestic pharmaceutical companies	19 (33.9)
Global pharmaceutical companies	37 (66.1)
Annual company sales (domestic sales revenue in 2021)[a]	
< KRW 100 billion	14 (25.0)
KRW 100 ~ 500 billion	28 (50.0)
≥ KRW 500 billion	14 (25.0)

[a]1 USD = KRW 1145.56 (2021).

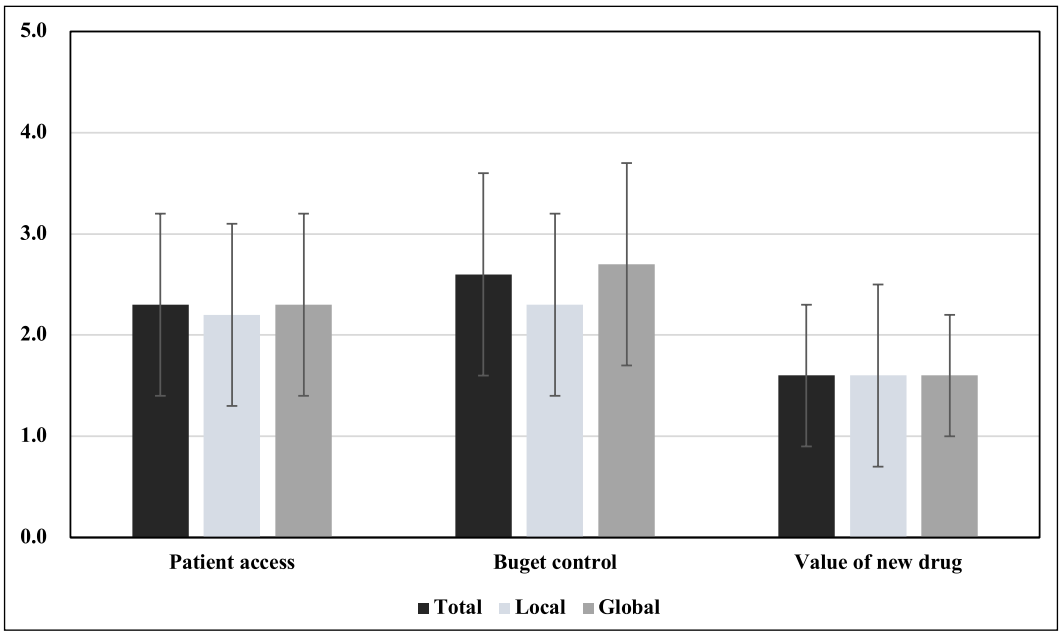

Figure 1. The mean and standard deviation of the survey results regarding the satisfactory levels pertaining to the new drug P&R system (5-points Likert scale).

Table 2. Need for improvement regarding each P&R pathway ($N = 56$).

Items	Needs improvement (4 or higher, %)	Likert scale mean points (SD)
PE pathway	83.9	4.2 (0.9)
Selection of comparator	87.5	4.2 (0.8)
ICER threshold	92.9	4.5 (0.8)
Discount rate	42.9	3.5 (0.8)
Design and assumptions of the PE model	55.4	3.6 (0.7)
Uncertainty in analysis	57.1	3.7 (0.8)
RSA pathway	87.5	4.4 (0.8)
Expanding eligible diseases	82.1	4.3 (0.8)
Determining the existence of alternative drugs	82.1	4.1 (0.7)
Standard for determining actual price	85.7	4.2 (0.7)
Standard for determining list price	75.0	3.9 (0.8)
Process for expanding reimbursement scope	91.1	4.6 (0.7)
PE exemption pathway	80.4	4.3 (0.9)
Expanding eligible diseases	89.3	4.4 (0.8)
Determining the existence of alternative drugs	80.4	4.0 (0.8)
Standard for determining actual price	87.5	4.3 (0.7)
Standard for determining list price	69.6	3.9 (0.9)
Listing requirement in at least 3 A7 countries	58.9	3.6 (1.0)
Process for expanding reimbursement scope	87.5	4.3 (0.8)

multi-national companies (Fisher's exact test, $p = 0.212$). Among the components of the different pathways, the one with the largest number of participants considered to require improvement was the ICER threshold (92.9%) for PE, the reimbursement scope expansion (91.9%) for RSA, and the disease expansion (89.3%) for PEE (Table 2).

A survey for assessing the need for improvement of the listing process, divided into cancer drugs and non-cancer

drugs, revealed that the demand for improvement of the drug price negotiation stage with the NHIS was the highest for non-cancer drugs (53.6%). The results also showed that demand for improvement in the appraisal stage confirming the reimbursement scope by the cancer assessment committee was the highest for anticancer drugs (83.9%) (Fig. 2).

Needs for Introducing New P&R Policies in South Korea

As specified in Table 3, indication-based pricing (IBP) was considered the most necessary among all the policies that have yet to be introduced in South Korea (83.9% answered 4 or more). Furthermore, 48.2% believed that IBP should be implemented for all diseases. As for wanting funds

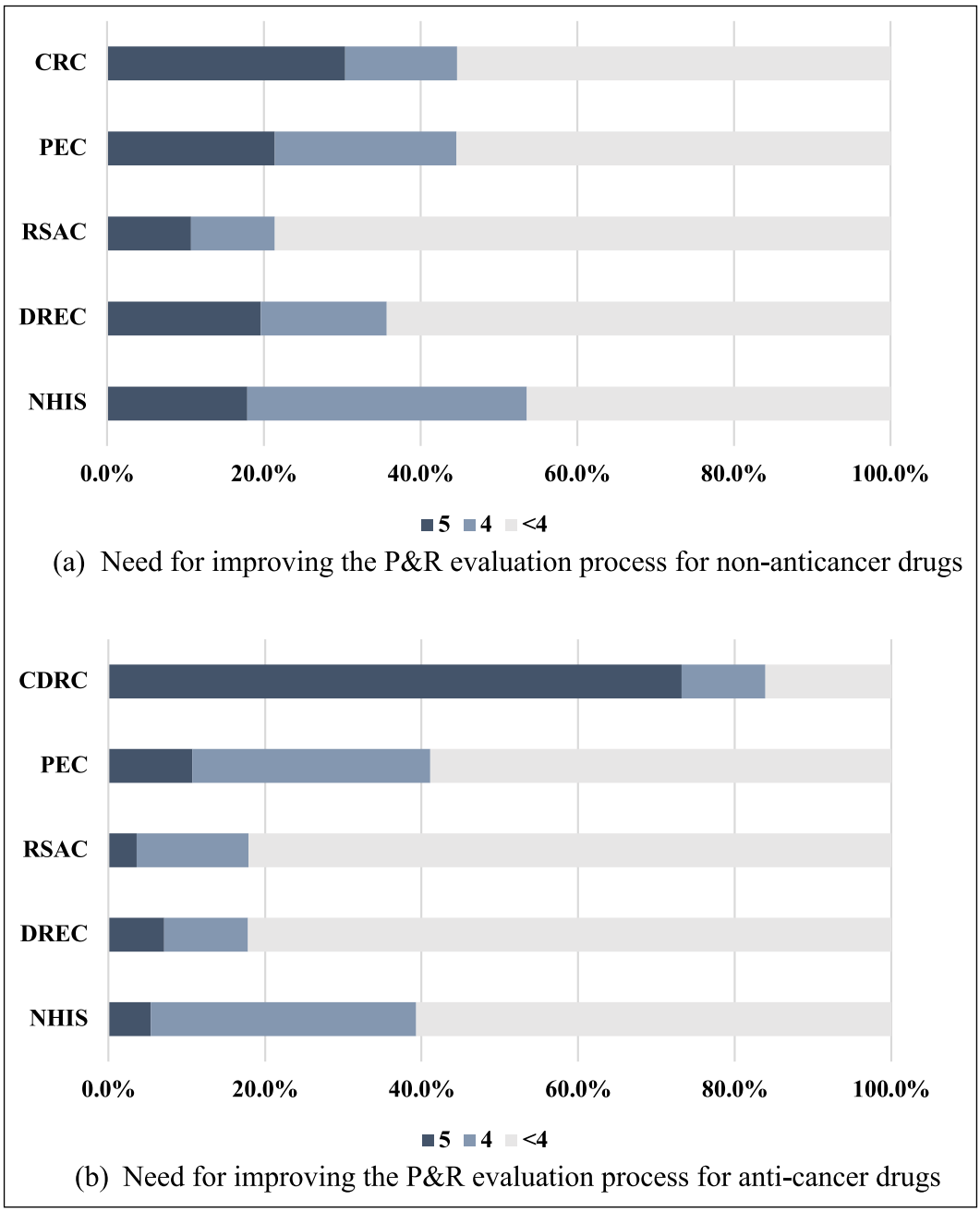

Figure 2. Survey results pertaining to the need for improving the P&R evaluation process for anticancer and non-anticancer drugs ($N=56$). *CRC* central review committee (reimbursement scope committee); *PEC* pharmacoeconomic evaluation committee; *RSAC* risk-sharing agreement committee; *DREC* drug reimbursement evaluation committee; *NHIS* national health insurance service; *CDRC* Cancer Disease Review Committee.

Table 3. The order of priority regarding the need for introducing P&R policies that have not yet been introduced in South Korea ($N=56$).

	Order of priority regarding the need for introduction (4 or more points, %)	Indication to be covered upon introduction (%)				
		Life-threatening or Progressive cancers and rare diseases	Life-threatening cancers and rare diseases	Progressive cancers and rare diseases	All cancers and rare diseases	All diseases
Fund[a]	76.8	19.7	21.4	12.5	39.3	7.1
Trade-off[b]	44.7	10.7	12.5	3.6	10.7	62.5
Indication-based pricing[c]	83.9	7.1	5.4	5.4	33.9	48.2
Pre-listing Post-assessment[d]	80.3	46.5	19.6	10.7	8.9	14.3

[a]Supports patients with cancer and severe diseases during the product's non-covered period using funds.

[b]Manipulates the prices of the applicant's other products to alleviate the financial burden of the new drug.

[c]Differentiates prices among indications.

[d]Initially lists with a temporary price and, thereafter, formally lists the product after completing the evaluation.

(established for purposes of financial support) to be introduced, the figure was 76.8; 39.3% believed that funds should be implemented for cancer or rare diseases. Among participants, 44.7% wanted trade-offs (this involves the reduction of the reimbursement price of another already listed drug of a company in order to compensate for the budget impact resulting from the new listing or reimbursement scope expansion of a reimbursement application drug of the company—it is a form of trade-off using the reimbursement price of another listed drug of the company) to be introduced, and 62.5% indicated that trade-offs should not be limited to certain diseases. Lastly, 80.3% wanted pre-listing & post-assessment (this would entail the pre-listing of a drug based on a tentative price, and thereafter, performing a post-assessment of the price—if the post-assessment price is lower than the pre-listed tentative price, then the company would refund such difference to the government) to be introduced; 46.5% suggested that these should be implemented for life-threatening diseases, including metastatic cancer.

Discussions

A survey on the satisfaction level of the South Korean new drug P&R system showed a low score for patient access, budget management, and value assessment of new drugs. These results should be understood within the context of the survey being conducted from the pharmaceutical industry's perspective. Strict control over the payer's budget is viewed as the underlying reason for dissatisfaction over new drug value assessment. In addition, overall dissatisfaction with the P&R system appeared to result from the failure of listing due to price control, which ultimately limits patient access to new drugs.

Next, a survey administered to various stakeholders—including the academy, the government, civilian society bodies, and industry P&R experts—was conducted in 2013, which was the sixth year after the PLS [15]. Participants replied that, while consistency and evidence-based assessment had indeed improved, transparency regarding the reimbursement assessment had actually been worsened by introducing the PLS. Remarkably, most (77.8%) P&R experts affiliated with pharmaceutical companies said that the PLS's purpose, which is to decide on reimbursements based on the value of the new drugs, had not been achieved. New drug value assessment was rated with the worst degree of satisfaction (1.6) in this study as well. These results show that, despite introducing new policies and the changes made during the last 10 years, the pharmaceutical industry still considers new drug value assessment as inadequate.

Risk-sharing agreement was the pathway considered by most to require improvement, from among the new drug listing pathways. Within RSA, the reimbursement scope expansion process was viewed by the majority (91%) as needing improvement. The reason behind this demand is that, in order to expand the reimbursement scope, PE is required. While the decision to apply for a reimbursement scope expansion in the case of an additional indication obtaining regulatory approval is reserved for the company, if the company proceeds with the reimbursement scope expansion, the reimbursement price of the drug will have to be reduced based on the government's budget impact additionally caused by such expansion. And in the case of an RSA product, PE is also required in addition to budget impact analysis. As a result, the price is cut each time the reimbursement scope expands, so that additional indication(s) for new drugs listed through the RSA pathway can be included [23]. South Korea's drug pricing system endows one price per drug and then requires the price to be cut when the

reimbursement scope expands. What is more, such a pricing system ultimately hinders reimbursement scope expansion. Modern anticancer drugs are often approved for multiple indications—sometimes up to as many as 20 [24, 25]. For these drugs, it becomes increasingly difficult for pharmaceutical companies to cover each indication, especially if each has to undergo a PE evaluation and price cut every time the reimbursement scope is expanded [10]. Additionally, as a result, such systematic limitations are viewed as ultimately hindering patient access to innovative therapies. For this reason, the survey participants indicated a demand for IBP, which may be a practical solution to this problem.

Recent studies have suggested alternatives, such as a flexible ICER threshold, IBP, post hoc reassessment, selective coverage system, and fundraising outside the health insurance [26–28]. Indication-based pricing was considered to be in most need, reflecting the difficulties in appreciating individual indications when the reimbursement scope of multi-indication drugs, such as immuno-oncology drugs, are expanded. Prescription rates for each indication are reflected in the drug's single price in Australia; in South Korea's case, given that RSA is actively used, adjustments to the reimbursement rate for each indication can be considered.

The incremental cost-effectiveness ratio threshold was considered by most to require improvement within the PE pathway. This reflects complaints with South Korea's current practice, where < KRW 50 million (QALY) is the pre-set ICER threshold without taking into account the new drugs' individual characteristics. The pharmaceutical industry wants variables, such as market size, R&D costs, revenue, and the innovativeness of the drug, to be reflected in the ICER threshold. However, the payer cannot overlook the budget impact presented by the new drug's coverage. The National Institute for Health and Care Excellence (NICE), in the United Kingdom, uses an ICER threshold higher than the standard for End of Life (EoL) criteria. In this context, a weighted QALY is applied for highly specialized technology (HST), allowing room for a higher ICER threshold [29–31]. The research was conducted on the relationship between the ICER threshold and the pharmaceutical companies' revenue. The findings revealed that certain orphan drugs with small market sizes should be allowed for upregulation of the ICER threshold [32].

Multiple respondents also indicated that RSA and PEE pathways should be expanded to other diseases. Among them, 41.1% believed that rare diseases are being sidelined in the context of coverage. This might be because chronic severe rare diseases are not considered "life-threatening" and, as a result, they cannot be easily listed through RSA and PEE pathways. Furthermore, most considered the appraisal of anticancer drugs as needing improvement within the P&R system. This is because anticancer drugs go through a separate and intensive process, such as assessing the budget impact, the price, and the cost-effectiveness, by the CDRC. Many survey respondents claimed that this process is used primarily for minimizing the budget impact of expensive anticancer drugs. What is more, there has been a controversy within the industry as to the scope of the CDRS' decision-making authority.

Among the P&R policies not yet introduced in South Korea, pre-listing and post-evaluation systems, funds, and IBP were considered as most needed. Regarding IBP and funds, many opined that it should be introduced to all diseases. For pre-listing and post-evaluation, however, the dominant view was that it should be limited to severe diseases.

The Korean pharmaceutical industry has repeatedly asked that P&R policies be improved [33]. More specifically, the industry has been insisting the addition of flexibility to cost-effectiveness assessment, the implementation of a more reasonable basis for selecting alternative drugs, and the expansion of the diseases eligible for PEE to improve patient access and facilitate research and development. A focus-group interview (FGI) conducted in 2015 on the problems and recommendations to improve by experts revealed that the pharmaceutical industry considered a stepwise approach, as opposed to an integrated approach, to assessment and decision-making was the largest single factor hindering patient access. Failure to reflect transparency and innovation in the DREC's decision-making process was likewise considered problematic. In particular, it was highlighted that the value of the new drug was devalued because the criteria for selecting a comparator was not reasonable [16]. Notably, the results of this study also confirmed that comparator selection in the PE pathway is still recognized as a factor that needs improvement, along with the ICER threshold.

While there have been studies that introduce European drug pricing and insurance policies through academic literature reviews or studies that propose increasing patient access, there are not yet any studies identifying the overall reform needs of a drug pricing and reimbursement system of a particular country or a region via surveying P&R experts in the pharmaceutical industry [5]. Studies conducted through surveys have often focused on a particular aspect of the drug pricing system, such as the introduction of health technology assessment (HTA), the status and objectives of managed entry agreement (MEA), or innovative pharmaceutical pricing agreements; additionally, the survey subjects of previous studies also consisted of a variety of groups, such as all stakeholders, the public, or the payer [34–40].

A study conducted in the Middle East and North African countries (MENA) areas introduced MEA, and it administered a survey to 44 persons, of which 25% were public officials working on drug appraisal and reimbursement listing, with the other 75% being pharmaceutical experts [41]. The survey's focus was on the perception of decision-makers toward MEA, and the uncertainty and challenges of

MEA within the MENA areas. A majority reported difficulties in conducting MEA in the process of data gathering, identifying and defining meaningful results, and measuring outcomes using limited data. While pharmaceutical experts believed improved access through stronger partnerships and reducing the payer uncertainty were the most important goals of MEA, payers believed that minimizing the budget impact, early access to patients, reducing uncertainty regarding product efficacy, and offering value-proven technology as the most important. The study expected MEA to be introduced to more countries, thereby resolving uncertainties over innovative medical technologies, notwithstanding the limitations of designing and operating MEA [14]. Likewise, it also seems necessary for South Korea to expand its scope of indications eligible for RSA to achieve greater patient access.

This study is the first in South Korea to conduct a survey of pharmaceutical industry experts about the P&R system after the introduction of various policies intended to improve patient access to new drugs, including RSA and PEE. Its strength is that its survey was conducted on both Korean and global companies alike, which enables it to better represent the opinion of the Korean pharmaceutical industry as a whole. Its limitation is that the survey was restricted to pharmaceutical companies, which is only a subsection of the stakeholders of the overall health insurance system. This study, therefore, does not claim to represent all stakeholders related to the new drug P&R process. Rather, it acknowledges that it is limited to the perspectives of the pharmaceutical industry, which explains why the answers regarding satisfaction with the current system and its improvements may be industry biased. Another potential limitation is that the survey was conducted online, which means that the answerers' logic may have been incompletely understood. The final limitation that we would like to note is the respondents with at least 5 cases of P&R listing experience being only about 50% of the respondents. However, considering the relatively small number of new drugs annually listed in Korea [9], the number of pharmaceutical company personnel with more than 5 cases of new drug listing experience is not large as displayed in the experience of our survey respondents. It should be noted that the survey for this study excluded gene and cell therapies from its scope to avoid any confusion arising from recent government policies issued in this regard. After the listing of both Kymriah and Zolgensma in 2022, the Ministry of Health and Welfare has issued in that same year a policy directive aimed at managing the listing of high priced innovative therapies [42]. Specifically, the policy directive aims to strengthen coverage for innovative products (e.g., expedited listing and performance-based RSA per patient) through strict post-listing management (e.g., strengthened monitoring of treatment efficacy and safety, strengthened reimbursement management). Further research that includes other stakeholders (e.g., the government, patients, and doctors) is needed to assess current policies from diverse perspectives.

Conclusions

South Korea's P&R policies need to improve in such a way as to enable better access to new drugs and facilitate their development. Given the nature of the current system, some innovative rare disease treatments and anticancer drugs are not reimbursed. As such, the satisfaction of the pharmaceutical industry is low. Hence, pathways to speed up the process of reimbursement assessment and to expand the range of reimbursable diseases are required. In particular, RSA is a tool that can be used both to improve access to new drugs and to address financial concerns effectively. Additionally, PEE is a system that can improve the accessibility of some rare disease treatments, which are difficult to prove cost-effectiveness. It is also necessary to expand the scope of diseases eligible for these pathways. Pharmaceutical companies are also important stakeholders, like in the case of clinicians and patients, and their opinions should also be considered in the process of P&R policy development.

Author Contributions

SK and JHL contributed to substantial contributions to the conception or design of the work; SK, JYL, SHC, and JHL contributed to substantial contributions to the acquisition, analysis, or interpretation of the data for the work; SK, and JHL contributed to drafting the work; SK, JYL, SHC, EJS, MK, and JHL contributed to revising the work critically for important intellectual content; SK, JYL, SHC, EJS, MK, and JHL contributed to the final approval of the version to be published; SK, JYL, SHC, EJS, MK, and JHL contributed to agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declarations

Conflict of interest

The authors declared that they have no conflict of interest.

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